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Journal of Pediatric Emergency and Intensive Care Medicine

TÜRK ÇOCUK ACİL TIP VE YOĞUN BAKIM DERNEĞİ

Volume / Cilt: 12 Issue / Sayı: 1 Year / Yıl: 2025

E-ISSN: 2148-7332

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Journal of Pediatric Emergency and Intensive Care Medicine

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Çocuk Acil ve Yoğun Bakım Dergisi, Çocuk Acil Tıp ve Yoğun Bakım Derneği'nin bilimsel yayınıdır.

The Journal of Pediatric Emergency and Intensive Care Medicine is a publication of "Society of Pediatric Emergency and Intensive Care Medicine".

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34093 İstanbul, Türkiye
Telefon/Phone: +90 (530) 177 30 97
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Web: www.galenos.com.tr
Yayıncı Sertifika No/Publisher Certificate Number: 14521

Yayın Tarihi/Publication Date: Nisan 2025/April 2025
ISSN: 2146-2399 **E-ISSN:** 2148-7332

Yılda üç kez yayımlanan süreli yayındır.
International periodical journal published three times in a year.

ÇOCUK ACİL ve YOĞUN BAKIM DERGİSİ

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Sahibi: Çocuk Acil Tıp ve Yoğun Bakım Derneği

Sorumlu Yönetici: Hayri Levent Yılmaz

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Owner: The Society of Pediatric Emergency and Intensive Care Medicine

Responsible Manager: Hayri Levent Yılmaz

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EDITORIAL

Dear Colleagues,

We are delighted to announce the first issue of the Journal of Pediatric Emergency and Intensive Care Medicine in 2025. Our journal continues to strengthen its position in the ESCI index while fulfilling its mission to share rapidly developing scientific knowledge in pediatric emergency medicine and intensive care on national and international platforms. This issue features valuable research articles, case reports, and a protocol paper focusing on common clinical situations in pediatric emergency departments and parent education themes.

Our journal continues to take strategic steps to increase its international visibility, raise citation rates, and become included in the Science Citation Index Expanded (SCIE) in the coming period. To achieve this goal, we are increasing the number of international reviewers, strengthening our double-blind peer review processes, and particularly encouraging multicenter studies. Additionally, we plan to publish special issues focusing on current topics in pediatric emergency medicine and intensive care.

Global trends in pediatric emergency medicine and intensive care are shaping toward the standardization of evidence-based protocols, integration of digital health technologies, and increase the resilience of healthcare systems in the post-pandemic period. Our journal aims to contribute to the development of practices in our country in line with international standards, by closely following global trends.

First, I address management changes in our association. We extend our gratitude to Prof. Dr. Dinçer Yıldızdaş, who has made great efforts and contributions to our association for many years and has successfully represented the Turkish Society of Pediatric Emergency and Intensive Care Medicine on national/international platforms with his visionary leadership, and to the board of directors for their dedicated work and valuable contributions. During Prof. Dr. Yıldızdaş's presidency, as in previous periods, our association and journal have achieved significant breakthroughs and progress in the scientific and academic field.

We wish to achieve success under the leadership of our association's new president, Prof. Dr. Özlem Tekşam, and its board of directors. We firmly believe that under Prof. Dr. Tekşam's leadership, with the support and collective energy of our community, our association and journal will develop further and increase their effectiveness in the national and international arenas. The support of all our members and readers is crucial for the future of our association and journal in this process.

We would like to share that the "1st Türkiye-Azerbaijan Pediatric Emergency and Intensive Care Conference" was successfully held in Baku, the capital of Azerbaijan, on April 7-9, 2025. The relations between Azerbaijan and the Pediatric Emergency and Intensive Care Association were initiated in 2015 by the then president of the association Prof. Dr. Hayri Levent Yılmaz and our association member Prof. Dr. Nurettin Onur Kutlu with the support of TIKA, moreover, many Advanced Life Support in Children courses were organized in various rayons of Azerbaijan, and the foundation of these scientific relations was strengthened by meeting with the Azerbaijani Ministry of Health. Within the scope of our association's strategy to develop international collaborations, scientific and education-oriented relations were initiated with Bosnia and Herzegovina in 2018 as a continuation of ongoing efforts, and significant contributions were made to the expansion of the regional pediatric emergency medicine network.

These mutual relations were developed by our association in the following years, and this year, they have been taken to a higher level at the conference, which was organized by the Turkish Pediatric Emergency Medicine and Intensive Care Association and the Azerbaijan Ministry of Health, TABIB, and supported by TIKA (Turkish Cooperation and Coordination Agency).

In addition, a meeting on "Management of Common Pediatric Emergencies" was successfully held in Sarajevo between October 4-6, 2024 in cooperation with the Turkish Society of Pediatric Emergency Medicine and Intensive Care and the Bosnia and Herzegovina Pediatric Society. This meeting is a continuation of the scientific cooperation with Bosnia and Herzegovina, which started in 2018 and has made significant contributions to the standardization of regional pediatric emergency medicine practices.

These international collaborations contribute to strengthening regional health capacity in line with the WHO recommendations on "Regional and Cross-Border Healthcare Collaboration." We would like to thank Prof. Dr. Tanıl Kendirli, Prof. Dr. Nurettin Onur Kutlu, Prof. Dr. Dinçer Yıldızdaş, Prof. Dr. Murat Duman, Prof. Dr. Özlem Tekşam, the boards of directors of our association and all colleagues of our community who have contributed to this.

Scientific studies on this issue have made important contributions to the field of pediatric emergencies and intensive care. The study by Ulusoy et al. titled "The Value of Serum Ischemia Modified Albumin Levels in the Diagnosis of Pediatric Testicular Torsion and Prediction of Post-operative Testicular Atrophy" showed that serum IMA levels can be a valuable biomarker for the diagnosis and prognosis prediction of pediatric testicular torsion. This finding is important for developing objective criteria for clinical decision-making.

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The study by Özden et al. titled "Evaluation of Patients Presenting to the Pediatric Emergency Department with Influenza-like Illness During the 2009 Influenza A/H1N1 Pandemic" provided valuable data for the management of pediatric emergency departments and identification of risk groups during pandemic periods. The findings of this study can contribute to global efforts to increase the resilience of health care systems in the post-COVID-19 era.

The study by Akça et al. titled "Comparison of Parental Anxiety Levels in Febrile Seizures and Epileptic Convulsions" showed that parents experience similar levels of anxiety regardless of the type of convulsion. This finding provides important clues for developing parental education and psychological support strategies in clinical practice and is consistent with the current literature emphasizing the importance of family centered care models in pediatric emergency departments.

The study by Yıldırım et al. titled "Determining Factors Affecting Fever Management of Parents Bringing Their Children to the Emergency Department with High Fever" revealed the impact of parents' education level, economic status, and place of residence on fever management. This study emphasizes the need to develop educational programs for parents living in rural areas with low educational levels and contribute to global efforts to reduce health inequalities.

The study by Dinçer et al. titled "Evaluation of Basic First Aid Knowledge Levels of Parents Presenting to the Pediatric Emergency Department" shows that the rate of parents receiving first aid training is low, and there is a significant relationship between education level and first aid knowledge. These findings reveal the need to expand community-based first aid training programs. This necessity directly aligns with the United Nations Sustainable Development Goals' "Good Health and Well-being' (SDG 3) target, particularly contributing to strengthening community capacity in reducing child mortality (SDG 3.2). The expansion of community-based first-aid training also serves the goal of education for sustainable development (SDG 4.7) by increasing health literacy.

This issue includes two important case reports. The case report by Döndü et al. titled "Use of Hyperbaric Oxygen Therapy to Prevent Amputation in Severe Crush Injury Due to Earthquake" demonstrates the effectiveness of hyperbaric oxygen therapy in a child injured during the February 6, 2023, Türkiye earthquake. This case contains important lessons for disaster medicine and pediatric trauma management, and provides a valuable contribution to the literature on the optimization of pediatric care in natural disasters.

The case report by Karabacak et al. titled "Successful Treatment of an Eleven-Year-Old Boy with Febrile Infection-Related Epilepsy Syndrome" shows the successful management of FIRES, which is rare and difficult to treat, using a multidisciplinary approach and ketogenic diet therapy. This case highlights the potential role of a ketogenic diet in the management of refractory epilepsy.

Finally, this issue includes a protocol paper titled "Status Epilepticus in the Critically Ill Pediatric Patient" prepared by our association's working group. This protocol, prepared by Özcan et al., provides current and comprehensive information regarding the definition, classification, and treatment approaches for status epilepticus. This protocol, meticulously prepared by our association's working group, is a valuable resource for ensuring standardization in clinical practice and will contribute to establishing a common language for the management of status epilepticus in pediatric emergency and intensive care units in our country.

The studies on this issue directly contribute to the United Nations Sustainable Development Goals, particularly the "Good Health and Well-being" (SDG 3). Parent education-focused research and community-based first-aid training recommendations are also aligned with the "Quality Education" (SDG 4) goal. Additionally, our case report in the field of disaster medicine provides an important contribution that can be evaluated within the scope of "Sustainable Cities and Communities" (SDG 11).

All studies in this issue of our journal make important contributions to the scientific knowledge in the field of pediatric emergency and intensive care. We thank the authors for sharing their valuable work with us. We are also grateful to our reviewers for their meticulous evaluation and to our editorial team for their dedicated work.

Your contributions as valued researchers are vital for increasing our journal's impact factor and strengthening its international visibility. We kindly request you to submit your studies to our journal, cite published articles, and promote our journal on international platforms. We will continue to share the current developments and valuable research in our field with you.

Respectfully,

Prof. Dr. Hayri Levent Yılmaz
Editor-in-Chief
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Değerli Meslektaşlarımız,

Çocuk Acil ve Yoğun Bakım Dergisi'nin 2025 yılının ilk sayısını sizlerle paylaşmanın mutluluğunu yaşıyoruz. Çocuk acil tıp ve yoğun bakım alanında küresel olarak hızla gelişen bilimsel bilgi birikimini ulusal ve uluslararası platformlarda paylaşma misyonuyla yayın hayatını sürdüren dergimiz, ESCI endeksinde yer alan konumunu güçlendirmeye devam etmektedir. Bu sayımızda, özellikle çocuk acil servislerinde sık karşılaşılan klinik durumlar ve ebeveyn eğitimi temaları etrafında şekillenen değerli araştırmalar, olgu sunumları ve bir protokol makalesi yer almaktadır.

Dergimiz, önümüzdeki dönemde uluslararası görünürlüğünü artırmak, atıf oranlarını yükseltmek ve Science Citation Index Expanded (SCIE) endeksine dahil olmak için stratejik adımlar atmaya devam etmektedir. Bu doğrultuda, uluslararası hakemlerimizin sayısını artırıyor, çift-kör hakem değerlendirme süreçlerimizi güçlendiriyor ve özellikle çok merkezli çalışmaları özendiriyoruz. Ayrıca, çocuk acil tıp ve yoğun bakım alanında güncel konulara odaklanan özel sayılar çıkarmayı planlıyoruz.

Çocuk acil tıp ve yoğun bakım alanında küresel eğilimler, kanıta dayalı protokollerin standardizasyonu, dijital sağlık teknolojilerinin entegrasyonu ve pandemi sonrası dönemde sağlık sistemlerinin dirençliliğinin artırılması yönünde şekillenmektedir. Dergimiz, bu küresel eğilimleri yakından takip ederek, ülkemizdeki uygulamaların uluslararası standartlarla uyumlu gelişmesine katkı sağlamayı hedeflemektedir.

