ÇOCUK ACİL ve YOĞUN BAKIM DERGİSİ

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AMAÇ VE KAPSAM

2014 yılında yayımlanmaya başlayan Çocuk Acil ve Yoğun Bakım Dergisi, "kritik hasta çocuk" konusundaki Türkiye'deki tek dergi olarak ulusal ve uluslararası makaleleri yayımlayan, hakemli-ön değerlendirmeli bir dergidir. İngilizce ve Türkçe dillerinde yayın kabul eden dergimiz, elektronik olarak yayımlanmaktadır. Yayın sıklığı dört ayda bir olmak üzere; yılda 3 sayı (Nisan, Ağustos, Aralık) şeklindedir. Çocuk Acil ve Yoğun Bakım Dergisi; çocuk acil tıp, çocuk acil sağlık hizmetleri, çocuk kritik hasta bakımı ve çocuk yoğun bakım hizmetleri konusunda bilimsel içerikli makaleleri yayınlamaktadır.

Dergi; özgün araştırma, olgu sunumu, derleme, editöre mektup türündeki makaleleri, klinik raporları, tıbbi düşünceleri ve ilgili eğitimsel ve bilimsel duyuruları yayınlar. Dergi içeriğinde temel bölümler; çocuk acil tıp sistemleri, akademik çocuk acil tıp ve çocuk acil tıp eğitimi, çocuk acil servis yönetimi, afet, çevresel aciller, travma, olgu sunumları, ergen acilleri, çocuk acilleri, yenidoğan acilleri, sağlık politikaları, etik, zehirlenme, çocuk acil hemşireliği, çocuk yoğun hemşireliği, koruyucu hekimlik, çocuk yoğun bakımı, kritik hastalıklar, kritik hasta yönetimi, tanı yöntemleri, sepsis ve septik şok, organ ve sistem yetersizlikleri, yoğun bakım teknolojisi, non-invazif ve invazif monitörizasyon, non-invazif ve invazif ventilasyon, vücut dışı destek sistemleri, etik değerlendirmeler, laboratuvar, acil radyoloji ve girişimsel işlemlerden oluşmaktadır.

Derginin editöryal ve yayın süreçleri ile etik kuralları International Committee of Medical Journal Editors (ICMJE), World Association of Medical Editors (WAME), Council of Science Editors (CSE), Committee on Publication Ethics (COPE), European Association of Science Editors (EASE), ve National Information Standards Organization (NISO) gibi uluslararası kuruluşların kurallarına uygun olarak şekillenmektedir. Dergimiz, şeffaf olma ilkeleri ve "DOAJ Akademik Yayıncılıkta En İyi Uygulama İlkeleri" ile uyum içindedir.

Çocuk Acil ve Yoğun Bakım Dergisi editörü veya editörleri Çocuk Acil Tıp ve Yoğun Bakım Derneği Yönetim Kurulu tarafından, üç yılda bir Ocak ayında belirlenir.

Çocuk Acil ve Yoğun Bakım Dergisi, **Tübitak-ULAKBİM TR Dizini, Directory of Open Access Journals (DOAJ), Scopus, CINAHL Complete, Gale, ProQuest, Embase, Index Copernicus, Directory of Research Journal Indexing (DRJI), J-Gate, Livivo-German National Library of Medicine (ZB MED), BASE - Bielefeld Academic Search Engine, Ulrich's Periodicals Directory, Ebsco, CiteFactor, IdealOnline, Türkiye Atıf Dizini, Hinari, GOALI, ARDI, OARE, AGORA, WorldCat ve Türk Medline** tarafından indekslenmektedir.

Dergi Adı: Çocuk Acil ve Yoğun Bakım Dergisi

Dergi Adı (İngilizce): The Journal of Pediatric Emergency and Intensive Care Medicine

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Açık Erişim Politikası

Bu dergi, araştırmaları halka ücretsiz olarak sunmanın daha büyük bir küresel bilgi alışverişini desteklediği ilkesine dayanarak içeriğine anında açık erişim sağlar.

Yazar(lar) ve telif hakkı sahibi/sahipleri, Çocuk Acil ve Yoğun Bakım Dergisi'nde yayınlanan makalelere tüm kullanıcıların ücretsiz olarak erişim sağlamasını onaylamış olur. Makaleler kaynak gösterilmek şartıyla kullanılabilir.

Açık Erişim Politikası, Budapeşte Açık Erişim Girişimi (BOAI) kurallarına dayanmaktadır. [Hakemli araştırma literatürüne] "açık erişim" ile, herhangi bir kullanıcının bu makalelerin tam metinlerini okumasına, indirmesine, kopyalamasına, dağıtmasına, yazdırmasına, aramasına veya bağlantı vermesine izin veren ve kamuya açık internet ortamında ücretsiz olarak erişilebilirliğini kastediyoruz. Bunları dizine eklemek için tarayabilir, yazılıma veri olarak iletebilir veya internete erişimin ayrılmaz bir parçası olmayanlar dışında finansal, yasal veya teknik engeller olmaksızın başka herhangi bir yasal amaç için kullanabilirsiniz. Çoğaltma ve dağıtım üzerindeki tek kısıtlama ve bu alandaki telif hakkının tek rolü, yazarlara çalışmalarının bütünlüğü üzerinde kontrol ve uygun şekilde tanınma ve alıntılanma hakkı vermek olmalıdır.

Çocuk Acil ve Yoğun Bakım Dergisi elektronik kaynaklara erişim için herhangi bir abonelik ücreti, yayın ücreti veya benzer bir ödeme talep etmez.

Açık erişim, disiplinler arası gelişimi destekleyen ve farklı disiplinler arasında işbirliğini teşvik eden bir yaklaşımdır. Bu nedenle Çocuk Acil ve Yoğun Bakım Dergisi, makalelerine daha fazla erişim ve daha şeffaf bir inceleme süreci sağlayarak bilimsel yayın literatürüne katkıda bulunmaktadır.

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Bu derginin reklam satışları ve editoryal süreçleri, editoryal bağımsızlığı sağlamak ve finansal çıkarların etkilerini azaltmak için ayrı tutulmuştur.

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Dergide yayınlanan makalelerde yer alan ifadeler veya görüşler editörlerin, yayın kurulunun ve/veya yayıncının görüşlerini yansıtmaz. Editörler, yayın kurulu ve yayıncı bu tür materyaller için herhangi bir sorumluluk veya yükümlülük kabul etmez. Dergide yayınlanan tüm görüşler, makalelerin yazarlarına aittir.

Çocuk Acil ve Yoğun Bakım Dergisi'nin mali giderleri Çocuk Acil Tıp ve Yoğun Bakım Derneği tarafından karşılanmaktadır.

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AIMS AND SCOPE

The Journal of Pediatric Emergency and Intensive Care Medicine is a peer-reviewed periodical journal that publishes national and international articles since 2014, and it is the first journal that is about "Critical pediatric patient" field in Turkey. Our journal, which accepts publications in English and Turkish languages, is published electronically. The publication frequency is 3 times a year (April, August, December) in every 4 months. The Journal of Pediatric Emergency and Intensive Care Medicine publishes the scientific articles that are written about pediatric emergency medicine, pediatric emergency health services, pediatric critical patient care, and pediatric intensive care issues.

The journal publishes original research, case reports, reviews, articles like letters to the editor, clinical reports, medical opinions and related educational and scientific notifications. The basic sections of the contents are composed of medical systems of pediatric emergency, academic pediatric emergency medicine and education, management of pediatric emergency department, disaster and environmental emergency, trauma, case reports, adolescence emergencies, pediatric emergencies, new born emergency, health policy, ethics, intoxication, pediatric emergency nursery, pediatric intensive care nursery, preventive medicine, pediatric intensive care, critical diseases, critical patient management, diagnostic methods, sepsis and septic shock, organ and system failures, intensive care technology, invasive and non-invasive monitorization, invasive and non-invasive ventilation, extra-corporal body support systems, ethical assessment, laboratory, emergent radiology and interventional procedures.

The editorial and publication processes of the journal are shaped in accordance with the guidelines of the International Committee of Medical Journal Editors (ICMJE), World Association of Medical Editors (WAME), Council of Science Editors (CSE), Committee on Publication Ethics (COPE), European Association of Science Editors (EASE), and National Information Standards Organization (NISO). The journal is in conformity with the Principles of Transparency and Best Practice in Scholarly Publishing.

The editors of the Journal of Pediatric Emergency and Intensive Care are determined by the Administrative Board of Society of Pediatric Emergency and Intensive Care Medicine periodically every 3 years at January.

The Journal of Pediatric Emergency and Intensive Care Medicine is indexed in **Tübitak-ULAKBİM TR Dizini, Directory of Open Access Journals (DOAJ), Scopus, CINAHL Complete, Gale, ProQuest, Embase, Index Copernicus, Directory of Research Journal Indexing (DRJI), J-Gate, Livivo-German National Library of Medicine (ZB MED), BASE - Bielefeld Academic Search Engine, Ulrich's Periodicals Directory, EBSCO Host, CiteFactor, IdealOnline, Türkiye Atıf Dizini, Hinari, GOALI, ARDI, OARE, AGORA, WorldCat** and **Türk Medline.**

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YAZARLARA BİLGİ

Yayımlanmaya 2014 yılında başlayan Çocuk Acil ve Yoğun Bakım Dergisi, ulusal ve uluslararası makaleleri yayımlayan, çift-kör hakemlik ilkeleri çerçevesinde yayın yapan bir dergidir. Dergi özgün araştırma, olgu sunumu, derleme, editöre mektup türündeki makaleleri, klinik raporları, tıbbi düşünceleri ve ilgili eğitimsel ve bilimsel duyuruları yayınlar.

Dergi içeriğinde temel bölümler çocuk acil tıp sistemleri, akademik çocuk acil tıp ve çocuk acil tıp eğitimi, çocuk acil servis yönetimi, afet, çevresel aciller, travma, olgu sunumları, ergen acilleri, çocuk acilleri, yenidoğan acilleri, sağlık politikaları, etik, zehirlenme, çocuk acil hemşireliği, çocuk yoğun hemşireliği, koruyucu hekimlik, Çocuk Yoğun Bakımı, kritik hastalıklar, kritik hasta yönetimi, tanı yöntemleri, sepsis ve septik şok, organ ve sistem yetersizlikleri, yoğun bakım teknolojisi, non-invazif ve invazif monitörizasyon, non-invazif ve invazif ventilasyon, vücut dışı destek sistemleri, etik değerlendirmeler, laboratuvar, acil radyoloji ve girişimsel işlemlerden oluşmaktadır.

Derginin İngilizce kısaltması; "J Pediatr Emerg Intensive Care Med" olarak kaydedilmiştir.

Editörler ve Yayın Kurulu üç yılda bir Ocak ayında Çocuk Acil Tıp ve Yoğun Bakım Derneği Yönetim Kurulu tarafından belirlenir.

Türkçe yazılarda Türk Dil Kurumu'nun Türkçe Sözlüğü ve Yazım Kılavuzu temel alınmalıdır.

Çocuk Acil ve Yoğun Bakım Dergisi, hiçbir makale başvuru veya işlem ücreti uygulamamaktadır.

Dergiye yayımlanmak üzere gönderilen tüm yazılar "iThenticate" programı ile taranarak intihal kontrolünden geçmektedir. İntihal taraması sonucuna göre yazılar ret ya da iade edilebilir.

Çocuk Acil ve Yoğun Bakım Dergisi, Türk Tıp Dizini koşullarına uygun olarak bir yıl içindeki toplam özgün araştırma makalesi sayısı 15'den az olmayacak ve toplam makale sayısının (özgün araştırma makalesi, olgu sunumu, kitap kritiği, editöre mektup, derleme, kılavuzlar) en az %50'sini oluşturacak şekilde yayımlanır. Her sayıda en az 5 araştırma, en fazla araştırma makalesi sayısı kadar olgu sunumu ve/veya derleme yayımlar. Derlemeler editörün daveti üzerine hazırlanır.

Derginin arşiv sisteminde tüm hakem kararları, başvuru yazılarının imzalı örnekleri ve düzeltme yazıları en az beş yıl süreyle saklanır.

Dergide yayımlanan makaleler, içindekiler sayfasında ve makale başlık sayfalarında türlerine göre (araştırma, olgu sunumu, kısa rapor, derleme, editöre mektup vb.) sınıflandırılır.

Yazarlar ilk gönderim sırasında aşağıdaki formalrı sağladığından emin olmalıdır:

- Telif Hakkı Devir ve Yazarlık Katkı Formu
- ICMJE Potansiyel Çıkar Çatışması Formu tüm yazarlar tarafından imzalanması gerekir.

HAKEM DEĞERLENDİRME SÜRECİ

Çocuk Acil ve Yoğun Bakım Dergisi'ne gönderilen yazılar ilk olarak editör tarafından değerlendirilir. Editör her yazıyı değerlendirmeye alınıp alınmaması konusunda gözden geçirir ve yazıya editör yardımcısı atar. Editör ve yazıya atanan editör yardımcısı yazıyı değerlendirmeye uygun bulursa, iki hakem veya bir hakem ve bir yayın/danışma kurulu üyesine değerlendirmek üzere gönderir. Eğer yazı bilimsel değerliliğinin ve orijinalliğinin olmaması, kritik hasta çocuk alanına ve dergi okuyucu kitlesine hitap etmemesi gibi nedenlerle yayın/danışma kurulu üyelerinin veya hakem değerlendirmesini gerektirmiyorsa yazı değerlendirme altına alınmaz.

Yazıların bilimsel ve etik sorumlulukları yazarlara, telif hakkı ise Çocuk Acil ve Yoğun Bakım Dergisi'ne aittir. Yazıların içeriğinden ve kaynakların doğruluğundan yazarlar sorumludur. Yazarlar, yayın haklarının devredildiğini belirten onay belgesini (Yayın Hakkı Devir Formu) yazıları ile birlikte göndermelidirler. Bu belgenin tüm yazarlar tarafından imzalanarak dergiye gönderilmesi ile birlikte yazarlar, gönderdikleri çalışmanın başka bir dergide yayınlanmadığı ve/veya yayınlanmak üzere incelemede olmadığı konusunda garanti vermiş, bilimsel katkı ve sorumluluklarını beyan etmiş sayılırlar.

MAKALE KATEGORİLERİ

Özgün Araştırma Makaleleri: Kritik hasta çocuk alanında yapılmış temel veya klinik araştırma makaleleridir. Kaynaklar ve İngilizce özet gereklidir (Bkz. Yazı hazırlığı bölümü). En fazla 5000 sözcük (20 çift aralıklı sayfa), yedi tablo ve/veya resim, ek olarak İngilizce, Türkçe özet ve kaynakları içermelidir. Etik kurul onayı çalışma içinde bahsedilmelidir.

Olgu Sunumları: Çocuk Acil Tıp ve Çocuk Yoğun Bakım alanında karşılaşılan eğitimsel yönü olan klinik olguların veya komplikasyonların sunumudur. Bu bölüme yayım için gönderilen yazılarda daha önce bilimsel literatürde sıklıkla bildirilmemiş klinik durumları, bilinen bir hastalığın bildirilmemiş klinik yansımaları veya komplikasyonlarını, bilinen tedavilerin bilinmeyen yan etkilerini veya yeni araştırmaları tetikleyebilecek bilimsel mesajlar içermesi gibi özellikler aranmaktadır. Olgu sunumları Türkçe ve İngilizce özet, giriş, olgu sunumu ve sunulan olguya yönelik tartışmayı içermelidir. En fazla uzunluk 2000 sözcük (8 çift aralıklı sayfa), 15 veya daha az kaynak, üç tablo veya resim içermelidir.

Özet Raporlar: Ön çalışma verileri ve bulguları, daha ileri araştırmaları gerektiren küçük sayılı araştırmalar. Kaynaklar ve İngilizce özet gereklidir (Bkz. yazı hazırlığı bölümü). En çok uzunluk 3000 sözcük (sekiz çift aralıklı sayfa), ek olarak İngilizce ve Türkçe özet, 15 veya aşağı sayıda referans, üç tablo ve/veya şekil. Etik kurul onayı gereklidir.

Konseptler: Çocuk acil tıp ve çocuk yoğun bakım ile ilgili ve bu alanı geliştirmeye yönelik klinik veya klinik olmayan konularda yazılardır. Kaynaklar ve İngilizce özet gereklidir. En çok uzunluk 4000 kelime (16 çift aralıklı sayfa), ek olarak İngilizce ve Türkçe özet (her biri 150 kelimenin altında) ve kaynaklar içermelidir.

Derleme Yazıları (Reviews): Çocuk acil tıp ve çocuk yoğun bakım ile ilgili ve konuyla ilgili son ulusal ve dünya literatürlerini içeren geniş inceleme yazılarıdır. Çocuk Acil ve Yoğun Bakım Dergisi davetli derleme yazısı yayımlamaktadır. Davetli olmayan derleme başvuruları öncesinde editör ile iletişime geçilmelidir. En çok 5000 kelime (20 çift aralıklı sayfa). Kaynak sayısı konusunda sınırlama yoktur. Derleme yazma konusunda gerekli bilgi aşağıdaki makaleden elde edilebilir;

Burney RF, Tintinalli JE: How to write a collective review. Ann Emerg Med 1987;16:1402.

Kanıta Dayalı Bilgi: Klinik ve tıbbi uygulamalara yönelik sorulara yanıt verebilen makaleler. Makale şu bölümleri içermelidir; Klinik senaryo, soru ve sorular, en iyi kanıtın araştırılması ve seçilmesi, kanıtın ayrıntılı incelenmesi ve kanıtın uygulanması. En çok 4000 kelime (15 çift aralıklı sayfa), ek olarak Türkçe ve İngilizce özet. Yazarlar kullandıkları makalelerin kopyasını da ekte editöre göndermelidir.

ÇOCUK ACİL ve YOĞUN BAKIM DERGİSİ

Journal of Pediatric Emergency and Intensive Care Medicine

ÇOCUK ACİL TIP VE YOĞUN BAKIM DERNEĞİ

Editöre Mektup: Çocuk acil tıp ve çocuk yoğun bakım ile ilgili konulardaki görüşler, çözüm önerileri, Çocuk Acil ve Yoğun Bakım Dergisi'nde veya diğer dergilerde yayımlanan makaleler hakkında yorumları içeren yazılardır. En çok 1500 kelime (altı çift aralıklı sayfa), ek olarak kaynaklar yer almalıdır.

Nöbet Öyküleri: Çocuk acil tıp ve çocuk yoğun bakımın doğasını ve dinamizmini yansıtan, çocuk acil tıbbın ve çocuk yoğun bakımın mizahi yönünü yakalamış kişisel ve/veya ekip deneyimleri. En çok 1000 sözcük içermelidir.

Makale Başvurusu

Makale Gönderim Sözleşmesi: Çocuk Acil ve Yoğun Bakım Dergisi'nin her yeni baskısında yer almakta olup, ihtiyaç duyulması halinde Çocuk Acil ve Yoğun Bakım Derneği ve internet sitesinde de yer almaktadır. Tüm makale gönderimlerinde doldurulmalıdır.

Kapak Mektubu: Yazar, bu mektupta, araştırmasının veya yazısının kısa bir açıklamasını, çalışmanın türünü (randomize, çift kör, kontrollü vb.), gönderildiği kategoriyi, bilimsel bir toplantıda sunulup sunulmadığını ayrıntılı olarak belirtmelidir. Ayrıca yazı ile ilgili iletişim kurulacak kişinin adresi, telefonu, faks numaraları ve e-posta adresi yazının alt kısmında yer almalıdır.

Makale gönderilirken yazışma yazarının ORCID (Open Researcher and Contributor ID) numarası verilmelidir. http://orcid.org adresinden ücretsiz kayıt oluşturulabilir.

MAKALE HAZIRLAMA

Biçim: Başvurusunu yaptığınız yazının kopyasını saklayın. Makale çift aralıklı olarak (1,5 aralık kullanmayın) A4 kağıdına standart kenar boşlukları (tüm kenarlardan ikişer santim) kullanılarak Arial yazı formatında 10 punto ile hazırlanmış olarak dört kopya gönderilmelidir. Online başvurularda basılı kopya gönderilmesine gerek yoktur.

Başlık Sayfası: Bu sayfa başlık, yazarların tam isimleri, bir yazar için ikiyi aşmayacak akademik derece, çalışma yapıldığı anda yazarların adresi şehri de içerecek şekilde, eğer yazı her hangi bir bilimsel toplantıda sunulmuş veya sunulmak için kabul edilmiş ise bu toplantı, kongre, vb.'nin tarih, yer ve adı (buna ilişkin kanıt), alınan finansal destek ve kimden olduğu, yazıya katkısı bulunan konsültan varsa ismi akademik derecesi ve adresi, makalenin kelime sayısı (Türkçe, İngilizce özetler ve referanslar hariç), yazı konusunda bağlantıya geçilecek kişinin ismi, adresi, telefon-faks numaraları ve varsa e-mail adresi mektubun alt bölümünde yer almalıdır.

Kör Ön Değerlendirme İçin: Makalenin sayfalarında ve Türkçe-İngilizce özet sayfalarında yazarların isminin, akademik derecesinin, adresinin, şehrinin yer almamasına dikkat edin. Bu şartı bulundurmayan makaleler geri gönderilebilir.

Türkçe ve İngilizce Özet: Özgün makaleler ve özet raporlar 250 sözcüğü aşmayan hipotez veya amaç, yöntemler, sonuçlar, tartışma içeren özet bulundurmalıdır. Konsept ve olgu sunumları için 150 kelimeyi aşmayan Türkçe ve İngilizce özet bulunmalıdır. Anahtar sözcükler, her türlü yazıda Türkçe ve İngilizce özetlerin altındaki sayfada 3-10 adet verilmelidir. Anahtar sözcük olarak Index Medicus'un Tıbbi Konu Başlıkları'nda (Medical Subject Headings, MeSH) yer alan terimler kullanılmalıdır.

İstatistiksel Testler: Çalışmalar istatistik alanında deneyimli kişilerin kontrolünde değerlendirilmelidir. Sonuçlar için güven aralığı, P değerleri verilmelidir.

Yazı İçeriği:

Araştırma makaleleri aşağıdaki bölümleri içermelidir;

- Giriş
- Gereç ve Yöntem
- Bulgular
- Tartışma
- Çalışmanın Kısıtlılıkları
- Sonuç

Değerler: Kullanılan madde, ilaç, laboratuvar sonuçları değerlerinde genel standartlara uyulmalıdır. İlaçlar: Jenerik isimler kullanılmalıdır.

Kaynaklar: Kaynaklar çift aralıkla ayrı bir sayfada yazılmalıdır. Kaynakları makale içinde kullanım sırasına göre numaralandırılmalıdır. Alfabetik sıralama yapılmamalıdır. Özet olarak yararlanılmış makaleler için parantez içinde İngilizce yazılar için "abstract", Türkçe yazılar için "öz" yazılmalıdır. Bir kaynaktaki yazarların sadece ilk beşi belirtilmeli, geri kalanlar için İngilizce kaynaklar için "et al.", Türkçe kaynaklar için "ve ark." kısaltmasını kullanın. Kaynakların doğruluğu yazarların sorumluluğundadır.

Örnekler;

- Makale: Raftery KA, Smith-Coggins R, Chen AHM. Gender-associated differences in emergency department pain management. Ann Emerg Med. 1995;26:414-21.
- Baskıdaki Makale için: Littlewhite HB, Donald JA. Pulmonary blood flow regulation in an aquatic snake. Science 2002 (baskıda)
- Kitap: Callaham ML. Current Practice of Emergency Medicine. 2nd ed. St. Luis, MO:Mosby;1991.
- Kitap Bölümü: Mengert TJ, Eisenberg MS. Prehospital and emergency medicine thrombolytic therapy. In: Tintinal-li JE, Ruiz E, Krome RL (eds). Emergency Medicine: A Comprehensive Study Guide. 4th ed. New York, NY:McGraw-Hill;1996:337-43.
- Kitaptan Bir Bölüm için, Bir Editör Varsa: Mc Nab S. Lacrimal surgery. In: Willshaw H (ed). Practical Ophthalmic Surgery. NewYork: Churchill Livingstone Inc, 1992: 191-211
- Türkçe Kitap Bölümü: Yilmaz HL. Çocuk Acil Mimarisi. İçinde: Karaböcüoğlu M, Yılmaz HL, Duman M (ed.ler). Çocuk Acil Tıp: Kapsamlı ve Kolay Yaklaşım. 1. Baskı. İstanbul, İstanbul Tıp Kitabevi, 2012:7-13
- Editörler Aynı Zamanda Kitabın İçindeki Metin ya da Metinlerin Yazarı ise: Önce alınan metin ve takiben kitabın ismi yine kelimeler büyük harfle başlatılarak yazılır: Diener HC, Wilkinson M (editors). Drug-induced headac-he. In Headache. First ed., New York: Springer-Verlag, 1988: 45-67
- Çeviri Kitaptan Alıntı için: Milkman HB, Sederer LI. Alkolizm ve Madde Bağımlılığında Tedavi Seçenekleri. Doğan Y, Özden A, İzmir M (Çevirenler) 1. Baskı, Ankara: Ankara Üniversitesi Basımevi, 1994: 79-96
- Kongre Bildirileri için: Felek S, Kılıç SS, Akbulut A, Yıldız M. Görsel halüsinasyonla seyreden bir şigelloz olgusu.

XXVI. Türk Mikrobiyoloji

- Basılmamış Kurslar, Sunumlar: Sokolove PE, Needlesticks and high-risk exposure. Course lecture presented at: American College of Emergency Physicians, Scientific Assembly, October 12, 1998, San Diego, CA.

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ÇOCUK ACİL ve YOĞUN BAKIM DERGİSİ

Journal of Pediatric Emergency and Intensive Care Medicine

- Tezden Alıntı için: Kılıç C. Genel Sağlık Anketi: Güvenirlik ve Geçerlilik Çalışması. Yayınlanmamış Uzmanlık Tezi, Hacettepe Üniversitesi Tıp Fakültesi, Psikiyatri AD, Ankara: 1992
- İnternet: Fingland MJ. ACEP opposes the House GOP managed care bill. American College of Emergency Physici-ans Web site. Available at: http://www.acep.org/press/pi980724.html . Accessed August 26,1999.
- Kişisel Danışmanlık: Kişisel danışmanları kaynak göstermekten kaçının. Fakat eğer çok gerekli ise kişinin adı, akademik derecesi, ay, yıl bilgilerine ek olarak kişiden yazılı olarak bu bilgiyi kullanabileceğinize dair mektubu makale ile birlikte gönderin.

Tablolar: Tablolar verileri özetleyen kolay okunur bir biçimde olmalıdır. Tablo'da yer alan veriler, makalenin metin kısmında yer almamalıdır. Tablo numaraları yazıda ardışık yer aldığı biçimde verilmelidir. Metinde tabloları işaret eden cümle bulunmalıdır. Her tablo "Kaynaklar" sayfasından sonra her sayfaya bir tablo gelecek şekilde gönderilmelidir. Tablolar hazırlanırken sayfa kenarı kurallarına uyulmalıdır. Metin içinde her tabloya atıfta bulunulduğuna emin olunmalıdır. Yazı içindeki grafik, şekil ve tablolar "Arabik" sayılarla numaralandırılmalıdır. Her tablo ayrı bir sayfaya çift aralıklı olarak basılmalıdır. Tabloları metindeki sıralarına göre numaralayıp, her birine kısa bir başlık verilmelidir. MS Word 2000 ve üstü sürümlerde otomatik tablo seçeneğinde "tablo klasik 1" ya da "tablo basit 1" seçeneklerine göre tablolar hazırlanmalıdır. Yazarlar açıklamaları başlıkta değil, dipnotlarda yapmalıdır. Dipnotlarda standart olmayan tüm kısaltmalar açıklanmalıdır. Dipnotlar için sırasıyla aşağıdaki semboller kullanılmalıdır: (*,+,^,§,ii,I,**,++,^^).

Şekiller/Resimler: Şeklin/Resmin içerdiği bilgi metinde tekrarlanmamalıdır. Metin ile şekilleri/resimleri işaret eden cümle bulunmalıdır. Resimler EPS veya TIF formatında kaydedilmelidir. Renkli resimler en az 300 DPI, gri tondaki resimleren az 300 DPI ve çizgi resimler en az 1200 DPI çözünürlükte olmalıdır.

DERGİ POLİTİKASI

Orijinal Araştırma Makalesi: Yeni bilgi ve veri içeren makaleler daha önce bir bilimsel dergide yayınlanmamış ve yayınlanması için aynı anda bir başka dergiye başvurulmamış olmalıdır. Bu sınırlama özet halinde bilimsel toplantı ve kongrelerde sunulmuş çalışmalar için geçerli değildir.

Birden Fazla Yazar: Makalede yer alan tüm yazarlar makalenin içeriğindeki bilgilerin sorumluluğunu ve makale hazırlanma basamaklarındaki görevleri paylaşırlar.

İstatistik Editörü: İstatistiksel analiz içeren tüm makaleler istatistik uzmanına danışılmış olmalıdır. Yazarlardan biri ya da yazarların dışında belirlenmiş ve istatistik konusunda deneyimli ve yetki sahibi bir kişi bu analizin sorumluluğunu üstlenmelidir. İstatistiksel değerlendirme için kullanılan istatistik uzmanının ismi başlık sayfasında belirtilmelidir.

Randomize Kontrollü Çalışmalar: Dergi bu tip çalışmaları yayınlamayı yeğlemektedir.

İzinler: Makalede yer alan herhangi bir resim, tablo vs. daha önceden başka bir bilimsel dergi veya kitapta yayınlanmış ise bu tablo ve resimlerin kullanılabilirliğine dair yazı alınması gerekmektedir.

Etik Komite Onayı İzni: Yazarlar, eğer çalışmaları insan ve hayvanlar üzerinde araştırmayı gerektiriyorsa, yayın değerlendirme kurulundan (araştırma etik kurulları) yazılı onay belgesini almalıdırlar.

DEĞERLENDİRME VE BASIM SÜRECİ

Ön değerlendirme: Dergi kör ön değerlendirmeyi tüm makale tipleri için uygulamaktadır. Tüm makaleler dergi editörü tarafından incelenir ve uygun bulunan makaleler ön değerlendirme amacıyla danışmanlara (editör yardımcılarına) iletilir. Dergi editöründen doğrudan yazara geri gönderilen yazılar Çocuk Acil ve Yoğun Bakım Dergisi'nde basılamaz. Başvuru ile derginin ön değerlendirmeye alınma arasında geçen süre en çok 15 gündür. Yazının alındığına ve durum bildirir mektup dergi editörünce yazara bu süre içinde bildirilir. Dergide basımı uygun bulunmayan makaleler geri gönderilmez.

Tüm makaleler editörlerce dergi yazım kuralları ve bilimsel içerik açısından değerlendirilirler. Gerekli görüldüğünde yazıda istenen değişiklikler yazara editörlerce yazılı olarak bildirilir.

Yazının Sorumluluğu: Yazarlar yayınlanmış halde olan makalelerinde bulunan bilgilerin tüm sorumluluğunu üstlenirler. Dergi bu makalelerin sorumluluğunu üstlenmez. Yazarlar basılı haldeki makalenin bir kopyasını alırlar.

Basım Hakkı: Dergide yayınlanmış bir makalenin tamamı veya bir kısmı, makaleye ait resimler veya tablolar Çocuk Acil ve Yoğun Bakım Dergisi editörü ve Çocuk Acil Tıp ve Yoğun Bakım Derneği Yönetim Kurulu, bilgisi ve yazılı izni olmadan başka bir dergide yayınlanamaz..

Gerekli Bilgiler: Dergi editörleri ön değerlendirme sürecinde gerek duyduklarında makalenin dayandırıldığı verileri incelemek için yazardan isteyebilirler. Bu nedenle yazara kolay ulaşımı sağlayacak adres ve diğer iletişim araçlarının başlık sayfasında yer alması önemlidir.

Ek: Yayın kurulu, yazarların iznini alarak yazıda değişiklikler yapabilir. Editör ve dil editörü dil, imla ve kaynakların Index Medicus'ta geçtiği gibi yazılmasında ve benzer konularda tam yetkilidir.

Makale yayınlanmak üzere gönderildikten sonra yazarlardan hiçbiri, tüm yazarların yazılı izni olmadan yazar listesinden silinemez, ayrıca yeni bir isim yazar olarak eklenemez ve yazar sırası değiştirilemez.

Ölçüm Birimleri: Uzunluk, ağırlık ve hacim birimleri metrik (metre, kilogram, litre) sistemde ve bunların onlu katları şeklinde rapor edilmelidir. Sıcaklıklar celsius derecesi, kan basıncı milimetre civa cinsinden olmalıdır. Ölçü birimlerinde hem yerel hem de Uluslararası Birim Sistemleri'ni (International System of Units, SI) kullanmalıdır. İlaç konsantrasyonları ya SI ya da kütle birimi olarak verilir, seçenek olarak parantez içinde verilebilir.

Kısaltmalar ve Semboller: Sadece standart kısaltmaları kullanın, standart olmayan kısaltmalar okuyucu için çok kafa karıştırıcı olabilir. Başlıkta kısaltmadan kaçınılmalıdır. Standart bir ölçüm birimi olmadıkça kısaltmaların uzun hali ilk kullanılışlarında açık, kısaltılmış hali parantez içinde verilmelidir.

Teşekkür(ler)/Acknowledgement(s): Yazının sonunda kaynaklardan önce teşekkür(ler)/ acknowledgement(s) bölümüne yer verilir. Bu bölümde yazı hazırlanırken içeriğe, düzene, bilgilerin istatistiksel analizine katkıları olanlar belirtilebilir.

Kaynaklara Ek: Tek tip kurallar esas olarak Amerikan Ulusal Tıp Kütüphanesi (National Library of Medicine, NLM) tarafından uyarlanmış olan bir ANSI standart stilini kabul etmiştir. Kaynak atıfta bulunma örnekleri için yazar(lar) http://www.nlm.nih.gov/bsd/uniform_requirements.html sitesine başvurabilir(ler).

Dergi isimleri Index Medicus'taki şekilleriyle kısaltılmalıdır. Ayrı bir yayın olarak yıllık basılan ve Index Medicus'un Ocak sayısında da liste olarak

yer alan Index Medicus'taki Dergiler Listesi'ne (List of Journals Indexed in Index Medicus) başvurulabilir. Liste ayrıca http://www.nlm.nih.gov sitesinden de elde edilebilir.

ETİK

Bilimsel Sorumluluk: Makalelerin bilimsel kurallara uygunluğu yazarların sorumluluğundadır. Tüm yazarların gönderilen makalede akademik ve bilimsel olarak doğrudan katkısı olmalıdır. Bu bağlamda "yazar" yayınlanan bir araştırmanın kavramsallaştırılmasına ve desenine, verilerin elde edilmesi, analizi ya da yorumlanmasına belirgin katkı yapan, yazının müsveddesi ya da bunun içerik açısından eleştirel biçimde gözden geçirilmesinde görev yapan birisi olarak görülür. Yazar olabilmenin diğer koşulları ise, makaledeki çalışmayı planlamak veya icra etmek ve/veya makaleyi yazmak veya revize etmektir.

Fon sağlanması, veri toplanması ya da araştırma grubunun genel süpervizyonu tek başlarına yazarlık hakkı kazandırmaz. Yazar olarak gösterilen tüm bireyler sayılan tüm ölçütleri karşılamalıdır ve yukarıdaki ölçütleri karşılayan her birey yazar olarak gösterilebilir. Çok merkezli çalışmalarda grubun tüm üyelerinin yukarıda belirtilen şartları karşılaması gereklidir. Yazarların isim sıralaması ortak verilen bir karar olmalıdır. Tüm yazarlar yazar sıralamasını Telif Hakkı Devir Formu'nda imzalı olarak belirtmek zorundadırlar.

Yazarlık için yeterli ölçütleri karşılamayan ancak çalışmaya katkısı olan tüm bireyler "teşekkür/bilgiler" kısmında sıralanmalıdır. Bunlara örnek olarak ise sadece teknik destek sağlayan, yazıma yardımcı olan ya da sadece genel bir destek sağlayan kişiler verilebilir. Finansal ve materyal destekleri de belirtilmelidir.

Yazıya materyal olarak destek veren ancak yazarlık için gerekli ölçütleri karşılamayan kişiler "klinik araştırıcılar" ya da "yardımcı araştırıcılar" gibi başlıklar altında toplanmalı ve bunların işlevleri ya da katılımları "bilimsel danışmanlık yaptı", "çalışma önerisini gözden geçirdi", "veri topladı" ya da "çalışma hastalarının bakımını üstlendi" gibi belirtilmelidir. Teşekkür (acknowledgement) kısmında belirtilecek bu bireylerden de yazılı izin alınması gerekir.

Etik Sorumluluk: Çocuk Acil ve Yoğun Bakım Dergisi, 1975 Helsinki Deklarasyonu'nun 2013 yılında revize edilen İnsan Deneyleri Komitesi'nin etik standartlarına uymayı ilke edinmiş bir dergidir.

Bu yüzden Çocuk Acil Ve Yoğun Bakım Dergisi'nde yayınlanmak üzere gönderilen klinik deneylere katılan sağlıklı bireyler/hastalarla ilgili olarak belirtilen komitenin etik standartlarına uyulduğunun mutlaka belirtilmesi ve deneyin türüne göre gerekli olan yerel veya ulusal etik komitelerden alınan onay yazılarının yazı ile birlikte gönderilmesi ve ayrıca deneye katılan kişi/hastalardan ve hastalar eğer temyiz kudretine sahip değilse hastaların vasilerinden yazılı bilgilendirilmiş onam (informed consent) alındığını belirten bir yazı ve tüm yazarlar tarafından imzalanmış bir belgenin editöre gönderilmesi gerekir.

Bu tip çalışmaların varlığında yazarlar, makalenin YÖNTEM(LER) bölümünde bu prensiplere uygun olarak çalışmayı yaptıklarını, kurumlarının etik kurullarından ve çalışmaya katılmış insanlardan bilgilendirilmiş onam (informed consent) aldıklarını belirtmek zorundadırlar. Çalışmada "deney hayvanı" kullanılmış ise yazarlar, makalenin YÖNTEM(LER) bölümünde "Guide for the Care and Use of Laboratory Animals" ilkeleri doğrultusunda çalışmalarında hayvan haklarını koruduklarını ve kurumlarının etik kurullarından onay aldıklarını belirtmek zorundadırlar.

Hayvan deneyleri rapor edilirken yazarlar laboratuvar hayvanlarının bakımı ve kullanımı ile ilgili kurumsal ve ulusal rehberlere uyup uymadıklarını yazılı olarak bildirmek zorundadırlar.

Makalelerin kurallara uygunluğu yazarın sorumluluğundadır. Çocuk Acil ve Yoğun Bakım Dergisi, ticari kaygılara bağlı olmaksızın makalelerin en iyi etik ve bilimsel standartlarda olmasını şart koşar.

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- For citation from a Thesis study: Kılıç C. General Health Survey: Reliability and Validity Study. Un-published Proficiency Thesis, Hacettepe University Faculty of Medicine, Department of Psychiatry, Ankara: 1992
- İnternet: Fingland MJ. ACEP opposes the House GOP managed care bill. American College of Emergency Physici-ans Web site. Available at: http://www.acep.org/press/pi980724.html Accessed August 26,1999.
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Research Article / Özgün Araştırma

DOI: 10.4274/cayd.galenos.2022.32650
J Pediatr Emerg Intensive Care Med 2023;10:1-7

Prediction of Febrile Seizures in Febrile Children with Upper Respiratory Infection

Üst Solunum Yolu Enfeksiyonu Olan Ateşli Çocuklarda Ateşli Nöbetin Öngörüsü

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Abstract

Introduction: Febrile seizures (FS) are the most frequently encountered childhood neurological problems. They cause stress and anxiety for parents and a considerable workload for healthcare providers. The purpose of this study was to identify useful markers capable of predicting the risk of FS in febrile children with upper respiratory infection using complete blood count parameters.