Öncelikle, derneğimizde gerçekleşen yönetim değişikliğine değinmek isterim. Uzun yıllar boyunca derneğimize büyük emek ve katkı sağlayan, vizyoner liderliğiyle Çocuk Acil Tıp ve Yoğun Bakım Derneği'ni ulusal/uluslararası platformlarda başarıyla temsil eden Prof. Dr. Dinçer Yıldızdaş'a ve yönetim kuruluna özverili çalışmaları ve değerli katkıları için teşekkürlerimizi sunarız. Prof. Dr. Yıldızdaş'ın başkanlığı döneminde, önceki dönemlerde de olduğu gibi derneğimiz ve dergimiz önemli atılımlar gerçekleştirmiş, bilimsel ve akademik alanda kayda değer ilerlemeler kaydetmiştir.

Derneğimizin yeni başkanı Prof. Dr. Özlem Tekşam'a ve yönetim kuruluna görevinde başarılar dileriz. Prof. Dr. Tekşam'ın liderliğinde, camiamızın desteği ve ortak enerjisiyle derneğimizin ve dergimizin daha da gelişeceğine, ulusal ve uluslararası alanda etkinliğini artıracağına olan inancımız tamdır. Bu süreçte tüm üyelerimizin ve okuyucularımızın desteği, derneğimizin ve dergimizin geleceği için büyük önem taşımaktadır.

Büyük bir memnuniyetle paylaşmak isteriz ki, 7-9 Nisan 2025 tarihlerinde Azerbaycan'ın başkenti Bakü'de "1. Türkiye-Azerbaycan Çocuk Acil ve Yoğun Bakım Konferansı" başarıyla gerçekleştirilmiştir. Azerbaycan ile Çocuk Acil ve Yoğun Bakım Derneği'nin ilişkileri 2015 yılında o zamanki dernek başkanı Prof. Dr. Hayri Levent Yılmaz ile dernek üyemiz Prof. Dr. Nurettin Onur Kutlu tarafından TİKA desteği ile başlatılmış, Azerbaycan'ın çeşitli reyonlarında çok sayıda Çocuklarda İleri Yaşam Desteği kursları düzenlenmiş, Azerbaycan Sıhhiye Nazırlığı ile görüşmeler yapılarak bu bilimsel ilişkilerin temeli güçlendirilmiştir. Derneğimizin uluslararası iş birliklerini geliştirme stratejisi kapsamında, 2018 yılında önceki girişimin devamı niteliğinde Bosna Hersek ile de bilimsel ve eğitim odaklı ilişkiler başlatılmış, bölgesel çocuk acil tıp ağının genişletilmesine önemli katkılar sağlanmıştır.

Bu karşılıklı ilişkiler sonraki yıllarda da derneğimiz tarafından önem verilerek geliştirilmiş ve bu yıl Türk Çocuk Acil Tıp ve Yoğun Bakım Derneği ile Azerbaycan Sıhhiye Nazırlığı, TABİB'in birlikte düzenlediği, TİKA (Türk İş Birliği ve Koordinasyon Ajansı) tarafından desteklenen konferans ile daha da ileri seviyelere taşınmıştır.

Ayrıca, geçtiğimiz yıl 04-06 Ekim 2024 tarihleri arasında Türk Çocuk Acil Tıp ve Yoğun Bakım Derneği ile Bosna-Hersek Pediatri Derneği'nin iş birliğiyle Saraybosna'da "Sık Görülen Çocuk Acillerin Yönetimi" konulu toplantı da başarıyla gerçekleştirilmiştir. Bu toplantı, Bosna Hersek ile 2018'de başlayan bilimsel iş birliğinin devamı niteliğinde olup, bölgesel çocuk acil tıp uygulamalarının standardizasyonuna önemli katkılar sağlamıştır.

Bu uluslararası iş birlikleri, WHO'nun "Bölgesel ve Sınır Ötesi Sağlık Hizmetleri İş Birliği" önerileriyle de uyumlu olarak bölgesel sağlık kapasitesinin güçlendirilmesine katkı sağlamaktadır. Bu konuda emeği geçen Prof. Dr. Tanıl Kendirli'ye, Prof. Dr. Nurettin Onur Kutlu'ya, Prof. Dr. Dinçer Yıldızdaş'a, Prof. Dr. Murat Duman'a, Prof. Dr. Özlem Tekşam'a, dernek yönetim kurullarımıza ve camiamızın tüm emektaşlarına teşekkür ederiz.

Bu sayımızda yer alan bilimsel çalışmalar, çocuk acil ve yoğun bakım alanında önemli katkılar sunmaktadır. Ulusoy ve arkadaşlarının "Pediatrik Testis Torsiyonunun Tanısında ve Ameliyat Sonrası Testis Atrofisinin Öngörülmesinde Serum İskemi Modifiye Albümin Düzeylerinin Değeri" başlıklı çalışması, serum IMA düzeylerinin pediatrik testis torsiyonu tanısında ve prognoz tahmininde kullanılabilecek değerli bir biyobelirteç olduğunu göstermektedir. Bu bulgu, klinik karar verme süreçlerinde objektif ölçütlerin geliştirilmesi açısından önemlidir.

Özden ve arkadaşlarının "2009 İnfluenza A/H1N1 Pandemisinde Çocuk Acil Servisine Grip Benzeri Hastalık Kliniği ile Başvuran Hastaların Değerlendirilmesi" başlıklı çalışması, pandemi dönemlerinde çocuk acil servislerinin yönetimi ve risk gruplarının belirlenmesi açısından

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değerli veriler sunmaktadır. Bu çalışmanın bulguları, COVID-19 sonrası dönemde sağlık sistemlerinin dirençliliğini artırmaya yönelik küresel çabalara katkı sağlayabilecek niteliktedir.

Akça ve arkadaşlarının "Febril Nöbet ve Epileptik Konvülziyonda Ebeveyn Kaygı Düzeylerinin Karşılaştırılması" başlıklı çalışması, ebeveynlerin konvülziyon türünden bağımsız olarak benzer kaygı düzeyleri yaşadıklarını göstermektedir. Bu bulgu, klinik pratikte ebeveyn eğitimi ve psikolojik destek stratejilerinin geliştirilmesi açısından önemli ipuçları sunmaktadır ve çocuk acil servislerde aile merkezli bakım modellerinin önemini vurgulayan güncel literatürle uyumludur.

Yıldırım ve arkadaşlarının "Çocuklarını Yüksek Ateş ile Acile Getiren Ebeveynlerin Ateş Yönetimini Etkileyen Faktörlerin Belirlenmesi" başlıklı çalışması, ebeveynlerin eğitim düzeyi, ekonomik durumu ve yaşadıkları yerin ateş yönetimi üzerindeki etkisini ortaya koymaktadır. Bu çalışma, özellikle kırsal kesimde yaşayan ve düşük eğitim düzeyine sahip ebeveynlere yönelik eğitim programlarının geliştirilmesi gerekliliğini vurgulamaktadır ve sağlık eşitsizliklerinin azaltılmasına yönelik küresel çabalara katkı sağlamaktadır.

Dinçer ve arkadaşlarının "Çocuk Acil Servise Başvuran Ebeveynlerin Temel İlk Yardım Bilgisi Düzeylerinin Değerlendirilmesi" başlıklı çalışması, ebeveynlerin ilk yardım eğitimi alma oranlarının düşük olduğunu ve eğitim düzeyi ile ilk yardım bilgisi arasında anlamlı bir ilişki olduğunu göstermektedir. Bu bulgular, toplum temelli ilk yardım eğitim programlarının yaygınlaştırılmasının gerekliliğini ortaya koymaktadır. Bu gereklilik, Birleşmiş Milletler'in Sürdürülebilir Kalkınma Amaçları'ndan "Sağlıklı ve Kaliteli Yaşam" (SKA 3) hedefiyle doğrudan örtüşmekte, özellikle çocuk ölümlerinin azaltılması (SKA 3.2) konusunda toplumsal kapasitenin güçlendirilmesine katkı sağlamaktadır. Toplum temelli ilk yardım eğitimlerinin yaygınlaştırılması, sağlık okuryazarlığını artırarak sürdürülebilir kalkınma için eğitim (SKA 4.7) hedefine de hizmet etmektedir.

Bu sayımızda ayrıca iki önemli olgu sunumu yer almaktadır. Döndü ve arkadaşlarının "Deprem Kaynaklı Şiddetli Ezilme Yaralanmasında Ampütasyonu Önlemek için Hiperbarik Oksijen Tedavisi Kullanımı" başlıklı olgu sunumu, 6 Şubat 2023 Türkiye depreminde yaralanan bir çocukta hiperbarik oksijen tedavisinin etkinliğini göstermektedir. Bu olgu, afet tıbbı ve çocuk travma yönetimi açısından önemli dersler içermektedir ve doğal afetlerde pediatrik bakımın optimizasyonu konusunda literatüre değerli bir katkı sunmaktadır.

Karabacak ve arkadaşlarının "On Bir Yaşında Febril Enfeksiyonla İlişkili Epilepsi Sendromu Tanılı Bir Erkek Çocuğun Başarılı Tedavisi" başlıklı olgu sunumu ise, nadir görülen ve tedavisi zor olan FIRES'in multidisipliner yaklaşım ve ketojenik diyet tedavisi ile başarılı yönetimini göstermektedir. Bu olgu, dirençli epilepsi yönetiminde ketojenik diyetin potansiyel rolünü vurgulamaktadır.

Son olarak, bu sayımızda derneğimizin çalışma grubunun hazırladığı "Kritik Çocuk Hastada Status Epileptikus" başlıklı protokol makalesi yer almaktadır. Özcan ve arkadaşları tarafından hazırlanan bu protokol, status epileptikus tanımı, sınıflandırması ve tedavi yaklaşımları hakkında güncel ve kapsamlı bilgiler sunmaktadır. Derneğimizin çalışma grubu tarafından titizlikle hazırlanan bu protokol, klinik uygulamada standardizasyonu sağlamak açısından değerli bir kaynak niteliğindedir ve ülkemizde çocuk acil ve yoğun bakım ünitelerinde status epileptikus yönetiminde ortak bir dil oluşturulmasına katkı sağlayacaktır.

Bu sayımızda yer alan çalışmalar, Birleşmiş Milletler Sürdürülebilir Kalkınma Hedefleri'nden özellikle "Sağlıklı Bireyler" (SKA 3) hedefine doğrudan katkı sağlamaktadır. Ebeveyn eğitimi odaklı araştırmalar ve toplum temelli ilk yardım eğitimi önerileri, "Nitelikli Eğitim" (SKA 4) hedefiyle de uyumludur. Ayrıca, afet tıbbı alanındaki olgu sunumumuz, "Sürdürülebilir Şehir ve Yaşam Alanları" (SKA 11) kapsamında değerlendirilebilecek önemli bir katkı sunmaktadır.

Dergimizin bu sayısında yer alan tüm çalışmalar, çocuk acil ve yoğun bakım alanında bilimsel bilgi birikimine önemli katkılar sunmaktadır. Yazarlarımıza değerli çalışmalarını bizimle paylaştıkları için teşekkür ederiz. Ayrıca, hakemlerimize titiz değerlendirmeleri ve editöryal ekibimize özverili çalışmaları için minnettarız.

Dergimizin etki faktörünü artırmak ve uluslararası görünürlüğünü güçlendirmek için siz değerli araştırmacılarımızın katkıları hayati önem taşımaktadır. Çalışmalarınızı dergimize göndermenizi, yayınlanan makalelere atıf yapmanızı ve dergimizi uluslararası platformlarda tanıtmanızı önemle rica ediyoruz. Gelecek sayılarımızda, alanımızdaki güncel gelişmeleri ve değerli araştırmaları sizlerle paylaşmaya devam edeceğiz.