Methods: Four hundred seventy-six children aged between 6 months and 5 years, 240 with a history of first FS, 121 with acute febrile upper respiratory tract infection without seizures (AFI), and 115 healthy controls were included in the study. Two age-and sex-matched control groups were recruited, one consisting of febrile patients without seizures and the other of healthy children.

Results: Logistic regression analysis of all participants together revealed that a hemoglobin (Hb) level ≤10.95 was associated with a 2.937 -fold greater risk of FS, and a neutrophil to lymphocyte ratio (NLR) ≥1.3969 with a 2.719-fold increase in FS (95% confidence interval: 1.885-4.576 vs. 1.873-3.949), (p<0.001).

Conclusion: Although low Hb levels and high NLR can be used to predict the risk of FS, these values alone are not sufficient to predict FS in children with AFI.

Keywords: Febrile seizure, prediction, hemoglobin, neutrophil/lymphocyte ratio

Öz

Giriş: Ateşli nöbetler (FS) çocukluk çağının en sık karşılaşılan nörolojik sorunudur. Ebeveynler için stres ve endişeye ve sağlık hizmeti sağlayıcıları için önemli bir iş yüküne neden olur. Bu çalışmanın amacı, tam kan sayımı parametrelerini kullanarak üst solunum yolu enfeksiyonu olan ateşli çocuklarda FS riskini öngörebilen faydalı belirteçleri belirlemektir.

Yöntemler: Çalışmaya 6 ay ile 5 yaş arasında, 240 ilk FS öyküsü olan, 121 nöbetsiz akut ateşli üst solunum yolu enfeksiyonu olan (AFI) ve 115 sağlıklı kontrolden oluşan toplam 476 çocuk çalışmaya dahil edildi. Çalışmaya yaş ve cinsiyet uyumlu biri nöbetsiz ateşli hastalardan ve diğeri sağlıklı çocuklardan oluşan iki kontrol grubu alındı.

Bulgular: Tüm katılımcılar birlikte değerlendirildiğinde, lojistik regresyon analizi, hemoglobin (Hb) seviyesinin ≤10,95 FS için 2,937 kat daha fazla riskle ve nötrofil/lenfosit oranı (NLR) ≥1,3969 ile 2,719 kat FS artışı ile ilişkili olduğunu ortaya koydu (%95 güven aralığı: 1,885-4,576 vs. 1,873-3,949), (p<0,001).

Sonuç: FS riskini öngörmek için düşük Hb seviyeleri ve yüksek NLR kullanılabilse de bu değerler AFI'lı çocuklarda FS'yi öngörmek için tek başına yeterli değildir.

Anahtar Kelimeler: Ateşli nöbet, öngörü, hemoglobin, nötrofil/lenfosit oranı

Introduction

Febrile seizures (FS) are the most frequent neurological problems in childhood.[1] They are most common at 12-18 months and in boys (M/F: 1.1/1-2/1).[2,3] Most cases consist of the simple FS (SFS) type, viral infections being the principal underlying cause.[4] Nutritional deficiencies such as iron deficiency, anemia, zinc deficiency, and vitamin B12 deficiency, and genetic factors also occupy an important place in the etiology of FS.[5]

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The febrile state is triggered by proinflammatory cytokines released during infections.[6] The most important cytokines in the development of FS are IL-1β and TNF-α.[7] These exhibit direct and indirect modulating effects on neurons and neurotoxic neurotransmitters released during excitation or inflammation.[8] Inflammation also involves the major immune system cells subtypes, including neutrophils and lymphocytes, and immune system activation is of considerable importance in patients with FS.[8]

Febrile seizures are rarely associated with significant morbidity or long-term health problems. However, they cause stress and anxiety in parents and increase healthcare providers' workloads.[9] It is therefore important to predict which children with fever will also undergo seizures.

Despite their being highly useful and important biomarkers, the accessibility of inflammatory cytokines is limited, and the costs involved are high. There is, therefore, growing interest in the use of low-cost complete blood count (CBC) inflammatory response markers for determining susceptibility to FS.[2,3,10,11]

The purpose of the present study was to identify useful markers capable of predicting the risk of FS in febrile children with upper respiratory infection using CBC parameters.

Materials and Methods

This retrospective study was conducted at the pediatric emergency department of a tertiary referral hospital in Turkey between October 2017 and October 2020. Four hundred seventy-six children aged between six months and five years, 240 with a history of first FS, 121 with acute febrile illness without seizures (AFI), and 115 healthy controls were enrolled.

The control group was recruited from two age-and-sex matched groups:

1. A healthy group was recruited from healthy children admitted to a general pediatric outpatient clinic for routine control.

2. An AFI without seizure group was recruited from children admitted to the general pediatric outpatient clinic with fever and diagnosed with an acute upper respiratory infection.

Definitions

FS were defined as seizures occurring at fever levels ≥38 °C, in children between six months and five years of age, with no previous history of afebrile seizure, and not accompanied by central nervous system infection or acute metabolic disease.[12]

Simple FS (SFS) were defined as seizures lasting less than 15 min, not recurring during 24 h or the same infectious process, and exhibiting a generalized characteristic.[7]

Complicated FS (CFS) were defined as seizures lasting ≥15 min or recurring within 24 h or in the same infectious process and exhibiting a focal characteristic.[12]

Diagnosis of anemia was based on hemoglobin (Hb) levels below 2 SD of age-matched values.[13]

Exclusion Criteria

Exclusion criteria in both the patient and control groups were: Prematurity (≤37 weeks), presence of any chronic diseases (bronchopulmonary dysplasia, neuromuscular diseases, epilepsy, congenital cardiovascular diseases, immunodeficiency, etc.), previous history of febrile and/or afebrile seizures, suspicion of meningitis, electrolyte imbalance, history of fever exceeding 48 h in duration, antibiotic use within the previous two weeks, and not being tested for CBC and C-reactive protein (CRP) blood levels.

Individuals with a fever origin other than acute upper respiratory infection in the FS and AFI groups, or with a history of any infection within the previous two weeks among healthy children were also excluded.

Study Design

Demographic characteristics including the patient's age, gender, duration and recurrence of FS episodes, family history of FS and epilepsy, parental consanguinity, and CBC and CRP values were retriev from the medical charts.

Laboratory Analysis

CBC and CRP tests were routinely performed for all children with and without FS in our hospital. These tests were performed from peripheral venous blood samples collected during hospital admission. CBC values were measured using an automatic hematology analyzer (MINDRAY BC-6800) with hydrodynamic focusing flow cytometry.

Serum CRP levels were assessed using the immunoturbimetric method (Abbott Architect-plus C8000, Diagnostic Inc., USA), values >5 mg/L being considered positive.

CBC findings including Hb, hematocrit, mean corpuscular volume (MCV), red blood cell distribution width (RDW), white blood cell count (WBC), neutrophil, and lymphocyte counts, and platelet count, values were retrieved from patients' medical records. The neutrophil to lymphocyte ratio (NLR) was calculated by dividing the absolute neutrophil count by the absolute lymphocyte count.

Ethics

Approval for the study was obtained from the Local Ethics Committee of Aydın Adnan Menderes University (decision no: 11, date: 17.01.2021). Informed consent was not obtained due to the retrospective design of the study.

Statistical Analysis

Statistical analyses were performed on SPSS 21 software (IBM Corporation, Armonk, NY, USA). Normality was assessed using the Kolmogorov-Smirnov test and descriptive statistics. Categorical variables were expressed as number and percentages. Continuous variables are expressed as mean plus standard deviations or median values and interquartile range (25 and 75 quartiles) depending on normality of distribution. Non-parametric or parametric tests were performed accordingly. Student's t-test or One-Way Analysis of Variance were used for normally distributed parameters, while quantitative variables were compared between the groups using either the Mann-Whitney U test or Student's t-test. Receiver operating curve (ROC) analysis was performed to determine CBC data cut-off values capable of predicting the development of FS. Risk analysis based on cut-off values was performed using logistic regression. P-values <0.05 were considered statistically significant.

Results

Patient Characteristics

Two hundred forty children with FS (171 SFS and 69 CFS), 121 with AFI, and 115 healthy age-and-sex matched children were included in the study.

The participants' demographic characteristics are shown in Table 1. There was no difference between the groups in terms of gender or age (p>0.05). Boys represented 57.9% of the patients. Median age at first FS was 25.42±14.95 months, and the median seizure duration was 1.86±1.49 min. Analysis showed that 71.3% of FS were simple and 28.7% complex.

A history of FS in first-degree relatives was determined in 55 (23.1%) patients, and in second-degree relatives in 20 (8.4%) (Table 1).

A comparison of laboratory parameters between children with FS, or AFI, and the healthy controls is shown in Table 2. Hb, MCV, and lymphocyte levels were lower, while RDW, WBC, neutrophil levels, and NLR were higher in children with FS compared to those with AFI and the healthy controls (p<0.05). Although CRP levels were lower in children with FS than in those with AFI, the difference was insignificant (p=0.127).

The cut-off, AUC, sensitivity, specificity, 95% confidence interval (CI) and p-values of the Hb, WBC, neutrophils, and NLR parameters for predicting FS in children with FS and AFI are shown in Table 3, while the ROC curves are presented in Figure 1.

A Hb cut-off value ≤10.95 g/dL predicted FS with 76.6% sensitivity and 34.6% specificity, a WBC value ≥9.405 with 63.8% sensitivity and 49.6% specificity, a neutrophil count ≥3.525 with 72.1% sensitivity and 48.8% specificity and NLR ≥1.3969 with 58.8% sensitivity and 52.1% specificity,

Logistic regression analysis of factors associated with risk of FS (Hb and NLR) is shown in Table 4. An Hb level ≤10.95 was associated with a 2.937 -fold increased risk of FS, and NLR ≥1.3969 with a 2.719-fold greater risk (95% CI: 1.885-4.576 vs 1.873-3.949, respectively), p<0.001).

However, when patients with fever (FS and AFI) were subjected to risk analysis based on CBC parameters, no parameter capable of increasing the risk was identified (OR: 1, p>0.05).

Table 1. Participants' demographic characteristics

Parameter	Children with FS (n=240) (mean ± SD)	Children with AFI (n=121) (mean ± SD)	Healthy children (n=115) (mean ± SD)	p-value
Age (months)	25.42±14.95	27.57±25.27	27.74±18.93	0.439*
Duration of seizure (minutes) (mean ± SD)	1.86±1.49	N/A	N/A	N/A
	n (%)	**n (%)**	**n (%)**	
Gender Male Female	 139 (57.9%) 101 (42.1%)	 67 (55.4%) 54 (44.6%)	 65 (56.5%) 50 (43.5%)	0.895
Type of seizure Simple Complex	 171 (71.3%) 69 (28.7%)	N/A	N/A	N/A
Family history of febrile seizure 1st degree relatives 2nd degree relatives	 55 (23.1%) 20 (8.4%)	N/A	N/A	N/A
Family history of epilepsy in first degree relatives	23 (9.7%)	N/A	N/A	N/A

n: Number, SD: Standard deviation, FS: Febrile seizure, AFI: Acute febrile illness, N/A: Non-applicable, Statistics: Cross tab chi score, *One-Way Analysis of Variance. Significance was set at p<0.05

Table 2. Comparison of laboratory parameters between children with FS, AFI and healthy controls

Parameter	Children with FS (n=240) (mean ± SD)	Children with AFI (n=121) (mean ± SD)	Healthy children (n=115) (mean ± SD)	p-value
Hb (g/dL)	11.31±1.01**	11.57±1.04**	11,94±0.94*	**<0.001**
Hct (%)	34.64±2.73	34.79±3.00	38.58±34.08	0.100
MCV (fl)	75.16±6.18**	77.53±5.98*	76.64±4.77	**0.001**
RDW (%)	15.03±3.27**	13.78±1.22*	13.81±1.40*	**<0.001**
WBC (10^3/mm^3)	11.98±5.407**	10.80±5.174*	10.04±3.118	**0.001**
Neuthrophils count (x10^3/mm^3)	6.866±4.792*	5.573±3.669*	3.610±1.827**	**<0.001**
Lymphocytes count (x10^3/mm^3)	3.857±2.599**	4.171±3.012**	5.201±2.075*	**<0.001**
PLT (10^9/L)	319.63±251.88	302.83±117.32	351.81±84.05	**0.139**
PCT (%)	0.267±0.106	0.254±0.095**	0.291±0.064*	**0.011**
MPV (fL)	8.871±0.94	8.49±0.79	8.54±0.84	0.051
PDW (fL)	14.05±2.45**	15.66±0.37*	15.53±0.32*	**<0.001**
NLR	2.806±3.410*	2.046±2.395*	0.866±0.780**	**<0.001**
PLR	109.79±73.92*	101.47±72.56*	77.91±34.65**	**<0.001**
MPV/PLT	0.032±0.012*	0.032±0.014*	0.026±0.008**	**<0.001**
CRP (mg/L)	15.352±25.307	19.664±25.191	-	**0.127**

Statistics: One-Way ANOVA, post-hoc test, Scheffe: (*is significantly larger than **p<0.05)
n: Number, SD: Standard deviation, FS: Febrile seizure, AFI: Acute febrile illness, Hb: Hemoglobin, Hct: Hematocrit, MCV: Mean corpuscular volume, RDW: Red blood cell distribution width, WBC: White blood cell, PLT: Platelet, PCT: Platelet crit, MPV: Mean platelet volume, PDW: Platelet distribution width, NLR: Neuthrophil to lymphocyte ratio

Table 3. ROC curves for Hb, WBC, neutrophils and NLR to predict febrile seizure in children with FS and AFI

Variable	Cut-off value	Sensitivity	Specificity	AUC, CI%	p-value*
Hb (g/dL)	≤10.95	0.766	0.346	0.374-0.499	**0.049**
WBC (10^3/mm^3)	≥9.405	0.638	0.496	0.524-0.628	**0.040**
Neuthrophil count (x10^3/mm^3)	≥3.525	0.721	0.488	0.507-0.631	**0.032**
NLR	≥1.3969	0.588	0.521	0.508-0.631	**0.031**

Hb: Hemoglobin, WBC: White blood cell, NLR: Neuthrophil to lymphocyte ratio, FS: Febrile seizure, AFI: Acute febrile illness, CI: Confidence interval, *ROC curve analysis. Significance was set at p<0.05

Table 4. Logistic regression analysis of Hb and NLR associations

Variable	OR	95% CI	p-value	Risk
Hb (≤10.95 g/dL)	2.937	1.885-4.576	**<0.001**	+
NLR (≥1.3969)	2.719	1.873-3.949	**<0.001**	+

Hb: Hemoglobin, NLR: Neutrophil to lymphocyte ratio, OR: Odds ratio, CI: Confidence interval. Significance value was set at p<0.05

Discussion

The present research is one of the few studies in the literature investigating all CBC parameters for predicting the risk of FS in febrile children with upper respiratory infection and comparing with AFI and healthy children

Previous studies have reported inconsistent results concerning the relationship between anemia and FS in children. Daoud et al.[14] and Vaswani et al.[15] reported significantly lower mean serum ferritin levels in children with first FS than in children with AFI without seizures. Additionally, Kumari et al.[16] reported significantly lower serum ferritin levels in children with first SFS compared to children with AFI without seizures, although no significant differences were observed in mean Hb values or mean blood indices. However, Derakhshanfar et al.[17] suggested that iron can play a protective role against FS. They attributed that role to the involvement of, iron in the activity of neurotransmitters such as monoamine oxidase and aldehyde oxidase. Those authors thus concluded that iron deficiency leads to a reduction in the excitation power of neurons and thus can play a protective role against FS in anemic patients.[17] Another study evaluating the relationship between anemia and first simple FS in 240 patients aged six months to five years, observed no association between anemia and seizure.[18]

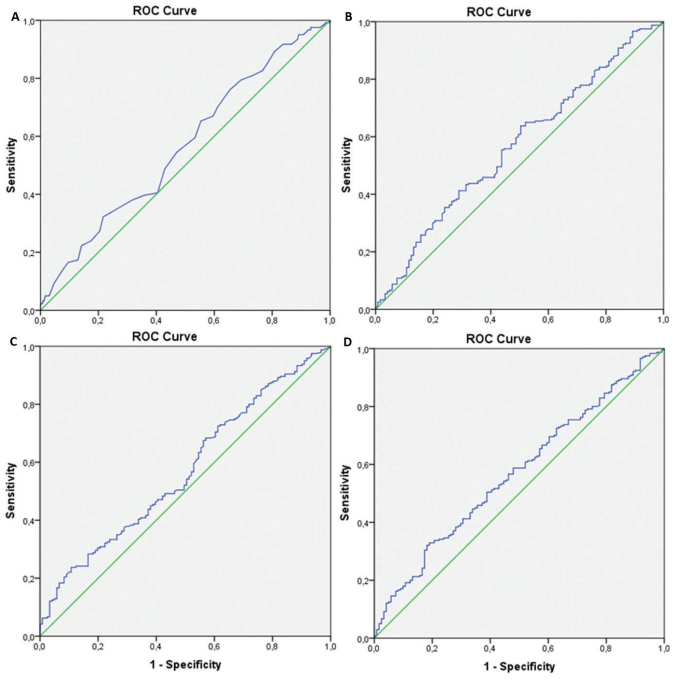

Figure 1. A: Receiver operating curve (ROC) curve for hemoglobin to predict febrile seizures (FS) in children with fever, **B:** ROC curve for white blood cell to predict FS in children with fever, **C:** ROC curve for neutrophil to predict FS in children with fever, **D:** ROC curve for neutrophil lymphocytes ratio to predict FS in children with fever

Animal studies have shown that iron deficiency affects myelination and the synthesis of neurotransmitters.[19] The first finding in the present study was lower Hb and MCV levels and higher RDW levels in children with FS compared to age-and-sex matched controls. When all the patients in the study were analyzed together, the optimal Hb cut-off value identified at ROC analysis was ≤10.95. Logistic regression analysis revealed that Hb level ≤10.95 was associated with a 2.937 -fold increased risk of FS (95% CI: 1.885-4.576).

In the light of the patients' age groups, the CBC parameters (low Hb and MCV and high RDW), and the causes of anemia, the findings of the present study suggest that anemia may derive from iron deficiency. We think that anemia developing in association with iron deficiency and fever may have made children more susceptible to seizures by reducing neuronal excitability in maturing brain cells and lowering the seizure threshold.[20]

IL-1β, one of the cytokines released during fever, stimulates cortisol secretion.[21] Cortisol in turn triggers an increase in neutrophils and leukocytes and a decrease in lymphocytes.[22] Woiciechowsky et al.[23] reported that intracerebroventricular IL-1β infusion significantly increased the numbers of peripheral neutrophils but reduced those of lymphocytes.

Gontko-Romanowska et al.[3] showed significantly higher neutrophil and significantly lower lymphocyte levels in children with FS compared to febrile children without seizures. Biyani et al.[24] concluded that increased leukocyte counts may be due to the stress caused by seizures. Similarity to Biyani et al.[24] Toyosawa[25] showed that electrically induced seizures immediately increased peripheral leukocyte counts in rabbits.

NLR is a measure of systemic inflammation.[7] Liu et al.[7] showed significantly higher NLR values in children with FS compared to febrile children without seizures. Another study of children with first seizure episodes of FS and febrile children reported higher WBC and NLR in children with FS.[20]

Another important finding in this study was that WBC, neutrophil counts and NLR were higher, while lymphocyte counts were lower in children with FS than in the control groups. Additionally, when all participants were evaluated together, the optimal WBC, neutrophil, and NLR cut-off values at ROC analysis were ≥9.405, ≥3.525, and ≥1.3969 respectively. Logistic regression analysis revealed that NLR ≥1.3969 was associated with a 2.719 -fold increased risk of FS (95% CI: 1.873-3.949).

The underlying mechanism of the relationship in FS is complex and is only gradually being elucidated. We think that the elevation in our results may not only indicate the presence of toxins in circulation as a result of an inflammatory reaction, but may also derive from a transient and rapid increase in catecholamine-derived neutrophils and leukocytes resulting from stress-induced by seizure and fever. Our CRP results (CRP was lower in children with FS than in those with AFI although the difference was not significant appear to support this idea.

CRP is an acute-phase reactant released during the course of infection and in several forms of inflammation.[26] Similarly to the findings of the present study, Yigit et al.[11] and Biyani et al.[24] observed no significant difference between groups with FS and with fever without seizure in terms of CRP levels (14.92 mg/dL vs 19.3 mg/dL and 11.67 vs 13.89, respectively). However, Gontko-Romanowska et al.[3] reported significantly lower CRP levels in children with FS compared to febrile children without seizures (15.73 vs. 58.50, respectively).

This is because viral infections are the principal underlying cause of FS and CRP elevation is not only a result of underlying infection but also of epinephrine release and demargination of neutrophils due to seizure stress. The higher CRP levels in children with AFI may be due to the inflammatory process increasing gradually to raise CRP to higher levels.[27]

Study Limitations

Due to the retrospective design of study, factors contributing to anemia, such as iron, ferritin, etc. levels, were not assessed therefore the etiology of anemia could not be determined precisely. Also causative micro-organism in upper respiratory infection was not identified.

Conclusion

Our findings suggest that low Hb levels and high NLR may be capable of use in predicting the risk of development of FS, but that these values are not by themselves sufficient for predicting FS in febrile children.

Clinicians must interpret blood tests results with care in order to predict FS in children from this age group. We think that, more advanced and extensive prospective studies including identifying the responsible micro-organism and evaluating the levels of IL-1β and TNF-α may ensure to elacuadiate underlying mechanism of FS and the inconsistant study results in the literature.

The strengths of this study included the fact that the febrile patients' group was homogeneous in terms of foci and duration of infection. Another strength is the presence of two control groups consisting of febrile and healthy children.

Ethics

Ethics Committee Approval: Approval for the study was obtained from the Local Ethics Committee of Aydın Adnan Menderes University (decision no: 11, date: 17.01.2021).

Informed Consent: Informed consent was not obtained due to the retrospective design of the study.

Peer-review: Externally and internally peer-reviewed.

Authorship Contributions

Concept: E.Ç., A.T., Design: E.Ç., Data Collection or Processing: E.Ç., Analysis or Interpretation: E.Ç., Ş.G., M.A., A.T., Literature Search: E.Ç., Ö.A., A.T., Writing: E.Ç.

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Evaluation of the Performance of PRISM III and PIM II Scores in a Tertiary Pediatric Intensive Care Unit

Üçüncü Basamak Çocuk Yoğun Bakım Ünitesinde PRISM III ve PIM II Skorlarının Performansının Değerlendirilmesi

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Abstract

Introduction: The most commonly used scoring systems for the assessment of predicted mortality (PDR) in the pediatric intensive care unit are the "pediatric risk of mortality" (PRISM) and the "pediatric index of mortality" (PIM) scores. The aim of this study is to evaluate the calibration and discrimination of PRISM III and PIM II scores in predicting mortality in a tertiary university hospital pediatric intensive care unit in Turkey.

Methods: Demographic data of patients hospitalized in the pediatric intensive care unit between January 1, 2015 and December 31, 2018 were scanned form the electronic records. PRISM III and PIM II score, PDR, and standardized mortality rate (SMR) were calculated. In order to show the discrimination of the scores, the area under the ROC curve (AUC) was calculated and the significance limit was accepted as 0.80. Hosmer-Lemeshow Goodness-of-fit test was used to evaluate the calibrations and p>0.05 was considered significant.

Results: After exclusions 825 patients included in the study. The mean value of the PRISM III was 9.5±6.8 and the mean value of the PIM II score was 1.9±8.2. The calculated SMR was 1.03 according to the PRISM III score and 0.76 according to the PIM II score. In the ROC analysis performed to evaluate the discrimination, the AUC values for PRISM III PDR and PIM II PDR were; 0.908±0.017 (p<0.001), 0.855±0.024 (p<0.001), respectively. When PRISM III and PIM II PDR values were analyzed in groups, the difference between predicted and observed mortality was not statistically significant (p=0>0.05).

Conclusion: In this study, it has been shown that the discrimination and calibration of the PRISM III and PIM II score is good in predicting mortality in a tertiary pediatric intensive care unit where medical and surgical patients are accepted.

Keywords: Mortality, score, PRISM, PIM, discrimination, calibration

Öz

Giriş: Çocuk yoğun bakım ünitesinde beklenen mortalitenin değerlendirilmesinde en yaygın kullanılan skorlama sistemleri "pediatric risk of mortality" (PRISM) ve "pediatric index of mortality" (PIM) skorlarıdır. Bu çalışmanın amacı, PRISM III ve PIM II skorlarının Türkiye'de üçüncü basamak bir üniversite hastanesi çocuk yoğun bakım ünitesinde mortaliteyi öngörmede kalibrasyonunun ve diskriminasyonunun değerlendirilmesidir.

Yöntemler: Çocuk yoğun bakım ünitesine 1 Ocak 2015-31 Aralık 2018 tarihleri arasında yatan hastaların demografik verileri elektronik kayıtlardan tarandı. PRISM III ve PIM II skoru, tahmini ölüm oranı (PDR), standardize mortalite oranı (SMR) hesaplandı. Skorların diskriminasyonlarını gösterebilmek için ROC eğrisi altında kalan alan (EAA) hesaplandı ve anlamlılık sınırı 0,80 kabul edildi. Kalibrasyonlarını değerlendirmek üzere Hosmer-Lemeshow Goodness-of-fit testi kullanıldı ve p>0,05 anlamlı kabul edildi.

Bulgular: Çalışma dışı bırakılan hastalar çıkarıldıktan sonra 825 hasta çalışmaya dahil edildi. PRISM III ortalama değeri 9,5±6,8 ve PIM II skorunun ortalama değeri 1,9±8,2 idi. Hesaplanan SMR, PRISM III skoruna göre 1,03 ve PIM II skoruna göre 0,76 idi. Diskriminasyonu değerlendirmek için yapılan ROC analizinde PRISM III PDR ve PIM II PDR için EAA değerleri; sırasıyla 0,908±0,017 (p<0,001), 0,855±0,024 (p<0,001) bulundu. PRISM III ve PIM II PDR değerleri gruplar halinde incelendiğinde, öngörülen ve gözlenen mortalite arasındaki fark istatistiksel olarak anlamlı değildi (p=0>0,05).

Sonuç: Bu çalışmada, ülkemizde tıbbi ve cerrahi hastaların kabul edildiği üçüncü basamak bir çocuk yoğun bakım ünitesinde PRISM III ve PIM II skorunun diskriminasyon ve kalibrasyonunun iyi olduğu gösterilmiştir.

Anahtar Kelimeler: Mortalite, skor, PRISM, PIM, diskriminasyon, kalibrasyon

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Introduction

Since the mid-1990s in Turkey, the number of pediatric intensive care units, which are structured independently of adult and neonatal intensive care units, has started to increase rapidly. In the following decade, it officially became a minor program in medical education and the education program was clearly defined. In this process, the minimum standards of the new intensive care units to be opened in the national health system have been defined and continuously inspected.[1] The main purpose of an intensive care unit is to reduce mortality.[2] For this reason, one of the defined standards is to evaluate the expected mortality rates in intensive care units with standard scoring systems and compare them with the actual mortality rates. The increase in infrastructure opportunities, the reflection of technological developments on patient care, and the increase of qualified health personnel have revealed the need to recalibrate and discriminate the scoring systems used in the evaluation of mortality. In addition, scoring systems are important to eliminate bias by selecting patients with similar disease severity when conducting clinical trials.[2,3] If the observed mortality number and distribution is similar to the number and distribution estimated from the results of the scores, it can be said that the performance of the institution is equivalent to the institutions in which the validity of these scores has been demonstrated elsewhere in the world.[4] The most commonly used scoring systems for the evaluation of mortality in the pediatric intensive care unit are the "pediatric risk of mortality" (PRISM) and the "pediatric index of mortality" (PIM) scores.[2] The PRISM III score uses the patient's most abnormal variants (PRISM III-24 score) during the first 12 or 24 hours in the intensive care unit, and it predicts possible mortality during this hospitalization.[5] The PIM II score estimates the risk of death from data available at the time of admission to the intensive care unit and has therefore been reported to be suitable for continuous monitoring of the quality of pediatric intensive care.[6] The aim of this study is to evaluate the calibration and discrimination of PRISM III and PIM II scores in predicting mortality in a tertiary university hospital pediatric intensive care unit in Turkey.

Materials and Methods

Patients and Data

The data of patients hospitalized in the Akdeniz University Pediatric Intensive Care Unit between January 1, 2015 and December 31, 2018 were scanned from electronic records. Their age, gender, underlying disease, reason for hospitalization in the intensive care unit, duration of invasive and non-invasive ventilation, length of stay in the intensive care unit, tracheostomy requirement and prognosis were recorded. Predicted death rate (PDR) was recorded using the PRISM III and PIM II scores, as well as the logarithmic formulas recommended for these scores.[7,8]

Standardized mortality rate (SMR) was calculated by dividing the mean of the PDR values obtained from the scores for both scoring systems by the actual mortality rate. Ideally, the SMR is expected to be close to 1. When this value was above 1, it was interpreted that the mortality predicted by the test was higher than the actual value, and when it was below 1, it was interpreted that the test predicted mortality (PDR) less than the actual value.

Features of the Unit Where the Study was Performed

Akdeniz University Pediatric Intensive Care Unit is an independent 8-room unit separated by an automatic door system. Two of these rooms are full isolation rooms. All beds are equipped with centrally connected advanced monitor system and advanced ventilators. During the period of the study, 1 lecturer, 1 minor specialist, 3 research assistants, one of whom was a senior, and 14 nurses worked in the unit. All medical and surgical patients aged 1 month to 18 years, including trauma, congenital heart surgery, and organ transplantation, are accepted. Advanced treatments such as high-frequency oscillatory ventilation, continuous renal replacement therapy, and extracorporeal membrane oxygenation (ECMO) are performed. The possibility of using ECMO is limited for economic reasons (less than 5 per year).

Exclusion Criteria

Patients who were hospitalized in the intensive care unit for less than 24 hours, whose cardio-pulmonary arrest status could not be stabilized at the end of the first 2 hours after admission, whose data could not be reached, who had undergone bone marrow transplantation or who had known chromosomal anomalies were excluded from the study.[3,9,10]

Statistical Analysis

Statistical evaluation was performed using the Statistical Package for Social Science (SPSS) 23 software. Descriptive statistics were made by using frequency and percentage (%) for categorical variables and by using mean and standard deviation (SD) values, and the median, minimum and maximum values for numerical variables. The chi-square test was employed to compare categorical variables with each other, while the Mann-Whitney U test was used for the analysis of numerical variables. A p-value below 0.05 was considered significant.

The area under the ROC curve (AUC) was calculated to evaluate how well the PRISM III and PIM II scores discriminated against the risk of death, and the significance limit was accepted as 0.80. When the AUC was higher than 0.80, it was considered

that the scores were able to discriminate adequately between the survivors and the non-survivors, and the scores had good discrimination.

In order to evaluate the calibrations of the scoring systems, the patients were divided into 5 different categories according to their risk groups, and the number of deaths, expected number of deaths, actual number of survivors and expected number of survivors were compared with the Hosmer-Lemeshow Goodness-of-fit test according to the total number of patients in the groups. In the case of p>0.05, it was evaluated that there was no statistically significant difference, and the calibration of the mortality test was considered good.

Consent was obtained for the study with the decision of the Akdeniz University Faculty of Medicine Clinical Research Ethics Committee, dated 09/04/2019 and numbered 70904504.

Results

Thirty-six patients with known chromosomal abnormalities, 55 patients who underwent bone marrow transplantation, and a total of 324 patients who were hospitalized in the intensive care unit for less than 24 hours or were unstable at the 2nd hour after cardiopulmonary resuscitation or had missing data were excluded from the study in accordance with the exclusion criteria (Figure 1). Three hundred seventy-eight (45.8%) of the patients included in the study were girls, and the mean age was 46.7 months (1-22) years. Among the reasons leading to intensive care hospitalization, respiratory failure (19.9%), trauma (18.4%), congenital heart surgery (16.1%), and postoperative follow-up (16%) were the most common ones (Table 1). Of the patients, 493 (59.75%) had a known chronic disease (Table 2). The duration of mechanical ventilation in the study group was 3.6 days (SD 6.0), and the mean intensive care unit stay was 7.1 days (SD 12.2). Tracheostomy was performed in 53 (6.42%) patients. The mortality observed in the study group was 8.60% (n=71). Mortality was 7.6% in males and 9.8% in females (p=0.265).

In the study group, the mean PRISM III score was 9.5 (SD 6.8), the mean PRISM III PDR was 8.3, and the PIM II score was 11.38. The SMR calculated according to the PRISM III score was 1.03, and the SMR according to the PIM II score was 0.76.

The area under the curve (AUC) was 0.908±0.017 (p<0.001) in the ROC analysis performed to evaluate the discrimination of the PRISM III score PDR. Similarly, when PIM II score PDRs were evaluated, AUC was found to be 0.855±0.024 (p<0.001). Since the AUC was above 0.80, it was seen that the discrimination of both scores was good (Table 3).

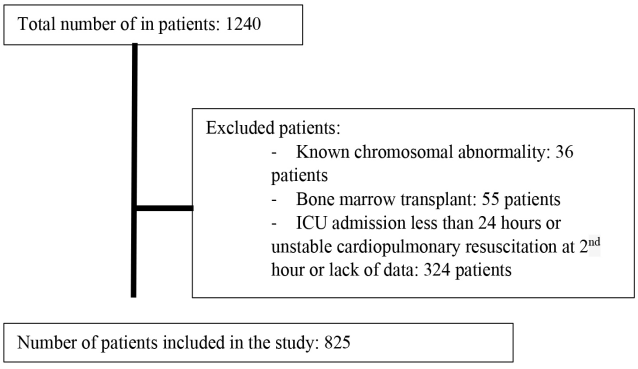

Figure 1. Selection of the study group and exclusion criteria
ICU: Intensive care unit

Table 1. Reasons for hospitalization in intensive care

Acute disease group	n=825 (%)	Mortality (%)
Respiratory failure	164 (19.9)	18 (10.97)
Trauma	152 (18.4)	12 (7.89)
Congenital heart surgery	133 (16.1)	2 (1.50)
Postoperative follow-up	132 (16)	5 (3.78)
Unconsciousness	99 (12)	6 (6.06)
Hemodynamic disorder	75 (9.1)	21 (28)
Poisonings	46 (5.6)	0 (0)
Follow-up after cardiopulmonary resuscitation	24 (2.9)	7 (29.16)

Table 2. Distribution of concomitant chronic diseases

Chronic disease group	n (%)	Mortality (%)
No known disease	332 (40.24)	17 (5.12)
Neurometabolic diseases	144 (17.45)	9 (6.25)
Acyanotic heart disease	143 (17.33)	6 (4.19)
Malignancy	74 (8.96)	18 (24.32)
Kidney diseases	39 (4.72)	5 (12.82)
Lower respiratory tract diseases	24 (2.90)	0 (0)
Immunodeficiency	21 (2.54)	3 (14.28)
Liver diseases	18 (2.18)	7 (38.88)
Cyanotic congenital heart diseases	17 (2.06)	3 (17.64)
Hematological diseases	13 (1.57)	3 (23.07)

Table 3. Discrimination of PRISM III and PIM II scores

Score	PDR*	#SMR	Discrimination (AUC&)
PRISM III	8.3%	1.03	0.908±0.017 (p<0.001)
PIM II	11.38%	0.76	0.855±0.024 (p<0.001)

*Actual mortality 8.60%, *PDR: Predicted death rate, #SMR: Standardized mortality rate, &Area under the curve (AUC) and p-value obtained from ROC analysis

The Hosmer-Lemeshow Goodness-of-fit test was applied to evaluate the calibration of the PRISM III score. When the PRISM PDR values of 825 patients were analyzed in groups, the difference between predicted and actual mortality was not significant (p=0.753). Calibration of the PIM II score was also similarly evaluated, and the difference between the predicted and actual mortality was similarly statistically insignificant (p=0.251). Since the p-values for both scores were insignificant, it was seen that their calibration was good (Table 4).

Discussion

Scoring systems are needed in pediatric intensive care units in order to evaluate the disease severity and response to treatment of study groups created for scientific research and to determine the expected mortality. It is seen that PRISM, PIM, PELOD and mSOFA scores are preferred in studies conducted in our country with critically ill children (Table 5). It is seen that most of these studies are retrospective, the number of patients is low, they are generally conducted on

Table 4. Calibration of PRISM III and PIM II scores (Hosmer Lemeshov Goodness-of-fit test)

	PDR %	Number of patients	Number of deaths occurred	Expected number of deaths	Actual number of survivors	Expected number of survivors
PRISM III*	0-1	129	0	0.492	129	128.508
	1-5	406	6	6.996	400	399.004
	5-15	172	15	12.784	157	159.216
	15-30	65	18	17.475	47	47.525
	>30	53	32	33.252	21	19.748
PIM II*	0-1	60	1	0.396	59	59.604
	1-5	401	10	8.404	391	392.596
	5-15	217	9	14.007	208	202.993
	15-30	56	13	10.190	43	45.810
	>30	91	38	38.003	53	52.997

According to the Hosmer Lemeshov Goodness-of-fit test result, p=0.753 for PRISM III, p=0.251 for PIM II score

Table 5. Studies evaluating mortality scores in critically ill children in Turkey and their results

Author and year of publication	The score used	Number and characteristics of patients	Design	Mortality rate	SMR*	Discrimination (AUC[&])	Calibration (Hosmer Lemeshov Goodness-of-fit test)
Anıl et al.[18]	PRISM I PIM II	277 patients between 2007-2008	Retrospective	14.7%	PRISM I: 1 PIM II: 1	PRISM I: 0.884 PIM II: 0.912	PRISM p=0.09 PIM II p=0.30
Köner et al.[13]	PIM I PIM II mSOFA[x]	373 postoperative congenital heart surgery patients between 2003-2009	Retrospective	13.4%	PIM I: 1.19 PIM II: 1.39	PIM I: 0.87, PIM II: 0.82 Baseline mSOFA: 0.92 Peak mSOFA: 0.93	PIM I: 0.0002 PIM II: 0.13
Ülgen Tekerek and Akyıldız[19]	PRISM III PIM II PELOD	454 patients in 2014	Retrospective	17%	PRISM III: 0.95	Not specified	PRISM III better than other scores in multiple binary logistic regression analysis (p<0.001)
Oymak and Bayrakci[11]	PRISM III-12 PRISM III-24 PIM II	389 patients between 2005-2006	Prospective	16%	PRISM III-12: 0.6 PRISM III-24: 0.6 PIM II: 0.4	PRISM III-12: 0.86 PRISM III-24: 0.89 PIM II: 0.84	Poor calibration of all three tests (p<0.05)
Kesici et al.[15]	PRISM III-24 PIM II OI[%]	150 patients undergoing mechanical ventilation	Retrospective	27.3%	PRISM III-24: 0.85	PRISM III-24: 0.66 PIM II: 0.52	PRISM III-24 p=0.002 PIM II p=0.68 Both tests are poorly calibrated, use of OI may be considered.
Alakaya and Arslanköylü[12]	PRISM III PELOD	372 patients between 2017-2018	Retrospective	7.8%	Not specified	PRISM III: 0.843 PELOD: 0.775	No significant difference between both tests (p=0.066), good correlations

*Standardized mortality rate, [&]Area under the curve (AUC from ROC analysis), [%] Oxygenation index, [x]Modified-sequential organ failure assessment score, SMR: Standardized mortality rate

Table 6. Examples and results of studies evaluating mortality scores in critically ill children in different countries

Author and year of publication/country	The score used	Number and characteristics of patients	Design	Mortality rate	SMR*	Discrimination (AUC&)	Calibration (Hosmer Lemeshov Goodness-of-fit test p-value)
Niederwanger et al.[17] 2020/Austria	PRISM III PRISM IV PIM II PIM III PELOD II	2019-2020 398 sepsis patients	Retrospective	13.6%		PRISM III: 0.75 PRISM IV: 0.7 PIM II: 0.78 PIM III: 0.76 PELOD II: 0.75	
Varma et al.[4] 2017/ India	PRISM III	2009-2011 723 patients	Prospective	14.8%	PRISM III: 0.98	PRISM III: 0.86	PRISM III: 0.638
Gonçalves et al.[3] 2015/Portugal	PRISM III PELOD II	2011-2012 556 patients	Prospective	5.21%	PRISM III: 0.94 PELOD II: 1.31	PRISM III: 0.92 PELOD II: 0.94	PRISM III: 0.282 PELOD II: 0.022
Slater et al.[20] 2003/ Austria, New Zealand	PIM PIM II PRISM PRISM III	2000-2001 26966 patients	Prospective	4.2%	PIM: 0.86 PIM II: 0.97 PRISM: 0.53 PRISM III: 0.77	PIM: 0.89 PIM II: 0.90 PRISM: 0.90 PRISM III: 0.93	PIM: <0.0001 PIM II: <0.025 PRISM: <0.0001 PRISM III: <0.0001
Tyagi et al.[21] 2018/ India	PIM II PIM III PRISM III	350 patients 18-month period	Prospective	39.4%	PIM II: 1.06 PIM III: 1.09 PRISM III: 0.9	PIM II: 0.728 PIM III: 0.726 PRISM III: 0.667	PIM II: 0.474 PIM III: 0.059 PRISM III: 0.747
Visser et al.[22] 2013/ Holland	PIM PIM II PRISM PRISM III	2006-2009 12040 patients	Retrospective	3.42%	PIM: 0.81 PIM II: 0.85 PRISM: 0.52 PRISM III: 0.87	PIM: 0.83 PIM II: 0.85 PRISM: 0.88 PRISM III: 0.90	
Nasser et al.[23] 2020/ Egypt	PRISM III PIM III	2015-2016 100 patients	Prospective	17%	PRISM III: 2.11 PIM III: 2.44	PRISM III: 0.987 PIM III: 0.973	PRISM III: 0.0001 PIM III: <0.0001
Jung et al.[24] 2018/ Korea	PIM II PIM III PRISM III	2009-2015 503 patients	Retrospective	19.8%	PIM II: 0.84 PIM III: 1.11	PIM II: 0.796 PIM III: 0.826 PRISM III: 0.775	PIM II: 0.249 PIM III: 0.337 PRISM III: 0.498
Zhang et al.[25] 2021/ China	PRISM III PELOD II	2014-2019 1253 patients	Retrospective	8.9%		PRISM III: 0.858 PELOD II: 0.721	PRISM III: 0.368 PELOD II: 0.276

SMR: Standardized mortality rate, AUC&: Area under the curve

non-homogeneous groups, and the facilities of the units are not sufficiently comparable. Similar to this study, although the discrimination of the PRISM III score was found to be good in studies in which the PRISM III score was evaluated, the calibration of the PRISM III score was not evaluated in one of the studies, and the calibration of the test was reported to be poor in another study conducted by Oymak and Bayrakci.[11,12] In the evaluation of expected and observed mortality rates in this study, both the calibration and discrimination of PRISM III and PIM II scores were found to be good. Similar to the studies conducted in our country, the results obtained in studies conducted outside the countries where the tests were developed are not homogeneous (Table 6).