Saygılarımızla,

Prof. Dr. Hayri Levent Yılmaz
Baş Editör
Çocuk Acil ve Yoğun Bakım Dergisi

Research Article / Özgün Araştırma

DOI: 10.4274/cayd.galenos.2024.02360
J Pediatr Emerg Intensive Care Med 2025;12:1-6

Comparison of Parents' Anxiety Levels During Febrile Seizure and Epileptic Convulsion

Febril Nöbet ve Epileptik Konvülziyonda Ebeveyn Kaygı Düzeylerinin Karşılaştırılması

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Abstract

Introduction: In childhood, convulsions are common neurological conditions in pediatric emergency service and cause stress in both families and healthcare professionals. The aim of this study was comparison of parents' anxiety level during febrile seizure and epileptic convulsion in pediatric emergency service.

Methods: A questionnaire which included socio-demographic-clinical data form and state-trait anxiety inventory was applied to the parents in the first 24 hours of convulsions. Comparisons were made between the febrile seizure and epileptic convulsion group and between the same group's mother and father.

Results: Total 133 patients included the study, 69 patient was febrile seizures and 64 patient was epileptic convulsions. A total of 183 parents agreed to participate in the study: 64 mothers and 33 fathers in the febrile seizure group, and 58 mothers and 28 fathers in the epileptic convulsion group. Parents' anxiety level was similar between febrile seizure and epileptic convulsion groups. The parents' state and trait anxiety scores were compared to determine the anxiety levels of before and during the convulsion, the differences were statistically significant. The state anxiety scores of the parents increased in both febrile seizure and epileptic convulsion group. The state and trait anxiety scores of the mothers were significantly higher than the fathers, regardless type, and repetition numbers of convulsion.

Conclusion: In our study, it was shown that all convulsions cause parental anxiety. Information and psychological support about convulsion should be equally given to all parents.

Keywords: Child, convulsion, parent, state anxiety, trait anxiety

Öz

Giriş: Çocukluk çağı konvülziyonları çocuk acil servisinde sık görülen nörolojik durumlardır ve hem ailelerde hem de sağlık çalışanlarında strese neden olmaktadır. Bu çalışmanın amacı çocuk acil servisinde febril nöbet ve epileptik konvülziyon sırasında ebeveynlerin kaygı düzeylerinin karşılaştırılmasıdır.

Yöntemler: Ebeveynlere, nöbetlerin ilk 24 saatinde sosyo-demografik-klinik veri formu ve durumluk-sürekli kaygı envanterini içeren anket uygulandı. Febril nöbet ve epileptik konvülziyon grubu arasında ve aynı grubun anne ve babası arasında karşılaştırmalar yapıldı.

Bulgular: Çalışmaya 69'u ateşli nöbet, 64'ü epileptik konvülziyon olmak üzere toplam 133 hasta dahil edildi. Febril konvülziyon grubunda 64 anne, 33 baba, epileptik konvülziyon grubunda 58 anne, 28 baba olmak üzere toplam 183 ebeveyn çalışmaya katılmayı kabul etti. Ebeveynlerin kaygı düzeyleri febril nöbet ve epileptik konvülziyon grupları arasında benzerdi. Konvülziyon öncesi ve sırasındaki kaygı düzeylerini belirlemek için ebeveynlerin durumluk ve sürekli kaygı puanları karşılaştırıldığında, aradaki fark istatistiksel olarak anlamlıydı. Ebeveynlerin durumluk kaygı puanları hem febril nöbet hem de epileptik konvülziyon grubunda artmıştı. Annelerin durumluk ve sürekli kaygı puanları, nöbetin türü ve tekrarlama sayısı ne olursa olsun babalara göre anlamlı derecede yüksekti.

Sonuç: Çalışmamızda tüm konvülziyonların ebeveyn kaygısına neden olduğu gösterilmiştir. Konvülziyonla ilgili bilgi ve psikolojik destek tüm ebeveynlere eşit şekilde verilmelidir.

Anahtar Kelimeler: Çocuk, konvülsiyon, ebeveyn, durumluk kaygı, sürekli kaygı

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Received/Geliş Tarihi: 19.07.2024 **Accepted/Kabul Tarihi:** 06.12.2024 **Epub:** 17.12.2024 **Publication Date/Yayınlanma Tarihi:** 21.04.2025
Cite this article as: Akça H, Tekeli A, Akca Çağlar A, Tural Hesapçıoğlu S, Çıtak Kurt AN, Karacan CN. Comparison of parents' anxiety levels during febrile seizure and epileptic convulsion. J Pediatr Emerg Intensive Care Med. 2025;12:1-6

Introduction

A seizure consists of temporarily abnormal and excessive brain neuronal activity. Convulsions involving motor activity are common neurological conditions in childhood and constitute an important part of pediatric emergency service admission. In childhood, the incidence of febrile seizure is 2-5%,[1] and that of epilepsy is 0.8%.[2] Febrile seizures are the most common and benign forms of convulsions in childhood.[3] There are no long-term adverse effects associated with having one or two simple febrile seizures.[4] Although it is usually self-limiting, it can be terrifying for parents to witness seizures in their children.[5,6] Although the condition is not perceived as a serious illness by healthcare professionals, parents believe that their child will be damaged or will die in the current clinical situation due to changes in consciousness. In addition, there is increasing concern about the recurrence of febrile seizures in children with febrile illnesses.[7,8] The coexistence of psychiatric and neurodevelopmental disorders, such as intellectual disability, attention deficit/hyperactivity, depression, and anxiety, in children with epilepsy affects their quality of life negatively.[9] The anxiety level of parents of children with epilepsy is higher than that of the general population, which is explained by the adaptation of the parents to the chronic disease in their children and its effects on the quality of life.[10,11] This study aimed to evaluate the parent's anxiety levels and factors affecting febrile seizures and epilepsy in patients with convulsions who applied to the pediatric emergency service.

Materials and Methods

Participants

The study was planned as a multicenter cross-sectional study with patients and their parents who applied to Pediatric Emergency Services, Yıldırım Beyazıt University Yenimahalle Training and Research Hospital and University of Health Sciences Türkiye, Ankara Dr. Sami Ulus Child Health and Diseases Training and Research Hospital between June 1, 2018 and October 1, 2018.

Individuals who were admitted to the pediatric emergency service due to convulsions in their children, who agreed to participate in the study, who were over 18 years of age, and who could read, write, and speak Turkish were included in the study. Exclusion criteria of the study; parents who refused to participate in the study, those with a chronic disease other than epilepsy in their children, and individuals who did not know how to read, write, or speak Turkish.

Ethical approval for this study was obtained from the Yıldırım Beyazıt University Yenimahalle Training and Research Hospital Clinical Research Ethics Committee (approval no: 2018/05/13, date: 15.05.2018). All participants were informed about the study and written consent was obtained.

Data Collection Tools

- **Socio-demographic and Clinical Data Form:** This form, which was developed by the researchers, included the socio-demographic information of the cases and parents and the patient's history, family history, and clinical information about convulsions. Forms were filled in within 24 hours of convulsion.
- **State trait anxiety inventory:** This scale was developed by Spielberger[12] to assess the state and trait anxiety levels of individuals. In translating this scale into Turkish texts, reliability and validity studies were conducted by Öner and Le Compte.[13] The scale includes 40 items from self-reporting. The four-point Likert scale consists of two parts: the 20-item "state anxiety form" created to determine the sense at that moment and the 20-item "trait anxiety form" to determine the sense in general.

Research Process

The number of patients admitted to the pediatric emergency service with febrile or epileptic convulsions between the study period was 151. The parents of the 133 patients agreed to participate in the study. Only the mother in 72 cases, only the father in 11 cases, and both parents in 50 cases completed the given forms. A total of 122 mothers and 61 fathers participated in the study.

Statistical Analysis

Data analyses were performed using SPSS software version 21.0 (Statistical Package for Social Sciences software for Windows). Socio-demographic and clinical data were used for descriptive analysis (mean and standard deviation). The frequency data are expressed as numbers and percentages. The Kolmogorov-Smirnov test was used to determine whether the cases and parents matched normal distribution variables, such as mean age and state and trait anxiety scores. A Student t-test was used to compare variables that provided parametric conditions. The paired t-test was used for the dependent variables. Nominal data, such as gender, parental education level, and convulsion type, were compared using the chi-squared test. Statistical significance was set as $p<0.05$.

Results

The mean age of the patients was 51.9±51.2 months and 55% of the patients were males. A total of 133 patients were included in the study; 69 patients had febrile seizures, and 64 patients had epileptic convulsions. A total of 121 convulsions

(91%) were generalized. Approximately half (49.6%) of the patients experienced convulsions for the first time. Thirty (22.5%) patients experienced convulsions at night (between 00.00-08.00). The duration of fever was less than 24 hours in 83.5% of 79 patients with fever. Intellectual and motor disability was present in 14 patients. Forty three patients were the only children of the family. Sixteen patients with epilepsy were taking antiepileptic drugs. A family history of convulsions was noted in siblings of 7 patients and parents of 27 patients.

A total of 183 parents agreed to participate in the study: 64 mothers and 33 fathers in the febrile seizure group and 58 mothers and 28 fathers in the epileptic convulsion group. The mean ages of the parents was 31.9±6.8 years in mothers and 35.6±6.2 years, respectively. The education level of 50% of the mothers and 33% of the fathers was high school and above. 25% of the mothers and 10% of the fathers had seen patients who had convulsions before. Furthermore, 20% of the mothers and 10% of the fathers stated that they had previous knowledge about convulsions.

The mothers' state anxiety score was 52.0±9.7 and the trait anxiety score was 43.8±7.9. The fathers' state anxiety score was 46.4±9.5 and the trait anxiety score was 38.4±7.1. The state and trait anxiety scores of the mothers were significantly higher than those of the fathers ($p<0.0001$). When the parents' own states and trait anxiety scores were compared, the differences were statistically significant ($p<0.0001$). The state anxiety scores of the parents did not differ significantly according to the gender of the patient, the age of the single child, and the time of convulsion.

First, the patients were divided into two groups: febrile seizure and epileptic convulsion. The socio-demographic and clinical characteristics and parental anxiety scores of the patients are presented in Table 1. The trait anxiety scores of mothers of children with epilepsy were higher than those of the other mothers. The state anxiety scores of the parents in both the febrile seizure and epilepsy groups increased during convulsions ($p<0.0001$) (Figure 1).

Second, patients were grouped according to first and recurrent convulsions. In the first convulsion group, the mean age was low, the duration of the convulsion was short, and the state anxiety score of the fathers was high (Table 2). The state anxiety scores of the parents increased in both the first and recurrent convulsions ($p<0.0001$) (Figure 2).

When comparing the parents of 50 patients whose both mothers and fathers participated in the study, it was seen that mothers' state and trait anxiety scores were higher than fathers' state and trait anxiety scores, regardless of the type and repetition number of convulsions ($p<0.01$).