There are also differences in the discrimination and calibration results of the tests in the studies conducted on the specific groups. Köner et al.[13] reported that the discrimination and calibration of the PIM II score was good in children followed up in the intensive care unit after congenital heart surgery, whereas the discrimination of the baseline and peak mSOFA score was superior to the PIM II score in predicting mortality. No comparison was made with the PRISM score in this study.[13] In another study conducted in the USA in children followed up for surgical and medical heart disease, it was detected that the PRISM III score was good in distinguishing mortality. However, when evaluated in terms of calibration, the expected mortality was lower than the observed in cardiac pathologies with lower risk and higher than the observed in pathologies with higher risk; therefore, the calibration was not good in the study group.[14] Kesici et al.[15] reported that the calibrations of PRISM III and PIM II scores were not good in children, all of whom were followed up on mechanical ventilators, and that the use of oxygenation index as a criterion in this group might be beneficial. In a retrospective study including 338 patients in a pediatric intensive care unit in Brazil where cancer patients were followed, mortality was reported as 18.34%, SMR as 0.78 and AUC as 0.71 for PRISM III score, and SMR as 0.77 and AUC as 0.76 for PIM II score. It was concluded that they were well calibrated, but they calculated the expected mortality higher.[16]

When PRISM, PIM and PELOD scores in 398 patients followed up for sepsis were evaluated together with their current and old versions, PIM score predicted lower mortality, and AUC

area values obtained in ROC analysis with PRISM III, PIM II and PELOD II scores were 0.75, 0.78 and 0.75, respectively.[17] The group included in our study did not consist of a homogeneous disease group, and the results obtained may have been affected by the distribution of the subgroups. In order to minimize this problem, patients with proven genetic disorders who underwent bone marrow transplantation, who were shown in previous studies to have unique risk factors, were excluded from the study group in this study.

Study Limitations

The most important limitation of this study is that it is a single-centered and retrospective evaluation and updated versions of the used scores are available. PRISM IV and PIM III scores have been developed and made available. On the other hand, in a study using the same scores, it was reported that the discrimination of PRISM IV and PIM III scores was not better than the previous versions, and the AUC values (0.70 and 0.76 for PRISM IV and PIM III, respectively) were similar.[17] The results obtained in our study could not be compared with other scoring systems and newer versions of existing scores.

Conclusion

In this study, it was shown that the discrimination and calibration of PRISM III and PIM II scores were good in a tertiary pediatric intensive care unit where medical and surgical patients were accepted. Discrimination and calibration of newly developed versions of these scores and less commonly used updated scores such as PELOD II and mSOFA should be evaluated in a multicenter national study. In this way, the scientific outputs of studies conducted in different units and on relatively small groups can be interpreted more accurately and used in the development of health policies.

Ethics

Ethics Committee Approval: Consent was obtained for the study with the decision of the Akdeniz University Faculty of Medicine Clinical Research Ethics Committee, dated 09/04/2019 and numbered 70904504.

Informed Consent: Informed consent was obtained.

Peer-review: Externally and internally peer-reviewed.

Authorship Contributions

Surgical and Medical Practices: B.U.G., O.D., N.Ü.T., L.D., Concept: B.U.G., O.D., Design: B.U.G., O.D., Data Collection or Processing: B.U.G., O.D., Analysis or Interpretation: B.U.G., O.D., N.Ü.T., L.D., Literature Search: B.U.G., O.D., N.Ü.T., Writing: B.U.G., O.D., N.Ü.T., L.D.

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Evaluation of Corrosive Substance Ingestion in the Pediatric Emergency Department

Çocuk Acil Servisinde Korozif Madde Alımının Değerlendirilmesi

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Abstract

Introduction: The management of the patient who applied to the emergency department with corrosive substance exposure varies according to the characteristics of the substance and the clinical conditions of the patient. In this study; demographic and clinical characteristics, patient management strategies and prognosis of the children presenting with corrosive substance ingestion are presented.

Methods: Cases who applied with corrosive substance intake and were under the age of 18 were included in the study. Demographic data of the patients, characteristics of the substance, presence of intraoral lesions or any symptoms or signs, treatment and prognosis, radiographs and hospital stay were examined. Drool scores were calculated.

Results: One hundred-ten patients were included. The mean age of the patients was 41±13 months and 56 (50.9%) were male. 53% of the patients were asymptomatic at presentation. The most common symptom was nausea-vomiting, the most common finding was hyperemia in the oropharynx. The mean Drool score of the patients was 8.9±1.7. Seventy-seven patients (70%) took alkaline, 33 patients (30%) took acidic substances; 45 patients sodium hydroxide, 27 patients sodium hypochlorite, 26 patients took hydrochloric acid. Findings were mostly observed in hydrochloric acid and sodium hydroxide intake. Endoscopy was performed in 3 of the patients. The mean Drool score of the patients who underwent endoscopy was 6.7. No complications were observed in any of the patients in the follow-up.

Conclusion: Ingestion of corrosive substances is one of the important and preventable causes of emergency department admissions with chemical poisoning. There is usually accidental and small amount of

Öz

Giriş: Korozif madde maruziyeti ile acil servise başvuran hastanın yönetimi maddenin özelliklerine ve hastanın klinik durumuna göre değişmektedir. Bu çalışmada; korozif madde alımı ile başvuran çocukların demografik ve klinik özellikleri, hasta yönetim stratejileri ve hastaların prognozu sunulmaktadır.

Yöntemler: Korozif madde alımı ile başvuran ve 18 yaşın altında olan olgular çalışmaya dahil edildi. Hastaların demografik verileri, maddenin özellikleri, ağız içi lezyonların veya herhangi bir semptom veya bulgunun varlığı, tedavi ve prognozu, grafileri ve hastanede kalış süreleri incelendi. Drool skorları hesaplandı.

Bulgular: Yüz on hasta çalışmaya dahil edildi. Hastaların yaş ortalaması 41±13 ay ve 56'sı (%50,9) erkekti. Hastaların %53'ü başvuru anında asemptomatikti. En sık görülen semptom bulantı-kusma, en sık bulgu orofarinkste hiperemiydi. Hastaların Drool skor ortalaması 8,9±1,7 idi. Yetmiş yedi hastanın (%70) alkali, 33 hastanın (%30) asidik madde alımı mevcuttu, içlerinden 45 hastanın (%40,9) sodyum hidroksit, 27 hastanın (%25) sodyum hipoklorit, 26 hastanın (%24) hidroklorik asit aldığı saptandı. Bulgular en fazla hidroklorik asit ve sodyum hidroksit alımında gözlendi (p=0,044). Hastaların 3'üne (%2,7) endoskopi yapıldı. Endoskopi yapılan hastaların Drool skor ortalaması 6,7 idi. Takiplerde hiçbir hastada komplikasyon görülmedi.

Sonuç: Korozif madde alımları kimyasal zehirlenmelerle olan acil servis başvurularının önemli ve önlenebilir nedenlerinden biridir. Erken çocukluk döneminde sıklıkla kazara ve az miktarda alımlar söz konusudur. Hastalar asemptomatik olabilir veya nadiren ciddi

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intake in early childhood. Patients may be asymptomatic or rarely present with severe symptoms. It is important to know the chemical content of the ingested substance in order to predict the risk of damage to the gastrointestinal tract and respiratory system and to provide appropriate management in emergency services.

Keywords: Corrosive, child, emergency, poisoning

semptomlar ile başvurabilirler. Gastrointestinal sistem ve solunum sistemi ile ilişkili hasar riskini öngörmek ve acil servislerde uygun yönetimi sağlamak için alınan maddenin kimyasal içeriğinin bilinmesi önemlidir.

Anahtar Kelimeler: Korozif, çocuk, acil servis, zehirlenme

Introduction

Corrosive damage remains a concern for pediatric emergency clinicians. Accidental ingestion of corrosive substances is common in young children. It can clinically occur in a wide spectrum. While patients may be asymptomatic, they may also present with conditions that require immediate intervention such as necrosis or perforation.[1] Corrosive substances can be acidic or alkaline and cause chemical burns by different mechanisms. The most commonly ingested corrosive substances, especially household cleaning products, are degreasers with a strong basic effect, dishwashing detergents, polishes and lime removers with a strong acidic effect.[2] The first intervention and management of the patient who applied to the emergency room due to corrosive ingestion varies according to the chemical and physical properties of the substance, its amount, concentration, contact time in the tissues, and the patient's signs and symptoms. In this study, demographic and clinical characteristics, patient management strategies and prognosis of the children admitted to the pediatric emergency department of our hospital with corrosive substance intake are presented.

Materials and Methods

It is a single-center retrospective descriptive study. Patients admitted to the pediatric emergency department with chemical poisoning between January 01, 2016 and December 31, 2018 were selected from our hospital database by using the ICD-10 codes of X49 (accidental poisoning and exposure by other and unspecified chemicals and harmful substances), T54.X (toxic effect: Corrosive acids/alkalis/unspecified/ others), T28.0-T28.2, T28.5-T28.7 (Corrosive Gastrointestinal Burns). The content of the exposed chemical substance was examined, those with strong acidic (<2) and strong alkaline (pH>11.5) structures were accepted as corrosive substances.[3] Cases under 18 years of age, who applied with corrosive substance intake, were included in the study. Patients with isolated inhalation, eye or skin contact, and those with missing data were excluded from the study.

Demographic data (age, sex) of all included patients, the time elapsed between the ingestion of the substance and admission, and the type and amount of the substance were recorded. Symptoms and/or signs of the patients (drooling, nausea, vomiting, difficulty in swallowing, burning sensation, erythema in the oropharynx, ulcer or respiratory symptoms such as hoarseness, cough, bruising, shortness of breath, chest pain, dysphonia, stridor, tachypnea), their treatment and prognosis were recorded. X-rays (postero-anterior chest X-ray and standing direct abdominal X-ray) and length of hospital stay were examined.

Drool Score

The Drool score is a tool that shows the risk of stricture in the esophagus according to the clinical findings in the child. It was developed by Uygun et al.[4] in a prospective study of 202 patients (Table 1). A score of ≤4 points as a result of this scoring is a predictor of esophageal stenosis. The Drool scores of all patients included in the study at the emergency service admission were calculated and recorded.

Corrosive substances ingested by the patients were examined. Chemical contents and pH values of the substances were recorded. They were divided into four groups as sodium hydroxide, sodium hypochlorite, hydrochloric acid and others. The clinical features and length of hospital stay of the cases were evaluated according to the groups.

This study was approved by the Ethics Committee of University of Health Sciences Turkey, Dr. Sami Ulus Gynecology, Child Health and Diseases Training and Research Hospital (date: E-21/09-208).

Statistical Analysis

Statistical analyses of the data obtained in the study were performed in IBM SPSS for Windows version 22.0 package program. Descriptive statistics were presented with frequency, percentage, mean, median, standard deviation, minimum and maximum values. The comparison between the groups was made using the Kruskal-Wallis test, since it did not conform to the normal distribution.

Results

Between January 2016 and December 2018, a total of 1100 patients were admitted to the pediatric emergency department of our hospital due to chemical substance exposure. Of these patients, 123 (11.1%) were exposed to corrosive substances. A total of 110 patients were included in the study. The mean age of the patients was 41±13 months and 56 (50.9%) were

Table 1. Drool score

Drool score			
Findings	**Score 0**	**Score 1**	**Score 2**
D (Drool) increased drooling	≥12 hours	<12 hours	None
R (Reluctant) loss of appetite	≥24 hours	<24 hours	None
O (Oropharyngeal) lesions	Serious lesions (bleeding, erosion, burn, necrosis, ulcer)	Edema/hyperemia	None
O (Other) number of other symptoms	Fever, hematemesis, abdominal pain, retrosternal pain, dyspnea (≥2)	1	None
L (Leukocytosis)	≥20000	<20000	None

Table 2. Demographic and clinical characteristics of the patients

Characteristics	n (%)
All patients	110
Age (month, mean ± SD)	41±13
Gender	
Female	54 (49)
Male	56 (50.9)
Time between ingestion and admission (minute, mean ± SD)	91.7±23
Symptom	
No symptom	58 (53)
Drooling	5 (4.5)
Dysphagia	1 (0.9)
Dyspepsia	2 (1.8)
Nausea-vomiting	52 (47.2)
Respiratory symptoms	8 (7.2)
Finding	
Hyperemia in the oropharynx	35 (31.8)
Respiratory findings	3 (2.7)
Drool score (mean ± SD)	8.9±1.7

SD: Standard deviation

Table 3. Swallowed corrosive substances

Corrosive agent	n (%)
All ingestions	110
Sodium hydroxide	45 (40.9)
Sodium hypochlorite	27 (25)
Hydrochloric acid	26 (24)
Other*	12 (16)
Corrosive agent form	
Solid	31 (28.1)
Liquid	79 (71.8)

* Potassium hydroxide, calcium hydroxide, alcohol benzene, nitric acid, sulfuric acid, hydrogen peroxide, aromatic hydrocarbon, sodium borate, citric acid

Table 4. Follow-up and treatment of patients

All patients	110
Patients admitted to the surgical service, n (%)	52 (47.2)
Length of stay in clinic (hour, mean ± SD)	35±9
Length of stay in the emergency room for patients not admitted to the clinic (hour, mean ± SD)	8.3±3.4
Treatment, n (%)	
Intravenous fluid	95 (86.3)
Proton pump inhibitor	90 (81.8)
Antibiotic	37 (33.6)
Complication	0

SD: Standard deviation

male. Ingestions of corrosive substance were all accidental/unintentional and at small amounts. The mean time from the ingestion of corrosive substances to admission to the emergency department was 91.7±23 minutes. 53% of the patients were asymptomatic at admission. The most common symptom was nausea-vomiting, and the most common finding was hyperemia in the oropharynx (Table 2). The mean Drool score of the patients was 8.9±1.7.

When the corrosive substance content was examined, it was detected that 77 patients (70%) had alkaline substance intake, 33 (30%) had acidic substance intake. It was found that 45 patients (40.9%) ingested sodium hydroxide, 27 patients (25%) had sodium hypochlorite, 26 patients (24%) had hydrochloric acid (Table 3). Medical treatments applied to all patients are presented in Table 4. Possible perforation and chemical pneumonia were excluded by chest and standing direct abdominal radiographs. Fifty-two patients (47.2%) were hospitalized in the pediatric surgery clinic and the mean length of hospital stay was 35±9 hours.

The comparison of the data according to the corrosive substance content is presented in Table 5. While the findings were mostly observed for the intake of hydrochloric acid and sodium hydroxide (p=0.044), 80.7% of the group that drank hydrochloric acid was hospitalized in the surgical service (p=0.002). Endoscopy was performed in 3 (2.7%) of the patients. The mean Drool score of the patients who underwent endoscopy was 6.7. Grade 1 erosion was detected in the middle part of the esophagus and the gastro-esophageal junction in one patient, and the Drool score was 6 at admission.

Table 5. Comparison of data according to corrosive substance content

	Sodium hydroxide	Sodium hypochlorite	Hydrochloric acid	Other	p
Patients (n)	45	27	26	12	
Symptoms (n)					
Drooling	1	1	2	1	0.325
Dysphagia	0	0	1	0	-
Dyspepsia	0	1	1	0	0.695
Nausea-vomiting	21	8	18	2	**0.044**
Respiratory symptoms	1	1	2	1	0.256
Finding (n)					
Oropharyngeal hyperemia	12	5	19	1	**0.026**
Respiratory findings	0	1	2	0	0.055
Drool score (mean ± SD)	9.1±0.6	8.9±0.8	8.6±1.1	9.5±0.4	0.765
Patients admitted to the service (n)	22	5	21	4	**0.002**
Length of stay in clinic (day, mean ± SD)	2±1	1.7±0.9	2.2±0.5	1.8±0.7	0.481

p<0.05 significant, SD: Standard deviation

No complications were observed in the follow-ups of the patients (Table 4). In the 3rd week after discharge, esophagus, stomach and duodenum radiographs were taken in 10 patients and no pathological findings were detected in any of them.

Discussion

Ingestion of corrosive substances is one of the important and preventable causes of pediatric emergency department admissions due to short- and long-term complications.[5] Patients may be asymptomatic or present with drooling or swallowing difficulty, oropharyngeal lesions or burns, retrosternal or abdominal pain, hematemesis, vomiting, agitation, dyspnea, tachycardia, fever, and leukocytosis.[1] It can be difficult to predict esophageal damage when no symptoms or signs are present. The lack of consensus on patient management in the literature can be challenging for pediatric surgeons and emergency room clinicians.

The rate of ingestion of corrosive substances in all poisoning cases is between 8.6% and 51.4%, and its incidence has increased gradually, especially in recent years.[6] It can be seen at any age, but it is common in children younger than 5 years old and boys constitute 50-62% of cases.[5] The majority of young children are brought to the emergency room for accidental ingestion or skin/eye contact, and exposure in these patients is usually low. In our study, 123 cases of exposure to corrosive substances were presented to the pediatric emergency service for 3 years, and the ratio of all chemical poisoning cases was 11.1%. Similar to the literature, most of the cases were in early childhood and all had accidental exposure to caustic substance. The most commonly exposed corrosive substances are household cleaning products such as bleach, dishwasher detergents and polishes, degreasers and lime removers.[2] These are products that are widely used and easily accessible in domestic cleaning today, they easily attract children's attention and cause unwanted situations.[7] In our study, degreasers (sodium hydroxide) with alkali content and bleach (hydrochloric acid) with acidic content were the most commonly ingested corrosive substances.

In the ingestion of corrosive substances, the severity of the injury is related to the corrosive nature of the ingested substance (pH, acidic, alkaline), its amount, concentration, physical form (solid or liquid), and the duration of contact with the mucosa.[8] Questioning these characteristics is a critical step in order to properly manage the follow-up and treatment process of patients and to predict the risk of damage. In this case, families should be encouraged to cooperate. It should be ensured that they bring the corrosive substance in question, show the photo of the product or say its name. Whether the substance taken is a branded product or not is not decisive in terms of burn rate.[9] However, the chemical content and pH value of the product can guide. In our study, the products in question were reached and their chemical properties were evaluated. Only the amount of the substance taken was not clearly stated, but the amount taken was expressed as "low" in all cases. Most of the cases were asymptomatic at emergency service admission. Nausea or vomiting was seen in half of the patients, while increased drooling and respiratory symptoms were rarely seen. The presence of clinical findings was observed mostly in sodium hydroxide and hydrochloric acid intake. Although the causative agent's being strongly acidic or alkaline affected the clinical features of the patients,

the prognosis of all patients was good due to the small amount swallowed and medical treatments.

The presence or absence of symptoms in corrosive substance exposures does not show a linear relationship with the extent of esophagus-stomach damage.[10] There are differences of opinion in the literature for the management of these patients. Some publications argue that clinical symptoms and the degree of esophageal damage are not correlated in this age group and emphasize that endoscopy should be performed in the pediatric age group whenever possible. On the other hand, it has been argued that endoscopy performed in the first 48 hours is unnecessary and does not make a significant contribution to the diagnosis, treatment and management of the patient.[11] The view supporting the use of non-invasive methods in these patients has suggested the use of the Drool scoring system, which is a new prognostic scoring system, and it has been accepted that this scoring is a high predictor of the development of esophageal stenosis.[12] In our study, the mean Drool score of all patients was 8.9. The mean Drool score of 3 patients who underwent endoscopy was 6.7, and the score of the patient with grade 1 injury was 6. Considering the general score average, the Drool score was lower in the patient who developed damage. No complications developed in any of the patients during the follow-up period. Therefore, we support the provision of supportive care in asymptomatic or rarely symptomatic patients and the use of the Drool scoring system, which is a practical and non-invasive tool for predicting clinical process.

Study Limitations

It is a single center, retrospective study. The number of patients undergoing endoscopy is small. This situation did not allow to discuss the necessity of endoscopy and the advantage of following only with Drool score. It can be guiding for future studies.

Conclusion

Ingestion of corrosive substances is one of the important and preventable causes of emergency department admissions with chemical poisoning. There are often accidental and small amounts of ingestion in early childhood. Patients may be asymptomatic or rarely present with severe symptoms. It is important to know the chemical content of the ingested substance in order to predict the risk of damage to the gastrointestinal tract and respiratory system and to ensure appropriate management in emergency departments.

Ethics

Ethics Committee Approval: This study was approved by the Ethics Committee of University of Health Sciences Turkey, Dr. Sami Ulus Gynecology, Child Health and Diseases Training and Research Hospital (date: E-21/09-208).

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Authorship Contributions

Surgical and Medical Practices: İ.B., M.M.G., N.T., Ö.B., D.E., Concept: R.M.Y., B.Ö., Design: R.M.Y., B.Ö., Data Collection or Processing: R.M.Y., A.Gü., Analysis or Interpretation: R.M.Y., C.D.K., Literature Search: R.M.Y., B.Ö., A.G., Writing: R.M.Y., A.Gü.

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Indications and Outcomes of Tracheostomy in Children After Congenital Heart Surgery

Doğuştan Kalp Cerrahisi Sonrası Çocuklarda Trakeostomi Endikasyonları ve Sonuçları

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Abstract

Introduction: In a minority of children after cardiovascular surgery may require prolonged mechanical ventilatory support and tracheostomy. We aim to describe indications, timing and, outcomes of the tracheostomy.

Methods: A retrospective review of 12 children requiring tracheostomy after cardiac surgery between January 2010-December 2019 was performed. The patients' characteristics, indications and timing for tracheostomy, and survival were reviewed.

Results: After cardiac surgery, 12 (0.5%) of 2.459 patients with a median age at surgery of 210 days (interquartile range: 75-262 days) underwent tracheostomy. The median time between cardiac surgery and tracheostomy was 25 days (interquartile range: 15-47 days). Diaphragmatic paralysis was the most common (42%) indication for tracheostomy. Genetic syndrome or at least one non-cardiac morbidity was present in 41.6% of patients. The duration of mechanical ventilation was shorter in patients who had tracheostomy within 30 days compared with >30 days following intubation (30 vs. 60 days, p=0.035). The median length of pediatric intensive care unit stays after the tracheostomy was 41 days (range, 21-289 days). Among all patients with congenital heart surgery undergoing tracheostomy, 6 (50%) of 12 were decannulated after a median time of 179 days (range, 34-463 days). The operative mortality was 8.3% (1/12) and the overall mortality during the first year of follow-up was 8.3% (1/12).

Conclusion: An early tracheostomy procedure may facilitates the weaning process and shorten the duration of positive pressure ventilation.

Keywords: Tracheostomy, congenital heart surgery, prolonged mechanical ventilation, children

Öz

Giriş: Kardiyovasküler cerrahi sonrası çocukların çok az bir kısmında uzun süreli mekanik ventilasyon desteği ve trakeostomi gerekmektedir. Bu çalışma ile trakeostominin endikasyonlarını, zamanlamasını ve sonuçlarını tanımlamayı hedefliyoruz.

Yöntemler: Ocak 2010-Aralık 2019 tarihleri arasında kalp cerrahisi sonrası trakeostomi gerektiren hasta verileri geriye dönük olarak değerlendirildi. Hastaların preoperatif özellikleri, trakeostomi endikasyonları, trakeostomi açılma zamanı ve klinik sonuçları analiz edildi.

Bulgular: Kalp cerrahisi uygulanan 2,459 hastanın 12'sine (%0,5) trakeostomi açıldı. Bu hastaların kalp cerrahisi sırasında ortanca yaşı 210 gün (çeyrek değerler genişliği: 75-262 gün) idi. Kalp cerrahisi ile trakeostomi arasındaki ortalama süre 25 gündü (çeyrek değerler genişliği: 15-47 gün). Trakeostomi için en sık endikasyon postoperatif gelişen diyafragma paralizisi (%42) idi. Hastaların %41,6'sında genetik sendrom veya en az bir kardiyak olmayan morbidite mevcuttu. Mekanik ventilatörde kalış süresi değerlendirildiğinde, çocuk yoğun bakım yatışlarının ilk 30 gün içinde trakeostomi açılan hastaların mekanik ventilatörde kalma süresi, 30. gün sonrasında trakeostomi açılan hasta grubuna göre daha kısaydı (sırasıyla 30 gün, 60 gün, p=0,035). Trakeostomiden sonra çocuk yoğun bakım ünitesinde ortalama kalış süresi 41 gündü (aralık, 21-289 gün). Doğuştan kalp cerrahisi sonrası trakeostomi açılan 12 hastanın 6'sı (%50) ortalama 179 gün (aralık, 34-463 gün) sonra dekanüle edildi. İzlem sonrası birinci yılda operatif mortalite %8,3 (1/12) ve genel mortalite %8,3 (1/12) idi.

Sonuç: Doğuştan kalp cerrahisi sonrası trakeostomi ihtiyacı olan hastalarda erken trakeostomi işlemi, pozitif basınçlı ventilasyondan ayrılma sürecini kolaylaştırır ve pozitif basınçlı ventilasyon süresini kısaltabilir.

Anahtar Kelimeler: Trakeostomi, doğuştan kalp cerrahisi, uzamış mekanik ventilasyon, çocuk

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Introduction

In the recent 20 years, improvement in the field of congenital heart surgery (CHS) and postoperative management result in improved survival in patients with congenital heart disease. Early extubation has advantages including reduced sedo-analgesia, decreased ventilator-associated pneumonia, and improved cardiovascular interactions. However, a small percentage of children who had CHS has a risk for prolonged ventilation. Prolonged mechanical ventilation is the most common indication for tracheostomy after CHS and occurs as a result of multiple etiologic factors. A large cohort of the patients who underwent tracheostomy after CHS reported that the incidence of tracheostomy increased from 0.11% to 0.76% between 2000-2012.[1]

Tracheostomy after cardiac operations appears to be associated with higher hospital mortality and higher mortality after discharge. Especially, children with single-ventricle physiology have lower long-term survival.[2] After CHS, in-hospital mortality following tracheostomy ranged from 7.7% to 28%.[3] However, the annual mortality rate of children with tracheostomy after CHS has not changed over time. It has reported 24.5% in 2010 and 27.5% in 2013.[1]

The purpose of the study is to describe the tracheostomy indications, complications, and long-term outcomes in children undergoing CHS.

Materials and Methods

We performed a retrospective chart review of all children who required tracheostomy after CHS from January 2010 to December 2019. Patients were identified from the pediatric intensive care unit (PICU) and cardiothoracic surgical database. All pediatric patients under the age of 14 years who underwent tracheostomy after CHS were included. Neonates and patients with tracheostomies placed before cardiac surgery were excluded. The demographic data, cardiac diagnosis, details of surgical procedures such as cross-clamp and cardiopulmonary bypass duration, and Risk Adjustment for Congenital Heart Surgery Score (RACHS)-1 were recorded.[4] Patients were evaluated for several extubation trials, tracheostomy timing, and duration of mechanical ventilation before and after the tracheostomy. We also recorded the Pediatric Risk of Mortality Score (PRISM)-III at PICU admission, which is a validated and physiology-based scoring system for rating the severity of medical illness for children.[5] The number of ventilator-associated pneumonia (VAP) episodes was recorded before and after tracheostomy. The indication for tracheostomy and, complications related to tracheostomy were recorded. This study was approved by the institutional review boards with the permission for the use of patient data for publication purposes (21-1T/26). Informed consent was received from the families.

Our primary outcomes included operative mortality and long-term survival, which was defined as 1-year survival. We reported operative mortality according to the definition of the Society of Thoracic Surgeons (STS) and Congenital Heart Surgery Database. Other outcomes include tracheostomy incidence, length of stay, time of decannulation if the patient had been decannulated, and mechanical ventilatory need after hospital discharge.

Statistical Analysis

Statistical analysis was performed using IBM SPSS Statistics version 20. Descriptive data are expressed as means (standard deviations) or medians (ranges) as appropriate. Categorical data were compared using the chi-squared test or Fisher's Exact test. Continuous data were analyzed using the Mann-Whitney U test for non-normally distributed data.

Results

A total of 12 patients underwent tracheostomy placement following cardiac surgery in the 9 year study period. During this period 2459 CHS performed in our center, the incidence of tracheostomy after CHS was 0.5%. Eight of the 12 patients (66.7%) were female. The median weight at the time of surgery was 6 kg (range, 4 kg-35 kg).

The median age at the time of surgery was 210 days [interquartile range (IQR): 75-262 days]. The median time between cardiac surgery and tracheostomy was 25 days (IQR: 15-47 days). The mean PRISM score was 7.1±5.5. Eleven patients (92%) RACHS-1 score were ≥2. A large proportion of patients (10/12, 83.3%) had biventricular anatomy, among these patients atrioventricular septal defect was the most common diagnose. Two patients had single ventricle anatomy. The details of cardiac diagnosis and the cardiac surgery performed are summarized in Table 1. The median duration of mechanical ventilation was 60 days (range, 30-261 days) and the median length of PICU stay was 68 days (range, 30-301 days). The median duration of mechanical ventilation after tracheostomy was 16 days (range, 12-215 days). Demographics and patient characteristics are shown in Table 2.

Three patients who had a neurological impairment and 2 patients who had a failure of weaning underwent tracheostomy before extubation trials. Seven patients had at least 2 extubation trials. Diaphragmatic paralysis was the most common (5/12, 42%) indication for tracheostomy. Neurological impairment and hypotonicity were the next common indication and were present in 4 patients (33.3%). Direct laryngo-bronchoscopy was performed in 6 patients,

Table 1. Cardiac diagnoses, procedures and outcomes for patients requiring tracheostomy after congenital heart surgery and, the timing and indications for tracheostomy in all patients

Case no	Cardiac diagnosis	Primary surgery	Tracheostomy indication	Comorbidity	Number of extubation trials	Duration of intubation before tracheostomy (days)	Outcome
1	Balanced AVSD	AVSD repair	Diaphragm paralysis (bilateral)	-	3	14	Home ventilation
2	ASD, VSD, PDA	PDA closure, pulmonary banding	Diaphragm paralysis	DiGeorge syndrome, chronic pulmonary disease	-	50	Decannulated
3	DORV, PA, PFO, PDA, MBT shunt	Glenn	Prolonged PPV	-	2	18	Decannulated
4	AVSD	AVSD repair	Hypotonicity, diaphragm paralysis	Down syndrome	-	22	Home ventilation
5	ASD, VSD, PDA	PDA closure, pulmonary banding	Tracheobronchomalacia	Malnutrition	3	45	Decannulated
6	Single Ventricle, Glenn	Fontan procedure	Neurological impairment	-	-	6	Decannulated
7	ASD, VSD	AVSD repair, tricuspid valvuloplasty	Prolonged PPV	Down syndrome	3	67	Died
8	Tetralogy of Fallot	MBT shunt	Neurogical impairment	-	-	17	Trach collar
9	Shone's complex, MS	Mitral valvulopla sty	Bronchomalacia	-	4	46	Decannulated
10	ASD, VSD	AVSD repair	Diaphragm paralysis Neurological impairment Prolonged PPV	-	-	15	Home ventilation
11	Truncus arteriosus	Repair of truncus arteriosus	Tracheobronchomalacia	-	2	48	Trach collar
12	D-TGA	Senning procedure	Diaphragm paralysis chylothorax	-	3	28	Decannulated

AVSD: Atrioventricular septal defect, ASD: Atrial septal defect, VSD: Ventricular septal defect, PDA: Patent ductus arteriosus, DORV: Double outlet right ventricle, PA: Pulmonary atresia, PFO: Patent foramen ovale, MBT: Modified blalock-taussig, PPV: Positive pressure ventilation, MS: Mitral stenosis, D-TGA: Dextrotransposition of great arteries

Table 2. Demographics and patients characteristics of children requiring tracheostomy after operation for congenital heart disease

Characteristics	n=12
Male gender, n (%)	4 (33.3)
Median weight at surgery (kg, range)	6 (4-35)
Median operation age, day (IQR)	210 (75-262)
Chromosomal abnormalities, n (%)	3 (25)
PRISM score (mean, SD)	7.1 (5.5)
CPB time, minute (mean, SD)	73.2 (33.5)
Cross-clemp time, minute (mean, SD)	60.8 (34.3)
Time between surgery and tracheostomy, day, median (IQR)	25 (15-47)
Median duration of MV (day, range)	60 (30-261)
Duration of MV after tracheostomy (day, range)	16 (12-215)
Median length of PICU stay (day, range)	68 (30-301)
Median length of hospital stay (day)	81.5 (43-310)

IQR: Interquartile range, PRISM: The Pediatric Risk of Mortality, SD: Standard deviation, CPB: Cardiopulmonary bypass, MV: Mechanical ventilation, PICU: Pediatric intensive care unit

3 patients were diagnosed with tracheobronchomalacia (25%). In 2 patients, persistent cardiac insufficiency and prolonged mechanical ventilation were considered as indications for tracheostomy. Three patients (25%) had confirmed chromosomal anomalies which revealed trisomy 21 in two patients and DiGeorge syndrome in one patient. Two patients had chronic lung disease, one of them operated for tracheoesophageal fistula. Tracheostomy indications are summarized in Table 1. Genetic syndrome or at least one non-cardiac morbidity were present in 41.6% of patients.

No procedure-related complications have occurred in any of the patients during tracheostomy insertion. There were no mediastinal wound infections. Only one patient with DiGeorge syndrome had a tracheostomy site infection. Tracheitis and pneumonia were the most common complications. Before tracheostomy 10 patients (83.3%) had 14 VAP episodes whereas 7 patients (58.3%) had 9 VAP episodes after tracheostomy, although this difference was not significant (p=0.152). *Pseudomonas aeruginosa* was the most common pathogen (10/23, 43.4%) followed by *Klebsiella pneumoniae*

Table 3. Outcomes measures based on the timing of tracheostomy

	Tracheostomy day <30 day (n=7)	Tracheostomy day >30 day (n=5)	p-value
Duration of MV (day)	30 (28-60)	60 (60-261)	0.035
Duration of MV after tracheostomy (day)	22 (15-35)	12 (10-215)	0.456
Length of PICU stay (day)	40 (30-76)	69 (68-301)	0.059
Length of hospital stay (day)	51 (43-99)	84 (68-310)	0.089

MV: Mechanical ventilation, PICU: Pediatric intensive care unit

(6/23, 26%), *Stenotrophomonas maltophilia* (3/23, 13%) and *Acinetobacter baumannii* (2/23, 8.6%).

The number of patients who underwent tracheostomy placement <14 days and <30 days were 2 (16.6%) and 7 (58.3%) respectively. Comparing VAP episodes before and after tracheostomy in patients who underwent tracheostomy within 30 days of ventilation with those who underwent tracheostomy >30 days after intubation yielded no differences (p=1.000 and p=1.000, respectively). When evaluating the duration of mechanical ventilation patients in patients who had tracheostomy within 30 days there was a reduction in the median days of mechanical ventilation (30 vs. 60 days, p=0.035). Also between this group's duration of mechanical ventilation after tracheostomy, length of PICU stay and length of hospital stay yielded no differences (Table 3).

The median length of PICU stays after the tracheostomy was 41 days (range, 21-289 days). During the PICU stay, one patient died due to sepsis and multiorgan failure on the postoperative 47th day. Three patients were weaned from mechanical ventilation and successfully decannulated. Four patients (33%) were discharged home on mechanical ventilation and four patients (33%) on a trach collar. Two patients on a trach collar and one patient on mechanical ventilation were decannulated after PICU discharge. Among all patients with CHS undergoing tracheostomy, 6 (50%) of 12 were decannulated after a median time of 179 days (range, 34-463 days). The operative mortality was 8.3% (1/12) and the overall mortality during the first year of follow-up was 8.3% (1/12).

Discussion

In children with CHS, there is no consensus on the indications and optimal timing for tracheostomy. Although there is limited data on tracheostomy practices and outcomes in the pediatric population, recent studies reported that in PICU patients early tracheostomy may have significant benefits without adversly effecting mortality.[6] Early tracheostomy placement may shorten the length of PICU stay and reduce the incidence of VAP.[7] Our study population has a shorter time to tracheostomy and subjects who had tracheostomy within 30 days have a significantly shorter duration of mechanical ventilation. Two patients (patients 6 and 12) who underwent tracheostomy within 30 days, have been decannulated during their stay in PICU. The timing of tracheostomy varies according to the experience and approach of the clinician, and this may cause unnecessary or delayed tracheostomy procedures. In our cohort, there were no life-threatening complications related to tracheostomy.