Discussion

We investigated parental anxiety levels and factors affecting pediatric patients admitted to the pediatric emergency service with febrile seizures versus epileptic convulsions. This is the first study in the literature to analyze parents' anxiety levels by convulsion type and number of repetitions. There were no significant differences in parents' anxiety caused by febrile seizure or epileptic convulsion. The mothers' state and trait anxiety scores were higher than the fathers'

Table 1. Socio-demographic and clinical characteristics and parental anxiety scores of patients diagnosed with febrile seizure or epilepsy

	Febrile seizure (n=69)	Epilepsy (n=64)	t or X^2	p
Gender, male	38 (55.1%)	35 (54.7%)	0.002	0.904
Age (months)	**26.6±14.3**	**79.2±61.8**	**-6.869**	**<0.0001**
Age at first convulsion (months)	**19.2±13.0**	**59.1±60.7**	**-5.329**	**<0.0001**
Convulsion type*	**67 (97.1%)**	**54 (84.4%)**	**6.551**	**0.010**
Convulsion duration (minutes)	7.26±8.7	10.4±17.2	-1.364	0.175
Convulsion time (%)**	16 (23.2%)	14 (21.9%)	0.033	0.856
Being the only child in the family	27 (39.1%)	16 (25.0%)	3.030	0.082
Mother's age (years)	**30.1±5.1**	**33.8±7.8**	**-3.139**	**0.002**
Father's age (years)	34.7±5.3	36.8±7.0	-1.364	0.178
Mother's education level***	39 (56.5%)	28 (43.8%)	1.970	0.160
Father's education level***	26 (36.7%)	18 (28.1%)	1.585	0.208
State anxiety score	50.6±9.9	53.5±9.4	-1.598	0.113
Trait anxiety score	**42.0±7.1**	**45.7±8.4**	**-2.677**	**0.008**
State anxiety score of father	45.6±8.6	47.3±10.6	-0.670	0.505
Trait anxiety score father	37.9±6.6	39.0±7.6	-0.597	0.553

*: Generalized, **: Between hours 24.00-08.00, ***: High school and above

anxiety scores in all cases, which was similar to previous studies.[10,14,15]

Epilepsy is not limited to convulsions in children; it can also affect cognitive and behavioral changes at different levels and affect school success. As with other chronic diseases of childhood, the effects of epilepsy can affect all family members psychosocially.[16] A previous study showed that the quality of life and psychological health of parents of children with epilepsy were severely affected, and anxiety and depression levels were increased.[17] In a systematic review by Jones and Reilly,[10] the anxiety level of parents with epileptic children was reported to be between 9% and 58%. The presence of depression symptoms among primary caregivers may lead to a decline in health-related quality of life in children.[18] Pekcanlar Akay et al. [14] showed that the depression and anxiety levels of mothers with children with epilepsy increased, and they failed to develop supportive and friendly relationships with their children. The results of our study revealed that state anxiety scores were high in both mothers and fathers with epileptic children. Moreover, trait anxiety scores were higher in mothers.

Anxiety symptoms increase in parents of children with febrile seizures. In the face-to-face meetings conducted by the pediatric emergency department nurses, it was stated that the families were worried that they were inadequate in terms of perception of the event and how to behave.[19] In a study involving mothers of 102 children with febrile seizures, increased anxiety levels were associated with uncertainty, frequency of febrile seizures, low income, and lack of knowledge.[20] The anxiety level of families who do not know about convulsions is higher than that of those who have prior experience.[21] If it is accepted that parents were

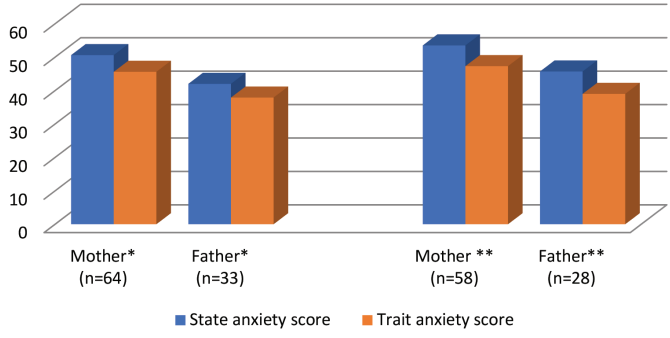

Figure 1. Comparison of state and trait anxiety scores of parents of patients diagnosed with febrile seizure or epilepsy

*: Febrile seizure group, **: Epilepsy group, p<0.0001

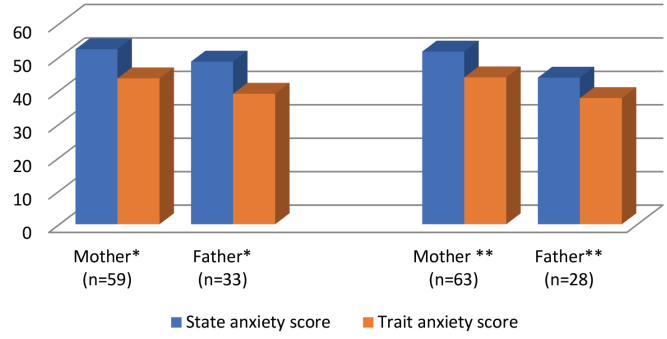

Figure 2. Comparison of state and trait anxiety scores of parents during first- or recurrent convulsions

*: First convulsion group, **: Recurrent convulsion group, p<0.0001

Table 2. Socio-demographic and clinical characteristics and parental anxiety scores of patients with first or recurrent convulsions

	First convulsion (n=65)	Recurrent convulsion (n=68)	t or X^2	p
Gender, male	39 (59.1%)	34 (50.7%)	0.935	0.334
Age (months)	**41.8±48.3**	**61.9±52.5**	**-2.188**	**0.023**
Age at first convulsion (months)	41.8±48.3	35.1±46.6	0.812	0.418
Convulsion type*	60 (90.9%)	61 (91.0%)	0.001	0.978
Convulsion duration (minutes)	**6.2±5.8**	**11.3±17.9**	**-2.188**	**0.030**
Convulsion time (%)**	14 (21.2%)	16 (23.9%)	0.136	0.836
Being the only child in the family	22 (33.3%)	21 (31.3%)	0.060	0.806
Mother's age (years)	31.6±6.8	32.1±6.8	-0.402	0.688
Father's age (years)	35.5±5.8	35.8±6.6	-0.235	0.815
Mother's education level***	40 (60.6%)	27 (40.3%)	7.654	0.006
Father's education level***	25 (37.9%)	19 (28.4%)	0.470	0.493
State anxiety score	52.3±9.6	51.6±9.9	0.398	0.691
Trait anxiety score	43.6±8.3	43.9±7.6	-0.223	0.824
State anxiety score of father	**48.6±10.0**	**43.8±8.4**	**2.009**	**0.049**
Trait anxiety score father	39.0±7.2	37.7±6.9	0.705	0.484

*: Generalized, **: Between hours 24.00-08.00, ***: High school and above

informed during the first convulsion, it could be expected that the anxiety level would decrease in recurrent convulsions. However, no significant change was observed in the parental trait anxiety level in the first and recurrent convulsions. For these reasons, it is stated that information about the disease can be obtained during the follow-up of healthy children, such as during pregnancy or vaccination. Higher levels of anxiety, especially among mothers, can be explained by the fact that mothers are responsible for the primary care of children, feel guilty due to illness, and have a responsibility toward other individuals in the family. In the present study, anxiety levels were high in both the mothers and fathers of patients who had febrile seizures.

The level of parent anxiety begins to increase in the first episode of febrile seizures.[22] Huang et al.[23] reported that when the number of repeats increased in febrile seizures, parents' anxiety levels increased further, and they believed their prognosis would be poor. The increase in the number of repetitions in the first three convulsions did not increase the risk of death, serious injury, brain damage, or learning disability.[24] Therefore, families should be informed about the recurrence and prognosis of febrile seizures. A previous study showed that the anxiety level of parents of patients who had convulsions for the first time was higher than that of parents of children with epilepsy.[25] In our study, state anxiety scores were similarly high in mothers during both the first and recurrent convulsions, whereas state anxiety scores were higher in fathers during the first convulsion. Compared to the anxiety of parents of patients with febrile and epileptic convulsions at the time of the event, both parents were found to have similar levels of anxiety. In our study, it was seen that the parents did not know enough about convulsions before the convulsions occurred, and there was no decrease in anxiety with the recurrence of the convulsions. Therefore, it is impossible to avoid the anxiety caused by inadequate parental knowledge.

Study Limitations

No comparison was made with the healthy control group.

Conclusion

Although febrile seizures have a good prognosis, they cause as much anxiety as epilepsy in parents. Because there was no difference between parents' education levels and anxiety scores, information and psychological support regarding convulsions should be given equally to all parents. Considering the intensive workload of emergency services in our country, we believe that easily accessible computers, brochures, or Internet-based training can be used to inform families about convulsions.

Ethics

Ethics Committee Approval: Ethical approval for this study was obtained from the Yıldırım Beyazıt University Yenimahalle Training and Research Hospital Clinical Research Ethics Committee (approval no: 2018/05/13, date: 15.05.2018).

Informed Consent: All participants were informed about the study and written consent was obtained.

Footnotes

Authorship Contributions

Surgical and Medical Practices: H.A., A.Ç.K., Concept: H.A., A.T., A.A.Ç., S.T.H., A.Ç.K., C.D.K., Design: H.A., A.T., A.A.Ç., S.T.H., A.Ç.K., C.D.K., Data Collection or Processing: H.A., A.T., A.A.Ç., Analysis or Interpretation: H.A., A.T., S.T.H., A.Ç.K., C.D.K., Literature Search: H.A., A.T., A.A.Ç. Writing: H.A., A.T., A.A.Ç., A.Ç.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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Research Article / Özgün Araştırma

DOI: 10.4274/cayd.galenos.2024.66487
J Pediatr Emerg Intensive Care Med 2025;12:7-13

Determination of Factors Affecting Fever Management of Parents Who Bring Their Children to the Emergency Department with High Fever

Çocuklarını Yüksek Ateş ile Acile Getiren Ebeveynlerin Ateş Yönetimini Etkileyen Faktörlerin Belirlenmesi

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Abstract

Introduction: This study was conducted to determine the factors affecting fever management of parents who bring their children to the emergency room with high fever.

Methods: This descriptive study was conducted with the parents of children aged 6 months to 5 years who presented to the pediatric emergency department of a state hospital in the southeastern region of our country with complaints of high fever. Data for the study were collected using the "descriptive characteristics form" prepared by the researcher and the "parent fever management scale". In the evaluation of the data, percentages, means, standard deviations, The study was completed with the participation of 252 parents. Percentage, mean, standard deviation, Kruskal-Wallis, Mann-Whitney U, ANOVA, t-test, and post hoc Scheffe and Jonckheere-Terpstra tests, which are advanced analysis techniques, were used in the evaluation of the data.

Results: As a result of the analysis, the average score of the participants on the parental fever management scale was calculated as 31.43±4.50. It was determined that parental fever management was influenced by factors such as the educational level of the mother and father, economic status, and place of residence.

Conclusion: Considering the minimum and maximum scores that can be obtained from the parent fever management scale, it can be stated that parents' fever management is above average.

Keywords: High fever, fever management, emergency, parent

Öz

Giriş: Bu çalışma çocuklarını yüksek ateş ile acile getiren ebeveynlerin ateş yönetimini etkileyen faktörlerin belirlenmesi amacıyla yapılmıştır.

Yöntemler: Tanımlayıcı türde yapılan bu çalışma ülkemizin güneydoğusundaki bir devlet hastanesinin çocuk acil servisine yüksek ateş şikayeti ile başvuran 6 ay-5 yaş aralığındaki çocukların ebeveynleri ile yürütülmüştür. Çalışmanın verileri araştırmacı tarafından hazırlanan "tanıtıcı özellikler formu" ve "ebeveyn ateş yönetimi ölçeği" kullanılarak toplanmıştır. Çalışma 252 ebeveynin katılımı ile tamamlanmıştır. Verilerin değerlendirilmesinde yüzde, ortalama, standart sapma, Kruskal-Wallis, Mann-Whitney U, ANOVA, t-testi, ileri analiz tekniklerinden olan post hoc Scheffe ve Jonckheere-Terpstra testleri kullanılmıştır.

Bulgular: Yapılan analizler sonucunda katılımcıların ebeveyn ateş yönetimi ölçeği puan ortalamaları 31,43±4,50 olarak hesaplanmıştır. Ebeveyn ateş yönetiminin anne ve baba eğitim durumu, ekonomik durum, yaşanılan yer gibi faktörlerden etkilendiği belirlenmiştir.

Sonuç: Ebeveyn ateş yönetimi ölçeğinden alınabilecek en az ve en çok puanlar göz önünde bulundurulduğunda ebeveynlerin ateş yönetimlerinin ortalamanın üstünde olduğu söylenebilir.

Anahtar Kelimeler: Yüksek ateş, ateş yönetimi, acil, ebeveyn

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Received/Geliş Tarihi: 08.09.2024 **Accepted/Kabul Tarihi:** 06.12.2024 **Epub:** 10.03.2025 **Publication Date/Yayınlanma Tarihi:** 21.04.2025
Cite this article as: Yıldırım M, Sevinç Akın HY, Kaya A, Gündüz B. Determination of factors affecting fever management of parents who bring their children to the emergency department with high fever. J Pediatr Emerg Intensive Care Med. 2025;12:7-13

Introduction

Fever, defined as a body temperature of ≥37.5 ^{0}C,[1] is not a disease but one of the body's important defense mechanisms.[2] Factors such as viral or bacterial infections, tissue damage and edema play a role in the etiology of fever, which can occur as a symptom of any disease.[2,3] The possibility that fever, which is usually self-limiting,[1] may cause seizures/convulsions, brain damage or physical damage in the child causes parents to worry.[4] Fever is one of the most common reasons for emergency admission in children.[3] It is thought that this may be due to the feeling of anxiety that fever creates in parents. In one study, it was found that the majority of the families participating in the study were afraid of their children's having fever, believed that fever was harmful and thought that fever could cause their children to have seizures.[5] In a study conducted in Türkiye, it was found that the majority of parents were overly anxious when their children had fever and were afraid that their children would have convulsions.[6] In a nationwide study conducted in Australia to examine parents' knowledge, beliefs and management of fever, it was found that parents thought that fever had harmful effects such as seizures, dehydration, serious illness and brain damage.[7] Parents' feelings of fear and anxiety related to fever and their knowledge or thoughts about the harms of fever may affect their management of fever. At the same time, the belief that fever may cause seizures, brain and physical damage may cause parents to experience anxiety and panic.[4] This state of anxiety and panic may cause parents to resort to wrong practices to reduce fever. In the literature, it has been reported that when children have fever, some parents apply warm shower, remove the child's clothes, and give antipyretics, while others use methods such as vinegar water, alcohol, and cologne.[5,8] In order to prevent parents from resorting to wrong practices related to fever management, it is important to investigate and reveal the factors affecting fever management and then inform parents about the identified factors. This study was conducted as a descriptive study to determine the factors affecting the fever management of parents who brought their children to the emergency room with high fever.

Materials and Methods

Aim and Type of the Study

This study was conducted as a descriptive study to "determine the factors affecting the fever management of parents who brought their children to the emergency room with high fever".

Population and Sampling of the Study

The data of the study were collected between March and June 2024. The population of the study consisted of parents (mother or father) of children between the ages of 6 months and 5 years who presented to the pediatric emergency department of a state hospital in the southeast of Türkiye with the complaint of high fever. The number of individuals to be included in the sample was calculated using the A-priori Sample Size Calculator for Multiple Regression program (alpha level 0.05, effect size 0.15, number of variables 13 and desired statistical power level 0.95) and it was determined that at least 190 individuals should be reached as a result of the calculation.[9] The study was completed with the participation of a total of 252 parents (mother or father).

Inclusion criteria were as follows: Parents who had a child between the ages of 6 months and 5 years, who brought their child to the emergency room with the complaint of high fever, who could read and write and who agreed to participate in the study were included in the study.

Data Collection Tools

The data of the study were collected in the pediatric emergency department of a state hospital in the southeast of Türkiye between March and June 2024 by the researchers conducting the study. The data were collected with face-to-face interview method using the "Descriptive Characteristics Form" and "Parent Fever Management Scale" prepared by the researchers. It took an average of 10-15 minutes to complete these forms.

Descriptive Characteristics Form: This form, prepared by the researcher, consists of 14 items about the socio-demographic characteristics of the participants.

Parent Fever Management Scale (PFMS): This scale, which aims to measure parents' practices related to the management of childhood fever, was developed by Walsh et al. in 2008. The Turkish validity and reliability study of the scale was conducted by Cinar et al.[10] in 2014. The scale consists of a total of eight items and is a five-point Likert-type scale. The minimum score is 8 and the maximum score is 40. As the score obtained from the scale increases, parents' fever management increases positively. In the validity and reliability study of the scale, Cronbach alpha value was calculated as 0.79.[10] In this study, Cronbach alpha value was found as 0.81.

Ethical Dimension of the Study

Before starting the study, the necessary permission were obtained from the Harran University Clinical Research Ethics Committee (decision no: HRU/24.02.30, date: 18.03.2024).

After the purpose of the study was explained to the participants, written and verbal consent was obtained from the participants who agreed to participate in the study. The study was conducted in accordance with the Declaration of Helsinki.

Statistical Analysis

After the data of the study were uploaded to the SPSS program, the necessary analyses were performed. Percentage, mean, standard deviation, Kruskall Wallis, Mann-Whitney U, One-Way ANOVA, t-test, post hoc Scheffe and Jonckheere-Terpstra tests, which are advanced analysis tests, were used in the evaluation of the data. Statistical significance level was accepted as $p<0.05$.

Results

Table 1 shows the sociodemographic characteristics of the participants. The mean age of the children of the participants was calculated as 27.80±14.61 (months). It was determined that the gender of the majority of the participants' children was female (52.2%), the degree of closeness was mother (58.3%), the mother's educational status was primary or secondary school (42.9%), and the father's educational status was high school (44.4%). It was determined that the majority of the parents' incomes were equal to their expenses (52.0%), they noticed when their child had fever by touching (42.1%), their children had not had febrile illnesses before (75.4%), their children had not had convulsions before (77.0%), their children did not have any chronic diseases (85.3%), and they were afraid of their children having convulsions when they had fever (54.4%). It was also found that the majority of the parents usually applied to the emergency unit between 16.00-24.00 hours when their child had fever (41.2%) and applied to the emergency room 2-6 hours after the child had fever (25.4%) (Table 1).

Table 1. Socio-demographic features

	Number (n)	Percentage (%)
Mean age of children (month)	27.80±14.61	
Gender of child		
Girl	131	52.0
Boy	121	48.0
Degree of affinity with child		
Mother	147	58.3
Father	105	41.7
Educational status of mother		
Pimary or secondary school graduate	108	42.9
High school graduate	106	42.1
University graduate	38	15.1
Educational status of father		
Pimary or secondary school graduate	76	30.2
High school graduate	112	44.4
University graduate	64	25.4
Economical status		
Income less than expense	68	27.0
Income equal to expense	131	52.0
Income more than expense	53	21.0
Place of residence		
Rural area	88	34.9
Urban area	164	65.1
Way of recognizing when the child has a fever		
By touching	106	42.1
By assessing general appearance (weakness, fatigue, etc.)	96	38.1
By taking temperature with a thermometer	50	19.8
The child's previous history of febrile illness		
Yes	62	24.6
No	190	75.4
The child's previous history of seizures		
Yes	58	23.0
No	194	77.0
The child's having a chronic disease		
Yes	36	14.3
No	216	85.3
The most feared situation when the child has a fever		
High fever doesn't scare me	6	2.4
Development of permanent brain damage	49	19.4
Convulsion	137	54.4
Loss of life	51	20.2
Other	9	3.8
Time of admission to the emergency unit		
8.00-16.00	74	29.4
16.00-24.00	104	41.2
24.00-08.00	74	29.4
Duration of emergency service admission after fever		
We came to the emergency room as soon as the fever broke	39	15.5
1 hour later	52	20.6
2-6 hours later	64	25.4
7-12 hours later	52	20.6
13-24 hours later or more	45	17.9

When the status of the participants according to the PFMS was evaluated, it was found that 47.2% of the parents mostly measured the child's temperature when the child had a fever, 52.4% mostly wanted to know what the child's temperature was, 41.3% mostly wanted to make sure that the child had plenty of fluids, 54.8% mostly used antipyretics, 53. 6% mostly checked the child's fever during the night, 42.1% mostly and 41.3% always slept in the same room with the child when the child had fever, 29.8% sometimes and 29.8% mostly woke the child at night to give antipyretics, and 51.6% mostly took the child to the doctor (Table 2).

Table 3 shows the fever management scale scores of the parents and the mean score of the parents on the PFMS was calculated as 31.43±4.50.

The comparison of the socio-demographic characteristics of the parents and the mean scores of the PFMS is shown in Table 4. It was determined that there was a statistically significant difference between mother's and father's education levels and PFMS, and the mean PFMS scores of those whose mother and father's education level was university and above were significantly higher (p≤0.001). In addition, it was found that there was a statistically significant difference between the economic status of the parents and the places where they lived and the mean scores of the parents whose incomes were higher than their expenses (p≤0.001) and who lived in urban areas (p=0.003) were significantly higher. It was determined that there was no significant difference between the PFMS and the gender of the child, the status of being the mother or father of the child, the methods of recognizing that the child had a fever, the child's previous febrile illnesses and convulsions and the presence of chronic diseases, the situation that the child was most afraid of when the child had a fever, the time of admission to the emergency unit and the time period from the onset of the child's fever to the application to the emergency service (Table 4).

Table 2. Parents' practices according to the parent fever management scale

	Never (%)	Rarely (%)	Sometimes (%)	Usually (%)	Always (%)	Mean ± SD
1. I take his/her temperature	0.4	4.8	24.2	47.2	23.4	3.88±0.83
2. I would like to know his/her temperature	0.0	2.8	17.5	52.4	27.4	4.04±0.74
3. I want to make sure he/she drinks plenty of fluids	0.4	9.1	25.0	41.3	24.2	3.79±0.92
4. I give him/her antipyretics	1.2	9.1	18.3	54.8	16.7	3.76±0.87
5. I check him/her during the night	0.0	3.6	11.5	53.6	31.3	4.12±0.74
6. I sleep in the same room with him/her	0.8	4.8	11.1	42.1	41.3	4.18±0.86
7. I wake him/her up to give antipyretics	2.4	19.0	29.8	29.8	19.0	3.44±1.07
8. I take him/her to the doctor	0.0	1.6	12.3	51.6	34.5	4.19±0.70

SD: Standard deviation

Table 3. Mean score for the parent fever management scale

Scale	Mean ± SD	Median (Min-max)
PFMS	31.43±4.50	32.00 (15.00-40.00)

PFMS: Parent fever management scale, SD: Standard deviation, Min-max: Minimum-maximum

Table 4. Socio-demographic features and parent fever management scale

	n	PFMS Mean±SD	Test
Gender of child			
Girl	131	31.40±4.63	U=7804.500 p=0.834
Boy	121	31.46±4.38	
Degree of affinity with child			
Mother	147	31.52±4.69	U=7515.000 p=0.722
Father	105	31.30±4.25	
Educational status of mother			
Pimary or secondary school graduate	108	30.24±4.53	F=10.846 **p≤0.001*** c>a=b
High school graduate	106	31.73±4.17	
University graduate	38	33.97±4.21	