Recent studies reported that patients with a history of cardiac surgery had a significantly longer duration of PICU admission to tracheostomy placement.[8,9] In a multicenter study that was evaluated to describe the use of tracheostomy, the median time between initiation of mechanical ventilation and tracheostomy placement was 14.4 days with significant variation in the primary diagnosis.[10] In literature, the median time for tracheostomy after CHS varies between 30-58 days.[11,12]

In this study, we identified a low rate of tracheostomy (0.5%) among patients after CHS and this result is comparable with previous studies. Although the incidence of tracheostomy after CHS is low, there is a significant increase over the years with possible attribution to the increased complexity of pediatric cardiac surgical procedures.[1,11] The incidence of tracheostomy after cardiac surgery has increased from 0.11% in 2000 to 0.76 in 2012, according to the STS congenital heart database.[1]

Infants and children undergoing cardiac surgery, especially patients with single ventricle physiology have a high risk for surgical complications and airway issues leading to prolonged mechanical ventilation. In a multicenter study that examined long-term mechanical ventilation and tracheostomy timing in PICU, they reported the majority of participants had underlying cardiac disease (57%) and 67% of those who underwent tracheostomy.[8] Published studies determined the several preoperative risk factors that are related to prolonged mechanical ventilation and the need for tracheostomy after CHS. Genetics and non-cardiac anomalies were present in 40-60% of the patients.[1,13] Additionally, postoperative morbidities including residual lesion, delayed sternal closure, cardiac arrest, sepsis and, airway issues related to the cardiovascular surgery may lead to prolonged mechanical ventilation and difficult weaning.[1,13,14] Hoskote et al.[12] described the postoperative

risk factors for tracheostomy after CHS as myocardial dysfunction (49%), tracheobronchomalacia (49%) and, diaphragmatic paralysis (35%). In our cohort, diaphragmatic paralysis was the most common indication for tracheostomy. Diaphragmatic plication is a successfull treatment option especially in infants with bilateral diaphragmatic paralysis.[15] Tracheobronchomalacia and prolonged mechanical ventilation due to neurological impairment were other indications for tracheostomy. Genetic syndrome or non-cardiac morbidities were present in 41.6% of patients. In 4 of 5 patients with diaphragm paralaysis, plication was not performed due to accompanying tracheostomy indication such as hypotonicity and neurological disorder that required positive pressure ventilatory support.

Although the rate of tracheostomy after CHS is increasing, tracheostomy requirement after CHS is still associated with a poor clinical course, high intra-hospital and extra-hospital mortality. In our cohort, the operative mortality was 8.3% that is lower than previously reported studies.[13,14] In our cohort, 11 patients (92%) RACHS-1 scores were ≥2 and 6 patients (50%) RACHS-1 scores were ≥3. Edwards et al.[16] reported children with more complex lesions and greater RACHS-1 scores had higher mortality rates. They reported the 5-year survival of 68% of children with home mechanical ventilation program after CHS, but the rate was only 12% in children with RACHS-1 of 4 or higher. However, in a study in which they analyzed the results of patients who needed tracheostomy and mechanical ventilation at home after CHS, they reported that there was no statistically significant difference in decannulation between patients with a RACHS-1 score >3 and patients with a RACHS-1 score ≤3.[17] In a large observational study, they demonstrated that subjects with congenital heart disease (CHD) had a 6.67 times higher risk of tracheostomy than those without CHD, and mortality risk was 3.8 times higher following tracheostomy in infants with CHD.[18]

In our study, the median length of PICU stay was 68 days. In our center, children requiring tracheostomy and mechanical ventilation are admitted in 5 beds intermediate unit facility. These patients have a high risk of death due to a tracheostomy-related complication after discharge. Therefore, in our clinic, the follow-up of patients with a high probability of decannulation and who may show reversibility for tracheostomy indication is followed up in this step-down unit. With this approach that patients can be followed for a longer period, it is aimed to prevent complications related to tracheostomy. In a single-center study, 5 out of 11 patients who underwent tracheostomy after CHS and died after initially being discharged home had tracheostomy-related complication.[11]

Study Limitations

There are some limitations of this study, as a result of it has retrospective design and a single-center study. As a result of the small number of patients in the study, a strong statistical evaluation could not be made. The study has a patient selection bias for age, the study cohort did not include the neonatal age group. Social conditions such as cooperation of the family, medical ward conditions may have affected the length of the PICU stay.

Conclusion

The early tracheostomy procedure facilitates the weaning process and shortens the duration of positive pressure ventilation. In this patient population, large scale studies are needed to identify risk factors for unsuccessful weaning and optimum timing for tracheostomy.

Ethics

Ethics Committee Approval: This study was approved by the institutional review boards with the permission for the use of patient data for publication purposes (21-1T/26, date: 07.01.2021 - Ege University Faculty of Medicine Medical Research Ethics Committee).

Informed Consent: Informed consent was received from the families.

Peer-review: Externally and internally peer-reviewed.

Authorship Contributions

Concept: P.Y.Ö., O.N.T., B.K., Design: P.Y.Ö., O.N.T., B.K., Data Collection or Processing: P.Y.Ö., E.E.T., İ.E., Analysis or Interpretation: P.Y.Ö., E.E.T., İ.E., Literature Search and Writing: P.Y.Ö.

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Retrospective Evaluation of Patients Who Underwent Bronchoscopy in a Tertiary Pediatric Intensive Care Unit

Üçüncü Basamak Bir Çocuk Yoğun Bakım Ünitesinde Bronkoskopi Yapılan Hastaların Geriye Dönük Olarak Değerlendirilmesi

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Abstract

Introduction: This study aims to evaluate bronchoscopy's indications and clinical results in patients who underwent bronchoscopy during their stay in the pediatric intensive care unit (PICU).

Methods: This study was carried out retrospectively in PICU between April 2019, and October 2021. The diagnoses of the patients, the reasons for bronchoscopy, where and by whom bronchoscopy was performed, complications related to bronchoscopy, and the contribution of bronchoscopy to diagnosis and treatment were determined.

Results: Thirty-seven patients underwent bronchoscopy. The median age was 20 (7-126) months. The children comprised 17 females (45.9%). We performed bronchoscopy in 17 (45.9%) patients in the PICU and in 20 (54.1%) patients in the operating room. Pediatric intensive care physicians, 13 (35.1%) performed fifteen (40.5%) of bronchoscopy procedures pediatric pulmonologists and 9 (24.3%) pediatric surgeons. Nine patients underwent rigid bronchoscopy, 28 patients underwent flexible bronchoscopy. The median bronchoscopy time was 10 minutes (7.5-15). Bronchomalacia was found in 5 of the patients and tracheomalacia in 2 of them. Three patients (8.1%) had extraluminal airway compression. Bronchoscopy was performed in six patients due to foreign body aspiration. In 13 patients, peak inspiratory pressure and positive end-expiratory pressure of mechanical ventilation were decreased after the bronchoscopy procedure. During the bronchoscopy procedure, desaturation showed in 19 patients, bleeding in 4 patients, bradycardia in 4 patients, and short-term cardiac arrest in 3 patients.

Öz

Giriş: Hava yolu bronkoskopisi, çocuk hasta grubunda çeşitli hava yolu bozukluklarının tedavisinin yanı sıra trakea ve bronşların görüntülenmesine izin veren önemli bir prosedürdür. Bu çalışmanın amacı çocuk yoğun bakım ünitesinde (ÇYBÜ) yatışı sırasında bronkoskopi işlemi yapılan hastalarda bronkoskopi endikasyonlarını ve klinik sonuçlarını değerlendirmektir.

Yöntemler: Bu çalışma geriye dönük olarak 1 Nisan 2019-1 Ekim 2021 tarihleri arasında ÇYBÜ'de gerçekleştirildi. Hastaların tanıları, bronkoskopi yapılma nedenleri, bronkoskopinin nerede ve kim tarafından yapıldığı, bronkoskopi ile ilişkili komplikasyonlar, bronkoskopinin tanı ve tedaviye katkısı belirlendi.

Bulgular: Otuz yedi hastaya bronkoskopi yapıldı. Olguların ortanca yaş değeri 20 (7-126) ay idi. Olguların %45,9'u kız (n=17) idi. Hastaların 17'sine (%45,9) ÇYBÜ'de, 20 (%54,1) hastaya ameliyathanede bronkoskopi işlemi yapıldı. Bronkoskopi işlemlerinin 15'i (%40,5) çocuk yoğun bakım doktoru, 13'ü (%35,1) çocuk göğüs hastalıkları doktoru ve 9'u (%24,3) çocuk cerrahi doktorları tarafından yapıldı. Dokuz hastaya rijit bronkoskopi 28 hastaya fleksibl bronkoskopi yapıldı. Ortalama bronkoskopi süresi 10 dk (7,5-15) idi. Hastaların 5'inde bronkomalazi, 2'sinde trakeomalazi saptandı. Üç hastada (%8,1) ekstraluminal hava yolu kompresyonu mevcuttu. Altı hastaya yabancı cisim aspirasyonu nedeniyle bronkoskopi yapıldı. On üç hastada bronkoskopi işlemi sonrası mekanik ventilasyonun inspiratuvar tepe basıncı ve-veya pozitif end-ekspiratuvar basınç azaltıldı. Bronkoskopi işleminde 19 hastada desaturasyon, 4 hastada kanama, 4 hastada bradikardi, 3 hastada kısa süreli kardiyak arrest

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Three patients with cardiac arrest were patients who underwent rigid bronchoscopy. The median PICU length of stay was 52 days. There were no bronchoscopy-related deaths, but 9 patients died due to their primary disease.

Conclusion: Bronchoscopy is a method that can be performed in PICU, both at the bedside and the operating room, to identify pathological changes in the airway in critical patients and to remove foreign bodies and life-threatening plugs in the airway. Its use for emergency or diagnostic purposes is increasing in PICUs.

Keywords: Bronchoscopy, pediatric intensive care, airway

gelişti. Kardiyak arrest olan 3 hasta da rijit bronkoskopi yapılan hastalardı. Hastaların ortanca yatış gün sayısı 52 (9-119) gün idi. Bronkoskopi ilişkili ölüm olmadı ancak 9 hasta primer hastalıkları nedeniyle kaybedildi.

Sonuç: Bronkoskopi, çocuk yoğun bakım ünitelerinde hem yatak başında hem de ameliyathane şartlarında yapılabilen kritik hastalarda havayolundaki patolojik değişiklikleri tanımlamaya yarayan, yabancı cisim ve hava yolundaki yaşamsal tehdit eden tıkaçların çıkartılması amacıyla kullanılan bir yöntemdir. Çocuk yoğun bakımlarda acil müdahale veya tanı amaçlı kullanımı giderek artmaktadır.

Anahtar Kelimeler: Bronkoskopi, çocuk yoğun bakım, hava yolu

Introduction

Bronchoscopy in children is an important procedure that allows imaging of the trachea and bronchi as well as the treatment of various airway disorders.[1] Flexible bronchoscopy (FB), using modern ultra-thin fiberoptic technology, has revolutionized the study of neonatal and pediatric airway disorders over the past two decades.[2] FB is recognized as an important tool for diagnosing and treating pediatric pulmonary disorders.[3] Although the first published report on the use of FB in children was in 1978, rigid bronchoscopy applied by surgeons remained as the standard practice for many years due to instrument size limitations.[3,4] With the advent of smaller size bronchoscopes, the use of FB in pediatric and neonatal patients has increased.[3] FB is increasingly used in critically ill patients, resulting in a wider range of therapeutic applications.[2] FB has been used in pediatric intensive care units in recent years as a safe and valuable diagnostic tool for anatomical airway problems.[5] Thus, it provides the opportunity to perform bronchoscopy in the intensive care unit for patients receiving extracorporeal treatment.[6]

Therapeutic interventions with FB effectively alleviate airway problems, by highlighting the potential benefits of FB administration in children who cannot be extubated. Although the use of FB has been recommended in preterm infants with recurrent extubation failures, reports of bronchoscopic findings in children who cannot be extubated are rare.[5]

Foreign body aspiration (FBA) is one of the usage areas of bronchoscopy in patients hospitalized in the pediatric intensive care unit. The current preferred procedure for the removal of the aspirated foreign body is rigid bronchoscopy, with reported complications.[7] However, in adults and children, FB may also be used for the removal of inhaled foreign body.[7]

The aim of this study is to evaluate the indications and techniques of bronchoscopy in patients hospitalized in our pediatric intensive care unit, and its contribution to the diagnosis and solution of patients' problems.

Materials and Methods

This study was carried out retrospectively in our pediatric intensive care unit (PICU) between April 1, 2019 and October 1, 2021. There are 20 tertiary care beds in our unit. The population of children in the city where our hospital is located is approximately 1.3 million. There are approximately 600-700 hospitalizations per year. Inclusion criteria were determined as being patients between 1 month and 18 years of age, who underwent bronchoscopy while in or during hospitalization in the pediatric intensive care unit. Written permission was obtained from the Clinical Research Ethics Committee of Ankara University Faculty of Medicine for the study (decision no: 2021/406).

Demographic information and information about the disease course of the patients hospitalized in the PICU unit and undergoing bronchoscopy were recorded as given below.

Patients' age, gender, primary diagnosis, status of mechanical ventilator connection and MV mode if connected, tracheostomy status in patients receiving invasive MV support, whether the intubation tube was cuffed, and sedation treatments during bronchoscopy were retrospectively recorded from patient files. Regarding bronchoscopy, indication for bronchoscopy, department performing bronchoscopy, duration of bronchoscopy, blood gases taken before and after bronchoscopy and mechanical ventilator settings, bronchoscopy type, bronchoscopy complications, bronchoalveolar lavage results obtained during bronchoscopy were recorded.

A portable fiber optic bronchoscope (Karl Storz Endoscopy, Germany) was used in the PICU.

Fiberoptic bronchoscope (Karl Storz Endoscopy, Germany) was used in pediatric chest diseases.

Pediatric rigid bronchoscope (Karl Storz Endoscopy, Tuttlingen, Germany) was used in pediatric surgery and the patients were ventilated with 100% oxygen through the bronchoscope during the procedure.

Heart rate and rhythm, blood pressure and peripheral oxygen saturation were routinely monitored. Intravenous sedation and analgesia were administered for all bronchoscopic examinations and procedures. The flexible bronchoscope was inserted into the ventilator breathing circuit by using a "Y" shaped tube and the inspired oxygen concentration was increased to 100%, but no other ventilator settings were changed.

Statistical Analysis

Statistical analyses were performed by entering the data into SPSS 26.0 (Statistical Package for Social Sciences for MacOS, Inc., USA) software. The expression n (%) was used for categorical variables. For continuous variables, mean ± standard deviation values were used in case of conformity with normal distribution, and median (minimum-maximum limit) values were used in the absence of conformity with normal distribution. The mean and standard deviations were determined by using descriptive analyses of the demographic and clinical data of the cases.

In the presence of more than two categorical variables, the Kruskal-Wallis test was used when the parametric tests did not show homogeneity. Statistical significance level was accepted as $p<0.05$ in all tests.

The chi-square test was employed to compare non-numerical parameters between categorical groups. The Fisher's Exact test was used when >20% of the expected value was less than 5. The Wilcoxon test was used for dependent variables.

Results

Thirty-seven patients underwent bronchoscopy. The median age of the cases was 20 (IQR 7-126) months (minimum 2 months, maximum 192 months). Twenty-three patients (62.2%) were younger than 3 years old and 17 patients (45.9%) were under one year old. 45.9% of the cases were girl (n=17) and 54.1% were boy (n=20). Bronchoscopy was performed for 17 (45.9%) patients in the pediatric intensive care unit, and for 20 (54.1%) patients in the operating room. Fifteen (40.5%) of the bronchoscopy procedures were performed by pediatric intensive care physicians, 13 (35.1%) by pediatric chest diseases physicians, and 9 (24.3%) by pediatric surgeons. Rigid bronchoscopy was performed in 9 patients and FB was performed in 28 patients (Table 1).

Thirty-four patients were followed up as intubated on a mechanical ventilator before bronchoscopy. Cuffed tube was used in 28 of intubated patients and uncuffed tube was used in 6 of them. Tracheostomy cannula was present in 6 patients. The number of intubated days in these patients was 34 (8.75-68.5) (minimum 1- maximum 201). All patients were given sedative and or analgesic treatment during the bronchoscopy procedure. Rocuronium was given to 8 patients, ketamine to 23 patients, fentanyl to 10 patients, and midazolam to 25 patients.

Twenty-five patients were monitored in pressure-SIMV mode and 9 patients were monitored in volume-SIMV mode.

Bronchoscopy was performed in 6 patients due to FBA. Peanuts in 2 patients, beans in 1 patient, and seeds in 1 patient were removed with bronchoscope. No foreign body was observed in two patients. Three of six patients were not intubated before and after bronchoscopy.

Cardiac arrest lasting 30 seconds to 1 minute was observed during the procedure in two of 6 patients. Two of these patients were admitted to the PICU as intubated and both were extubated on the first day of hospitalization.

Bronchoscopy was performed at night in 6 patients, outside of working hours. In these patients, the procedure was performed by pediatric surgeon in 2 patients and by pediatric intensive care physician in 3 patients.

Bronchoscopy was performed in 5 patients while being followed in ECMO. Three of these procedures were performed by a pediatric intensive care physician, one by a pediatric chest diseases physician, and one by a pediatric surgeon.

Table 1. Clinical and demographic characteristics of the patients

Demographic data	
Sex: Boy, n (%), girl n (%)	20 (54.1), 17 (45.9)
Age (month), median (IQR 25-75)	20 (7-126)
Time of bronchoscopy	
Daytime	31 (83.7)
Night	6 (16.3)
Indication	
Diagnostic	23 (62.1)
Therapeutic	14 (38.9)
Department performing bronchoscopy n (%)	
Pediatric intensive care	15 (40.3)
Pediatric chest diseases	13 (35.1)
Pediatric surgery	9 (24.4)
Place of bronchoscopy	
Pediatric intensive care unit	17 (45.9)
Operating room	20 (54.1)
Bronchoscopy type: n (%)	
Rigid	9 (24.3)
Flexible	28 (75.7)
Complication of bronchoscopy	
Desaturation	20 (54.1)
Bleeding	4 (10.8)
Bradycardia	4 (10.8)
Cardiac arrest	3 (8.1)

IQR: Interquartile range

Table 2. Comparison of blood gas parameters and mechanical ventilator settings before and after bronchoscopy

	Before bronchoscopy	After bronchoscopy	p
pH	7.40 (7.32-7.42)	7.39 (7.34-7.44)	0.1
$PaCO_2$	46 (37-55)	39.7 (34-49.8)	0.062
HCO_3	24.5 (18.8-28.8)	23 (19.7-26.4)	0.568
Lactate	1.4 (1.1-2.5)	1.6 (1.1-2.45)	0.156
Respiratory rate	30 (20-30.5)	26 (20-31)	0.752
PIP	24 (22-27.5)	22 (22-28)	0.943
PEEP	6 (6-8)	6 (6-8)	0.366

PIP: Peak inspiratory pressure, PEEP: Positive end-expiratory pressure, $PaCO_2$: Partial pressure of carbon dioxide, HCO_3: Bicarbonate

Table 3. Comparison of complications according to bronchoscopy type

	Rigid (n=9)	Flexible (n=28)	
Desaturation	6	14	0.659
Bleeding	2	2	0.291*
Bradycardia	3	1	0.022
Cardiac arrest	3	0	**0.015***
Pediatric intensive care unit	2	15	0.054
Operating room	8	12	

*Fisher's Exact test

In 23 patients, the plug was removed during the bronchoscopy procedure. Atelectasis appearance regressed in 8 patients after bronchoscopy. Peak inspiratory pressure (PIP) of mechanical ventilation and/or positive end-expiratory pressure (PEEP) were reduced in 13 patients. When the patients' blood gas parameters and mechanical ventilator settings such as respiratory rate, PIP and PEEP were compared before and after bronchoscopy, no significant difference was found (Table 2).

In the bronchoalveolar lavage samples taken, *Streptococcus* mitis grew in 1 patient, *Klebsiella pneumoniae* in 3 patients, *Klebsiella oxytoca* in 1 patient, *Pseudomonas aeruginosa* in 1 patient, coagulase negative *Staphylococci* in 1 patient, *Stenotrophomonas maltophilia* in 1 patient, and *Candida albicans* in 1 patient.

The mean duration of bronchoscopy was 10 minutes (7.5-15). Bronchoscopy was beneficial in 31 patients. Desaturation was observed in 20 patients, bleeding in 4 patients, bradycardia in 4 patients, and cardiac arrest in 3 patients during bronchoscopy. All 3 patients developing cardiac arrest were those who underwent rigid bronchoscopy by the pediatric surgeon.

It was determined that there was a significant difference in the frequency of cardiac arrest between patients who underwent rigid bronchoscopy and those who underwent FB (p=0.015) (Table 3).

Bedside bronchoscopy was performed in 17 patients in the pediatric intensive care unit. Twelve of these patients were girls and the median age of the patients was 32 months. Fifteen of the bronchoscopy procedures were performed during the daytime and 2 of them were performed at night. It was performed for diagnostic purposes in 13 patients and for therapeutic purposes in 4 patients. All patients were performed with FB. Significant atelectasis appearance in 5 patients regressed after bronchoscopy procedure. As a complication of bronchoscopy, desaturation was observed in 9 patients, bleeding in 2 patients, and bradycardia in 1 patient. Bronchoscopy was performed in 14 patients by a pediatric intensive care physician, and in 3 patients by a pediatric chest diseases physician (Table 4).

One patient was found to have a kinked intubation tube during the bronchoscopy procedure. The bronchoscopy procedure was terminated and the patient's intubation tube was changed. Bronchomalacia was found in 5 patients and tracheomalacia in 2 patients. All of these patients were performed bronchoscopy by pediatric chest diseases physician and the median number of intubated days of these patients was 50 (26-11) (minimum 25-maximum 192 days). Cardiac disease was present in 6 of 7 patients with malaise. One patient was diagnosed with lissencephaly. Tracheostomy cannula was inserted in 3 of 7 patients. Two of the 7 patients died (one had a tracheostomy).

One of our patients who underwent fiberoptic bronchoscopy had granulation tissue that almost completely covered the trachea (Figure 1). This patient was a one-year-old boy patient, who was admitted to the PICU for postoperative follow-up after the closure of the ventricular septal defect and patent ductus

Table 4. Clinical and demographic characteristics of patients who underwent bedside bronchoscopy	
Demographic data	
Sex: Boy, n (%), girl n (%)	5 (29.5%) 12 (70.5%)
Age (month), median (IQR 25-75)	32 (7-156)
Number of days intubated	45 (20-118)
Number of hospitalization days	54 (28.5-179)
Time of bronchoscopy	
Daytime	15
Night	2
Indication	
Diagnostic	13
Therapeutic	4
Department performing bronchoscopy n (%)	
Pediatric intensive care	14 (82.3%)
Pediatric chest diseases	3 (17.7%)
Pediatric surgery	
Bronchoscopy type: n (%)	
Rigid	2 (11.8%)
Flexible	15 (88.2%)
Duration of bronchoscopy (min)	**10 (6-19)**
Complication of bronchoscopy	
Desaturation	9 (52.9%)
Bleeding	2 (11.8%)
Bradycardia	1 (5.9%)
Cardiac arrest	0
IQR: Interquartile range	

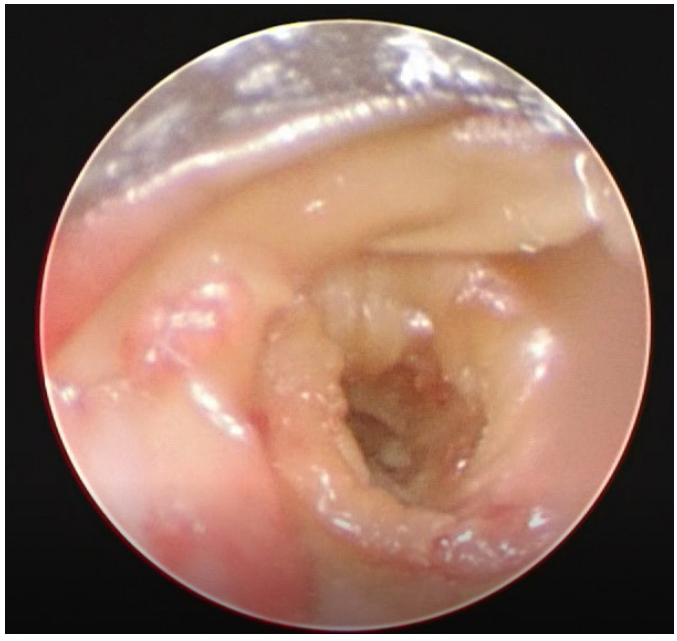

Figure 1. Pseudomembrane causing tracheal stenosis in the middle and lower part of the trachea

arteriosus. After being admitted to the PICU, the patient had poor ventilation despite being on a mechanical ventilator, and although pressure support was increased, his lungs were not well ventilated. It was observed that the intubation tube did not progress during re-intubation, and tracheal granulation tissue was observed in the rigid bronchoscopy. A chest tube was inserted because he had pneumothorax on the third day of his hospitalization. On the 4th day of his hospitalization, the patient who developed respiratory arrest and then cardiac arrest was connected to Veno-Arterial Extracorporeal Membrane Oxygenation (VA-ECMO) by performing CPR for 8 minutes. He was extubated on the 14th day of ECMO administration and decannulated on the 16th day of ECMO administration. After ECMO decannulation, the patient was given non-invasive mechanical ventilation for one month.

Tracheal dilatation was performed by the pediatric surgeon because of the increase in tracheal stenosis every 2 weeks during the patient's hospitalization. He was re-intubated on the 49th day of his hospitalization due to cardiac arrest and CPR was performed for 15 minutes. Tracheostomy was opened on the 60th day of hospitalization and then he was connected to a home mechanical ventilator. On the 95th day of his hospitalization, the patient with normal vital signs was transferred to the pediatric surgery unit on the 95th day of his admission to the PICU.

In our study, 3 patients (8.1%) had extraluminal airway compression. Two of these patients were postoperative cardiac surgery patients. The other patient was a patient with a hemangioma that almost completely occupied the trachea and propranolol was started by oncology (Figure 2).

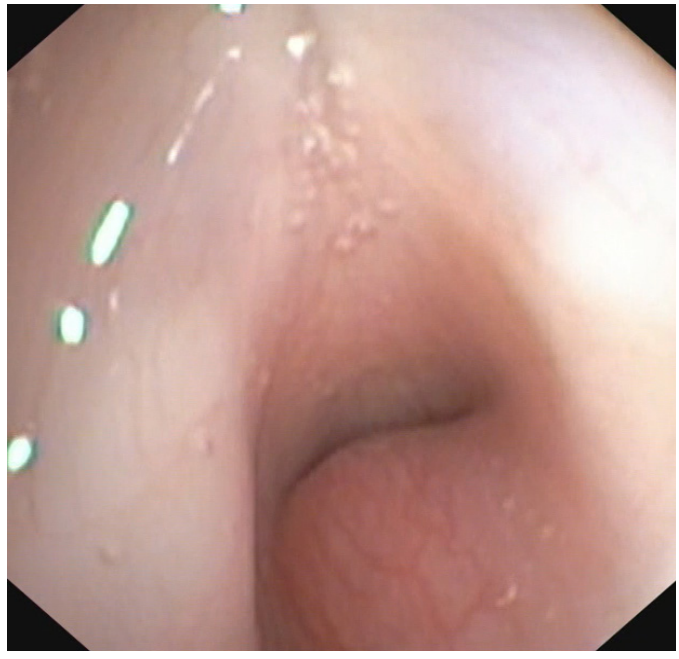

Figure 2. The appearance of a smooth and soft subglottic hemangioma covered with normal mucosa, causing subglottic stenosis at the stage 3 level

Considering the number of intubated days of the patients according to the departments performing the bronchoscopy procedure, it was found that there was no significant difference.

The median number of hospitalization days of the patients was 52 (9-119) (minimum: 1, maximum: 210). Nine of our patients who underwent bronchoscopy died due to their primary disease.

Discussion

Traditional FB is usually performed by pediatric chest diseases physicians under elective conditions in operating rooms and intensive care units.[2] Under these conditions, FB procedure is generally a low-risk procedure with high efficiency and low complications (<1-2%).[2] In addition, FB is increasingly used by pediatric intensive care physicians because of its diagnostic and therapeutic value and high safety profile.[8] In recent years, studies emphasizing the importance of FB in pediatric intensive care have been published.[9] The first study on pediatric intensive care inpatients only was conducted between 1982 and 1986.[10] In this study, 87 patients were evaluated with FB and reported minimal morbidity and no mortality.[10] This study demonstrated the benefit of the bedside technique in critically ill pediatric patients.[10]

The most common complications during bronchoscopy are related to oxygenation and ventilation.[1,11] Patients may become hypoxic or hypercapnic, which can cause bradycardia and possibly cardiac arrest.[1] Barotrauma (e.g., pneumothorax, pneumomediastinum) may result from inadequate air outflow from oxygen insufflation during bronchoscopy.[1]

Fortunately, the mortality rate for both flexible and rigid bronchoscopy in the pediatric population has been reported to be quite low.[1] In addition, complications such as perforation, bleeding, lung abscess, and epistaxis may also be observed.[11]

In our study, despite the difference in patient populations, a higher rate of critical illness compared to previous studies was proven by our mechanical ventilation (91.9%) and ECMO (13.5%) rates. Not surprisingly, this was associated with higher complication rates. Desaturation was observed in 20 patients, bleeding in 4 patients, bradycardia in 4 patients, and cardiac arrest in 3 patients during bronchoscopy. Three patients with cardiac arrest were those who were performed rigid bronchoscopy by the pediatric surgeon. Two of these patients were followed up with a diagnosis of FBA and one with a diagnosis of Hemophagocytic lymphohistiocytosis. In these three patients, the heart rate was observed as >60/min after CPR. However, most physiological impairments were short-lived, responsive to standard therapy, and not associated with long-term sequelae.

The diversity of inpatients in the PICU has changed significantly in recent years.[9] As in our study group, long-term mechanical ventilation may be required in patients after cardiac surgery and in patients receiving extracorporeal therapy.[6] Long-term mechanical ventilation is associated with high mortality and morbidity, and extubation should be planned as early as possible to minimize these risks.[12] However, extubation failure is an important problem in these patients. Visualization of the upper and lower airways with FB, assessment of BAL, and removal of mucous plugs provide accurate diagnosis and facilitate appropriate management of patients.[8,12]

In our study, 14 (37.8%) patients were hospitalized for cardiac reasons. In a study, it was reported that the frequency of airway abnormalities was 87% in cardiac patients undergoing bronchoscopy.[9] In our study, this rate was 71% (10 patients). FB may provide therapeutic benefit in patients with mucus plug alone as the cause of atelectasis.[6] It has been reported that the incidence of atelectasis is high in mechanically ventilated children with severe pneumonia, and the main causes may be mucus and sputum plugs.[13] In cases where medical treatments fail, FB should be performed to identify the cause of atelectasis and to remove mucus plugs, and to prevent prolonged atelectasis that can cause irreversible lung damage.[12,14] In this study, mucus plug was removed in 23 patients (62.1%). A decrease in atelectatic area was detected in 13 patients (35.1%) after bronchoscopy. In 13 patients (35.1%), PIP or PEEP was reduced in mechanical ventilation after bronchoscopy.

Early and accurate diagnosis is essential to ensure optimal treatment given in children with recurrent pneumonia and to minimize the risk of progressive or irreversible lung injury.[15] Congenital airway anomalies such as tracheomalacia, tracheobronchomalacia, tracheal bronchus, tracheoesophageal fistula, tracheal stenosis, and unilateral lung hypoplasia, FBAs, hemosiderosis, and middle lobe syndrome are among the causes of recurrent pneumonia.[15]

FB is considered the gold standard for the diagnosis of airway malaise.[12] Airway malaise is one of the causes of airway obstructions and can cause a wide variety of symptoms, from persistent cough and lower respiratory tract infections to respiratory failure, depending on the length, location and severity of the malacic segment.[12] Airway malaise may be primary (congenital) or secondary to external compression to the airways, positive pressure ventilation, or respiratory tract infections, resulting in high rates of malaise in the newborn and PICU.[12] Airway malaise can cause unsuccessful extubation attempts, decreased mucociliary clearance, and secondary infections in intensive care units.[12] In our study, bronchomalacia was found in 5 patients and tracheomalacia

in 2 patients. Six of these patients were cardiac patients. All of these patients had prolonged intubation times.

One of the indications for bronchoscopy was FBA. FBA is one of the most common causes of unintentional injuries and carries a significant morbidity and mortality burden, especially in the first 3 years of life.[16] Although modern bronchoscopy techniques have resulted in an important reduction in mortality, FBAs are still responsible for more than 100 deaths per year in the United States and can lead to serious complications.[16] Rigid bronchoscopy is indicated in patients with a history of positive FBA, such as asphyxia, or in those with unilateral decreased breath sounds, obstructive emphysema, and atelectasis.[17] However, in some children, the diagnosis may not be so easily understood and for these patients, FB is the procedure that is preferred.[15] Up to 50% of patients with FBA may not have a typical history of aspiration.[15] In our series, foreign body was not observed in 2 of 6 (16.2%) patients with suspected FBA. Short-term cardiac arrest was observed in two of 6 patients. Both patients were extubated on the first day of hospitalization in the pediatric intensive care unit.

The occurrence of atelectasis is common in patients on ECMO due to heart failure or respiratory failure, and there are studies showing that atelectasis is treated with FB to prevent barotrauma due to high PEEP in these patients.[6]

In our study, bronchoscopy was performed on 5 patients followed up on ECMO by a pediatric intensive care physician (3 patients), a pediatric chest diseases physician (1 patient), and a pediatric surgeon (1 patient). Atelectasis was observed in 4 patients after bronchoscopy procedure. In these patients, systemic anticoagulation was interrupted for 1 hour before the procedure and no active major bleeding was observed in any of the patients.

Study Limitations

The limitations of our study are its retrospective nature and the small number of cases.

Conclusion

Bronchoscopy is a safe procedure that provides direct imaging of the airways in patients who are followed up on mechanical ventilators for a long time in pediatric intensive care units, thus enabling the recognition of airway anomalies, and also providing appropriate treatment options by aspirating mucous plugs and allowing BAL sample to be taken. In addition, it can prevent unnecessary intubation tube changes by allowing us to see directly whether the intubation tube is clogged or mucus plugs. We think that it may be a routine practice for intubated patients in pediatric intensive care units in the coming years.

Ethics

Ethics Committee Approval: Written permission was obtained from the Clinical Research Ethics Committee of Ankara University Faculty of Medicine for the study (decision no: 2021/406).

Informed Consent: Retrospective study.

Peer-review: Externally and internally peer-reviewed.

Authorship Contributions

Concept: T.K., E.G., H.U., F.K., E.B., A.G., B.B., H.Ö., F.A., G.Ç., G.Ö., F.Z., S.S., Design: E.G., H.U., F.K., E.B., A.G., B.B., H.Ö., F.A., G.Ç., G.Ö., F.Z., S.S., Data Collection or Processing: E.G., H.U., F.K., E.B., A.G., B.B., H.Ö., F.A., G.Ç., G.Ö., F.Z., S.S., Analysis or Interpretation: T.K., E.E., E.G., H.U., F.K., E.B., A.G., B.B., H.Ö., F.A., G.Ç., G.Ö., F.Z., S.S., Literature Search: T.K., E.G., H.U., F.K., E.B., A.G., B.B., H.Ö., F.A., G.Ç., G.Ö., F.Z., S.S., Writing: E.G., H.U., F.K., E.B., A.G., B.B., H.Ö., F.A., G.Ç., G.Ö., F.Z., S.S, E.E., N.Ç., T.K.

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Ultrasound Guided Pleural Drainage with the Seldinger Technique Using a Central Venous Catheter

Santral Venöz Kateter Kullanılarak Seldinger Tekniği ile Ultrason Eşliğinde Plevral Drenaj

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Abstract

Introduction: Pigtail catheters are currently recommended for draining pleural effusions. However, specific catheters manufactured for this purpose may not be feasible in resource-limited settings. This study evaluated the safety and effectiveness of a central venous catheter for treating uncomplicated pleural effusions with point-of-care ultrasound in children.

Methods: The study was a single-center retrospective review of the clinical records of pediatric patients with symptomatic uncomplicated pleural effusion who had underwent bed-side ultrasound guided pleural drainage with a central venous catheter, between 2014 and 2019.

Results: We determined 93 patients who had undergone 98 central venous catheter insertions during the study period. The patient's median age was 4.5 years (range, 7 days to 15 years) and median weight was 19 kg (range, 3 to 60 kg). The most underlying cause was cardiovascular surgery. The technical success rate was 95.9% and only 2 (2.2%) complications were observed.

Conclusion: Point of care ultrasound guided pleural drainage with a central venous catheter is safe and effective in critically ill children with uncomplicated pleural effusion.

Keywords: Pleural effusion, ultrasound, Seldinger, central venous catheter

Öz

Giriş: Plevral efüzyonların drenajında pigtail kateterlerin kullanılması önerilmektedir. Ancak, bu amaç için üretilmiş kateterler, kaynakların kısıtlı olduğu yerlerde temin edilemeyebilir. Bu çalışmada, hasta başı ultrason rehberliğinde basit plevral efüzyonların tedavisinde santral venöz kateter kullanımının güvenirliliği ve etkinliği değerlendirilmiştir.

Yöntemler: Çalışma, 2014 ve 2019 yılları arasında santral venöz kateter ile yatak başında ultrason rehberliğinde plevral drenaj uygulanan bulguya yönelik basit plevral efüzyonlu çocuk hastaların klinik kayıtlarının tek merkezli geriye dönük bir incelemesidir.

Bulgular: Çalışma süresi boyunca plevral drenaj amacı ile santral venöz kateter takılan 93 hasta (98 girişim) belirledik. Hastaların ortanca yaşı 4,5 yıl (7 gün ile 15 yıl arası) ve ortanca ağırlığı 19 kg (3 ile 60 kg arası) idi. En sık altta yatan neden kalp damar cerrahisi sonrası izlemdi. Teknik başarı oranı %95,9 olup sadece iki işlemde (%2,2) komplikasyon gözlendi.

Sonuç: Santral venöz kateter ile yatak başı ultrason rehberliğinde plevral drenaj, komplike olmayan plevral efüzyonlu kritik hasta çocuklarda güvenli ve etkilidir.

Anahtar Kelimeler: Plevral efüzyon, ultrason, Seldinger, santral venöz kateter

Introduction

Pleural effusion (PE) is a significant morbidity and is frequently caused by infections, cardiac failure, volume overload, heart-liver surgery, and trauma in pediatric critically ill patients.[1] Indeed, PE impinge on lung volumes, impact gas exchange resulting in hypoventilation and hypoxemia.[2] Drainage by varying techniques improve oxygenation, lung mechanics and compliance by enhancing the ventilation: Perfusion ratio.[3]

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Rapid diagnosis of the effusion and determining the nature are crucial for the best therapeutic choice. Point of care ultrasound (POCUS) is a non-invasive bedside tool for diagnosis and procedural guidance, by the clinician himself, at the point of care, in real time allowing for direct correlation with signs and symptoms. Many studies have shown that lung ultrasound has better diagnostic accuracy over the chest X-ray for the diagnosis of PEs.[4,5] Furthermore, the amount and nature of the PE can be established by lung ultrasound.[6] Although pleural fluid volume can be estimated using sonographic measurements, these formulas are uncommonly used in clinical practice. A qualitative assessment is adequate for most clinical decision making. According to sonographic view, PEs are categorized as simple or complex. Simple effusions are anechoic and typically transudative. Complex PEs are heterogeneously echogenic, with or without septations and often exudative.[7]

Although large bore chest tubes provide effective treatment, it may cause pain and incision infection.[8] Pleural drainage with specific pigtail catheters is much safer than repeated thoracentesis and large bore chest tubes inserted by blunt dissection. Pigtail catheters have over 90% success rate and less than 5% complication rate in pleural drainage.[9-12] Also, many studies have shown that the use of POCUS during pigtail insertion increases the success rate and decreases the complication rate.[11,12]

Despite the success of pigtail catheters, we investigated the treatment of simple PE by closed thoracic drainage using a central venous catheter (CVC) instead of traditional large bore chest tubes. The aim of this study was to evaluate the efficacy and safety of using a CVC in the treatment of simple PE in resource limited settings.

Materials and Methods

Patients

We reviewed all CVC insertions performed for pleural drainage between 2014 and 2019 in a pediatric intensive care unit of a tertiary medical center. The indications for pleural drainage with a CVC were inability to wean from mechanical ventilation, high ventilator settings, and non-purulent effusions over 20 mm on ultrasound. A plateau pressure over 28 cm H_2O and a maximum inspiratory pressure over 30 cm H_2O were considered as "high ventilator settings". Patients with purulent effusions on ultrasound were excluded. A total of 93 patients who underwent pleural drainage with a CVC using POCUS guided Seldinger technique included in this study. This study was conducted in accordance with the amended Declaration of Helsinki and approved by the Local Ethical Committee of Dokuz Eylül University (4721-GOA/2019/11-37).

Procedure

All patients were sedated with midazolam and fentanyl before the procedure, and local anesthesia was provided with lidocaine. The catheter size was determined according to the patient size. Braun CertoFix, double lumen 5 Fr-13 cm (patients under 30 kg) and double lumen 7 Fr-20 cm (patients over 30 kg) CVCs inserted under full aseptic conditions. In the supine position with ultrasound guidance, the needle was inserted into the pleural space from 4th or 5th intercostal space midaxillary line. After aspiration of the pleural fluid, soft guidewire was inserted into the needle about 10 cm in length. While holding the guidewire in, the needle was removed and a stiff dilatator used to enlarge the entry route. After removal of the dilatator, CVC was put into the pleural space over the guidewire. The guidewire was removed and CVC sutured on the chest wall and connected to the standard thoracic drainage systems. The position of the catheter was confirmed with thoracic ultrasound and chest X-ray (Figure 1).

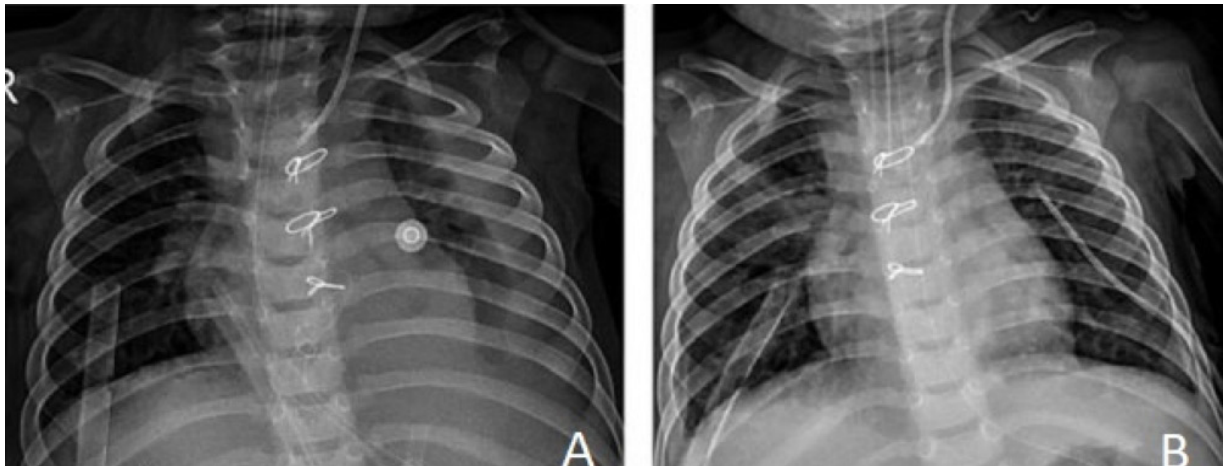

Figure 1. A. Left pleural effusion on chest X-ray, **B.** Successful drainage of the pleural effusion with a central venous catheter in place on chest X-ray

Table 1. Characteristics of the patients underwent pleural drainage with a central venous catheter	
Characteristics	**n**
Gender, n (%)	
Male	52 (55.9)
Female	41 (44.1)
Age-years (median-IQR)	4.5 (1-15)
Weight-kg (median-IQR)	19 (3-60)
Pediatric index of mortality - 3 score (median-IQR)	3.78 (1.88-12.14)
Pediatric risk of mortality - 4 score (median-IQR)	3.66 (1.90-11.69)
Underlying disease	
Post-surgery	
- Cardiovascular, n (%)	35 (37.6)
- Liver transplantation, n (%)	8 (8.6)
Cardiac failure, n (%)	19 (20.4)
Volume overload, n (%)	14 (15.1)
Acute respiratory distress syndrome, n (%)	10 (10.7)
Other, n (%)	7 (7.5)
Major indication for pleural drainage	
High ventilator settings	13 (14.0)
Inability to wean from mechanical ventilation	36 (38.7)
Effusion over 20 mm	33 (35.7)
Persistent effusion	11 (11.8)
On mechanical ventilation	
Yes	70 (75.3)
No	23 (24.7)
IQR: Interquartile range	

Adequate drainage and resolution of the effusion (confirmed by daily bedside thoracic ultrasound and chest X-ray) were defined as successful intervention and persistence or increasing PE or requiring another intervention defined as unsuccessful intervention. Pneumothorax, hemothorax, and pulmonary edema were accepted as complications.

Statistical Analysis

Statistical analysis was performed using SPSS software version 22.0 (SPSS, Chicago, IL) for Windows. The demographic characteristics, primary diagnosis, success and complication rates of the patients were summarized using standard descriptive statistics. The amount of effusion and drainage time were defined as mean (± standard deviation) and categorical data was defined as frequency (percentage).

Results

During the study period, 93 patients had 98 insertions. While the most common underlying disease was post-operative follow-up, the most common indication for pleural drainage was inability to wean from mechanical ventilation (Table 1). All pleural fluid analysis showed transudative properties on the biochemical analysis. Of them, 98 CVC insertions, 4 (4.4%) procedures were unsuccessful (two patients had pneumothorax after the procedure and two patients had insufficient drainage) and needed large bore-chest tube insertion (Table 2). Among the insertions, 12 (12.2%) had inadequate drainage from the main lumen and required the use of the second line, however 2 of them could not achieve adequate drainage despite using both lumens. The

Table 2. Clinical details of the pleural effusions treated with a central venous catheter	
Characteristics	**n**
Transude, n (%)	
- Yes	98 (100)
Drainage time (days) (mean ± SD)	8.1±5.1
Effusion length (mm) (mean ± SD)	25±8.2
Mean intervention time (min) (mean ± SD)	4.4±1.5
Insertion site, n (%)	
Right	57 (58.2)
Left	35 (35.7)
Bilateral	6 (6.4)
Success	
Yes, n (%)	94 (95.9)
Increased need for sedation and analgesia	
Yes, n (%)	5 (5.1)
SD: Standard deviation	

mean intervention time was 4.4±1.5 min, 5 of them (5.1%) required sedation and analgesia dose increase, and wound infection was not observed in any of the patients.

Discussion

Large bore chest tubes have traditionally been recommended in almost all cases to treat various pleural diseases requiring large skin incision, blunt dissection and insertion. Small bore catheter insertion using the Seldinger technique is a much easier and less invasive method than traditional large bore tubes.[12,13] Consequently, specially developed chest drains "pigtails" are recommended due to high complication rates of large bore chest tubes.[14]

In 1986, Fuhrman et al.[15] introduced pigtail catheter insertion with the Seldinger technique for pleural space diseases. And in 1989, Lawless et al.[16] assessed the method in a prospective interventional study of 16 pediatric patients and demonstrated successful drainage of air and fluid without any complication. Subsequently, Roberts et al.[17] inserted pigtail catheters in pediatric patients who have chylothorax, serious fluid, hemothorax with a success rate of 96%, 72% and 81% respectively. Over the past two decades, pleural drainage with small catheters shown that they have high success rates with lower complication rates on different studies.[12,18]

As POCUS becomes widespread in pediatric intensive care units, thus physicians had the chance to provide interventions under ultrasound guidance to reduce complications and increase success rate.[19] Sonographic guidance enables visualization of the needle insertion to the pleural space and is associated with a reduced risk of complications such as pneumothorax. An adult study demonstrated that ultrasound guided thoracentesis reduced pneumothorax incidence from 8.89% to 0.97% in 445 procedures.[20]

All data propose specially designed pigtail catheters and there are only two studies had evaluated CVC for pleural drainage. First, Singh et al.[21] used 15 CVC insertions to drain PEs in adult patients and they have 100% success rate without any complications. Shwaihet and Ingram[22] evaluated double lumen CVCs for the drainage of uncomplicated PEs in pediatric post cardiac patients. They had 47 patients included in the study, one case (2.1%) had pneumothorax on insertion, three cases (6.38%) had a line dislodgement and one case (2.1%) had line blockage during the follow-up period. In our study, we used double lumen catheters, which allowed us to use another line if the main lumen was blocked.

Since there are publications showing the success of a CVC in the treatment of pneumothorax,[23,24] we started using a CVC for pleural drainage, considering that it may be less invasive compared to large bore chest tubes and can provide adequate pleural drainage especially in transudative fluids. We knew we had to use specially manufactured pigtail catheters; however, limited availability of pigtail catheters led us to perform pleural drainage using CVC. Also, CVCs have small caliber and clinicians may be concerned about obstruction. Although considerably thinner than traditional chest tubes, CVCs are made from polyurethane with excellent biocompatibility. In our study, we had a high success rate and no obstruction were observed. If a catheter occlusion does occur, it can be easily removed by flushing with serum physiologic.

Our data revealed many advantages of using ultrasound guided pleural drainage with a CVC. We had 96.4% success rate on various etiologies with transudative PE's and only two patients had pneumothorax during insertion and two needed another intervention due to inadequate drainage that suggested that this method is effective and safe in draining PE. Especially, ultrasound guidance and inserting double lumen catheters were the major key points of our study. We had a suspicion but higher awareness of our team and nurses about this procedure prevent us from mis-using lines and any medication was administered during follow-up. Finally, this procedure is considered as safe and effective like pigtail catheters under ultrasound guidance.

Study Limitations

There are some limitations of our study, first the study was retrospective and had a relatively small population. Also, we could not have the opportunity to compare CVCs with other techniques. Therefore, future comparative prospective studies with larger samples needed to compare CVCs against other techniques in pleural drainage. These studies would help in more reliable and powerful evidence.

Conclusion

Ultrasound-guided pleural drainage with the Seldinger technique using a CVC is a safe and effective method. There were less complications and high success rate. In the lack of pigtail catheters, CVCs should be used for treating simple PEs in PICU settings with a high success and low complication rates under ultrasound guidance.

Ethics

Ethics Committee Approval: This study was conducted in accordance with the amended Declaration of Helsinki and approved by the Local Ethical Committee (4721-GOA/2019/11-37 - Dokuz Eylül University Non-Invasive Research Ethics Committee).

Informed Consent: Informed consent was not obtained from the patients given the retrospective study design.

Peer-review: Externally and internally peer-reviewed.

Authorship Contributions

Concept: G.A., G.E., A.K., M.D., T.F.K., Design: G.A., G.E., A.K., T.F.K., Data Collection or Processing: G.A., G.E., A.K., Analysis and Interpretation: G.A., M.D., T.F.K., Literature Search: G.A., G.E., A.K., Writing: G.A., G.E., A.K., M.D., T.F.K.

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Investigation of the Role of Nesfatin-1 Levels in the Evaluation of Nutrition Monitoring in the PICU

Nesfatin-1 Düzeylerinin ÇYBÜ'de Beslenme Monitorizasyonu Değerlendirilmesindeki Rolünün Araştırılması

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Abstract

Introduction: Although nutrition is very effective on mortality in critically ill children, patients cannot be fed adequately. There is no suitable biomarker for enteral nutrition monitoring and management. The aim of this study; To investigate the usability of nefsatin-1 for nutritional monitoring and management in critically ill children.

Methods: In the January-September 2019 period, 35 critically ill children who were hospitalized in the tertiary pediatric intensive care unit without any signs of inflammation were included in the study. Nesfatin-1, vitamin D level, prealbumin, albumin was evaluated for the study.

Results: Thirty-five patients who were admitted to the pediatric intensive care unit and whose hospitalization reasons had regressed were evaluated. The mean nesfatin-1 values of the patients were measured as 9.95±0.78 ng/mL (4.25-18.93 ng/mL). There was a negative and low (r=-0.214) relationship between target calorie intake and nesfatin-1, a positive and low (r=0.172) relationship with prealbumin, and a positive and high relationship with vitamin D (r=0.529). Similar relationships were determined between the weight change ratio and nesfatin-1 (r=-0.266), prealbumin (r=0.154) and vitamin D (r=0.337).

Conclusion: Based on the study findings, it was concluded that serum nefsatin-1, albumin and prealbumin are not appropriate indicators for nutritional monitoring and management in critically ill children.

Keywords: Nesfatin-1, child critical ilness, nutrition

Öz

Giriş: Kritik hasta çocuklarda beslenme mortalite üzerinde oldukça etkili olmasına rağmen, hastalar yeterince beslenememektedir. Enteral beslenme monitorizasyonu ve yönetimi için uygun bir biyobelirteç mevcut değildir. Bu çalışmanın amacı; nefsatin-1'in kritik hasta çocuklarda nütrisyonel monitorizasyon ve yönetimi için kullanılabilirliğini araştırmaktır.

Yöntemler: Ocak-Eylül 2019 periyodunda 3. basamak çocuk yoğun bakım ünitesinde yatan, enflamasyon bulgusu olmayan 35 kritik hasta çocuk çalışmaya alınmıştır. Nesfatin-1, vitamin D düzeyi, prealbümin, albümin, çalışma için değerlendirilmiştir.

Bulgular: Çocuk yoğun bakım ünitesine yatan, enfeksiyon belirteçlerinin gerilediği 35 hasta değerlendirilmiştir. Hastaların ortalama nesfatin-1 değerleri 9,95±0,78 ng/mL (4,25-18,93 ng/mL) olarak ölçülmüştür. Hedef kalori alım oranı ile nesfatin-1 arasında negatif ve düşük (r=-0,214), prealbümin ile pozitif ve düşük (r=0,172), vitamin D ile ise pozitif ve yüksek (r=0,529) ilişki bulunmuştur. Benzer ilişkiler ağırlık değişim oranı ile nesfatin-1 (r=-0,266), prealbümin (r=0,154) ve vitamin D (r=0,337) arasında belirlenmiştir.

Sonuç: Çalışma bulgularına göre, kritik hasta çocuklarda, nutrisyon monitorizasyonu ve yönetimi için serum nefsatin-1, albümin ve prealbüminin uygun göstergeler olmadığı sonucuna varılmıştır.

Anahtar Kelimeler: Nesfatin-1, kritik hasta çocuk, beslenme

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Introduction

Despite recent technological developments, malnutrition is commonly seen in pediatric intensive care units. Acute or chronic malnutrition is observed at a rate of 24-55% with deterioration of nutritional status during hospital stay.[1]

Malnutrition observed at the time of hospitalization, increased basal metabolic rate during critical illness, severe protein catabolization, and limited energy stores of the pediatric patient increase the severity of malnutrition and thus the mortality and morbidity of the patient.[2]

Monitoring is recommended in order to start feeding in the early period and to achieve ideal nutritional goals in critical pediatric patient follow-up. However, no method has been identified as the ideal method.[3] The condition of the critically ill child is even more complex, and fluid leaks into the third space make accurate anthropometric evaluation difficult.[4]

Some peptides and neurotransmitters play a role in both appetite regulation and stress response, and nesfatin is one of these peptides. Nesfatin-1, which was first described by Oh et al.[5] in 2006, is a satiety molecule found in the hypothalamus, with a molecular weight of 9.7 kDa, consisting of 82 amino acids. Nesfatin-1 is found not only in brain tissues, but also in peripheral tissues such as adipose tissue, stomach, pancreatic islets, liver and testis.

Nesfatin-1, originating from NEFA/nucleobindin2, is a recently discovered hormone that suppresses food intake via melanocortin in the hypothalamus.[5]

The relationship of the nesfatin-1 molecule with thermogenesis, especially in ischemic brain injuries, neuroprotective, reproductive physiology, cardiovascular functions, blood glucose balance, gastrointestinal functions, energy metabolism, and even anxiety and depression has been investigated.[6,7] Nesfatin-1, which was considered an anorexigenic hormone when it was first discovered, has been shown to have an effect on many systems in later studies. Especially in animal studies, it was observed that food intake decreased when serum and tissue nesfatin levels increased.[8,9]

Low levels of albumin in serum are known as an indicator of malnutrition. In emergency and critical situations, albumin level decreases by 30% in a very short time. Prealbumin level (normal range: 16-35 mg/dL) is not considered as a marker for malnutrition since it is also affected by inflammation; however, it has been stated that it can be useful to determine the nutritional level by measuring it with C-reactive protein (CRP) at certain periods even in cases where inflammation persists.[10]

Nutrition is an important part of treatment in the critically ill patients. During the enteral nutrition period, the difference between the planned/calculated nutrient formulation to be given to the patient and the amount that the patient can take in practice is quite high. In addition, the effect of nutrition on the patient emerges in the future. Therefore, monitoring and standardization are very important in intensive care nutrition management from the first day of the hospitalization of critically ill patient.[10]

The aim of this study is to investigate the usability of nesfatin-1 in nutritional monitoring and management by examining the relationship between serum nesfatin-1 levels and anthropometric measurements and some blood parameters in patients hospitalized in the pediatric intensive care unit. Studies on nesfatin-1, which is reported to be closely related to nutrition and affect almost all systems in the literature, almost completely examine the issue of obesity in adults and children. According to the published literature, this study was carried out on pediatric intensive care patients for the first time.

Materials and Methods

The study was planned as a controlled prospective clinical trial. In the January-September 2019 period, 35 critically ill children, who were hospitalized in the tertiary pediatric intensive care unit and had no signs of inflammation, were included in the study. Informed consent was obtained from their families.

Body weights, height measurements, demographic data, complications, daily calorie intake, and reasons for admission to the intensive care unit of the patients included in the study were recorded. After the patient's inflammation markers (CRP, procalcitonin) regressed, routine biochemistry and hematological examinations were performed. Vitamin D level, prealbumin, and albumin were evaluated for the study. During these tests, serum was separated for serum nesfatin-1 level. The serums were stored at -40 °C. After the study was completed, serum nesfatin-1 levels were measured with Bio-Tek ELX-800 brand ELISA method in Van Yüzüncü Yıl University Health Services Vocational School, Research and Application Laboratory.

The study was approved by the Hatay Mustafa Kemal University, Tayfur Ata Sökmen Faculty of Medicine Clinical Research Ethics Committee (approval number: 03, date: 20.02.2020).

Statistical Analysis

The daily calorie intake and the required calorie intake were determined according to the Schofield method (target calorie) and recorded. In order to prevent differences between patients, the caloric intake-target calorie/target calorie*100 was formulated. Entry and exit weights of the patients were formulated with exit weight-entry weight/entry weight*100. Patients were considered to have lost weight if they had a weight loss of more than 10%.

The normality test of nesfatin-1 values was performed with the Shapiro-Wilk and it was determined that it did not show normal distribution. The correlation between demographic and blood parameters and nesfatin-1 was calculated using the Spearman's rho. The differences in nesfatin-1 between those who maintained their weight and those who lost their weight were analyzed by using the Mann-Whitney U test, one of the non-parametric tests, and the difference between the percentage of reaching the target calorie (95% and above, 94-75% and below 75%) and nesfatin-1 by using the Kruskal-Wallis test. Normally distributed albumin, prealbumin and vitamin D levels were compared with t-test for pairwise comparison, with One-Way ANOVA for triple comparison, and with Duncan test for multiple comparison test. Values below p<0.05 were considered significant in the multiple comparison test. The analysis of the obtained data was made with the SPSS 22.0 statistical program.

Results

In 35 patients included in the study, the number of boys/girls was 19/16 and their mean age was calculated as 40.6±7.1 months (12 months-144 months). Eighteen of the patients were hospitalized in the intensive care unit for central nervous system diseases, 10 for respiratory failure, 4 for cardiogenic reasons, and 3 for renal reasons. 88.5% (n=31) of the patients were fed enterally. Two patients were fed only parenterally, and 2 patients were fed enterally + parenterally. The mean nesfatin value of the patients included in the study was measured as 9.958±0.78 ng/mL (4.25-18.93 ng/mL).

The correlation coefficient values calculated between measured levels of nesfatin-1, albumin, prealbumin and vitamin D and some nutritional parameters are presented in Table 1.

Targeted calorie intake had a negative and low correlation with nesfatin-1 (r=-0.214; p>0.05), a positive and low correlation with prealbumin (r=0.172; p>0.05), and a positive and high correlation with vitamin D (r=0.529; p<0.01). Similar relationships were determined between weight change ratio and nesfatin-1 (r=-0.266; p>0.05), prealbumin (r=0.154; p>0.05) and vitamin D (r=0.337; p>0.05). Correlation coefficient was calculated as r=-0.337 between serum nesfatin-1 level and vitamin D (p<0.05). A positive and moderate correlation (r=0.329) was found between hospitalization time and prealbumin level (p<0.05).

Nesfatin-1, albumin, prealbumin and vitamin D levels of those who maintained their weight and lost weight during the intensive care period are presented in Table 2.

It was observed that weight change during hospitalization did not affect serum nesfatin-1, albumin, prealbumin and vitamin D levels (p<0.05).

Table 1. Relationships between some parameters of patients and nesfatin-1, prealbumin, albumin, and vitamin D levels

	Age (month)	PELOD2	PIM3	Weight-1 (kg)	Weight-2 (kg)	AF (%)	HKF (%)	Length of hospitalization (day)	Nesfatin-1 (ng/mL)	Prealbumin (mg/dL)	Albumin (mg/dL)	Vitamin D (ng/mL)
PELOD2	-0.18											
PIM3	-0.17	0.81**										
Weight-1 (kg)	0.37*	0.17	0.15									
Weight-2 (kg)	0.42*	0.18	0.19	0.99**								
AF (%)	0.18	0.13	0.29	-0.07	0.09							
HKF (%)	0.13	-0.14	-0.11	-0.18	-0.10	0.44**						
Length of hospitalizaiton (day)	-0.02	0.15	0.08	0.00	0.03	0.16	0.43*					
Nesfatin-1 (ng/mL)	-0.11	0.18	0.15	0.01	-0.04	-0.32	-0.21	-0.12				
Prealbumin (mg/dL)	0.29	-0.17	-0.11	0.07	0.10	0.13	0.17	0.33	0.01			
Albumin (mg/dL)	0.11	-0.21	-0.22	0.17	0.15	-0.08	0.09	0.23	-0.08	0.60**		
Vitamin D (ng/mL)	0.03	-0.09	-0.08	-0.24	-0.21	0.17	0.52**	0.52**	-0.34	0.42*	0.40*	
CRP	0.21	0.17	0.21	0.15	0.15	0.01	-0.16	-0.02	0.20	0.19	-0.15	0.06

PELOD2: Pediatric logistic organ dysfunction 2, PIM3: Pediatric index of mortality 3, Weight-1: Weight on the first day of hospitalization in the intensive care unit, Weight-2: Weight on the day when blood sample was collected for nesfatin-1, AF: (Weight2 - Weight1)/Weight1*100, HKF: (Calorie intake- target calorie)/target calorie, CRP: C-reactive protein, *: p<0.05, **: p<0.01

Table 2. Serum nesfatin-1, prealbumin, albumin and vitamin D levels of patients who could maintain their weight (normal) and lost weight during hospitalization

	n	Nesfatin-1 (ng/mL)	Prealbumin (mg/dL)	Albumin (mg/dL)	Vitamin D (ng/mL)
Normal	28	9.54±4.41	17.93±7.85	3.34±0.61	28.14±13.30
Weight loss	7	11.61±5.63	17.43±5.62	3.40±0.39	31.43±6.80
p		0.219	0.299	0.176	0.056

Table 3. Nesfatin-1, albumin, prealbumin and vitamin D levels with the rate of reaching the target calorie

Rate of reaching the target calorie	n	Nesfatin (ng/mL)	Prealbumin (mg/dL)	Albumin (mg/dL)	Vitamin D (ng/mL)
>95%	10	8.169±1.160	19.5±2.271	3.42±0.44	37.00±2.923[a]
94-75%	13	12.691±1.541	15.60±2.609	3.18±0.21	25.90±3.089[b]
<75%	12	9.506±1.219	18.00±1.747	3.35±0.57	23.46±3.459[b]
p		0.177	0.478	0.533	0.011

[a,b]Mean values followed by different letters within a column are significantly different (p<0.05)

In Table 3, the rates of reaching the targeted calories and nesfatin-1, albumin, prealbumin and vitamin D levels of patients who could take the targeted daily calorie amount are presented. It was determined that target calorie intake rates did not change nesfatin-1, albumin and prealbumin levels. It was calculated that the vitamin D level of patients who reached at least 95% of their target calorie intake (37.00±2.923 ng/mL) was higher than those with lower calorie intake (25.90±3.089 and 23.46±3.459 ng/mL) (p<0.05).

Discussion

It is known that nesfatin-1 is effective on appetite tendencies, simple carbohydrate and fat intake behavior that will cause obesity in experimental animals. However, the mechanism of action has not yet been clearly explained. In addition, most studies have aimed to find new therapeutic solutions for obesity.[11,12]

Studies in experimental animals have shown that increased levels of nesfatin-1 suppress appetite and play a role in the regulation of eating behavior and body weight in rats.[5]

Nesfatin-1 level was found to be significantly lower in obese children compared to those with normal body mass index.[12] On the contrary, another study reported a positive and high correlation between the amount of body fat and serum nesfatin-1 concentration.[13]

In the literature, there are many studies on serum nesfatin-1 levels in obese adults. However, the number of studies measuring blood nesfatin-1 levels in obese children and adolescents is extremely limited. First, the relationships between anthropometric and metabolic characteristics and serum nesfatin-1 were investigated in obese children and adolescents in South Korea.[14]

All of these studies aimed to understand the relationship between the mechanism of obesity and nesfatin-1 secretion. In one of the studies conducted on this subject,[14] the mean serum nesfatin-1 level was found to be 1.4 ng/mL (0.1-10.7 ng/mL) in obese children and 2.0 ng/mL (0.1-20.0 ng/mL) in children with a normal body mass index. The difference between the two groups was found to be statistically very significant. According to the findings of the same study, it was stated that the serum nesfatin-1 level tended to decrease as the adolescent period approached.[14] In our study, the mean blood nesfatin-1 level was found to be 9.95±0.78 ng/mL (4.25-18.93 ng/mL), which was higher than in previous studies. This result was attributed to the fact that the patients were prepubertal and they had baseline malnutrition.

There are conflicting reports in the results of studies to determine the relationship between childhood serum nesfatin-1 and anthropometric properties. For example, Anwar et al.[15] reported a positive relationship between serum nesfatin-1 level and body mass index in obese children.

In our study, in critically ill children, no difference was detected in serum nesfatin-1 levels between those with and without weight loss and between those who reached the target calories and those who did not. It was thought that the results of our study could not be compared to those of previous studies since they were performed in healthy and homogeneous (age-physiological period-sex etc.) populations and/or groups of obese children. However, based on the current findings, it has been evaluated that nesfatin-1 cannot be used as a marker for nutritional monitoring and management to monitor the feeding level in the intensive care unit. On the other hand, nesfatin-1 level was found to be significant in terms of measuring it for the first time in critically ill children and it provided a reference value.

In our study, it was observed that weight differences during hospitalization did not change serum albumin and prealbumin levels and were among the reference values in all groups.

However, a positive and moderate correlation was calculated between the length of stay in the intensive care unit and the serum prealbumin level. However, Keller[16] reported that although albumin and prealbumin levels were associated with nutritional levels in non-diseased individuals, these two parameters should be used as an indicator of inflammation rather than nutritional level in acute diseases. In this study, the increased prealbumin with longer hospitalization period and the short half-life of prealbumin (2-3 days) were explained by the effectiveness of enteral nutrition during hospitalization. Researchers reported that there was no difference in blood vitamin D levels in obese and normal children.[14] Currently, vitamin D supplementation is given in enteral formulas used in intensive care nutrition and the current research. However, in the current study, children who lost weight and did not achieve their target caloric intake had significantly lower vitamin D levels than patients who achieved the target caloric intake and did not lose weight.

Study Limitations

The limitations of this study are that the basal nesfatin-1 levels of the patients were not determined and the number of patients was low.

Conclusion

This is the first study to evaluate nesfatin-1 as a nutritional indicator in critically ill children. According to the study findings, serum nesfatin-1, albumin and prealbumin, which are selected as biomarkers for nutritional monitoring and management in critically ill children, are not appropriate indicators; however, it was concluded that the level of vitamin D could indicate the level of reaching the target calorie. Traditionally, calorie and weight monitoring have already been considered a good indicator.

Ethics

Ethics Committee Approval: The study was approved by the Hatay Mustafa Kemal University, Tayfur Ata Sökmen Faculty of Medicine Clinical Research Ethics Committee (approval number: 03, date: 20.02.2020).

Informed Consent: Informed consent was obtained from their families.

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Authorship Contributions

Surgical and Medical Practices: Y.Ç., A.K., Y.A., Concept: Y.Ç., A.K., Y.A., Design: Y.Ç., A.K., Y.A., Data Collection or Processing: Y.Ç., A.K., A.U.K., Analysis or Interpretation: Y.Ç., A.K., A.U.K., Literature Search: Y.Ç., S.A., Writing: Y.Ç.

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Case Report / Olgu Sunumu

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Critically Affected Children Owing to Butane Abuse in Pediatric Intensive Care: Clinical Courses and Outcomes

Çocuk Yoğun Bakımda Bütan Kötüye Kullanımı Nedeniyle Kritik Etkilenen Çocuklar: Klinik Seyirleri ve Sonuçlar

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Abstract

One of the most common health problems today is volatile substance abuse and toxic gas inhalation. Butane gas, also known as lighter gas, is increasingly used because it causes euphoria, pleasure and joy among adolescents. The most important reasons for this situation are the fact that it is cheap and easy to obtain, and at the same time the legal audit is not very serious. In this article, two adolescent male patients who were followed up in our pediatric intensive care unit after lighter gas inhalation are presented. The first case was discharged, and the second case died despite extracorporeal cardiopulmonary resuscitation due to cardiac arrest during admission to our hospital from another center. In our study, it was aimed to draw attention to the fact that butane gas inhalation, which has been increasingly common in childhood, is responsible for significant morbidity and mortality.

Keywords: Butane gase, lighter gas, pediatric intensive care

Öz

Günümüzde sık karşılaşılan sağlık sorunlarından biri uçucu madde kullanımı ve toksik gaz inhalasyonudur. Çakmak gazı olarak da bilinen bütan gazının ergenler arasında öfori, keyif ve neşe oluşturması nedeni ile kullanımı giderek artmaktadır. Bu durumun en önemli nedenleri ucuz ve temininin kolay olması ile beraber aynı zamanda yasal denetimin çok ciddi olmamasıdır. Bu yazıda çakmak gazı inhalasyonu sonrası çocuk yoğun bakım ünitemizde takip edilen iki olgu sunulmuştur. Birinci olgunun taburculuğu yapılmış, ikinci olgu ise başka bir merkezden hastanemize kabulü sırasında kardiyak arrest olmasına yönelik ekstrakorporeal kardiyoakciğer resüsitasyon uygulanmasına rağmen kaybedilmiştir. Çalışmamızda çocukluk çağında son zamanlarda giderek yaygınlığı artan bütan gazı inhalasyonunun önemli ölçüde morbidite ve mortaliteden sorumlu olduğuna dikkat çekilmesi amaçlanmıştır.

Anahtar Kelimeler: Butan gazı, çakmak gazı, çocuk yoğun bakım

Introduction

The use of volatile substances and toxic gas inhalation is a significant social problem in Turkey, as it is in many countries. Inhalant use is most common among 7-19-year olds and prevalent among the male population.[1] Adolescents usually inhale gas for curiosity or to experience feelings of euphoria. In addition, butane gas is the most preferred choice, which is cheaper and easier to obtain. Lighter gas is associated with the highest mortality rate among abused substances.[2] Depending on the method and duration of use, mild symptoms such as dizziness, nausea, vomiting, euphoria and hallucination can be observed, whereas reasons such as suffocation, vagal inhibition, respiratory depression, trauma and cardiac arrhythmia might result in sudden death.[3] Here, we present the clinical follow-up and results of two adolescent male cases who were admitted to our paediatric intensive care unit (PICU) due to it's the critical impact from butane gas inhalation. In our study we draw attention to the fact that butane gas inhalation, which is increasing in use among youths and adolescents, is responsible for significant morbidity and mortality.

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Case Reports

Case 1

A 16-year-old male patient, who was previously healthy, was taken to hospital four hours after inhaling lighter gas with complaints of recurrent vomiting, stagnation, and general disturbance in his general condition. On admission to the hospital, the patient, whose general condition was poor and who was unconscious. He was intubated and an adrenaline infusion was started due to circulatory disorder. The patient, who was started with insulin and whose inotropic support was given as adrenaline, noradrenaline, dopamine and hydrocortisone, was admitted to the PICU because of the possibility of needing extracorporeal membrane oxygenation (ECMO).

On physical examination, the patient's overall condition was poor. He was intubated with oxygen saturation 98%, body temperature was 36.5 °C, heart rate was 96/min, and his blood pressure was 106/54 mmHg. The patient received adrenaline, noradrenaline, dopamine and hydrocortisone as inotrope support; in addition, he received insulin infusion due to high blood sugar, and bicarbonate was given because metabolic acidosis was found in his laboratory examinations. By starting hypertonic saline infusion to avoid the risk of cerebral edema no pathology was detected except subgaleal edema in the occipitoparietal region measuring 2.5 cm in its thickest part in the taken brain CT. In the first admission, the creatinine value increased to 3.2 mg/dL, the control creatinine value increased to 4.2 mg/dL after four hours, and the urine output was less than 0.5 cc/kg/hour. Despite the treatments, the patient was placed on a central venous catheter and continuous veno venous hemodialysis (CVVHD) was started. Pain localization was better on the second day of follow-up. Due to its normotensive and neuroglycemic course, dopamine, hydrocortisone and insulin infusions were discontinued and adrenaline and noradrenaline doses were reduced. Since the patient whose CVVHD was stopped on the third day of his admission, due to the spontaneous urine output, furosemide infusion was started. When compared with the previous examination, it was observed that the subgaleal edema in the occipitoparietal region increased by 3.5 cm in the thickest part of the control brain computed tomography. Neurosurgery said that there is no need for any invasive intervention. On the fourth day of hospitalization the patient regained normal sinus rhythm after the application of cardioversion, due to the presence of pulsating ventricular tachycardia (VT), prophylactic amiodarone infusion was started, and due to oliguria CVVHD was restarted. On the fifth day of his hospitalization, for the purpose of evaluating his state of consciousness, sedation was stopped. We could see his fluctuating consciousness and after that eye blinking and extremity movements due to our commands. Although there were widespread encephalopathic findings in electroencephalography, no epileptic activity was detected. Due to high blood pressure, the inotropic supplements he was taking were gradually stopped. The patient, whose consciousness was better on the sixth day of the follow-up, was continued on dialysis due to the absence of urine, although haemodialysis was intermittently stopped. Extubation was performed on the seventh day. Dialysis was interrupted when the diuretic infusion was initiated on the ninth day of his follow-up and his haemodialysis was stopped on the ninth day of his follow-up. He was transferred to the paediatric nephrology service on the tenth day of his admission. During the follow-up, he was fully conscious and his kidney functions improved. The patient is now clinically normal.

Case 2

A 15-year-old male patient, two days before his admission to our hospital, was brought to the emergency department after being informed to the 112-emergency team, due to the development of confusion after inhalation of lighter gas with his friends in another city. As the patient's heart rhythm was in pulseless VT, the patient received cardiopulmonary resuscitation (CPR) and defibrillation for up to 5 minutes, subsequently the patient's heart rate returned to normal. The patient was intubated and hospitalized in the PICU. Dopamine infusion was initiated in the hypotensive patient and the ejection fraction was measured as 18 in echocardiography. In laboratory tests, cardiac enzymes were found to be too high to be measured. The patient was given triple inotrope (dopamine, dobutamine and milrinone) support due to resistant hypotension, and adenosine was administered due to the development of supra VT, and then amiodarone infusion was initiated. After two days of follow-up, the patient, whose heart functions did not change despite receiving high doses of inotrope support, was admitted to our hospital due to the need for ECMO. The patient was transported from a hospital located in another city y air-ambulance. We started CPR due to the development of cardiac arrest (CA) in the emergency room, and after 10 minutes of CPR, we decided on extracorporeal cardiopulmonary resuscitation (ECPR). The patient who was admitted to the PICU with was performing CPR. ECMO was installed on the left femoral artery and vein as VA ECMO in 115th minutes of CPR. However, since the heart rhythm of the patient did not return under ECMO, he was pronounced dead. The demographic, clinical characteristics, treatments and results of both patients are given in Table 1.

Table 1. Patients' demographic, clinical features, interventions and outcomes

Parameters	Cases	
	1	2
Gender	Male	Male
Age (years)	16	15
History of cardiac arrest	No	Yes
Length of PICU stay* (days)	10	1
Length of hospital stay (days)	31	1
Mechanical ventilation time (days)	7	1
CRRT⁺	Yes	No
ECMO^	No	Yes
Mortality	No	Yes
Sequel	No	-

*PICU: Pediatric intensive care unit, ⁺CRRT: Continues renal replacement therapy, ^ECMO: Extracorporeal membrane oxygenation

Discussion

The fact that volatile substances are the ones used in our daily life, that they constitute a step toward the use of heavier substances, and the early onset of abuse are social problems all over the world, but also an important health problem in adolescents and young adults. The frequency of inhalant use varies in societies. In a study conducted in Australia among students aged 12-17, it was reported that 27.3% of adolescents inhaled lighter gas at least once in their life.[4] Although the abuse of butane gas is seen in different age groups, it is more common in children between the ages of 7-19 and male (1,2). In the article in which 282 deaths related to inhalant use were reported in the United Kingdom, it was shown that 95% of the participants were male.[5] Our cases were also in line with the studies conducted on this subject, either in terms of age or gender.

Although the mechanism of sudden death due to inhalant use is not fully known, different mechanisms have been reported for the emergence of "sudden sniffing death syndrome". "Sudden sniffing death syndrome", first described by Bass in the literature, is responsible for 55% of deaths caused by the abuse of volatile substances.[6] Studies have reported that butane gas increases the sensitization of the myocardium to the arrhythmogenic effects of endogenous catecholamines. The increase in sympathetic activity in users, whether due to hallucination due to the effect of toxic gas, running from the scene after inhalation to conceal substance use, and other reasons, increases the secretion of endogenous catecholamines. It is thought that these rapid fluctuations in adrenaline level may cause severe vasospasm, arrhythmia and sudden death.[3,7]

One of the conditions that need to be considered due to lighter gas inhalation is the administration of antiarrhythmic drugs such as amiodarone or beta blockers because of reducing the risk of recurrent ventricular fibrillation together with classical adrenaline applications in CPR applied to these patients.[8,9] In our study, pulsed VT was detected in the first case and pulseless VT was detected in the follow-up of the second. In the first case, amiodarone infusion was started after cardioversion, and in the second case only defibrillation was applied.