Table 4. Continued

	n	PFMS Mean±SD	Test
Educational status of father			
Pimary or secondary school graduate	76	30.14±4.85	F=8.478 **p≤0.001*** c>a=b
High school graduate	112	31.30±4.13	
University graduate	64	33.18±4.18	
Economical status			
Income less than expense	68	29.95±4.86	KW=16.159 **p≤0.001**** a<b<c
Income equal to expense	131	31.38±4.17	
Income more than expense	53	33.45±4.10	
Place of residence			
Rural area	88	29.97±4.69	U=5560.500 **p=0.003**
Urban area	164	32.21±4.21	
Way of recognizing when the child has a fever			
By touching	106	31.34±4.63	F=2.892 p=0.057
By assessing general appearance (weakness, fatigue, etc.)	96	30.85±4.11	
By taking temperature with a thermometer	50	32.72±4.76	
The child's previous history of febrile illness			
Yes	62	30.50±5.67	t=-1.590 p=0.116
No	190	31.73±4.02	
The child's previous history of seizures			
Yes	58	30.67±6.00	t=-1.178 p=0.243
No	194	31.65±3.94	
The child's having a chronic disease			
Yes	36	31.38±5.12	t=-0.063 p=0.950
No	216	31.43±4.40	

*: Post Hoc-Scheffe, **: Jonckheere-Terpstra test, PFMS: Parent fever management scale, SD: Standard deviation, KW: Kruskal-Wallis, U: Mann-Whitney U, F: ANOVA

Discussion

The approach of parents is very important in the management of fever[3], which is one of the most common causes of emergency admission in childhood. For this reason, it is important to determine the knowledge and attitudes of parents about fever management and to correct any mistakes with trainings in terms of child health and then public health. In our study in which we examined the factors affecting the fever management of the parents of children admitted to the emergency department with the complaint of high fever, it was determined that the majority of the parents knew that their child had fever by touching the child and they were afraid that their children would have convulsions when they had fever. In some studies, conducted in Türkiye, similar to our findings, it was found that the majority of parents recognized that their child had fever by touching the child and that they were most afraid of their child having convulsions.[6,11,12] In a study conducted in Malaysia, it was reported that very few parents recognized that their child had fever by touching the child.[13] It is thought that this difference in the literature may be due to cultural and economic factors between countries. Detection of fever by parents by touching may lead to inaccurate detection of fever and thus delays in early intervention for fever. Failure to intervene early in fever will lead to the development of convulsions, which is an important complication of fever and a condition that parents fear. Therefore, it is recommended that practices or trainings should be planned to increase the level of knowledge of parents about fever management. In addition, in our study, it was found that the majority of parents usually applied to the emergency room between 16.00 and 24.00 when their children had fever and applied to the emergency room approximately 2-6 hours after the child's fever broke out. It is thought that the reason why they applied to the emergency room between 16.00 and 24.00 is due to the fact that outpatient clinics are closed after working hours. It is thought that when the child's fever first broke out, the parents tried to reduce the fever at home with their own means, so they applied to the emergency room approximately 2-6 hours later. In a study, it was determined that the majority

of parents applied to the emergency room if the child's fever did not decrease for a day.[16] When the studies examining the fever management of parents were examined, it was found that the mean scale scores of the fever management method of the parents ranged between 33.71±3.40 and 36.22±3.46.[8,14-16] In this study, the mean score of the parents in the PFMS was calculated as 31.43±4.50. Based on the minimum and maximum mean scores that can be obtained from the scale, it is seen that the mean scores of the parents are above the average.

In our study, when the mean PFMS scores of the parents according to the socio-demographic characteristics of the parents were compared, it was determined that there was a significant difference between maternal and paternal education levels and PFMS, and the mean PFMS scores of the parents with university and higher education level were significantly higher. When the literature was examined, similar to our study findings, studies indicating a relationship between parental education level and parental fever management were found.[14,17,18] In these studies, it was determined that as the level of education increased, the fever management of parents increased positively. It is thought that the possibility that parents' reading and research potential or awareness on health may have increased as their educational level increased, which might be the reason for this difference. In the literature, unlike our findings, there are also studies in which it was determined that there was no relationship between parental education level and parental fever management.[2,8] In our study, it was also found that there was a statistical difference between the economic status of the parents and the places where they lived and PFMS scores, and that the mean PFMS scores of parents whose incomes were higher than their expenses and who lived in urban areas were higher. The fact that parents have higher income levels or live in urban areas may facilitate their access to accurate information about childcare. Therefore, it is thought that the mean fever management scores of parents having higher income levels and living in urban areas may be higher. Similar to our findings, Yiğit and Sarıalioğlu[14] found that parents whose income was higher than expenses and who lived in urban areas had higher mean fever management scores. Higher mean fever management scores were reported for parents living in urban areas by Yazıcı and Kutlu[17] and for parents whose income was higher than expense by Kayhanlar Gulcan and Canbulat Sahiner.[18] In our study, it was determined that there was no significant difference between the gender of the child, the status of being the mother or father of the child, the methods of recognizing that the child had fever, the child's previous febrile illness and convulsions, and the presence of chronic disease and the PFMS. When the literature was examined, similar to our findings, it was found that some studies stated that there was no relationship between the gender of the child,[8,14] being a mother or father,[14] having a chronic disease[8] and parental fever management. In contrast to this study, Ekim and Üstünel[2] found that the mean fever management scores of parents whose children did not have a history of previous febrile illness were higher.

Study Limitations

The limitation of this study is that it was conducted in a single center and only with the parents of children who were admitted to the emergency unit.

Conclusion

If fever, which is an important symptom of childhood diseases, is not treated correctly, many complications may occur. For this reason, it is important that parents, who are with the child at every moment, have the right information about fever and can make the right interventions in case of fever. The first step to be taken in this regard is to determine the status of parents regarding fever management and then to eliminate the problems identified. In our study, it was determined that fever management was at a better level for parents who were university graduates, whose income was higher than their expenses and who lived in urban areas. It is thought that this difference is due to the fact that parents living in urban areas have more opportunities to obtain information, and individuals whose income is more than their expenses and who are university graduates have a higher awareness of accessing correct information. In this direction, it is recommended that all parents, especially parents living in rural areas and parents with low educational and economic levels, should be given training on fever management.

Ethics

Ethics Committee Approval: Before starting the study, the necessary permission were obtained from the Harran University Clinical Research Ethics Committee (decision no: HRU/24.02.30, date: 18.03.2024).

Informed Consent: After the purpose of the study was explained to the participants, written and verbal consent was obtained from the participants who agreed to participate in the study.

Footnotes

Authorship Contributions

Concept: M.Y., H.Y.S.A., A.K., B.G., Design: M.Y., H.Y.S.A., Data Collection or Processing: A.K., B.G., Analysis or Interpretation: M.Y., Literature Search: M.Y., H.Y.S.A., Writing: M.Y.

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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Research Article / Özgün Araştırma

DOI: 10.4274/cayd.galenos.2025.27132
J Pediatr Emerg Intensive Care Med 2025;12:14-21

Evaluation of the Level of Basic First Aid Knowledge of Parents Applying to Paediatric Emergency Department

Çocuk Acil Servise Başvuran Ebeveynlerin Temel İlk Yardım Bilgisi Düzeylerinin Değerlendirilmesi

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Abstract

Introduction: First aid is a set of practices that all members of society should know under all circumstances. Our aim was to evaluate the level of basic first aid knowledge of parents of patients admitted to the pediatric emergency department and to raise awareness about first aid knowledge.

Methods: The study was conducted in University of Health Sciences Türkiye, İzmir Tepecik Education and Research Hospital, Clinic of Pediatric Emergency between December 15, 2017 and March 15, 2018. A descriptive and cross-sectional questionnaire was applied to question the socio-demographic characteristics of the parents who participated in the study, the situations requiring first aid encountered by their children and their level of first aid knowledge. Ethics committee approval was obtained (2017-30).

Results: The mean age of the 350 parents included in the study was 35.57±8.21 years and 157 of them were male. Sixty-one (17.4%) of the parents had first aid training. It was found that 32.9% of university graduates had first aid training (p<0.001). There was no statistically significant difference between the working status of the mother and the caregiving parent and the event requiring first aid (p=0.133, p=0.930, respectively). A significant relationship was found between the educational level of the parents and first aid, and between first aid training and finding oneself competent (p<0.001 and p<0.001, respectively).

Conclusion: The results of the study showed that there was a relationship between the level of education and first aid, first aid training and self-perception of adequacy and the importance of education. First of all, the level of education in the society should be increased, accidents frequently encountered by children should be identified and first aid training should be given to parents.

Keywords: Child, parent, education, awareness, first aid

Öz

Giriş: İlk yardım, toplumun tüm bireylerinin her koşulda bilmesi gereken bir uygulamalar bütünüdür. Amacımız çocuk acil servisine başvuran hastaların ebeveynlerinin temel ilk yardım bilgi düzeyini değerlendirmek, ilk yardım bilgisi konusunda farkındalık yaratmaktır.

Yöntemler: Araştırma, Sağlık Bilimleri Üniversitesi, İzmir Tepecik Eğitim ve Araştırma Hastanesi, Pediatri Acil Kliniği'ne 15 Aralık 2017-15 Mart 2018 tarihleri arasında gerçekleştirildi. Tanımlayıcı ve kesitsel tipte olan çalışmaya katılan ebeveynlerin sosyo-demografik özelliklerini, çocuklarının karşılaştıkları ilk yardım gerektiren durumları ve ilk yardım bilgi düzeylerini sorgulayan anket uygulandı. Etik kurul onayı alındı (2017-30).

Bulgular: Çalışmaya dahil edilen 350 ebeveynin yaş ortalaması 35,57±8,21 yıl, 157'si erkekti. Ebeveynlerin 61'inin (%17,4) ilk yardım eğitimi vardı. Üniversite mezunu olanların %32,9'unun ilk yardım eğitimi aldığı saptandı (p<0,001). Annenin çalışma durumu ve bakım veren ebeveyn ile ilk yardım gerektiren olay arasında istatistiksel olarak anlamlı bir fark bulunmadı (sırasıyla p=0,133, p=0,930). Ebeveynlerin eğitim düzeyi ile ilk yardım arasında, ilk yardım eğitimi ile kendini yeterli bulma arasında anlamlı ilişki bulundu (sırasıyla p<0,001; p<0,001).

Sonuç: Çalışmanın sonuçları eğitim düzeyi ile ilk yardım, ilk yardım eğitimi ile kendini yeterli görme arasındaki ilişki saptandığını ve eğitimin önemini göstermiştir. Öncelikle toplumda eğitim düzeyi yükseltilmeli, çocukların sık karşılaştığı kazalar saptanarak ebeveynlere bunlara yönelik ilk yardım eğitimi verilmelidir.

Anahtar Kelimeler: Çocuk, ebeveyn, eğitim, farkındalık, ilk yardım

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Received/Geliş Tarihi: 17.05.2024 **Accepted/Kabul Tarihi:** 17.01.2025 **Epub:** 20.03.2025 **Publication Date/Yayınlanma Tarihi:** 21.04.2025
Cite this article as: Dinçer İ, Balcı UG, Harputluoğlu N, Anıl M. Evaluation of the level of basic first aid knowledge of parents applying to paediatric emergency department. J Pediatr Emerg Intensive Care Med. 2025;12:14-21

Introduction

Parents have an important role in providing a safe environment for children, preventing accidents and providing first aid in case of accidents. Although some conscious or unconscious behaviors may cause accidents, it is important to educate family members, to prevent accidents or to provide first aid in case of accidents and to raise awareness on this issue.[1] Despite protective measures, accidents can still occur and cause injuries and deaths of children. Therefore, correct and effective first aid at the time of an accident or life-threatening event is very important to reduce death and disability.[2]

In a sudden accident, illness or life-threatening situation, first aid is defined as the interventions made with the facilities available in the environment without medical equipment and without the use of drugs in order to save the life of the person and/or prevent the situation from getting worse until medical support arrives.[3] First aid is a set of practices that all members of the society should know under all conditions, regardless of whether they receive health education or not, and situations that require first aid can be encountered at any time throughout life. The aim of this study is to evaluate the level of basic first aid knowledge of parents of patients admitted to the pediatric emergency department, to determine the relationship with various factors, to raise awareness about first aid knowledge, and to ensure that the necessary steps are taken in terms of knowledge, attitude and behavior.