Although patients have serious systemic side effects, especially cardiac, and fatal complications, it is seen in case one that patients can return to their normal life if they survive this process. In both cases, it is observed that cardiac involvement is the basis of the events that cause life-threatening patients. The main reasons for the death in case two, are the occurring of cardiac arrest before entering the emergency room, the absence of a response to CPR, the possibility of ECPR being set up at the 115th minute, the use of multiple and high doses of inotropes in the previous hospital. However, as seen in case 1, if the patient comes to the hospital without CA, even if multiple organ failure develops and CRRT is applied, the patient can return to normal life with good care.

Conclusion

After butane gas inhalation, life-threatening systemic effects, especially cardiac, occur in children. This causes fatal or permanent neurological sequelae, especially as it causes out-ofhospital arrest. Although it does not have a special antidote, it can be ensured that patients survive with respiratory and circulatory support and regain normal health. In addition, the regulation of laws on the sale of volatile substances from government offices and educating the public on this issue by health professionals are among the measures to prevent adolescent deaths.

Ethics

Informed Consent: We was approved informed consent from the child's parents.

Peer-review: Externally peer-reviewed.

Authorship Contributions

Concept: A.G., T.K., Design: T.K., Data Collection or Processing: A.G., Analysis or Interpretation: A.G., T.K., E.B., E.G., Literature Search: A.G., E.B., E.G., T.K., Writing: A.G., T.K.

Conflict of Interest: No conflict of interest was declared by the authors.

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Case Report / Olgu Sunumu

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Severe Asthma Attack-associated Middle Lobe Syndrome in an Uncontrolled Asthma Patient

Uzun Süreli Takipsiz Astım Hastasında Ağır Astım Atağı İlişkili Orta Lob Sendromu

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Abstract

Middle lobe syndrome is a well-defined clinical and radiological entity in the pediatric literature, The causes include many pathologies such as asthma, lymphadenopathy, tumor, foreign body aspiration, granulation tissue, mucus plug, bronchopulmonary dysplasia, and cystic fibrosis. A nine-year-old girl with a diagnosis of asthma, who lack regular follow-up visits and a regular treatment, was admitted to the pediatric emergency department with respiratory distress. On physical examination; tachipnea, dyspnea, bilateral wheezing was revealed. Oxygen saturation was 80% in room air. Chest X-ray showed atelectasis in the right middle lobe and bilateral pneumonic infiltrates, more prominently in the right lung. The patient was started a non-invasive mechanical ventilation support, a broad-spectrum antibiotic therapy, asthma medication, N-acetylcysteine nebule therapy and chest physiotherapy. The chest X-ray showed improvement in atelectasis on the 5th day of treatment. Middle lobe syndrome has a very good prognosis when diagnosed early and treated appropriately. It should be kept in mind in patients with recurrent or persistent respiratory symptoms. Asthma is one of the most common causes of middle lobe syndrome in children, and uncontrolled asthma patients constitute a high risk. It is very important for asthma patients to continue their regular follow-up and to receive appropriate treatment according to their disease control.

Keywords: Asthma, atelectasis, middle lobe syndrome

Öz

Orta lob sendromu sıklıkla sağ orta bronşun dıştan bası ya da içeriden mukus tıkacı ile tıkanması sonucu ortaya çıkan bir klinik tablodur. Etiyolojide astım, lenfadenopati, tümör, yabancı cisim aspirasyonu, granülasyon dokusu, mukus tıkacı, bronkoakciğer displazi, kistik fibrozis gibi pek çok patoloji yer almaktadır. Astım tanılı ancak takipsiz olan ve düzenli tedavi almayan dokuz yaşında kız hasta çocuk acil servise solunum sıkıntısı şikayetiyle başvurdu. Oksijen satürasyonu oda havasında %80 olan hastanın fizik muayenesinde; takipne, dispne, akciğerlerde sağda daha belirgin olmak üzere yaygın ronküsler ve ekspiryum uzunluğu mevcuttu. Akciğer grafisinde sağ akciğer orta lobda atelektazi ve sağda daha belirgin olmak üzere bilateral pnömonik infiltrasyon olduğu görüldü. Non-invaziv mekanik ventilasyon desteği verilen hastaya geniş spektrumlu antibiyotik tedavisi ve astım atağına yönelik tedavinin yanı sıra N-asetilsistein nebül tedavisi verildi ve göğüs fizyoterapisi uygulandı. Tedavini beşinci gününde çekilen akciğer grafisinde atelektazinin düzeldiği görüldü. Orta lob sendromu erken tanı ve uygun tedavi ile prognozu oldukça iyi olan bir tablo olup, tekrarlayıcı ya da persistan solunum semptomu olan hastalarda mutlaka akılda tutulmalıdır. Astım çocuklarda orta lob sendromuna en sık yol açan tablolardan birisidir ve kontrolsüz astım hastaları riskli gurubu oluşturmaktadır. Astım hastalarının düzenli kontrollerine devam etmeleri ve hastalık kontrolüne göre uygun tedavi almaları oldukça önemlidir.

Anahtar Kelimeler: Astım, atelektazi, orta lob sendromu

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Introduction

Middle lobe syndrome (MLS) is a well-defined clinical and radiological condition in the pediatric literature.[1] The features of lung involvement were first described in 1937 by Brock et al.[2] in children with tuberculous lymphadenitis, but the term MLS was first used by Graham et al.[3] in a series of 12 cases published in 1948, in which atelectasis developed as a result of compression of the peribronchial lymph nodes to the middle lobe bronchus. Culiner[4] stated in 1966 that the main cause of MLS was bronchial compression and that this picture emerged as isolated in the right middle lobe due to the absence of collateral ventilation. Then, Wagner and Johnson[5] expanded the definition of this syndrome by stating that atelectasis could develop without external pressure on the bronchi. It has been observed over time that although this clinical picture is mostly in the right middle lobe, it can also occur in other areas of the lung.

It is usually seen with a history of asthma or atopy in the childhood age group. Also, in etiology, many pathological conditions such as lymphadenopathy, tumor, foreign body aspiration, granulation tissue, mucus plug, bronchopulmonary dysplasia, cystic fibrosis play a role, and the exact prevalence is unknown. It is more common in the preschool age group in children, and the median age of diagnosis varies between 3.3 and 5.5 years.[4,5] Middle lobe syndrome is a clinically overlooked diagnosis, and delay in diagnosis is responsible for both the high economic burden of drug overuse and potentially poor long-term outcomes. This case was presented and discussed in the light of the literature, in order to draw attention to severe asthma attack and related MLS in asthma patients without follow-up.

Case Report

A nine-year-old female patient was admitted to the pediatric emergency department of our hospital with the complaint of respiratory distress. It was learned from the patient's history that she had recurrent wheezing attacks since she was 2 years old, she received nebular treatments in the emergency department at the time of the attack, she never received regular inhaled corticosteroid treatment, and she did not apply to the hospital because she had no attacks for 3 years. Her vital signs at the time of admission were as follows; temperature: 37.6 °C, respiratory rate: 60/min, pulse: 140/min, blood pressure: 115/50 mmHg, oxygen saturation: 80% in room air, 94% with oxygen. In the physical examination, her general condition was moderate-poor, dyspneic, with diffuse rhonchi and expiratory length in the lungs, more prominently on the right side. In the laboratory tests of the patient whose other system examinations were normal, hemoglobin was 12.7 g/dL, leukocyte was 16300/mm^3, neutrophil was 14780/mm^3 lymphocyte was 1100/mm^3, platelet was 331000/mm^3 and crp was 2.1 mg/dL. There was mild lactic acidosis in blood gas. Chest X-ray showed atelectasis in the middle lobe of the right lung (Figure 1A).

In the thorax computed tomography, there was an increase in density consistent with diffuse atelectasis, including air bronchograms observed as extending from the posterior of the upper lobe apical segment in the right lung to the hilar section and to the middle lobe to the lower lobe anterobasal segment on the right and at the level of the lower lobe anterobasal segments on the left, and there were findings consistent with prominent bilateral bronchopneumonic infiltration on the right (Figure 2).

The patient, whose Coronavirus type-19 (Coronavirus disease-2019) polymerase chain reaction test was performed twice and was found to be negative, was hospitalized in the pediatric intensive care unit with the preliminary diagnosis of asthma attack and right middle lobe syndrome. Meropenem and teicoplanin antibiotics were started. Respiratory support was given with Bilevel positive airway pressure. 2 mg/kg/day methylprednisolone, continuous salbutamol nebulization, ipratropium bromide nebulization, intravenous (iv) magnesium sulfate ($MgSO_4$), and iv aminophylline infusion treatments together with N-acetylcysteine nebules were started for asthma attack. Chest physiotherapy and postural drainage were applied to the patient. According to the improvement in the patient's auscultation findings, iv aminophylline and $MgSO_4$ treatments were discontinued on the 2nd day of hospitalization, respectively. On the fifth day of hospitalization, chest X-ray showed improvement in atelectasis (Figure 1B). Antibiotherapy and steroid treatment of the patient, who was transferred to the ward after a seven-day intensive care follow-up, was discontinued on the tenth day, and nebular salbutamol and ipratropium treatments were gradually decreased and discontinued on the eleventh day.

In the bronchoscopy performed on the patient for the differential diagnosis of foreign body aspiration or intrabronchial obstructive lesion, edema and occasional sticky occlusive secretions were observed in both bronchial systems, and no foreign body, external compression appearance or mass was detected. Purified protein derivative test performed for tuberculosis exclusion, and acid-fast bacillus staining taken from fasting gastric juice for 3 days and tuberculosis cultures were negative. The patient's immunoglobulin A, G, M levels were 1.18 g/L, 10.84 g/L, and 1.37 g/L, respectively, and were within normal limits for her age. It was observed that IgE level was 569 IU/L, *Dermatophagoides pharynea* specific IgE level was 22 kU/L, and *Dermatophagoides pteronyssinus* specific IgE level was 40.2 kU/L.

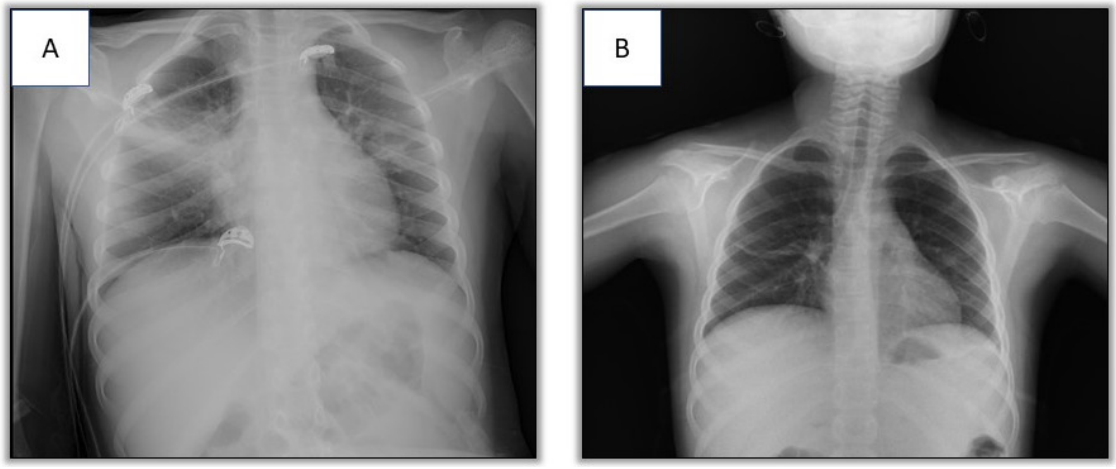

Figure 1. A) On the patient's chest X-ray taken at the time of admission, view of atelectasis in the middle lobe of the right lung and bilateral paracardiac infiltration, more prominently on the right, **B)** On the chest X-ray taken on the fifth day of the patient's treatment, it is seen that atelectasis has improved

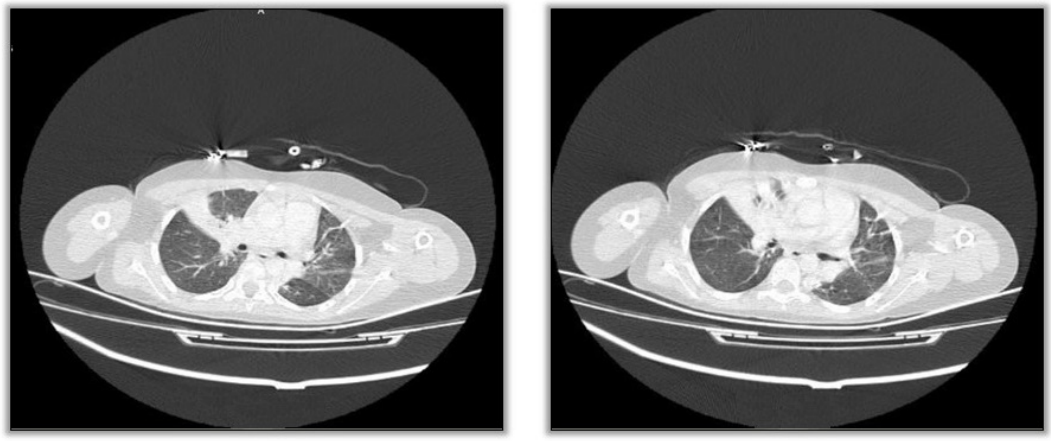

Figure 2. In the thorax computed tomography, there was an increase in density consistent with diffuse atelectasis, including air bronchograms observed as extending from the posterior of the upper lobe apical segment in the right lung to the hilar section and to the middle lobe to the lower lobe anterobasal segment on the right and at the level of the lower lobe anterobasal segments on the left, and there were findings consistent with prominent bilateral bronchopneumonic infiltration on the right

Fluticasone propionate (250 mcg) + salmeterol (50 mcg) metered dose inhaler treatment was started during discharge, and no pathology was detected in the physical examination and chest X-rays in the 3rd and 6th month control examinations, and she is being followed by the department of pediatric immunology and allergy diseases.

Discussion

Although middle lobe syndrome is a complication of childhood asthma, its exact prevalence and incidence are unknown. Studies have reported that 5-10% of patients hospitalized with acute asthma attack have radiological findings of lobar collapse.[6,7] However, these studies are quite old and were conducted before preventive anti-inflammatory treatments for asthma were begun to be widely used.

In a study conducted in Turkey in 2004, 3.528 patients who applied to the pediatric allergy clinic for a two-year period were evaluated and it was observed that the middle lobe syndrome was found in 56 (1.58%) patients, emerging only once in 50 patients, 2 times in 5, and 3 times in 1 patient.[8] It was stated that the symptoms of the patients at the time of admission were respiratory distress, cough, sputum, fever and wheezing.[8] Our patient applied to the emergency department with respiratory distress. Again, in the same study, it was observed that atelectasis continued for an average of 45 days in 36.5% of the patients, and although it was not statistically significant, patients who took systemic corticosteroids for 10 days recovered faster than those who did not receive corticosteroids. The authors have stated that the most important clinical clue for middle lobe syndrome is prolonged asthma symptoms and that the complaint or recovery period lasting more than 2 weeks can be used as a limit to investigate the complication of atelectasis. Early initiation of corticosteroid therapy was thought to be effective in the rapid recovery of atelectasis in our patient.

Reasons suggesting that young children are more prone to atelectasis are that in early childhood, the airways tend to be closed with smaller and larger peripheral airway resistance, the chest wall is more compliant, and collateral ventilation is not fully developed.[9] Although the clinical findings in middle lobe syndrome are variable and may be asymptomatic, chronic/recurrent cough, sputum, recurrent wheezing or recurrent/persistent pneumonia are the most common findings.[10] Since the symptoms are quite non-specific, the diagnosis is made late in about half of the patients.[10] Delays in taking chest X-ray in patients with non-specific, mild persistent symptoms may result in missed diagnosis of long-standing middle lobe syndrome. Findings such as mild fever, weight loss, malaise, chest pain or hemoptysis suggest complications associated with suppurative infection. The history usually includes having taken antibiotics, anti-mucolytic or anti-asthmatic drug therapy several times. The physical examination of the patients is usually normal, and rales and rhonchi localized to the middle lobe can be heard.[11]

In asthmatic patients, the airway lumen may be partially or completely obstructed due to viral infections, poor clearance of inflammatory debris, smooth muscle contraction, and edema in the bronchial wall.[1] Since the right middle lobe bronchus is separated from the main bronchus at a steeper angle and is shorter, drainage is more difficult. Therefore, the most affected lobe is the right middle lobe. In the differential diagnosis of patients with middle lobe syndrome, foreign body aspiration, cystic fibrosis, primary ciliary dyskinesia, primary immune deficiencies, neuromuscular diseases, mass causing external compression to the bronchus, lymphadenopathy or endobronchial tumors should be kept in mind.[1] No external or internal compression was detected in the bronchoscopy of the patient, no foreign body was observed, her tomography revealed no pathology in the lung parenchyma, bronchiectasis or enlarged lymph node, there was no pathology in the examinations carried out for tuberculosis and immune deficiency.

In the presence of concomitant infection in middle lobe syndrome, treatment is in the form of antibiotherapy including bacteria such as "*Streptococcus pneumoniae, Haemophilus influenzae, Moraxella catarralis*", bronchodilator and inhaled corticosteroid treatments for asthma patients. It is very important to ensure airway clearance in patients with chronic productive cough or mucus plug findings. Inhalation of 3-14% hypertonic saline or dry powdered mannitol together with chest physiotherapy may be beneficial. While flexible bronchoscopy is diagnostically important, recovery is seen in the majority of patients after bronchoalveolar lavage. Although mucolytic therapy is not recommended in asthma, there are studies showing that it is beneficial in middle lobe syndrome. In addition to its mucolytic effect, N-acetyl-cysteine also has strong antioxidant properties, and it has also been shown to have positive effects on preventing airway hypersensitivity, inflammation and goblet cell hyperplasia in asthma mouse models.[12] In our patient, in addition to the treatments for asthma attack, acetylcysteine nebul and postural drainage techniques applied together were thought to have an effect on the early recovery of atelectasis.

The prognosis of middle lobe syndrome is quite good. In a study in which 17 patients were evaluated, it was reported that mild obstructive airway symptoms persisted in 1/3 of the patients, and cylindrical bronchiectasis developed in only 1 patient in a 10-year follow-up.[13] In a study of 55 patients by Priftis et al.[10], the rate of bronchiectasis was reported as 27.3%. The development of bronchiectasis was found to be less in patients who underwent early bronchoscopy and bronchoalveolar lavage. In the 3rd and 6th month follow-ups of our patient, the physical examination was normal, no atelectasis or bronchiectasis was detected in the chest radiographs, and her regular follow-up is being continued.

In conclusion, middle lobe syndrome is a picture with a very good prognosis with early diagnosis and appropriate treatment, and it should definitely be kept in mind in patients with recurrent or persistent respiratory symptoms. It is especially important to regulate the treatment of asthma patients for disease control.

Ethics

Informed Consent: Permission was obtained from the patient's family.

Peer-review: Externally and internally peer-reviewed.

Authorship Contributions

Concept: B.B., Design: B.B., Data Collection or Processing: M.Y.M., T.S., İ.B., C.Ö., H.G., B.B., Analysis or Interpretation: B.B., Literature Search: B.B., Writing: M.Y.M., T.S., İ.B., C.Ö., H.G., B.B.

Conflict of Interest: No conflict of interest was declared by the authors.

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Case Report / Olgu Sunumu

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Postpericardiotomy Syndrome in an Infant with Down Syndrome Presenting with Recurrent Pericardial Effusion

Tekrarlayan Perikardial Effüzyon ile Prezente Olan Down Sendromlu Bebekte Postperikardiyotomi Sendromu

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Abstract

Postpericardiotomy syndrome (PPS) is a hypersensitivity reaction characterized by inflammation in pleural, pericardial or lung tissue following cardiac surgery or myocardial infarction. Clinically; fever, chest pain, findings related to pleural or pericardial effusion may be seen. In this case report, we wanted to present a case of Down syndrome who was followed up with PPS causing recurrent pericardial effusion after cardiac surgery for 5 months and was successfully treated by opening a pericardial window. PPS is one of the leading causes of post-cardiac morbidity in developed countries, despite all the advances in diagnosis and treatment. The earliest clinical finding is the development of pericardial effusion after the operation. Although pericardiocentesis is performed many times, PPS should be kept in mind in patients with recurrent pericardial effusion, and pericardial window opening should be considered in the treatment.

Keywords: Postpericardiotomy syndrome, pericardial effusion, recurrent effusion

Öz

Postperikardiyotomi sendromu (PPS) kardiyak cerrahi veya miyokard enfarktüsünü takiben plevral, perikardiyal veya akciğer dokusunda enflamasyonla karakterize bir hipersensitivite reaksiyonudur. Klinik olarak; ateş, göğüs ağrısı, plevral veya perikardiyal effüzyona bağlı bulgular görülebilir. Bu olgu sunumunda 5 aylık Down sendromu olan kardiyak cerrahi sonrasında tekrarlayan perikardiyal effüzyona yol açan PPS ile izlenen ve perikardiyal pencere açılarak başarılı bir şekilde tedavi edilen bir olguyu sunmak istedik. PPS, tanı ve tedavi yöntemlerindeki tüm gelişmelere rağmen gelişmiş ülkelerde kardiyak cerrahi sonrası morbiditenin başta gelen nedenlerindendir. En erken klinik bulgusu operasyon sonrası perikardiyal effüzyon gelişimidir. Birçok kez perikardiyosentez işlemi yapılmasına rağmen, tekrarlayan perikardiyal effüzyonu olan hastalarda PPS akılda tutulmalı, perikardiyal pencere açılması tedavide düşünülmelidir.

Anahtar Kelimeler: Postperikardiyotomi sendromu, perdikardiyal effüzyon, tekrarlayan effüzyon

Introduction

Postpericardiotomy syndrome is also defined as postacute myocardial syndrome or post cardiac injury syndrome. Postpericardiotomy syndrome is a clinical picture characterized by fever, pleuropericarditis and parenchymal infiltration, which develops within weeks following pericardial and/or myocardial injury. This syndrome has been described in the literature after myocardial infarction, cardiac surgery, blunt chest trauma, pacemaker implantation, coronary stent implantation, heart punctures and angioplasty.[1]

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Although the exact etiology of the syndrome is not known, it is accepted that it is an immune event caused by autoantibodies formed against antigens released after pericardial damage.[2]

Pericardial effusion is defined as an increase in fluid between the pericardial leaves. Various factors play a role in the etiology. Tuberculosis (primary cause especially in developing countries), viral infections and postoperative complications may cause effusion.[3]

In this study, we wanted to present a case of postpericardiotomy syndrome, which caused recurrent pericardial effusion resistant to medical treatment after cardiac surgery and required 4 pericardiocentesis and interventional tube insertion, with clinical and radiological findings.

Case Report

It was learned from the history of the patient, who was diagnosed with complete atrioventricular septal defect for the first time at the age of 4 months, that the patient was born prematurely, had Down syndrome, had body weight below the 3rd percentile in the follow-ups, and received thyroid hormone LT4 replacement therapy due to hypothyroidism. Since the atrioventricular valve structure was not suitable for full correction, pulmonary banding surgery was performed 2 weeks after the diagnosis.

A pericardial effusion of 11 mm was detected in the patient who applied to the outpatient clinic with respiratory distress 14 days after discharge. The patient was admitted to the pediatric cardiology service and methylprednisolone, furosemide and angiotensin converting enzyme inhibitor treatments were started.

The patient's blood tests taken at the time of hospitalization were as follows: White blood cell: 5400/mm^3, polymorphonuclear cell count: 2180/mm^3, hemoglobin: 11.2 g/dL, C-reactive protein: 4.9 mg/L, albumin: 3.1 g/dL, serum electrolytes: normal. Considering that the etiology of the effusion might be hypothyroidism, the patient's current drug treatment was continued, since the thyroid function test results were between normal intervals, as T4: 1.4 ng/dL and thyroid-stimulating hormone: 4.9 ng/dL. During the follow-up, the patient's pericardial effusion increased and respiratory distress occurred despite the treatment, and the patient's effusion was drained with an appropriate technique. After the procedure, it was determined with echocardiography that the effusion was not present and the condition of the patient was improved. When it was determined that the pericardial effusion increased to 7 mm on the 4th day following the procedure, ibuprofen was started at a dose of 10 mg/kg/day in addition to the steroid. Ten days after the first pericardiocentesis, the patient had tachycardia and tachypnea, and pericardiocentesis was performed for the second time, as a 14.5 mm effusion was observed on echocardiography. When tachycardia (170-180/min) and tachypnea developed during the follow-up of the patient, echocardiography was repeated. Since pericardial fluid did not impair ventricular functions on echocardiography, 55 mL of serous fluid was drained with pericardiocentesis for the third time. Pericardial fluid was in the nature of transudate, as in the first pericardiocentesis (Table 1). Thyroid function tests, metabolic tests, and immunological tests, which were ordered for etiology, were found to be normal. The bone marrow examination was normal in terms of malignancy in the patient, and no malignant cells were seen in the pericardial fluid cytology.

As the patient's respiratory distress continued, he was transferred to the intensive care unit. During the intensive care follow-ups, effusion was drained for the 4th time by puncture in the patient who developed tamponade clinic on the 10th day. There was no growth in the culture, gram staining was negative (Figures 1a, 1b). After clinically relieved patient re-developed effusion, a pigtail catheter with a 3F intraducer sheath was placed to drain the effusion permanently. Pericardial window was opened because the patient had repeated pericardiocentesis procedures for 4 times in total and effusion did not improve despite the medical treatment given (Figure 2). The patient was discharged asymptomatically on the 13th day of hospitalization.

Discussion

Postpericardiotomy syndrome is characterized by fever, chest pain, pericarditis, pleuritis and pneumonia, which usually occur after cardiac trauma.[4] Symptoms are observed in the first 3 weeks after cardiac operations. The two main symptoms of the syndrome are fever and chest pain.[5] Chest

Table 1. Fluid characteristics after pericardiocentesis

	Density	Fluid/serum protein	Fluid/serum lactate dehydrogenase	pH	Amount of drained fluid (milliliter)
1. pericardiocentesis	1014	0.4	0.5	7.4	20
2. pericardiocentesis	1015	0.4	0.5	7.5	25
3. pericardiocentesis	1015	0.3	0.4	7.5	55
4. pericardiocentesis	1013	0.4	0.4	7.4	30

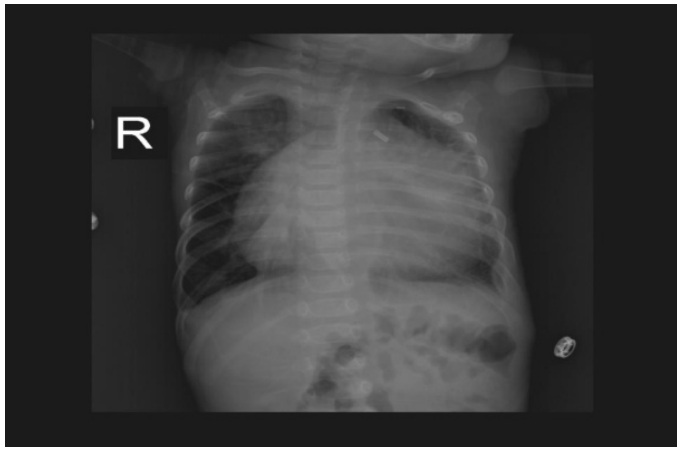

Figure 1a. Chest X-ray before pericardiocentesis

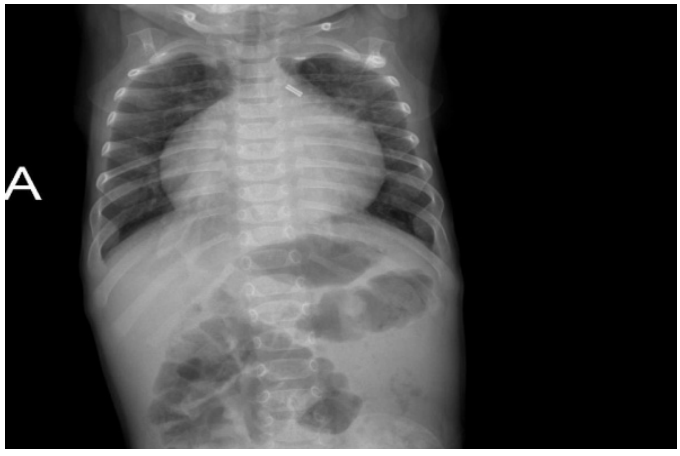

Figure 1b. Chest X-ray after pericardiocentesis

pain in infants can manifest itself as irritability. Almost all cases have pericardial friction rub and most of them have pericardial effusion.[6]

Systemic fluid retention, hepatomegaly, and hypoxemia may be observed. Laboratory examination usually reveals 10-20 thousand leukocytosis and moderately increased sedimentation rate.[7]

Some criteria are used in the diagnosis of postpericardiotomy syndrome. These are classified as major and minor criteria. Major criteria include the presence of pericardial or pleural friction rub, chest pain and fever over 38 degrees. The minor criteria include an increase in erythrocyte sedimentation rate, C-reactive protein level and leukocyte count. It is stated that the presence of two major and one minor criteria is sufficient for diagnosis after excluding the conditions such as pneumonia, heart failure, pulmonary embolism etc.[8]

Although postpericardiotomy syndrome has a self-limiting course in most cases, it carries a potential risk for cardiac tamponade due to the rapid accumulation of pericardial

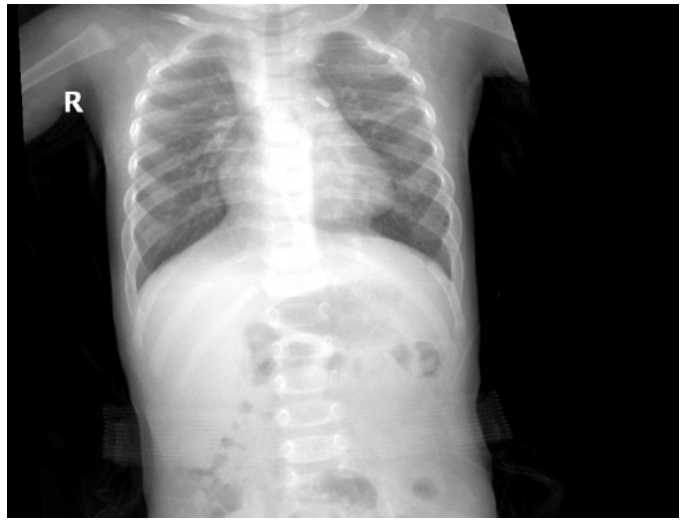

Figure 2. Control chest X-ray after pericardial window operation

fluid. Pericardiocentesis may be required, although it is not common, in the course of the disease. Although late recurrence may be seen, it is very rare. There is almost no data on this syndrome in childhood. In studies conducted to date, the presence of surgical trauma and autoimmune pathogenesis has been blamed as risk factors in the development of the disease.[8] Today, thanks to the developing intensive care units and advanced surgical techniques, the chance of complete surgical correction for congenital heart diseases has increased, which has also increased the incidence of postpericardiotomy syndrome. For this reason, it is very important to know the risk factor or factors for the development of postpericardiotomy syndrome, to prevent complications such as tamponade with close follow-up, early diagnosis and treatment in order to prevent the development of serious complications such as pericardial tamponade in patients with risk factors.[1]

For the reason for the development of pericardial effusion in our patient, it was thought that the patient had postpericardiotomy syndrome, considering the presence of subfebrile fever, irritability, and high acute phase reactants under ibuprofen in the first 3 weeks after the pulmonary banding operation. In addition, the presence of underlying hypothyroidism due to Down syndrome facilitated the development of pericardial effusion.

This syndrome should be considered in patients with recurrent pericardial effusion and congenital heart surgery, and rapid intervention is required to shorten the length of stay in the pediatric intensive care unit.

Ethics

Informed Consent: Verbal consent was obtained from the patient's family.

Peer-review: Externally peer-reviewed.

Authorship Contributions

Concept: Ş.K., M.U.Y., Design: Ş.K., U.A.Ö., Analysis or Interpretation: Ş.K, M.U.Y., U.A.Ö., M.T., Literature Search: Ş.K., M.U.Y., Writing: Ş.K.

Conflict of Interest: No conflict of interest was declared by the authors.

Financial Disclosure: The authors declared that this study received no financial support.

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A Case of Measles Initially Diagnosed as MIS-C in the COVID-19 Pandemics

COVID-19 Pandemisinde MİS-C ile Karışan Bir Kızamık Olgusu

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Abstract

Fever and rash are a common symptom combination in children. Etiological studies are carried out primarily for the most common diseases. For this reason, in the period of the new Coronavirus disease-2019 (COVID-19) pandemic, especially COVID-19-related multi-inflammatory syndrome (MIS-C) comes to mind in children with this combination. Measles infection was detected in an 18-month-old Syrian girl who was hospitalized with the diagnosis of fever, conjunctivitis, pneumonia, maculopapular rash during the COVID-19 pandemic period. The case died with pneumonia and septic shock. With this case, we wanted to emphasize that during the COVID-19 pandemic, and measles should also be considered in the differential diagnosis of MIS-C in cases with fever, maculopapular rash and conjunctivitis.

Keywords: Measles, COVID-19, MIS-C, pediatric intensive care, pneumonia

Öz

Çocuklarda ateş ve döküntü sık görülen belirti kombinasyonudur. Etiyolojik araştırmalar öncelikle en yaygın görülen hastalıklara yönelik yapılmaktadır. Bu nedenle yeni Koronavirüs hastalığı-2019 (COVID-19) pandemisi döneminde bu kombinasyonu taşıyan çocuklarda özellikle COVID-19 ilişkili multi-enflamatuvar sendrom (MİS-C) akla gelmektedir. COVID-19 pandemi döneminde ateş, konjonktivit, pnömoni, makulopapüler döküntü ile yatan 18 aylık Suriyeli kız olguda, kızamık enfeksiyonu saptanmıştır. Olgu pnömoni ve septik şok kliniği ile kaybedilmiştir. Biz bu olgu ile COVID-19 pandemisi döneminde özellikle ateş, makülopapüler döküntü ve konjonktivitle gelen olgularda MİS-C ayırıcı tanısında kızamığın da düşünülmesi gerektiğini amaçladık.

Anahtar Kelimeler: Kızamık, COVID-19, MİS-C, çocuk yoğun bakım, pnömoni

Introduction

The "Novel Coronavirus disease-2019 (COVID-19)" spread rapidly all over the world, starting from the city of Wuhan, Hubei province of China, at the end of 2019 and caused many deaths.[1] The World Health Organization (WHO) declared COVID-19 as a pandemic on 11 March 2020.[2]

COVID-19 in children usually has a mild course. However, towards the end of April 2020, serious cases of COVID-19-related illness in previously healthy children began to be reported in many countries. Later, the Center for Disease Control and Prevention and WHO defined COVID-19-associated multi-inflammatory syndrome (MIS-C), presenting with fever, maculopapular rash, conjunctivitis and various organ involvements in children.[3]

It is stated that many infectious and inflammatory conditions such as Kawasaki disease, other viral infections, sepsis, and

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vasculitis should be considered in the differential diagnosis of MIS-C. The presence of many diseases in the differential diagnosis complicates the diagnosis of MIS-C.[4]

Measles is a highly contagious rash disease caused by an RNA virus of the paramyxoviridae family.[5]

In measles, a prodrome period manifested by cough, cold, conjunctivitis and fever are followed by the formation of typical maculopapular rashes.[6] Measles infection, which can cause serious complications, can result in death, especially due to panencephalitis and pneumonia.[7]

Our aim in this article is to present an 18-month-old Syrian patient, who presented with fever, pneumonia, conjunctivitis, and maculopapular rash and died due to septic shock, and to remind the necessity of considering measles infection in the differential diagnosis of MIS-C.

Case Report

An 18-month-old female patient was admitted to our hospital because of high fever, diarrhea and insufficient nutrition that had been going on for 3 days. She was weak and had cachectic appearance. Her body weight was 7 kg (<3 percentile), her height was 72 cm (<3 percentile), her body temperature was 39.5 °C, her heart rate was 140/min/rhythmic, her blood pressure was 85/50 mmHg, her respiration rate was 36/min, and SpO_2 was 98% (at room air). The patient had dry oral mucosa, cracked lips, sunken eyeballs, and a maculopapular rash (Figures 1, 2). On respiratory examination, there were prominent rales in the bilateral middle zone on auscultation, and diaper dermatitis was observed in the genital area.

Although the anamnesis reliability was low due to the fact that the family was from Syria, it was learned that the child was healthy before, there was no one in the family with similar symptoms, and they lived in a tent. There was no history of contact person in terms of COVID-19. The patient was considered as a possible COVID-19 case due to fever and respiratory distress, and droplet and contact isolation precautions were taken and she was hospitalized.

In the initial laboratory tests, the results were as follows: leukocyte: 13.000/mm^3, 57% neutrophil dominance, lymphocyte 38.9%, Hb: 10.4 gr/dL, Htc: 33%, platelet: 57.8000/mm^3, blood glucose: 83 mg/dL, urea: 48 mg/dL, creatinine: 0.6 mg/dL, Na: 131 mmol/L, K: 4.26 mmol/L, Ca: 9.4 mg/dL, aspartate transaminase (AST) 67 U/L, alanine transaminase (ALT) 27 U/L, C-reactive protein 88 mg/L (0.10-2.80), procalcitonin 37.1 ng/L (0.04-0.1), Pz: 14 sec, aPTZ: 47.7 sec, international normalized ratio (INR): 1.18, D-dimer 1.540 µg/mL (0-440) troponin was <2.5 ng/L (negative), BNP: 155.28 ng/L (2-100). Complete urinalysis was normal, electrocardiogram was consistent with sinus tachycardia. There was infiltration in the bilateral lower zones on the chest X-ray (Figure 3a). Thorax computed tomography (CT) revealed peripheral and centrally located multifocal consolidated areas in the bilateral lung parenchyma and ground glass densities around it. Thorax CT was reported by the radiology department as consistent with COVID-19 pneumonia (Figure 3b).