Materials and Methods

The study was a descriptive and cross-sectional study planned to evaluate the level of basic first aid knowledge of the parents of patients admitted to the Pediatric Emergency Clinic of University of Health Sciences Türkiye, İzmir Tepecik Education and Research Hospital between December 15, 2017 and March 15, 2018. The study included 350 parents who met the inclusion criteria and agreed to participate in the study without time limitation and after explaining the purpose of the study. The personal information form included a total of 8 questions about demographic characteristics; gender, age, number of children, education level, income level, employment status, and the person who undertakes child care.

The form that evaluates first aid knowledge consists of 23 questions on the parameters such as the first aid training status, the person who applied the first aid, having any previous experience on a situation requiring first aid and if so, what this situation is, the first intervention after encountering with the situation requiring first aid, the approach to head trauma, the approach to the case of obstruction of the trachea, the approach to the case of foreign body in the ear, the approach after nosebleed, the approach to bee sting, the approach after cat or dog bite, the approach after foreign body sting, the approach to bleeding after any incision, the approach to drug poisoning, the approach to fainting, the approach to drowning, the approach to swelling in the body after trauma, the approach to burn, the approach to electric shock, and the approach to foreign body in the eye (Supplementary Table 1). Parents admitted to the emergency department due to accidents, parents who agreed to participate in the study and parents aged 18-65 years were included in the study. Parents who presented to the emergency department for reasons other than accidents, parents who refused to participate in the study, and parents outside the age range of 18-65 years were excluded from the study.

Ethical approval was obtained from the Ethics Committee of University of Health Sciences Türkiye, İzmir Tepecik Education and Research Hospital to participate in the study (decision no: 30, date: 11.12.2017). Informed consent forms were obtained from the subjects included in the study.

Statistical Analysis

The data obtained were coded and saved in SPSS for Windows (Statistical Package for Social Sciences for Windows) 24.0 package program and statistical analysis was performed. Descriptive statistics were given as arithmetic mean ± standard deviation and median (minimum-maximum) for numerical variables and as numbers and percentages for categorical data. The compatibility of numerical variables with normal distribution was analyzed with the Shapiro-Wilk test. Differences between groups in terms of categorical variables were analyzed with the chi-square test and Fisher's exact exact test. Variables were analyzed at 95% confidence level and $p \leq 0.05$ was considered significant.

Results

The mean age of the parents (n=350) participating in the study was 35.57±8.21 years and 157 were male (44.9%) and 193 were female (55.1%). Demographic characteristics of the study group are presented in Table 1. Of the parents who participated in the study, 61 (17.4%) stated that they had first aid training, while 289 (82.6%) stated that they did not receive any training. Of the parents who participated in the study, 8% (n=28) considered themselves adequate in first aid, 45.7% (n=160) did not consider themselves adequate, and 46.3% (n=192) considered themselves partially adequate. Among the children of the parents who participated in the study, 47.7% stated that they encountered a situation requiring first aid at least once. The most frequently encountered events requiring first aid by the children of the parents participating in the study are presented in Table 2. After encountering

a situation requiring first aid, 46.1% (n=77) of the parents stated that they took their children to the hospital without any intervention, and the first interventions made by the parents are presented in Table 3. When the educational status of the parents and first aid training status were examined, it was found that 32.9% of those with a university degree received first aid training, which was statistically significant (p<0.001) (Table 4). When the distribution of parents' first aid training and first aid competence status was examined, the competence of those who received training was found to be significantly related (p<0.001). There was no statistically significant difference between the educational level of the parents and the situation requiring first aid (p=0.146).

Table 1. Socio-demographic features of the parents

Demographic features	Number (n=350)	%
Gender		
Male	157	44.9
Female	193	55.1
Educational status		
Illiterate	15	4.3
Primary school	75	21.4
Secondary school	65	18.6
High school	122	34.9
University	73	20.9
Number of children in the family		
1	148	42.3
2	121	34.6
3	57	16.3
4	21	6.0
5	3	0.9
Income level of the family		
Below minimum wage	16	4.6
Minimum wage	74	21.1
Between minimum wage and 2000 ₺	96	27.4
Over 2000 ₺	164	46.9
Mother's employment status		
Working	110	31.4
Not-working	240	68.6
The person who gives care to the child		
Mother	250	71.4
Father	3	0.9
Grandmother	46	13.1
Caregiver	21	6.0
Other	30	8.6

*The minimum wage was set at 1604.12 ₺ in the working year

No statistically significant difference was found between the number of children and income status of the parents participating in the study and the situation requiring first aid (p=0.711, p=0887, respectively). There was no statistically significant difference between the employment status of the mother and the caregiver and the situation requiring first aid (p=0.133, p=0930, respectively). The accuracy distribution of the events requiring first aid and the first interventions performed by the parents are presented in Table 5.

Table 2. Distribution of situations requiring first aid in children

Event requiring first-aid	Number (n=167)	%
Poisoning	13	7.8
Head trauma	30	18
Fainting	16	9.6
Nose bleeding	15	9
Bleeding due to incision anywhere in the body	4	2.4
Cat or dog bite	12	7.2
Foreign body in the ear or nose	12	7.2
Burn	12	7.2
Electric shock	2	1.2
Drowning	5	3
Post-traumatic swelling in any part of the body (arm, hand, leg, foot, etc.)	15	9
Foreign body in the eye	5	3
Bee and insect stings	1	0.6
Nail puncture	5	3
Swallowing a foreign body (coin, bead)	20	12

Table 3. Distribution of parents' first interventions after an incident requiring first aid

Intervention	Number (n=167)	%
I take him/her to the hospital	77	46.1
I make him/her vomit	3	1.8
I put a tampon in his/her nose	9	5.4
I press on the bleeding area	5	3
I wash the eye with water	4	2.4
I wash the bite site with soap and water	6	3.6
I apply cold	28	16.8
I remove the foreign body	6	3.6
I pour water on his/her face	1	0.6
I wash with cold water	6	3.6
I hit him/her in the back	2	1.2
Other	10	6
I take it out of his/her mouth	2	1.2
I cut the power	2	1.2
I intervene and take him/her to hospital	6	3.6

Table 4. Distribution of parents' level of education and first aid training status

		First-aid training				
		Yes		No		p
		Number	%	Number	%	
Educational status	Illiterate	1	6.7	14	93.3	<0.001
	Primary school	7	9.3	68	90.7	
	Secondary school	3	4.6	62	95.4	
	High school	26	21.3	96	78.7	
	University	24	32.9	49	67.1	

Table 5. Distribution of accuracy of first aid provided by parents at the time of the incident

Intervention	Giving the correct answer (n=350)	%
Head trauma	246	70.3
Respiratory distress/aspiration	143	40.9
Cuts	229	65.4
Foreign body in the ear	181	51.7
Cat/dog bite	107	30.6
Bee sting	114	32.6
Nose bleeding	195	55.7
Nail punctuation	238	68
Poisoning	172	49.1
Burns	248	70.9
Fainting	129	36.9
Swelling due to trauma	289	82.6
Electric shock	198	56.6
Drowning	192	54.9
Foreign body in the eye	146	41.7

Discussion

The results of this study showed the importance of education and that parents were more likely to receive education as their level of education increased. It was shown that encountering situations requiring first aid was not associated with educational level, socio-economic level, number of caregivers and number of children.

It has been reported that parents who received first aid training were similar in terms of mean age, educational status and socio-economic level.[4-6] Mothers are the most common caregivers and they have to intervene in case of an event requiring first aid.[7] Similarly, mothers were the caregivers in our study and more than half of the participants were women. This may be related to the average age at marriage, having children and the similar likelihood of encountering situations requiring first aid. The attribution of the duty of taking care of children to mothers may be due to women's working rate, cultural approach, and the idea that this is the natural thing to do.

Parents' interest in receiving first aid training is low. In studies, while the rate of parents who received first aid training was reported to be between 5.9% and 9%, higher rates (17.4%) were found in our study.[7-10] It is known that education is related to low socio-economic status.[11] In the literature, the importance of adding first aid training to the curriculum for pre-school and primary school teachers and parents has been reported.[12] In addition to low rates of first aid training, it has been shown that the rates of updated training are also low, and the rates of being able to perform cardiopulmonary resuscitation are very low.[13] In our study, the rates of first aid training were found to be higher, and in addition, the self-sufficiency of those who received first aid training was significantly higher than those who did not receive first aid training. These results may be due to the fact that our study was conducted in the west of the country, in a region where education is relatively high and women play a more active role in business life. Therefore, providing and updating first aid training starting from the primary education period may increase the number of parents who receive first aid training and the number of parents who feel competent.

In our study, the rate of parental referral to the emergency department in case of an event requiring first aid was observed in approximately half of the cases (46.1%). In one study, the rate of seeking help from a physician in case of a situation requiring first aid was found to be quite high (70%) and burn cases were evaluated.[4] The rate of encountering a situation requiring first aid was found to be similar to the literature.[4,14] One study showed high rates because it was conducted in a physical education and sports teaching department.[14] Among the situations encountered, the most common situations requiring first aid were reported as falls and nosebleeding.[4,10,15,16] In our study, head trauma was found to be the most common condition requiring first aid. Different results may have been found due to the region where the study was conducted and the socio-cultural characteristics of the region.

Approximately half of the parents who encounter a situation requiring first aid take their children to the hospital. In only one study in the literature, the rate of application to a health institution was found to be low.[9] It has been reported that approximately half of the parents who were questioned about head trauma gave correct answers, and this rate was found to be as high as 70.3% in our study.[17] In our study, head trauma was found to be the most common condition requiring first

aid, and this may be due to the fact that parents think that it is a high-risk situation and that they have knowledge about it from the information and experiences on this subject because it poses a life risk.

Working mothers are less likely to encounter a situation requiring first aid than non-working mothers. Spending less time with the child reduces the likelihood of encountering a situation requiring first aid.[5] The frequency of accidents is high in children who receive care from people and institutions other than the mother.[18] It has been shown that first aid training should be widespread in the society and the use of training videos for this purpose is effective.[19] In our study, considering the fact that the caregiver parent was a mother, that the level of education was low, that the level of first aid training was low, and the characteristics of the region, the lack of basic and first aid training of mothers emerged as an important factor.

Study Limitations

The fact that the study was single centered and conducted in a province in the west of Türkiye is a limitation of the study. It cannot be generalized to all parents without multicenter studies with high numbers of participants.

Conclusion

First aid training of parents is important for children to receive first aid in accidents. First aid training of mothers seems to be a priority. Our study showed that parents were more prone to receive training as their level of education increased. Raising public awareness about first aid, creating awareness, brochures, social media and establishing a national policy are important for providing first aid to children.

Ethics

Ethics Committee Approval: Ethical approval was obtained from the Ethics Committee of University of Health Sciences Türkiye, İzmir Tepecik Education and Research Hospital to participate in the study (decision no: 30, date: 11.12.2017).

Informed Consent: Informed consent forms were obtained from the subjects included in the study.

Footnotes

Authorship Contributions

Concept: İ.D., U.G.B., M.A., Design: İ.D., U.G.B., M.A., Data Collection or Processing: İ.D., Analysis or Interpretation: İ.D., U.G.B., N.H., Literature Search: İ.D., U.G.B., M.A., Writing: N.H.