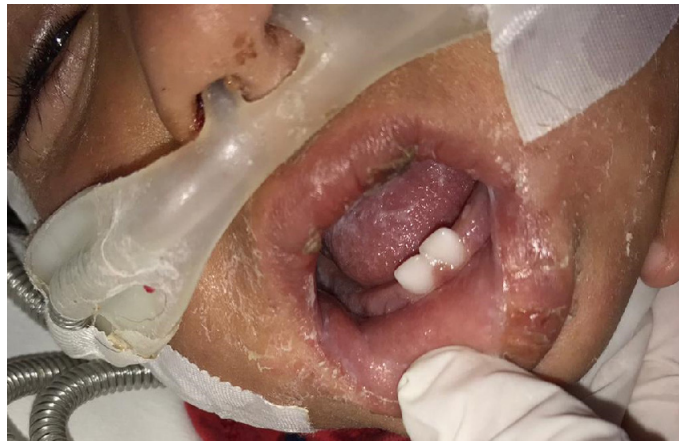

Figure 1. Koplik spot, dried and cracked lips

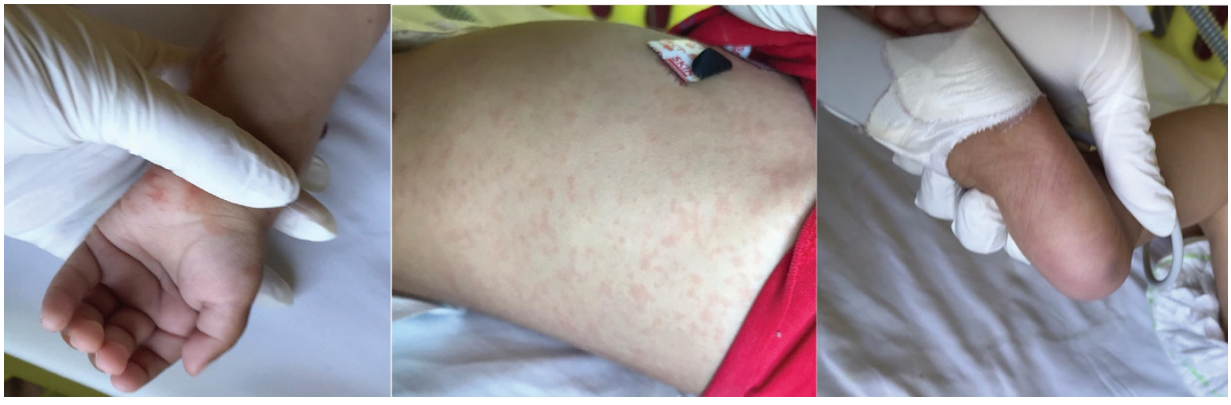

Figure 2. Exanthema appearance on the erythematous ground on the trunk

In the nasopharyngeal and oropharyngeal swab samples taken twice, COVID-19 polymerase chain reaction (PCR) was negative. High-flow nasal cannula (HFNC) oxygen therapy was initiated to the patient with respiratory distress. Considering pneumonia and possible COVID-19, oseltamivir, teicoplanin, cefotaxime and hydroxychloroquine treatments were started. The patient was hydrated. On the 3rd day of the follow-up, the patient developed increased respiratory distress and impaired consciousness; The child was intubated due to respiratory failure and was taken to the intensive care unit. Adrenaline infusion was started to the patient with fluid-resistant septic shock. In the examinations, leukocytes: 4.700/mm^3, lymphocytes: 3.000/mm^3, Hb: 7.5 gr/dL, Htc: 23%, platelets: 331.000/mm^3, blood glucose: 100 mg/dL, urea: 20 mg/dL, creatinine: 0.4 mg/dL, Na: 143 mmol/L, K: 4.1 mmol/L, Ca: 7.4 mg/dL , AST 86 U/L, ALT 21 U/L, C-reactive protein 18 mg/L (0.10-2.80), procalcitonin 16.9 ng/L (0.04-0.1), Pz: 13 sec, aPTZ: 43.6 sec, INR: 1.15, fibrinogen: 270 mg/dL, D-dimer: 2.380 µg/mL (0-440) troponin: <2.5 ng/L (negative), BNP: 200 ng/L (2-100). In the new chest radiograph, there was an increase in infiltration in the bilateral pericardiac area. On echocardiography, systolic functions were normal, jet flow in the mitral valve was 1st degree mitral insufficiency and there was no myocardial dysfunction.

In the differential diagnosis of the patient who was in the septic shock, toxic shock, Kawasaki disease, MIS-C, and viral eruptive diseases were considered. Immune globulin levels were within normal limits for age. CMV, HIV, hepatitis, EBV, and Parvovirus serologies were sent. Antibiotic therapy was changed to meropenem, vancomycin, and clindamycin. Intravenous immunoglobulin 2 g/kg and acetylsalicylic acid 5 mg/kg/day were started. The severe acute respiratory syndrome coronavirus-2 bronchoalveolar lavage PCR test for the patient who was followed up on mechanical ventilator was negative. Since she had fever, maculopapular rash, and pneumonia clinic and the vaccination status of the patient could not be known because she was from Syria, measles serology was sent. There was no growth in the blood, urine and bronchoalveolar lavage cultures of the patient. The patient died in the 12th hour of the intensive care monitorization. COVID-19 immunoglobulin M and G were found to be negative, measles IgM >200 U/L (>25) was high titer positive as postmortem. No pathology was detected in other viral serology tests. Based on the current findings, it was thought that the patient died due to complications of measles infection (pneumonia, septic shock).

Discussion

Fever, rash, conjunctivitis, pneumonia and shock seen in our patient made us think of the diagnosis of MIS-C in the current period. Because the patient was Syrian and her vaccination status was unknown, measles was suspected, but the diagnosis was made postmortem. Our patient died due to pneumonia and septic shock. This case is presented to emphasize that measles should not be forgotten among the rash diseases that can be confused with MIS-C.

In MIS-C cases, findings related to many systems are seen together with fever. These findings are not specific and the differential diagnosis includes non-infectious etiologies such as Kawasaki disease, severe acute COVID-19 infection, bacterial sepsis, toxic shock syndrome, other viral infectious diseases as well as oncological or inflammatory conditions.[8,9] Measles infection is one of the infectious viral rash diseases that should be considered in the differential diagnosis of MIS-C. Fever, cough, non-purulent conjunctivitis, diarrhea, and maculopapular rashes seen in measles infection are the most common findings in MIS-C. In the skin findings of MIS-C, papulovesicular, varicella-like rash and urticarial lesions can also be seen apart from a maculopapular rash. While koplik spot is seen specifically in oral mucosal involvement of measles infection, non-specific oral mucosal changes and dry red lips

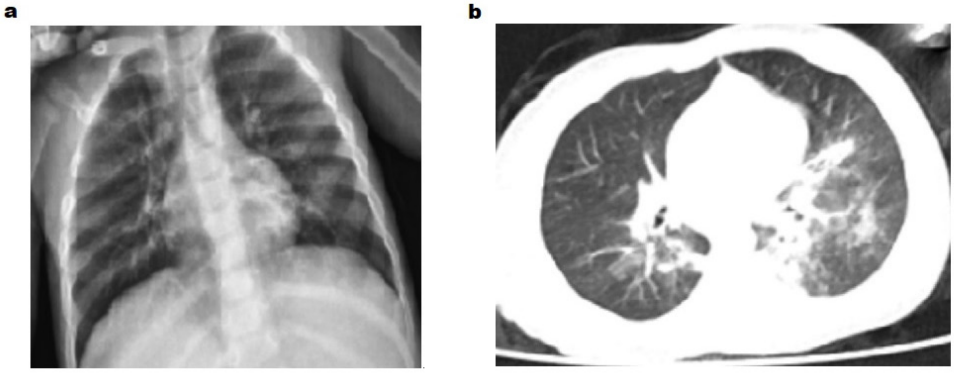

Figure 3. a. Pneumonic infiltration in bilateral lower zone in a posterior anterior chest X-ray, **b.** Consolidated area in bilateral lung parenchyma and ground-glass density image around it in thorax CT

CT: Computed tomography

Table 1. Comparison of the case in terms of MIS-C and measles

	Case	MIS-C	Measles
Findings	Fever, cough, diarrhoea, conjunctivitis, respiratory distress, rash, pneumonia, shock	Fever Two or more system involvement (rash, conjunctivitis, shock, abdominal pain, diarrhea, cough, dyspnea, cardiac dysfunction, renal-neurological-hematological findings)	Fever, malaise, cough, flu, conjunctivitis, diarrhea, pneumonia and maculopapular rash
Laboratory	Leukopenia, anemia high CRP and procalcitonin, hypoalbuminemia Measles, IgM positivity	High lymphopenia, neutrophilia, anemia, thrombocytopenia, CRP, D-dimer, procalcitonin, ferritin, fibrinogen, Hypoalbuminemia, high liver enzymes, High troponin and BNP, history of COVID-19 infection or contact (positive serology, antigen or PCR test)	Thrombocytopenia, leukopenia measles, IgM positivity
Radiology	Ground-glass appearance around the consolidated area in the lung parenchyma (interstitial pneumonia)	Diffuse consolidation, pleural effusion, ground glass opacities	Diffuse consolidated area in lung parenchyma consistent with interstitial pneumonia

MIS-C: Multi-inflammatory syndrome, COVID-19: Coronavirus disease-2019, PCR: Polymerase chain reaction, CRP: C-reactive protein, Ig: Immunoglobulin

are present in MIS-C. In addition, hand and foot edema, which is not seen in measles, can develop in MIS-C.[10] There are also similarities in laboratory and chest radiography findings of MIS-C and measles infection. Table 1 shows the comparison of our case in terms of MIS-C and measles findings. In the light of these findings, MIS-C was first considered in our patient due to the COVID-19 pandemic period, and measles infection was also investigated in the differential diagnosis.

The diagnosis of measles is made clinically. However, it is necessary to apply to the laboratory in different clinical courses. Serology (measles IgM positivity) is the most common laboratory method for diagnosing measles infection.[7] Due to the similarity of our case with MIS-C, the diagnosis could only be made postmortem with measles IgM positivity.

There is no specific antiviral drug against measles and its complications, but ribavirin treatment may be preferred for patients younger than 12 months, who have pneumonia due to measles and require respiratory support.[11] WHO recommends that all children with acute measles infection be given vitamin A.[12] Vitamin A acts as a kind of immune modulator and increases the antibody response.[13] Our patient died due to pneumonia and septic shock at the 12th hour of her intensive care hospitalization, and vitamin A treatment could not be given since the diagnosis was made postmortem.

Vaccination is the most effective way to prevent measles. The measles vaccine has been in the vaccine program since the 1970s. Since 2006, measles- mumps- rubella triple vaccine has been administered as a total of 2 doses in the 12th month and the first grade of primary education. As of July 1, 2020, it has been administered as an additional dose in the 9th-11th months in epidemic regions[14] WHO recommends that all routine vaccines be administered as planned during the COVID-19 outbreak. Our patient was thought to be unvaccinated because she was Syrian and lived in poor socioeconomic conditions.

Conclusion

Apart from MIS-C, measles infection should be considered in children presenting with fever, conjunctivitis, rash and respiratory symptoms during the COVID-19 pandemic period.

Ethics

Informed Consent: Written informed consent was obtained from the parents for the publication of their personal and clinical details with any identifying images in this study.

Peer-review: Externally peer-reviewed.

Authorship Contributions

Concept: D.L., A.B.A., Design: D.L, A.B.A., P.K., Ç.K., Data Collection or Processing: D.L., A.B.A., F.G.U., Analysis or Interpretation: A.B.A., B.G., D.Y.Ç., G.Ü., Literature Search: D.L., A.B.A., Writing: D.L., A.B.A.

Conflict of Interest: No conflict of interest was declared by the authors.

Financial Disclosure: The authors declared that this study received no financial support.

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Case Report / Olgu Sunumu

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Foreign Body of the Heart

Kalpte Yabancı Cisim

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Abstract

Foreign bodies in the heart is rare and can be life threatening. Early diagnosis and removal are very important. X-ray, computed tomography and echocardiography are the main diagnostic methods. In this article, a 14-year-old male patient who had chest pain for ten days, whose pain increased when lying down for the last two days, and who was found to have a foreign body needle in the heart in the pediatric emergency service is presented. It was learned that the needle was voluntarily inserted by our patient, who was diagnosed with attention deficit hyperactivity syndrome seven years ago and did not follow-up regularly. It was learned that the chest X-ray taken at another hospital 2 days before applying to our hospital was evaluated as normal. The needle that caused lung contusion, right pleural effusion, right ventricular contusion, right coronary artery injury and pericardial effusion was successfully removed by open heart surgery. It is presented to draw attention to the rarity of cases with a foreign body in the heart in the literature and the careful evaluation of the X-rays.

Keywords: Foreign body, heart, needle, child

Öz

Yabancı cisimlerin kalbe girmesi nadir olup, yaşamı tehdit edebilir. Erken teşhis ve çıkarılması çok önemlidir. Röntgen, bilgisayarlı tomografi ve ekokardiyografi başlıca tanı yöntemleridir. Bu yazıda on gündür göğüs ağrısı yakınması olan, son iki gündür uzandığında ağrısı artan ve çocuk acil servisinde kalpte yabancı cisim olarak iğne saptanan 14 yaşındaki erkek olgu sunuldu. İğnenin, yedi yıl önce dikkat eksikliği hiperaktivite sendromu tanısı alan ve takiplerine düzenli gitmeyen olgumuz tarafından kendisine isteyerek batırılmış olduğu öğrenildi. Hastanemize başvurmadan 2 gün önce gittiği klinikte çekilen akciğer grafisinin normal olarak değerlendirildiği öğrenildi. Akciğer kontüzyonu, sağ plevral effüzyon, sağ ventrikülde kontüzyon, sağ koroner arterde yaralanma ve perikardiyal effüzyona neden olan iğne, açık kalp ameliyatı ile başarıyla çıkarıldı. Literatürde kalpte yabancı cisim olan olgularının nadir rastlanması ve çekilen grafilerin dikkatli değerlendirilmesine dikkat çekmek için sunuldu.

Anahtar Kelimeler: Yabancı cisim, kalp, iğne, çocuk

Introduction

Chest pain in children is a common cause of emergency admission and is generally divided into two main groups as traumatic and non-traumatic. The most common source of chest pain due to non-traumatic causes is musculoskeletal diseases, and most of them are not life-threatening. Diseases of the respiratory system, cardiovascular system, gastrointestinal system, and nervous system can be seen less frequently. The most feared pains of cardiac origin are rarely seen in children.[1]

The penetration of foreign bodies into the heart is life-threatening and is very rare. Early diagnosis and removal of them are very important for these rare cases.[2] Foreign bodies reach the heart in three ways. It may remain in the heart after direct penetration, intravenous migration, or medical procedures. With local penetration, it can be a

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firearm or trauma-induced bullet, shrapnel, needle, etc.[3] It is rare for the sewing needle to accidentally penetrate into the heart. The needle can migrate rapidly between tissues and cause serious consequences such as hemopericardium, hemothorax, pneumothorax, and cardiac tamponade.[4] The main diagnostic methods are X-ray, computed tomography, and echocardiography.[3] In this article, a case admitted for chest pain and found to have a needle penetrated as a foreign body in the heart is reported since these kinds of cases are rarely found in the literature.

Case Report

A previously healthy 14-year-old male patient was brought to our pediatric emergency clinic by his family due to chest pain. In his history, it was learned that the chest X-ray taken at a private health center due to the complaint of chest pain lasting for 10 days was normal and the chest pain increased when he was lying down for two days. In his history, it was stated that he had been diagnosed with attention deficit disorder in the 2nd grade of primary school, but he had not used medication and had not been followed up regularly. No significant finding was seen in the family history. On his initial physical examination, the Glasgow Coma score was 15. The patient had no fever, was normotensive, and had an SpO_2 of 97% at room temperature. No trace was detected on the skin of the patient's chest wall. In the respiratory system examination, his both lungs were equally involved in respiration, respiratory sounds were normal, and there was no respiratory distress. In the cardiovascular system examination, heart sounds were normal, S1 and S2 were rhythmic, and S3 was absent. The patient's biochemistry, hemogram, cardiac enzymes, and coagulation parameters were found to be normal. Electrocardiogram revealed normal sinus rhythm. First of all, posterior-anterior and lateral chest radiographs was taken and the needle was visualized (Figure 1). In bedside echocardiography, a band-shaped hyperechoic area extending to the right ventricle and pericardial fluid without any signs of compression around the right ventricle and right atrium were detected (Figure 2). In order to determine the intrathoracic location of the foreign body, non-contrast thorax computed tomography was performed. Linear density that may belong to the foreign body extending towards the pericardial space in the right paracardiac area and possible contusional ground glass areas in the surrounding lung parenchyma, a mildly high-density appearance reaching 6 mm in thickness at the pericardial level and minimal pleural effusion on the right were detected (Figure 3). The patient, who had a significant increase in pericardial fluid during clinical follow-ups, was taken to the emergency operation by pediatric cardiovascular surgery after excluding surgical contraindications. It was planned to remove the foreign body by open heart surgery under cardiopulmonary bypass. The pericardium was seen to be lacerated by emergency median sternotomy under general anesthesia and approximately 300 cc of hemorrhagic fluid was drained. A 4 cm long needle, which created a focus of bleeding and laceration on the acute margin surface of the right ventricle and the lateral wall of the right coronary artery, was detected. A foreign body was removed. The right ventricle, right coronary artery and pericardium were repaired. The patient was discharged after two days of intensive care and 5 days of hospitalization. He was consulted with a child psychiatrist during his hospitalization. During the psychiatry control, the parents stated that they did not know how the needle entered the body. The patient, on the other hand, said that he pricked the needle because he was angry with his mother. Borderline mental retardation and accompanying

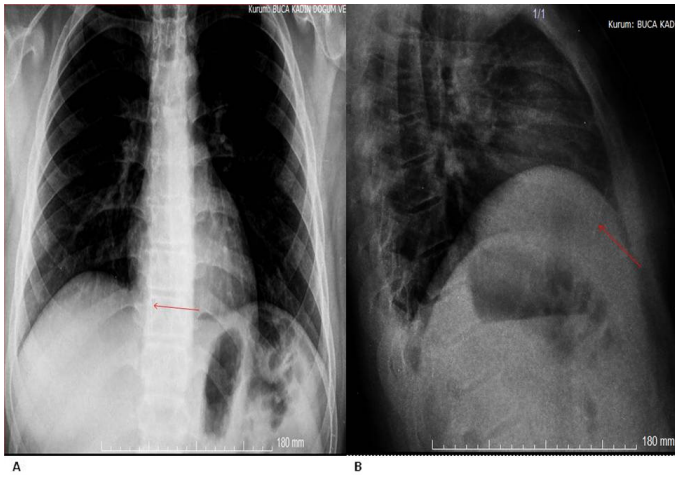

Figure 1. A high-density foreign body superposed on the anterior mediastinum in the area marked with the arrow in the posterior-anterior (A) and lateral (B) chest X-ray images

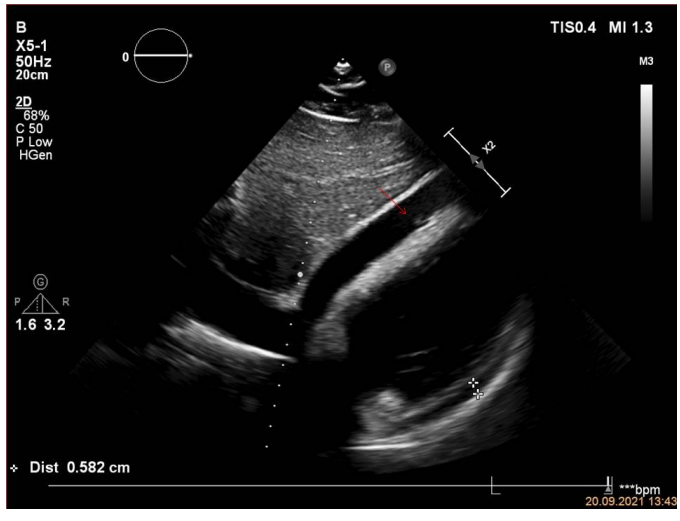

Figure 2. Foreign body in the right ventricle and its acoustic shadow are seen in the area marked with the arrow in the transthoracic echocardiography image

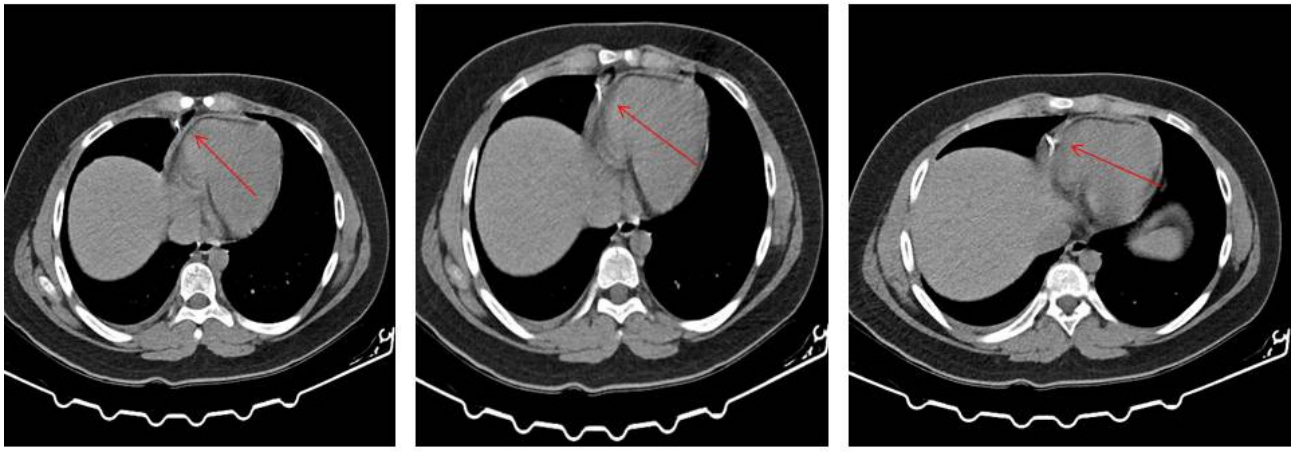

Figure 3. Right pleural effusion indicated by arrow and linear high-density foreign body adjacent to the right ventricle are seen in the heart computed tomography image

adjustment problems were found in the patient. His history of self-harm was deepened and it was determined that it was the first attempt since there were no previous incision marks on the skin. Citalopram 20 mg was started. After discharge, psychiatry and cardiology controls were performed at the 1st week, 1st month, and 2nd month. No sequela was observed in the patient. Written informed consent was obtained from the patient and his family.

Discussion

To the best of our knowledge, penetrating heart injury caused by self-inserted needles is rare.[5] Foreign bodies in the heart can present with a wide variety of symptoms. Physicians should be aware of these rare complications, which can be fatal. Foreign bodies in the heart are rare, they can reach the heart by accident or traumatic ways. Most reported foreign bodies are catheter fragments or broken guidewires.[6] Foreign bodies that are self-inserted into the chest wall are usually caused by suicide attempts, mental illnesses, or substance abuse.[7,8]

If left untreated, it can cause hemothorax due to needle movement, cardiac tamponade and pneumothorax. In addition, thrombus may form and cause repetitive embolization. Rarely, valve insufficiency or infective endocarditis may develop.[9] Diagnosis of cardiac foreign bodies can be made by radiological examination. Echocardiography is superior to other types of radiological examinations in that it directly visualizes the intracardiac structure, evaluates heart function, and does not contain radiation.[5] Echocardiography has almost 100% sensitivity in assessing the size, location and mobility of foreign bodies. In the review performed by Soren et al.[10], depression was reported to be the most common psychiatric disorder in 40 cases in the literature, and mental retardation was found in only 2 cases. The most common presenting symptom was chest pain, as in our case. Unlike our case, intracardiac foreign body is more common in female patients. A single needle was detected in approximately 70% of the cases, and second attempts have been reported very rarely. Most of these patients are treated with surgery. However, mortality has been reported at the rate of 5%.[10] Especially sharp-edged foreign bodies can cause serious complications in the heart, and early removal of the needles is recommended to avoid further damage to the heart. However, there is no consensus on surgical procedures for removing the metallic foreign body in the heart. Foreign bodies can sometimes be directly removed by minimally invasive surgery[5] or, as in our case, by invasive intervention.[11]

Conclusion

Foreign bodies in the heart can have fatal consequences. Intracardiac foreign body due to self-injury is mostly seen as a result of psychiatric diseases. Intrathoracic foreign body should be considered in the differential diagnosis of patients who present with chest pain and have or are thought to have an underlying psychiatric disease. In such a case, careful evaluation of the medical history, physical examination, and chest X-ray is very important.

Ethics

Informed Consent: Written informed consent was obtained from the patient and his family.

Peer-review: Externally peer-reviewed.

Authorship Contributions

Concept: G.Y., E.G., E.A., Ü.D., M.B.B., M.A., Design: G.Y., E.G., E.A., Ü.D., M.B.B., M.A., Data Collection or Processing: G.Y., E.G., E.A., Ü.D., M.B.B., M.A., Analysis or Interpretation: G.Y., E.G., E.A., Ü.D., M.B.B., M.A., Literature Search: G.Y., E.G.,

E.A., Ü.D., M.B.B., M.A., Writing: G.Y., E.G., E.A., Ü.D., M.B.B., M.A.

Conflict of Interest: No conflict of interest was declared by the authors.

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Review / Derleme

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Nutrition in Pediatric Intensive Care Units

Çocuk Yoğun Bakım Ünitelerinde Beslenme

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Abstract

The limited energy stores and fast metabolism of sick children in the intensive care unit, as well as the intense stress caused by the critical illness, reveal the importance of nutrition. Adequate and balanced nutritional care for critically ill children improves the clinical course and prognosis. In order to provide appropriate nutritional support, it is important to evaluate the nutritional status of the critical patient in detail and integrity. In the critically ill child with a functioning gastrointestinal tract, the enteral route is preferable to parenteral nutrition. In cases where the digestive system is not used completely or adequately, parenteral nutrition should be applied.

Keywords: Pediatric intensive care, nutrition, malnutrition

Öz

Çocuk yoğun bakım ünitelerinde izlenen kritik hasta çocukların kısıtlı enerji depoları ve hızlı metabolizmaları yanı sıra kritik hastalığın yarattığı yoğun stres durumu beslenmenin önemini ortaya koymaktadır. Kritik hasta çocuklara yönelik yeterli ve dengeli nutrisyonel bakım hastalık sürecini olumlu yönde etkiler. Uygun beslenme desteğinin sağlanabilmesi için kritik hastanın beslenme durumunun değerlendirilmesinin ayrıntılı ve bütünlük içerisinde yapılması önemlidir. Sindirim sistemi işlev gören kritik hasta bir çocukta enteral yol parenteral beslenmeye tercih edilmelidir. Sindirim sisteminin tümüyle ya da yeterince kullanılmadığı durumlarda ise parenteral beslenmeye başvurulmalıdır.

Anahtar Kelimeler: Çocuk yoğun bakım, beslenme, malnutrisyon

Introduction

It is known that nutrition is among the important factors affecting morbidity and mortality in critically ill patients followed in pediatric intensive care units. Children need adequate and balanced nutrition not only for their basal metabolism, organ functions and daily movements, but also for their growth. For this reason, ensuring optimal nutrition of patients treated in pediatric intensive care units forms the basis of patient care. While malnutrition of the critically ill patient causes an increase in the frequency of infection, prolongation of the wound healing process, deterioration in digestive system functions, secondary immunodeficiency, prolonged stay on mechanical ventilator and hospitalization, thus increased morbidity and mortality, overnutrition will also cause hyperglycemia, hyperlipidemia, fatty liver, congestive heart failure due to volume overload, increase in respiratory

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workload due to increased carbon dioxide production, prolongation of mechanical ventilation, and increase in morbidity and mortality. Nutrient requirements should be able to meet the needs of the growing organism and should be meticulously planned individually after evaluating the current nutritional status for each patient.

Evaluation of Nutritional Status

Malnutrition is defined as a nutritional disorder that causes measurable adverse effects on body mass and functions due to a deficiency or excess of protein, energy and other nutrients. Children's macronutrient reserves are lower than adults, while their energy needs are higher. Malnutrition is reported to be as high as 35-72% in critically ill children during hospitalization in the intensive care unit.[1,2] In addition, compared to baseline values, a decrease in nutritional parameters is observed in approximately one third of the patients during intensive care hospitalization.[3] It is known that both the nutritional status at the time of admission and the nutritional support given in the intensive care unit are effective on the prognosis of the patients. Negative nutritional status is associated with increased hospital-associated infection, mortality, prolonged intensive care stay and duration of ventilation.[4,5] While malnutrition is more common in this group, overnutrition is also associated with increased morbidity. Evaluation of nutritional status and providing adequate and appropriate nutrition are very important, especially in the management of critically ill children. In patients hospitalized in the pediatric intensive care unit, the nutritional status should be evaluated in detail as soon as possible (in the first 48 hours at the latest).[6] It is recommended to repeat the nutritional assessments of all patients once a week in terms of nutritional problems that may develop during the intensive care unit stay.

When assessing the need for any nutritional support, both the current nutritional status should be evaluated and the underlying causes of nutritional deficiency should be examined. This process includes a detailed dietary history, physical examination, and anthropometric measurements (weight, height, head circumference in young children). In addition, in some cases, measurement of skinfold thickness and mid-upper arm circumference can be used to determine body composition. Anthropometric measurements should be done carefully and appropriately and the measurements should be evaluated in standard growth charts. It is appropriate to use a corrected age up to 2 years in the evaluation of the measurements of premature babies. In patients with ascites and edema, such as chronic liver disease and nephrotic syndrome, anthropometric measurements that are not affected by these, such as middle-upper arm circumference and triceps skinfold thickness, should be preferred. Head circumference of infants younger than 36 months should also be measured. The patient's nutritional status is evaluated by calculating the body mass index (BMI) Z-score (<2 years, weight for height Z-score) by measuring the body weight and height of the patient during hospitalization in the pediatric intensive care unit. If the patient's height is unknown, the patient's nutritional status is evaluated by calculating the weight Z-score for age.[6,7] There are different classifications for assessing the degree of malnutrition. The GOMEZ classification uses weight for age, the Waterlow classification uses height for age, and the WHO classification uses weight for height (Table 1).

Along with malnutrition, obesity has also become a serious health problem worldwide. The most accepted method in obesity screening is BMI calculation. Abnormal BMI is evaluated in specific percentile curves for age and sex. Children over two years of age are considered overweight if their BMI is above the 85th percentile, obese or overweight if they are above the 95th percentile, and morbidly obese if they are above the 99th percentile.

Critically ill children have a high risk of malnutrition during their hospitalization in the intensive care unit, as well as at admission. Disease-related malnutrition in children is associated with nutrient loss, increased energy consumption, decreased food intake, or altered food use. Early recognition and intervention of malnutrition or preventing its development by foreseeing it will both contribute to the recovery process of the patient's primary disease and reduce morbidity and mortality. For this reason, it is important to evaluate the nutritional status of inpatients at frequent intervals. This evaluation can be made with nutrition-oriented physical examination considering nutritional history, changes in anthropometric measurements, and functional status.

Numerous nutritional screening methods have been developed to predict malnutrition that may develop and to identify malnutrition risk early. Some of them are the pediatric

Table 1. Gomez, Waterlow and WHO classifications

Degree of malnutrition	Weight for age (%) (Gomez)	Height for age (%) (Waterlow)	Weight for height (%) (WHO)
Normal	>90%	>95%	>90%
Mild	75-90%	90-95%	81-90%
Moderate	60-74%	85-89%	70-80%
Severe	<60%	<85%	<70%

Yorkhill malnutrition score (PYMS)[8], screening tool for risk of impaired nutritional status and growth (STRONGkids)[9], pediatric nutrition screening tool (PNST)[10] and screening tool for the assessment of malnutrition in pediatrics (STAMP).[11] Of these methods, PYMS and STRONGkids can be preferred due to ease of application, standardization, high specificity and sensitivity. PYMS is a 4-step screening method, which can be applied between the ages of 1 and 16 years and one of whose criteria is BMI. When the total risk score is calculated as 0, there is no risk and a repeat PYMS is recommended after 1 week. If the score is 1, the test is repeated after 3 days. Cases with a score of >2 are in the risk group for malnutrition and immediate evaluation is required (Table 2). STRONGkids can be applied between the ages of 1 month and 18 years and it consists of 4 separate steps. When the total risk score is calculated as 0, nutritional intervention is not required, weekly evaluation is recommended. For those with a score between 1 and 3, weight control should be done twice a week, taking into account the nutritional intervention. Cases with a score of 4-5 are in the risk group in terms of malnutrition and it is recommended to be evaluated immediately (Tables 2, 3).

Timing in Enteral and Parenteral Nutrition

The delivery of nutrients to the digestive organs through the oral route or gastric tubes is called enteral nutrition. Enteral nutrition (EN) should be preferred for the delivery of nutrients in pediatric intensive care units (PICU). EN meets the energy and protein needs of the patient, and it also provides additional contributions such as protecting the integrity of the intestine, preventing bacterial translocation and creating a trophic effect in the intestinal villi. It is also more economical than parenteral nutrition (PN) and is better tolerated by patients.[12] If the patient is hemodynamically and respiratoryly stable, enteral feeding can be started within the first 24-48 hours after admission to the PICU, if there are no contraindications for enteral nutrition. The amount of nutrition should be increased in a way that takes into account food intolerance with a stepwise feeding algorithm.[6,7]

EN contraindications:

- Increased vasoactive/inotropic support
- Hemodynamic instability with ongoing fluid resuscitation
- Suspicion or diagnosis of necrotizing enterocolitis

Table 2. Pediatric Yorkhill malnutrition score (PYMS)*

Is BMI below the lower limit value?	No Yes	0 2
Is there a loss in body weight recently?	No Yes	0 2
Has there been a decrease in food intake in the last one week?	No Yes, food intake decreased in the last 1 week Yes, no food intake in the last 1 week	0 1 2
Will next week's nutrition be affected by current hospitalization/ health condition?	No Yes, decreased food intake and/or increased nutrient requirements and/or increased losses Yes, no food intake	0 1 2

*When the total risk score is calculated as 0, there is no risk and a repeated PYMS is recommended after 1 week. If the score is 1, the test is repeated after 3 days. Cases with a score of >2 are in the risk group in terms of malnutrition and should be evaluated immediately, BMI: Body mass index

Table 3. *Screening tool for risk of impaired nutritional status and growth

1-Subjective clinical assessment (1 point) Is the patient in a poor nutritional status (diminished subcutaneous fat and/or muscle mass and/or hollow face)?	No Yes	0 1
2-High-risk disease (2 points) Is there an underlying illness with a risk of malnutrition or expected major surgery?	No Yes	0 2
3-Nutritional intake and losses (1 point) Is one of the following items present? Excessive diarrhea (>5 times/day) and/or vomiting (>3 times/day) in the last few days Reduced food intake in the last few days Previously advised nutritional intervention Inability to consume adequate food because of pain	No Yes	0 1
4-Is there weight loss or no weight gain during the last few weeks/months (for infants aged <1 year)?	No Yes	0 1

*When the total risk score is calculated as 0, nutritional intervention is not required, weekly evaluation is recommended. For those with a score between 1-3, weight control should be done twice a week, taking into account the nutritional intervention. Cases with a score of 4-5 are in the risk group in terms of malnutrition and it is recommended to be evaluated immediately

- Mechanical intestinal obstruction
- Significant gastrointestinal bleeding
- Ischemic intestine

EN can be applied in pediatric intensive care patients if no fluid loading has been performed in the last two hours and the general condition of the patient is stable despite receiving inotropic therapy. If active fluid replacement or general resuscitation is performed, and the general condition of the patient is not stable despite the use of more than one vasoactive agent, EN is not continued.[6,7] It is not recommended to start PN within the first 24 hours in the PICU. PN should be given to patients for whom enteral feeding is contraindicated or inadequate. The initiation time of PN should be individualized according to the patient, and PD can be delayed for up to one week after admission to the PICU for patients who are in a normal nutritional state at the time of hospitalization.[6,7] However, if patients with malnutrition or a high risk of nutritional deficiency cannot be fed enterally during hospitalization in the PICU, it is recommended that PN can be started within the first week.[6]

EN

a- Energy requirement

Indirect calorimetry is the first choice for determining energy needs. If indirect calorimetry cannot be measured, the Schofield and WHO equations can be used. Stress factors should not be added when using these equations. During EN, the aim should be to provide at least 2/3 of the energy requirement calculated at the end of a week.[6]

Schofield equation (Kcal/day):

<3 years	Men: 60.9 x weight (kg) - 54
	Women: 61.0 x weight (kg) - 51
3-10 years	Men: 22.7 x weight (kg) + 495
	Women: 22.5 x weight (kg) + 499
10-18 years	Men: 17.5 x weight (kg) +651
	Women: 12.2 x weight (kg) + 746

When calculating the energy need of the patients, factors that decrease or increase the energy need should be taken into consideration. In case of obesity in the patient, energy and protein requirements should be calculated according to the ideal weight for the patient's age.

Factors that increase energy need

- Fever
- Sepsis
- Burn
- Trauma
- Cardiac/pulmonary disease
- Major surgery

Factors that reduce energy need

- Sedation
- Mechanical ventilation
- Paralysis
- Pentobarbital coma

b- Protein need

0-2 years: 3 g/kg/day protein intake provides positive nitrogen balance

2-13 years: 2 gr/kg/day protein intake provides positive nitrogen balance.

At least 1.5 g/kg/day of protein should be given to patients to ensure positive nitrogen balance in patients followed up in the pediatric intensive care unit.[6]

c- Selection of enteral feeding method and route

A stepwise algorithmic approach should be applied in the selection of enteral feeding method and route. The application of algorithms that start with a small amount and gradually increase the EN will ensure that the feeding is done safely and that the goals are achieved. A multidisciplinary nutrition support team should be established for nutritional practices in the PICU. A dietitian responsible for the intensive care unit together with the pediatric intensive care team must be in this team. After deciding to start EN, the route in which the nutrients will be given should be determined. EN can be performed by the gastric or postpyloric route. The first choice for EN in patients followed up in the PICU is gastric feeding.[6]

Gastric route

- Orogastric/nasogastric tube
- Gastrostomy

Postpyloric route

- Nasojejunal/basoduodenal tube
- Jejunostomy

Advantages of gastric feeding

- Physiological
- Anti-microbial effect
- Trophic effect (hormonal)
- Being a reservoir
- Ability to provide hyperosmolar feeding due to osmotic tolerence
- Being suitable for bolus feeding and not requiring the use of a pump.
- Easy to place and allowing free activity

Risks of gastric feeding

- Gastroesophageal reflux and aspiration

Postpyloric feeding using a nasoduodenal or nasojejunal tube should be preferred in cases in which gastric feeding cannot be tolerated and in cases with very high aspiration risk.

Indications for postpyloric nutrition

- Aspiration history
- Gastroparesis
- Gastric outlet obstruction
- Previous gastric surgery

Disadvantages of postpyloric nutrition

- Difficulty in placement
- Able to gradually increase nutrition with continuous infusion
- Inability to apply high-energy-hyperosmolar nutrition
- Lack of taste/oral motor function development

Nasoduodenal/nasojejunal tube

The most common indications are aspiration risk and gastroparesis. Only continuous feeding can be done with the postpyloric route. Bolus feeding cannot be performed. The most important disadvantage of postpyloric feeding is the difficulty of placing the nasoduodenal and nasojejunal tube, which also causes a delay in the initiation of feeding. The following methods can be used for the placement of postpyloric feeding tubes. It is aimed to place the transpyloric feeding tube on the distal to the ligament of Treitz.

Nasoduodenal/nasojejunal tube placement methods

- Blind method using peristaltism or tube weight
- Fluoroscopic
- Endoscopic
- With medication (metaclopromide, erythromycin)

Gastrostomy/Jejunostomy

While it is appropriate for short-term EN to be made by tube, enterostomy tubes placed by endoscopic or surgical method are used in patients who need long-term nutrition. Considering the patient's underlying disease, gastrostomy/jejunostomy is indicated in cases for which EN is required for more than 6-12 weeks.[13] Gastrostomy can be opened through percutaneous endoscopic, radiological (fluoroscopic), surgical or laparoscopic surgical methods. The algorithm for deciding the EN location and method is given in Figure 1.

Nutritional method

Feeding can be performed as intermittent bolus or continuous infusion. Bolus feeding is a feeding made in specific amounts at specific intervals. Continuous nutrition, on the other hand, is the delivery of nutrients 24 hours a day as a continuous infusion of nutrients at a constant rate via a pump. There is no recommended method in the first place, as there is insufficient evidence that one of the two feeding methods is superior to the other.[6,14]

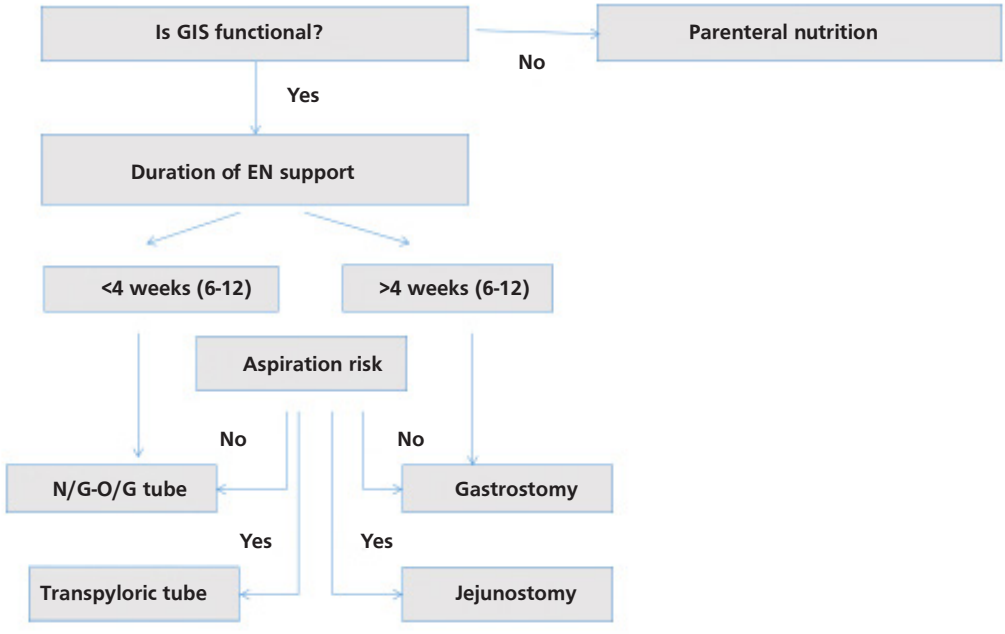

Figure 1. Algorithm for deciding the place and method of enteral nutrition

Features of bolus feeding:

- It can imitate meals, be supplement
- It is more physiological
- It may not require a pump
- It provides freedom between meals
- It may predispose to osmotic diarrhea
- It is not suitable for jejunal feeding

Features of continuous feeding:

- Slow infusion may increase tolerance and absorption.
- It can be given during the night not to prevent daytime activity.
- It promotes intestinal adaptation with mucosal stimulation.

When bolus or continuous feeding is applied, it will be appropriate to use feeding algorithms, such as starting the feeding with a small amount and increasing it gradually.

d- Nutritional intolerance

One of the main reasons for termination or interruption of EN in the pediatric intensive care unit is nutritional intolerance, which is generally assessed by gastrointestinal symptoms and/or gastric residual volume (GRV).

GIS findings of nutritional intolerance

- Vomiting/nausea
- Diarrhea (>2 mL/kg)
- Abdominal distention
- Abdominal discomfort
- Constipation
- Aspiration
- Gastrointestinal bleeding

Gastric residual volume

Measurement of the amount of residue cannot be a clinical indicator of gastric emptying or an accurate indicator of nutritional intolerance. The correlation between the clinical findings of nutritional intolerance, such as abdominal distention and decreased bowel sounds, and the amount of residue is weak. The correlation between radiological findings such as air-fluid levels and the amount of residue is also not significant. A low GRV will not guarantee tolerance, nor can a normal GRV rule out intolerance. For these reasons, routine GRV testing is not recommended to show nutritional intolerance.[15-17] However, it is still widely used in practice in many PICUs. Although there is no broad agreement on how much GRV means a nutritional intolerance, a GRV of ≥150 mL or >3-5 mL/kg is considered significant.

There are also centers that consider GRV more than half of the previous feeding amount in bolus feeding and more than 2-hour total feeding rate in continuous feeding as significant.[18]

Situations for which feeding should be interrupted with gastrostomy or jejunostomy include the presence of pain during feeding, fresh bleeding, leakage of gastric contents, prolonged or severe pain after the procedure, and physiological instability.[19]

e- Pediatric enteral nutrition products and selection of product

Human breast milk, age-appropriate formulas and age-appropriate enteral products can be used for enteral nutrition. For enteral nutrition, polymeric products are most often used. Unless there is a contraindicated situation, polymeric products should be the first choice in the nutrition of critically ill patients.[7] In the following special cases, oligomeric and monomeric products can be used.[19] In order to reach nutritional goals in children with fluid restriction, products with high protein and energy concentrations can be preferred (Table 4).

The following factors should be considered in the selection of enteral products.

- Age
- Degree of nutrient requirement
- Intestine, liver and pancreas functions
- Presence of food intolerance or allergies
- Enteral product delivery route and method
- Enteral product features
- Taste, cost, osmolarity, renal solute load

Standard polymeric products contain complete protein, complex carbohydrates and long chain fatty acids. They are isoosmolar solutions containing 1 kcal energy in one milliliter and they meet all needs because their nutritional content is balanced. Polymeric products can be classified as follows.

Classification of Polymeric Products

According to energy content

- Standard polymeric products
- High energy polymeric products

According to age group

- Infantile period
- 1-12 years
- ≥12 years

According to fiber content

- Fibre containing products
- Fibre-free products

Oligomeric Products

Oligomeric products are the products that have been hydrolyzed to varying degrees. It is recommended in cases

Table 4. Nutritional product recommendations according to age and bowel functions of patients*	
First 1 year of age	
Normal bowel function	**Bowel dysfunction**
Human breast milk	Human breast milk
Standard infant formula at >6 month	Lactose-free formula Semi-elemental formula Highly hydrolyzed formula Elemental formula Modular products if no formula can be tolerated
1-6 years of age	
Normal bowel function	**Bowel dysfunction**
Standard pediatric formula +/- fiber 1-1.5 kcal/mL	Semi-elemental/elemental pediatric formula 1 kcal/mL, can be increased to 1.5 kcal/mL if necessary
>10 years of age	
Normal bowel function	**Bowel dysfunction**
Standard pediatric formula/product may continue to be used. Adult products can be used.	Semi-elemental pediatric formula Elemental pediatric formula Adult semi-elemental/elemental products
*Adapted from the references of[20,21]	

where complete protein cannot be tolerated. There is no need for pancreatic and bile secretion.

Content;

- Protein; dipeptide or tripeptide
- Carbohydrate; glucose polymers-maltodextrin, disaccharides
- Fat; MCT (30-50%) - LCT
- They are expensive and taste bad.

Monomeric Products

They are fully hydrolyzed products (aa based). They are recommended in cases where complete protein cannot be tolerated. There is no need for pancreatic and bile secretion.

Content;

- Protein; free amino acids
- Carbohydrate; glucose polymers-maltodextrin, disaccharides
- Fat; MCT (30%)-LCT
- They have high osmolarity
- They are expensive and taste bad.

Indications for Using Oligomeric and Monomeric Product

- Malabsorption Syndromes
- Short bowel syndrome

- Intestinal insufficiency
- Chronic congenital diarrhea

- Pancreatic Diseases

- Cystic fibrosis
- Acute-chronic pancreatitis

- Chronic liver diseases
- Crohn's disease complicated by fistula
- Cow's milk protein allergy

Immune nutrition is defined as practices for reducing inflammation by using various dietary components (Arginine, glutamine, etc.) to correct the immune response in patients followed in the pediatric intensive care unit and replacing the nutrients that have been reduced due to stress. However, since the benefit of immune nutrition has not been proven yet, immune nutrition is not recommended in intensive care patients.[6,7] There is also insufficient evidence for the use of prokinetics to facilitate gastric emptying and prevent nutritional intolerance.[7]

EN monitoring is given in Table 5, and possible complications and precautions are listed in Table 6.

Parenteral Nutrition

In cases in which the digestive system cannot be used completely or adequately, the delivery of nutrients necessary for life via the intravenous (IV) route is called PN. PN is not physiological in nature, as nutrients are delivered directly into the systemic circulation, bypassing the digestive tract and portal circulation. Parenteral nutrients given IV in this way do not have the "first pass" effect in the liver. In addition, malnutrition is known to cause thinning of the digestive system mucosa, blunting of the villi and an increase in bacterial translocation.[22]

Total PN should be the last choice when the combination of oral intake, EN and PN is not possible. Indications for PN or total PN are given in Table 7.

Table 5. Enteral nutrition monitoring

		At admission	At hospital	Outside hospital
Anthropometric measurements	Weight Height	Daily Initially	Daily Weekly	Weekly/monthly Monthly
Intake	Calories, protein, fluid	Daily	Weekly	Monthly
Tolerance	Abdominal circumference, vomiting, residue	In the presence of intolerance findings		
Stool/ostomy	Volume, frequency, consistency	Daily	Daily	In the occurrence of changes in stool
Tube placement		Before each nutrition		
Tube field		Daily	Daily	Daily

Table 6. Enteral nutrition complications and precautions

Complication	Prevention/intervention
Diarrhea/abdominal cramp	Decrease delivery rate Review and discontinue medications that may cause diarrhea Choose products containing fibre Review osmolarity, add modular additives Semi-elemental or elemental formulas if necessary
Nausea/vomiting	Make sure that the product is brought to room temperature before tube feeding. Raise the head of the bed (30-45 °C) Post-pyloric or continuous feeding
Hyperglycemia	Decrease delivery rate Prefer formulas containing minimal simple sugar. Insulin if clinically indicated
Blockage in nutrition tube	Check tube diameter Make sure to wash the tube every 4-8 hours for residue control, boluses or continuous feeding. Post-pyloric or continuous feeding
Gastric retention	Check tube location If the amount of residue is high, stop feeding 1 hour later, see the residue again. Post-pyloric or continuous feeding Lay the patient on his/her right side
Constipation	Make sure the patient is getting optimal fluids Increase the amount of free water Products containing fibre

Table 7. Indications for parenteral nutrition in children

Congenital anomalies of the gastrointestinal system that can be corrected surgically	
- Gastrointestinal atresia - Tracheo-esophageal fistula - Malrotation and volvulus - Omphalocele	- Gastroschisis - Diaphragmatic hernia - Meconium ileus and peritonitis - Hirschsprung's disease
Intestinal diseases	
- Necrotizing enterocolitis - Chronic resistant diarrhea - Pancreatitis	- Inflammatory bowel diseases - Short bowel syndrome - Pseudomembranous enterocolitis
Situations in which nutritional needs cannot be met with maximum enteral nutrition	
Severe burns	
Multiple organ failure	
Bone marrow and organ transplantation	
Malignant diseases	
- Radiation enteritis - Effects of chemotherapy on the digestive mucosa	- Cancer cachexia

If it is anticipated that infants and children who cannot be fed enterally will need nutritional support for 7 days or more, it means that there is an indication for PN. PN should not be used for short periods of time, as the risks may outweigh the benefits.[23] Unless the patient has severe malnutrition, there is no need to initiate PN to prepare for surgery.[24]

Whether administered peripherally or centrally, PN should be administered only in patients who are hemodynamically stable and can tolerate the required fluid. Particular attention should be paid to children with electrolyte imbalance, kidney or liver failure, metabolic acidosis or alkalosis, and it should not be administered to correct metabolic imbalances. Acid-base and electrolyte abnormalities must be corrected before starting PN. PN is not more effective than EN in children and adolescents receiving cancer treatment, whether or not they have malnutrition.[25]

a. Route of Delivery

Ensuring reliable venous access is extremely important for PN. PN can be administered through a peripheral or central vein. In general, the choice of peripheral or central venous access depends on the anticipated duration of nutritional therapy. Although the main advantages of peripheral catheters are ease of insertion, low infection and complication rates, the maximum osmolarity that can be delivered through a peripheral vein is 900 mOsm/L, which limits the amount of nutrients that can be delivered through the peripheral vein. The osmolarity of a PN solution can be determined with the following equation.[6]

mOsm/L = (gram amino acid/L × 10) + (gram dextro/L × 5) + [(mEq Na + mEq K) × 2] / L + (mEq Ca × 1.4)/L

Considering this osmolarity restriction, it is often impossible to provide all essential nutrients with peripheral PN and central venous access will be required to fully meet the nutritional needs of the child. Therefore, if PN support is anticipated for more than two weeks, a central venous catheter (CVC) should be placed to meet the patient's nutritional needs.

In addition, it should be noted that the presence of a CVC is the main risk factor for major, potentially fatal complications such as nosocomial bloodstream infection and venous thrombosis. Moreover, the most important risks associated with complications arising from the use of CVC are PBN administration, young age, and long-term use.[26,27] CVC-related complications, patient morbidity and mortality, and health care costs increase significantly in children receiving long-term PN treatment.

A catheter with a minimum number of ports or lumens for PN should be used for only PN administration if possible. If a multi-lumen CVC is present, it is necessary to reserve a lumen for PN and avoid blood sampling, transfusion, and central venous pressure monitoring from that lumen. In order to improve the quality of life of patients with long-term PN, blood sampling from CVC for routine follow-up can only be recommended if a full aseptic protocol is followed.[28]

Use of routine heparin has not been shown to be superior to saline flushing for the prevention of thrombotic occlusions in CVC in children. Moreover, there is insufficient evidence to justify the use of prophylactic anticoagulants to prevent catheter-related thrombosis, occlusion, and infection in children undergoing PN at home.[28] Recombinant tissue plasminogen activator or urokinase can be used to open a blocked catheter.[29]

Before and after vascular intervention, skin cleaning should be done with 2% chlorhexidine solution in 70% isopropyl alcohol. After applying the antiseptic (before catheter placement or dressing), it should be allowed to air dry.[30]

Sterile gauze or transparent semi-permeable polyurethane dressing can be used to cover the catheter application site. If there is bleeding or leakage at the catheter site, sterile gauze should be preferred. For short-term CVCs, sterile gauze should be replaced every 2 days and a transparent dressing every seven days. If it becomes damp, loose or soiled, it should be replaced sooner.[31] Routine topical antimicrobial therapy is not applied to the catheter insertion site, as it may increase the risk of Candida infection and antimicrobial resistance, and damage the catheter surface.[28]

b. PN Preparation

The energy provided to the patient by nutrition should meet the patient's nutritional needs, including basal metabolic rate, physical activity, growth, diet-induced thermogenesis, and correction of pre-existing malnutrition. Generally, for pediatric critically ill patients, PN is arranged considering the needs of the patient.

Energy

A practical approach to the determination of energy needs in PN is to identify the approximate range of energy needs based on the patient's age, body weight, and stage of the disease. Table 8 shows the predicted values, in accordance with the recently published ESPGHAN guideline, for energy needs of acute, clinically stable patients and those at the recovery phase for different age groups.[32]

Fluid-electrolyte

Total fluid requirement in infants apart from those in the neonatal period and children: Maintenance fluid is based on the replacement of ongoing losses (drain, urine and stool losses) and existing losses. During maintenance fluid therapy, the target should be to prevent dehydration, electrolyte disturbances, ketoacidosis, and protein breakdown. Loss

from urine and stool and insensible losses from the skin and lungs should be replaced, the volume of maintenance fluid administered should put minimal burden on the kidney and ensure that the urine is isotonic.[33]

Although the Holliday-Segar method is most commonly used to calculate the maintenance fluid, many individual factors such as age, disease status, fluid balance, latent water losses, and changes in metabolic rate and respiratory rate affect fluid requirement. Infants and children generally need at least 115 mL of fluid for the 100 kcal of energy provided. Appropriate fluid management requires constant monitoring and regulation according to the patient's fluid losses and hydration level. The hydration and electrolyte status of the patient should be evaluated clinically, considering body weight, serum electrolyte and acid-base balance, hematocrit and blood urea nitrogen (BUN) values, urine output and density, osmolarity and ions, and if possible, with ultrasonography (vena cava inferior collapsibility index, etc.). Fluid losses should be measured frequently and replaced exactly. For a critically ill child, applied medical treatments and blood and blood products must be taken into account and deducted from the total fluid to be given to the patient. Digestive system losses due to stoma, fistula or short bowel syndrome can reach 1-3 liters per day. In this case, the measured net loss amount should be replaced separately from the PN solution. The fluid and electrolyte content of the PN solution should be calculated individually, and should not be used as the sole fluid source in metabolically variable patients or to correct electrolyte abnormalities.

Sodium-potassium-chlorine

Conventional parenteral fluids have been administered as hypotonic saline (Na 35-77 mmol/L in 5% dextrose), but a potential risk for hospital-acquired hyponatremia has been observed.[34-36] However, there is some concern that normal saline solution is not physiological as it contains equal concentrations of Na and Cl. It is on the agenda that it would be more appropriate to use IV solutions containing less Cl than Na, as increased Cl load may cause hyperchloremia and acidosis.[37] To avoid a sodium concentration in the PN solution, which could cause hyponatremia, the use of balanced solutions has recently been recommended.

In critically ill children fed parenterally, serum electrolyte concentrations are monitored daily during the first days of treatment and subsequent monitoring intervals are adapted to the clinical condition of the patient.

Calcium-phosphorus-magnesium

Sufficient amounts of Ca, P and Mg should be provided to ensure optimal growth and bone mineralization in children and adolescents fed parenterally. The recommended amounts according to age groups are given in Table 9. Due to the risk of metabolic bone disease in children who have been treated with PN for a long time, Ca, P, ALP and vitamin D levels and bone mineral contents should be monitored as well as routine serum and urinary electrolytes.[38]

The targeted Ca/P ratio (in mg) in PN is 1.7/1. The solubility of calcium and phosphorus varies with temperature, type and concentration of amino acid solution, glucose concentration,

Table 8. Energy needs for different age groups in parenteral nutrition according to the stages of the disease (kcal/kg/day)*

	Acute phase[a]	Stable phase[b]	Recovery phase
0-1 year	45-50	60-65	75-85
1-7 years	40-45	55-60	65-75
7-12 years	30-40	40-55	55-65
12-18 years	20-30	25-40	30-55

[a]The patient needs vital support (sedation, mechanical ventilation, fluid resuscitation, vasopressor). [b]The patient is stable but unable to wean from vital support. *Taken from reference[32]

Table 9. Recommended daily amounts of calcium, phosphorus and magnesium for children on parenteral nutrition mmol (mg)/kg/day*

	Ca	P	Mg
0-6 months	0.8-1.5 (30-60)	0.7-1.3 (20-40)	0.1-0.2 (2.4-5)
7-12 months	0.5 (20)	0.5 (15)	0.15 (4)
1-18 years	0.25-0.4 (10-16)	0.2-0.7 (6-22)	0.1 (2.4)
Preparate contents			
1 mL 10% Ca gluconate	9.8 mg (0.45 mEq) elemental calcium		
1 mL 10% Ca chloride	27 mg (1.4 mEq) elemental calcium		
1 mL 15% $MgSO_4$	150 mg elemental magnesium		
1 mL potassium phosphate	0.6 mmol phosphorus and 1 mmol potassium		

*Adapted from reference[38]

pH, type of calcium salt, order of addition of calcium and phosphorus, calcium/phosphorus ratio, and presence of lipids. Since amino acid solutions increase the acidity of the fluid, higher calcium and phosphorus can be given with high amino acid solutions. In modern mix preparation devices in total PN preparation units, the system can calculate the precipitation itself and give a warning.

The precipitation factor is calculated as follows:

If the amount of amino acids in the liquid is ≤2.5%, the precipitation factor should be adjusted as ≤26 and if >2.5% then the factor should be kept ≤35.

Carbohydrate

Carbohydrates are the only energy source for the brain, renal medulla and erythrocytes. Adequate carbohydrate supply should be provided in critical illness. While determining the amount of glucose to be given in PN, the balance between meeting energy needs and the risks of overfeeding/excessive glucose load, the stage of the critical illness (acute, stable, recovery), growth, and the amount of glucose administered with treatments other than nutrition should be considered.[39]

In parenteral nutrition, the dextrose monohydrate form, which contains slightly less energy (3.4 kcal/g) than the carbohydrate concentration in foods (4 kcal/g), is used. The recommended parenteral glucose amount according to body weight and disease stage in infants and children is given in Table 10.

Recurrent and/or prolonged hypoglycemia (<60 mg/dL) should be avoided in all critically ill patients. Excess glucose and hyperglycemia should be avoided as well as. Hyperglycemia causes increased lipogenesis and hepatic steatosis with adipose tissue deposition and increased production of VLDL triglycerides in the liver. In critically ill children, these adverse effects appear in the form of increased CO_2 production and minute ventilation. Since it may cause an increase in morbidity and mortality in critically ill children, blood glucose values above 145 mg/dL should be avoided, and insulin therapy should be initiated when recurrent hyperglycemic values above 180 mg/dL are detected.[39]

Since glucose concentrations above 12.5% and high osmolarity in PN may damage the vessels, it should not be given peripherally. The upper limit of glucose concentration to be administered via the central vein is 30%. Starting glucose infusion and concentration at low dose and gradually increasing it prevents the development of hyperosmolarity, hyperglycemia and osmotic diuresis, and gives time for hormonal adaptation.[39]

Protein

Proteins are essential structural and functional components of all cells in the body. Protein needs may vary depending on the severity of the disease. Stress factors such as sepsis, burns, surgery, trauma and stomal losses increase the protein need. Urinary nitrogen excretion due to primary kidney disease with the use of steroids or diuretics may also increase protein requirement. In kidney diseases, liver failure and congenital metabolic diseases, it may be necessary to reduce the amount of protein given.[40] It is necessary to give 0.3-0.6 g/kg amino acids per day in chronic kidney patients who need protein restriction. On the other hand, in patients who receive continuous renal support treatments, amino acid should be given as 2-3 gr/kg/day for 0-2 years of age, 1.5-2 gr/kg/day for 2-13 years of age, and 1.5 gr/kg/day for 13-18 years of age.[41] Although protein solutions rich in branched-chain amino acids are recommended as 0.8-1.2 g/kg per day in liver failure, it would be more rational to determine the amount of amino acids to be given according to ammonia levels.[42]

In order to avoid negative protein balance, it is recommended to give at least 1.0 g/kg of protein daily in infants aged 1 month to 3 years with stable general condition, and at least 1.0 g/kg and at most 2.0 g/kg of protein in older children and adolescents. It has been shown that at least 57 kcal/kg of energy and 1.5 g/kg of protein should be given daily to ensure positive protein balance in critically ill children on mechanical ventilators.[43] In children with normal organ functions, daily protein targets per weight should be 2.5 g/kg till 3 years of age and 2 g/kg between 3 and 18 years of age.

Table 10. Recommended glucose amounts according to body weight and disease stage in children fed parenterally (mg/kg/min-g/kg/day)*

	Acute phase[a]	Stable phase[b]	Recovery phase
28 days-10 kg	2-4 (2.9-5.8)	4-6 (5.8-8.6)	6-10 (8.6-14)
11-30 kg	1.5-2.5 (2.2-3.6)	2-4 (2.8-5.8)	3-6 (4.3-8.6)
31-45 kg	1-1.5 (1.4-2.2)	1.5-3 (2.2-4.3)	3-4 (4.3-5.8)
>45 kg	0.5-1 (0.7-1.4)	1-2 (1.4-2.9)	2-3 (2.9-4.3)

[a]Life-threatening condition or organ failure and need for vital support (sedation, mechanical ventilation, fluid resuscitation, vasopressor, etc.). [b]The patient is clinically stable but still needs vital support. *Taken from reference [39]

Lipid

Intravenous lipid emulsions (ILEs) are an indispensable part of pediatric PN due to their high caloric content and low osmolality. For most patients, it is initially started at 1 g/kg/day. If necessary, the dose of fat can be increased up to 3 g/kg/day (2 g/kg/day in children over 10 years of age) to ensure adequate energy intake.[44]

Carnitine facilitates the transport of long-chain fatty acids across the mitochondrial membrane, making them suitable for β-oxidation. Carnitine is found in human breast milk and cow's milk formulas, but PN solutions usually do not contain carnitine. Carnitine is synthesized in the liver and kidney from lysine and methionine. Therefore, patients with renal or hepatic failure may be at risk of carnitine deficiency. Carnitine supplementation may be considered in pediatric patients expected to receive PN for more than 4 weeks.[44]

In critically ill children fed parenterally, the amount of ILE should be reduced if serum triglyceride concentrations exceed 265 mg/dL in infants and 400 mg/dL in older children.[44]

Malnourished children have low lipoprotein lipase levels, which reduces the clearance of intravenously administered lipid. In patients with metabolic stress such as sepsis and trauma, or organ dysfunction such as liver and kidney, the production of cortisol, catecholamines and cytokines that cause lipolysis is increased, and the risk of hypertriglyceridemia increases during IV lipid administration.[45]

In patients with severe unexplained thrombocytopenia, serum triglyceride concentrations should be monitored and parenteral lipid dose reduction should be considered. Although lipid emulsions do not appear to affect platelet count and function, some concerns have been expressed regarding their effect on platelet aggregation. Long-term administration of PN with pure soy-based lipid emulsions may stimulate hemophagocytosis in the bone marrow by inducing recurrent thrombocytopenia due to shortened platelet lifespan and the activation of the monocyte-macrophage system.[45]

Fat overload syndrome is a well-known complication of IV administration of lipid emulsions at high dosages or at excessive infusion rates. It is characterized by headache, fever, jaundice, enlarged liver-spleen, respiratory distress and bleeding tendency. Other symptoms include anemia, leukopenia, thrombocytopenia, low fibrinogen levels, and coagulopathy. Although mostly associated with the use of soy-based lipid emulsions, it has recently been shown to be related to the rate of infusion and not the type of lipid emulsion.[46]

It has been reported that administration of IV lipid emulsions mixed with other nutrients in total PN bags does not cause an increase in the risk of bloodstream infection rates.[47] In pediatric patients, heparin should not be routinely given with lipid infusion.

The amino acid and lipid solutions available in our country and their properties are listed in Table 11.

Table 11. Amino acid and lipid solutions available in our country and can be used in the childhood age group

Amino acid solutions
• PF pediatriamine
• TrophAmine® 6%
• Primene 10%
• PF hiperalamine 8.5% and 10%
• Aminoven® 5%, 10%, 15%
• PF Nephricamine 5.4% (contains high concentration of aromatic amino acids and methionine)
• Nephrotect® 10% (The dipeptide glycyl-tyrosine in its content meets the increased tyrosine requirement in renal failure)
• 6% PF K-Camine 8% (contains high concentration of branched-chain amino acids, low concentration of methionine and aromatic amino acids)
• Aminoplasmal® Hepa 10% (contains high concentration of branched-chain amino acids, low concentration of methionine and aromatic amino acids)
• Aminosteril® N-Hepa 8% (contains high concentration of branched-chain amino acids, low concentration of methionine and aromatic amino acids)
Lipid solutions
• Intralipid® 10%, 20% (contains 100% soya oil) • Lipofundin® 10%, 20% (contains 50% MCT, 50% soya oil) • Lipoplus® 20% (contains 50% MCT, 40% soya oil, 10% fish oil) • SMOFlipid® 20% (contains 30% soya oil, 30% MCT, 25% olive oil, 15% fish oil) • Clinoleic 20% lipid (contains 20% soya oil, 80% olive oil)
• Omegaven (contains long-chain omega-3 fatty acids especially EPA and DHA)
MCT: Medium chain fatty acids (coconut oil is used), EPA: Eicosapentaenoic acid, DHA: Docosahexaenoic acid

Vitamins

Children on PN should be given vitamin preparates daily. Vitamin stability should be ensured by adding both water-soluble and fat-soluble vitamins to lipid emulsions or mixtures containing lipids. Although optimal vitamin doses for children have not been fully determined, daily recommended parenteral vitamin doses based on expert opinion are given in Table 12. Patients on long-term PN should be monitored periodically for vitamin D deficiency and patients with serum 25(OH) vitamin D levels of <50 nmol/L should be provided with vitamin D supplementation.[48]

Trace Elements

Trace elements play a role in wound healing and immune response. Although parenteral doses have not been determined exactly, the recommended daily doses according to expert opinion are given in Table 13. Commercial preparates are in the form of ampoules containing all these trace elements and added to the PN solution.[49]

a. Standard PN Solutions

Standard PN solutions are commercially available as two-in-one (carbohydrate and protein) or three-in-one (carbohydrate, protein and lipid) bag systems. The advantages of these products are lower cost and longer shelf life (up to 28 days). These formulations will generally meet the needs of some pediatric patients and can be safely used for short periods of up to 2-3 weeks in stable pediatric patients. It should be stated that they are also suitable for patients undergoing PN at home. In intensive care patients, they can be used as initial formulas for PN until an individual PN solution is prepared, but individual PN solutions should definitely be preferred for

Table 12. Daily recommended parenteral doses of fat and water soluble vitamins for children and content of parenteral vitamin preparates in our country *

	<12 months	1-18 years	Soluvit ®N (10 mL)	Vitalipid ®N infant (10 mL)	Cernevit® Venavit® Todavit® (5 mL)
Vitamin A	150-300 mcg/kg/day or 2300 IU/day	150 mcg/day	-	690 mcg 2300 IU	3500 IU
Vitamin D	400 IU/ day or 40-150 IU/kg/day	400-600 IU/day	-	400 IU	220 IU
Vitamin E	2.8-3.5 mg/kg/day	11 mg/day	-	6.4 mg	10.2 mg
Vitamin K	10 mcg/kg/day	200 mcg/day	-	200 mcg	-
Vitamin C	15-25 mg/kg/day	80 mg/day	100 mg	-	125 mg
Thiamine	0.35-0.50 mg/kg/day	1.2 mg/day	2.5 mg	-	3.51 mg
Riboflavin	0.15-0.2 mg/kg/day	1.4 mg/day	3.6 mg	-	4.14 mg
Pyridoxine	0.15-0.2 mg/kg/day	1.0 mg/day	4 mg	-	4.53 mg
Niacin	4-6.8 mg/kg/day	17 mg/day	40 mg	-	46 mg
Vitamin B12	0.3 mcg/kg/day	1 mcg/day	5 mcg	-	6 mcg
Pantothenic acid	2.5 mg/kg/day	5 mg/day	15 mg	-	17.25 mg
Biotin	5-8 mcg/kg/day	20 mcg/day	60 mcg	-	69 mcg
Folic acid	56 mcg/kg/day	140 mcg/day	400 mcg	-	414 mcg

*Adapted from reference [48]

Table 13. Daily recommended amounts of trace elements (mcg/kg/day) for children fed parenterally and contents of parenteral trace element preparates in our country*

	0-3 months	3-12 months	1-18 years	Tracutil® (mg/10 mL)
Iron	50-100	50-100	50-100	1.95
Zinc	250	100	50	3.27
Copper	20	20	20	0.76
Iodine	1	1	1	0.13
Selenium	2-3	2-3	2-3	0.02
Manganese	≤1	≤1	≤1	0.55
Molybdenum	0.25	0.25	0.25	0.01
Chromium	0.2	0.2	0.2	0.01

*Adapted from reference [49]

critically ill children who are metabolically unstable and have abnormal fluid-electrolyte losses.[50]

b. Cyclic Parenteral Nutrition

Cyclic feeding means that the PN solution is given in less than 24 hours and then left for several hours without PN for the patient. Cyclical feeding can be initiated after patients have tolerated the full amount of PN and have stabilized both clinically and biochemically for at least one week. In general, while the duration of PN-free time is increased, the infusion rate of the PN solution is increased to compensate, so that the total daily PN volume remains unchanged. Cyclic PN allows the increase and decrease of meal-related hormones, and has a protective effect against intestinal failure-associated liver disease. Thanks to the night infusion, it gives freedom to the patient during the daytime and improves the quality of life. Children can usually tolerate the night infusion for more than 10-14 hours. Cyclical PN should definetly be tried while the patient is in the hospital, its tolerance and safety should be determined before being discharged home.[51]

c. Follow-up of the Parenterally Fed Patient

Follow-up of the parenterally fed patient requires frequent clinical evaluation together with the evaluation of nutritional status and laboratory findings. The biochemical tests requested should be adjusted according to the underlying clinical condition and also to the duration of PN (Table 14).

Before starting parenteral nutrition, basic biochemical values and anthropometric measurements should be recorded. After starting parenteral nutrition, electrolytes, glucose, BUN, creatinine, triglyceride, glucose and ketone presence in the urine, and urine density should be checked every day for the first week, and if C-reactive protein is >1 mg/L, weekly pre-albumin level can be checked. Weight follow-up and intake-output monitoring should be done. Daily biochemistry control is required until the targeted amounts are reached or when changes are made, and weekly biochemistry control is required after the patient is stable. Vitamin and trace element levels should be checked once a week until clinical and metabolic stabilization is achieved, and monthly thereafter,

Table 14. Laboratory monitoring of parenterally fed children

Test	Sample	Before PN	During PN, before clinical and metabolic stabilization			During PN, during clinical and metabolic stabilization		
			Every 1-2 days	At least once a week	As needed	Every 1-2 weeks	Once a month	As needed
Na, K, Ca	S	X	X			X		
P	S	X	X					
Cl	S	X	X					X
Mg	S	X			X	X		
Zinc	S				X			X
Blood gas	CapB	X				X		
Glucose	CB, CapB	X	X			X		
T. protein	S	X		X		X		
Albumin	S	X		X			X	
BUN, creatinine	S	X		X			X	
Triglyceride, cholesterol	S	X			X			X
Bilirubin, AST, ALT	S	X			X		X	
GGT, ALP	S	X			X			X
Complete blood count	CB	X		X		X		
INR	S	X			X		X	
CRP	S	X			X			X
Vitamin B12	S				X			X
Fe, ferritin	S				X			X
PTH	S							X
25 OHD_3	S				X			X
Trace elements	S			X				X
Urine	US	X		X			X	
Urine electrolytes	US				X			X

X: Time of test, S: Serum, plasma, CB: Complete blood, CapB: Capillary blood, US: Urine sample, AST: Aspartate aminotransferase, ALT: Alanine aminotransferase, GGT: Gamma-glutamyl transferase, PN: Parenteral nutrition, BUN: Blood urea nitrogen

and anthropometric measurements should be repeated.[51] Sudden changes in biochemical status are rare in stable patients.

a- Transition from PN to Enteral Nutrition

Even if the patient is in the process of PN, minimal EN should be administered whenever possible to preserve the intestinal mucosal structure, promote adaptation, and reduce the risk of PN-related liver disease. The volume should be increased as soon as a small amount of EN is tolerated. The transition to EN should be carefully planned, should be slow and gradual. Since abrupt termination of PN may cause hypoglycemia, the transition period should not be less than one week. The EN product should be given in normal concentrations and should not be diluted, otherwise the child will achieve normal fluid volume intake without adequate nutrition. The decrease in PN solution should be proportional to or slightly greater than the increase in enteral nutrition. If the chosen strategy fails, it is necessary to try again in smaller increases.[51]

b- Complications of PN

Despite very good application and follow-up, PN is a method with many complications. These complications can be examined in three main groups as mechanical, septic and metabolic complications.

Mechanical complications

Among the early complications that may be encountered during the application of the catheter are bleeding, arterial puncture, arrhythmia, air embolism, thoracic duct injury, malposition, hemothorax and pneumothorax. Late mechanical complications include improper functioning of the catheter, venous thrombosis, embolism, cardiac injuries, and nerve damage. About a quarter of catheters become clogged during use. The most common cause of these obstructions is thrombus. Lipid emulsions, calcium-phosphorus precipitates and drug residues are also among the causes. There is insufficient evidence to support the use of heparin instead of saline to keep catheters open. However, it is recommended to wash the catheters 1-2 times a week with 3-5 mL saline containing 5-10 IU/mL heparin. Regular flushing of in-use catheters with heparinized SP is not recommended. Recombinant tissue plasminogen activator is recommended primarily in the presence of thrombus, but urokinase and recombinant urokinase can also be used. 0.1 N hydrochloric acid can be used for drug or calcium precipitation. Clogged catheters should not be attempted to be opened with a guidewire.[52] Drugs that are frequently used in intensive care units but incompatible with PN solution are acetazolamide, amphotericin, acyclovir, ganciclovir, phenytoin, mannitol, metronidazole and sodium bicarbonate.

Infectious complications

Catheter-related bloodstream infections (CR-BSI) are among the most important complications associated with catheters in intensive care units. They are the most serious cause of morbidity and mortality for PN-dependent patients with intestinal failure. The most common infectious agents are *Staphylococcus epidermidis*, as well as *Staphylococcuc aureus* and *Candida* strains, *enterococci* and *enterobacter* strains. The usual approach should be primarily to start treatment with broad-spectrum antibiotics while the catheter is in place. The catheter should be removed if there is clinical worsening despite 72-hour antimicrobial therapy to which the infectious agent is susceptible, or if there is persistent or recurrent bacteremia, severe sepsis, suppurative thrombophlebitis, endocarditis, or bloodstream infection.[52]

In patients with a long-term catheter, who have CR-BSI due to *Staphylococcus aureus, Pseudomonas*, or *Candida* spp., the infected catheter should be removed immediately, except in rare cases where alternative venous access is not available. Treatment of catheter-related fungemia without catheter removal has a low success rate and is associated with higher mortality.

There are no randomized studies on antifungal lock therapy in critically ill pediatric patients with CR-BSI due to *Candida* strains, publications are insufficient, and results are controversial.

Since prevention will be easier than treatment, maximum sterile barrier precautions and aseptic technique should be considered during the intervention.[52] A precautionary package (bundle) including catheter site dressing applications, use of needle-free vascular intervention devices, disposable washing systems and washing technique must be defined.

Metabolic complications

Metabolic complications that may develop in association with PN are as follows:[52]

- Hypo-hyperglycemia
- Thrombocytopenia
- Mineral-vitamin deficiencies
- Coagulopathy
- Electrolyte and acid-base balance disorders
- Essential fatty acid deficiency
- Hepatobiliary dysfunction
- Refeeding syndrome
- Osteopenia
- Hyperlipidemia

Hepatobiliary dysfunction is the most common and serious complication of parenteral nutrition. Early signs of liver injury are elevated ALP and GGT values, bilirubin level rises later; it

can lead to cirrhosis and liver failure. While cholestasis is more common in young children and infants, steatosis is common in adolescents. If there are no contraindications in the treatment approach, EN should be started even if it is little. If long-term PN is to be administered, cyclic feeding can be tried. If the bilirubin is rising and no other cause can be found, the lipid infusion may be discontinued and ursodeoxycholic acid may be started.

Refeeding syndrome, on the other hand, defines metabolic disorders that occur with rapid PN administration, especially to patients with malnutrition. Low serum phosphorus, magnesium and potassium levels and life-threatening results such as disorders of fluid balance and glucose metabolism can be seen. In order to prevent the development of refeeding syndrome, risky patients should be identified beforehand and fluid-electrolyte replacement with PN should be monitored by an experienced, multi-disciplinary team.[52] It should not be rushed to reach the daily calorie target needed; it should be started with low energy and gradually increased over 4-10 days.

c- Home-PN

In particular, pediatric patients who have nutritional problems related to short bowel syndrome, inflammatory bowel disease, AIDS or cancer, who need long-term PN and who do not have any other problems that require hospitalization can continue to be fed at home. A child expected to need PN for more than three months can be discharged as soon as he/she is clinically stable for better quality of life with fewer complications and provided that the following conditions are met:

- The underlying disease taken under control,

- Absence of fluid-electrolyte imbalance, having a reliable vascular access,

- Education of at least one of the parents by a specialist nutrition nurse or team,

- Having been provided appropriate social support,

- Availability of regionally trained health teams that families can reach 7/24 in case of a possible negativity.

Education of families includes the topics of hygiene, catheter care, infusion pumps, PN solutions, and recognition and prevention of potential complications. Physical examinations, biochemical anayses and anthropometric measurements of patients should be performed by home care teams at appropriate intervals (planned as 4 times a year for an uneventful patient) at home or in the hospital when necessary.[53]

Providing PN in this way outside the hospital setting supports a normal lifestyle and reduces complications and medical costs. Moreover, it ensures that nutritional support is continued in a more normal environment, facilitates the development of the child, and allows participation in social activities in the family environment.

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Peer-review: Internally peer-reviewed.

Authorship Contributions

Surgical and Medical Practices: H.A., A.E.A., A.B.A., O.D., T.K., D.Y., Concept: H.A., A.E.A., O.D., D.Y., Design: H.A., A.E.A., N.A.Y., A.B.A., O.D., T.K., Data Collection or Processing: H.A., A.E.A., D.Y., Analysis or Interpretation: H.A., N.A.Y., A.B.A., Literature Search: H.A., A.E.A., N.A.Y., O.D., D.Y., Writing: H.A., A.E.A., N.A.Y., T.K.

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