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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Supplementary Table 1. Questionnaire on the approach of parents of pediatric patients brought to the emergency department for basic first aid

1.	Name/Surname	
2.	Gender	
3.	Age	
4.	Educational status	1. Illiterate 2. Primary school 3. Secondary school 4. High school 5. University
5.	Number of children in the family	
6.	Income level of the family	1. Below minimum wage 2. Minimum wage 3. Minimum wage of 2000 ₺ 4. Over 2000 ₺
7.	Mother's employment	1. Working 2. Not working
8.	The person who gives care to the child	1. Mother 2. Father 3. Grandmother 4. Caregiver 5. Other
9.	What is first aid?	
10.	Who are the first aid practitioners?	Doctor Nurse Those having first aid certificate Other
11.	Do you consider yourself competent in first aid?	Yes No I know a little Other
12.	Have you experienced an incident at home or on the street that required first aid to your child?	a) Yes b) No
13.	If yes, which of the following events did you experience?	a) Poisoning b) Head trauma c) Fainting d) Nose bleeding e) Bleeding due to cut f) Cat/dog bite g) Foreign body in the ear h) Burn ı) Electric shock j) Drowning k) Swelling due to trauma l) Foreign body in the eye m) Traffic accident n) Multiple trauma
14.	What was your first intervention?	
15.	Which health facility did you contact after the intervention?	a) Emergency unit of a hospital b) Health Center c) Polyclinic d) Did not apply

Supplementary Table 1. Continued		
16.	Suppose that your child fell down while playing at home and hit his/her head, and his/her forehead was swollen, what would your first intervention be?	a) I would put ice on his/her forehead b) I would wrap his/her head in a cloth c) I would take him/her to the hospital without doing anything. d) Other
17.	Suppose you were feeding your child and suddenly he/she started coughing and turning purple, what would you do first?	a) I would hit him/her hard on the back b) I would put my hand in his/her mouth c) I would pass behind him/her and pull my hands in front of his/her abdomen d) I would give water
18.	What would you do if you saw your child swallowing coin?	a) I would put my hand in his/her mouth to check b) I would have him/her eat bread c) I would give water to drink d) I would observe the child and act accordingly
19.	What is your first intervention when a bead gets in your child's ear?	a) I try to pull it out with tweezers or a Q-tip. b) I drip Vaseline or glycerin to make the bead come out. c) I never intervene, thinking that I will damage the eardrum. d) Other
20.	Suppose your child was bitten by a cat while playing on the street, what are the first things to do?	a) I would wash the bite with soap and water b) If the bite site is bleeding, I try to stitch it up c) I would press tobacco on the bleeding area d) I would not intervene at all
21.	In the case of bee sting in the garden, what are the first things to do?	a) If the bee-sting is left, I remove it b) I apply ammonia to the bee sting c) I apply cold to the bee sting d) I apply salt to the bee sting
22.	What do you do for the first treatment of nose bleeding?	a) I squeeze the wings of the nose and tilt the head forward b) I put cotton in the nose c) I clean his/her nose d) I wash his/her nose with cold water
23.	Suppose your child was pricked by a nail while playing in the street, what would you do in the first intervention?	a) I would remove the nail immediately b) I would not remove the nail c) I would wipe the wound with tincture of iodine d) I would take him/her to the hospital immediately
24.	You see your child at home with a medicine box in his/her hand and chewing medicine in his/her mouth, what is your first intervention?	a) I make him/her vomit b) I put my finger in his/her mouth and try to get any leftovers c) I make the child drink water d) I call poison counseling
25.	Suppose hot water was spilled on your child's hand, what would you do as a first intervention?	a) I would wash his/her hand with cold water b) I would wash his/her hand with warm water c) I would put ice in his/her hand d) I would cut the child's contact with hot water
26.	What do you do in case of your child's fainting?	a) I check his/her consciousness b) I control his/her breathing c) I pour cold water on him/her d) I give him/her water in his/her mouth
27.	Your child has a fever, what is the first thing to do?	a) I give antipyretics b) I wash with vinegar water c) I cover the child with a wet sheet d) I undress the child and apply cold to the groin and armpit with wet cotton
28.	What do you do as the first intervention in case of drowning in water?	a) I get him/her out of the water safely b) I inform the lifeguard c) I do not intervene at all d) I start CPR after I get him/her out of the water
29.	You pulled your child out of the water, what is your first intervention?	a) I check if he/she is breathing b) I press on the abdomen to let the excess water out c) I start CPR immediately d) I do not intervene at all
30.	What is the first thing you do when you see your child's foot hit the table and swell up?	a) I apply cold to the swollen area b) I rub the swollen place with olive oil c) I bandage his/her foot tightly d) I elevate his/her foot up

Supplementary Table 1. Continued		
31.	What is the first thing to do in case of your child's being exposed to electric shock?	a) I cut the electricity b) I immediately remove from the place of electric shock by holding him/her with my hands c) I check the child's breathing after removing him/her d) I do not intervene at all
32.	What do you do for your child who comes with a cut on his/her hand and says that a toy cut him/her while playing?	a) I apply tobacco on the injury b) I wash with water c) I apply pressure with a clean cloth d) I pour cologne on the injury

Research Article / Özgün Araştırma

DOI: 10.4274/cayd.galenos.2025.72324
J Pediatr Emerg Intensive Care Med 2025;12:22-8

Evaluation of the Patients Admitted to the Pediatric Emergency Department with Influenza Like Illness During 2009 Influenza A/H1N1 Pandemic Period

2009 İnfluenza A/H1N1 Pandemisinde Çocuk Acil Servisine Grip Benzeri Hastalık Kliniği ile Başvuran Hastaların Değerlendirilmesi

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Abstract

Introduction: In this study, the aim is evaluation of clinical and epidemiological characteristics of the patients presenting to pediatric emergency service with flu like findings.

Methods: Demographical, clinical, laboratory, treatment, hospitalization, and vaccination characteristics of the patients of 1 month-18 years old presenting to Pediatric Emergency Department of Dokuz Eylül University Hospital with influenza-like symptoms in between September 2009-March 2010 have been evaluated.

Results: In the pandemic period 3,646 patients were presented with influenza like illness and 902 patients were evaluated in this study. The mean age was 73.4±56.1 (median: 60.0) (1-204) months. The most affected age group was school children of age between 5 and 14. The age, 42% of admitted patients were under one year of age. Presenting symptoms of the patients were determined fever (92%), cough (89%), rhinorrhea (64%), sore throat (40%), myalgia (26%), headache (26%), vomiting-diarrhea (26%), and respiratory distress (3%) in respectively. The rapid antigen test was used in 487 (54%) patients and founded positive in 203 (42%) of them. The pandemic influenza A/H1N1 real time-polymerase chain reaction test was performed in twenty-four (3%) patients, 16 (67%) of them had positive result. The antiviral treatment was started in 357 (90.4%) patients for having a risk factor, in 27 (6.8%) patients for having symptoms of serious illness and in 11 (2.8%) patients as a prophylactic. No patient was died due to pandemic influenza. Twenty-two (2.4%) patients were vaccinated by seasonal influenza vaccine and pandemic virus vaccine while 15 (1.7%) patients were vaccinated by only seasonal influenza vaccine.

Öz

Giriş: Bu çalışmada, çocuk acil servisine pandemik influenza döneminde grip benzeri hastalık bulguları ile başvuran hastaların klinik ve epidemiyolojik özelliklerinin değerlendirilmesi amaçlanmıştır.

Yöntemler: Dokuz Eylül Üniversitesi Hastanesi Çocuk Acil Servisi'ne Eylül 2009-Mart 2010 tarihleri arasında grip benzeri hastalık bulguları ile başvuran 1 ay-18 yaş arası hastaların demografik, klinik, laboratuvar, tedavi, hastaneye yatış ve aşılanma özellikleri değerlendirildi.

Bulgular: Pandemi döneminde grip benzeri hastalık tanısıyla başvuran toplam 3.646 hastadan 902 tanesi değerlendirmeye alındı. Değerlendirilen hastaların yaş ortalaması 73,4±56,1 (ortanca: 60,0 ay) (1-204 ay) ve en çok etkilenen yaş grubu 5-14 yaş (%44) arası okul çocuklarıydı. Yatırılan hastaların ise %42'sinin yaşı bir yaşın altında idi. Hastaların başvuru semptomları sıklık sırasına göre; ateş (%92), öksürük (%89), burun akıntısı (%64), boğaz ağrısı (%40), miyalji (%26), baş ağrısı (%26), kusma-ishal (%26) ve solunum sıkıntısı (%3) olarak belirlendi. Çalışmada 487 (%54) hastaya hızlı antijen testi yapıldı ve 203 (%42) hastada sonucun pozitif olduğu görüldü. Yirmi dört (%3) hastaya pandemik influenza A/H1N1 gerçek zamanlı-polimeraz zincir reaksiyonu testi yapıldı, 16 (%67) tanesinin sonucu pozitif saptandı. Hastaların 357'sine (%90,4) influenza ilişkili komplikasyonlar için risk faktörü olması, 27'sine (%6,8) ciddi hastalık bulgusu olması ve 11'ine (%2,8) ise profilaktik amaçla olmak üzere toplam 395 (%44) hastaya antiviral tedavi verildi. Pandemik influenzaya bağlı hiç hasta kaybedilmedi. Yirmi iki (%2,4) hastanın mevsimsel influenza ve pandemik virüs aşısı olduğu, 15 (%1,7) hastanın ise sadece mevsimsel influenza aşısı olduğu görüldü.

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Received/Geliş Tarihi: 09.10.2024 **Accepted/Kabul Tarihi:** 13.02.2025 **Epub:** 09.04.2025 **Publication Date/Yayınlanma Tarihi:** 21.04.2025
Cite this article as: Özden Ö, Duman M, Gençpınar P, Çağlayan Sözmen Ş, Yılmaz D. Evaluation of the patients admitted to the pediatric emergency department with influenza like illness during 2009 influenza A/H1N1 pandemic period. J Pediatr Emerg Intensive Care Med. 2025;12:22-8

***One of the authors of this article (M.D.) is a member of the Editorial Board of this journal. He was completely blinded to the peer review process of the article.**

Abstract

Conclusion: The study has been shown that the most affected group was the school age due to pandemic influenza, and the majority of patients admitted to hospital were the age under one year. We thought that early initiation of treatment was important to prevent complications because of the influenza especially in the risk groups.

Keywords: Pandemic influenza, pediatric emergency, influenza rapid test

Öz

Sonuç: Çalışmamızda pandemik influenzadan en çok okul çağı çocuklarının etkilendiği, ciddi hastalık bulguları ile hastaneye yatırılan olguların çoğunluğunun ise bir yaş altı çocuklar olduğu bulunmuştur. İnfluenza komplikasyon gelişimi açısından risk taşıyan hastalarda erken tedavi başlanmasının, komplikasyon gelişiminin önlenmesi açısından önemli olduğu düşünülmüştür.

Anahtar Kelimeler: İnfluenza pandemisi, çocuk acil, influenza hızlı test

Introduction

Influenza virus infections are a public health problem worldwide due to epidemics. The most important feature of the influenza virus is antigenic change. In this way, influenza virus causes epidemics affecting the whole society every year. In addition, it also causes pandemics that affect the whole world every 10-40 years. There have been three influenza pandemics in the last century. These pandemics, which affected large masses, caused significant economic losses, morbidity, and mortality.[1]

Pandemic influenza A/H1N1 virus was first identified in Mexico in February 2009 and rapidly spread throughout the world.[2,3] The World Health Organization (WHO) raised the influenza pandemic alert level to phase-6 on June 11, 2009. Thus, the first pandemic of the 21st century was declared.[4]

The spread of the virus is by droplet, like classical influenza agents.[5] The incubation period of the pandemic virus is 1-7 days. In the first 2-3 days of the disease, the amount of virus excreted in respiratory secretions is the highest and this is known to be correlated with fever. Therefore, the period of influenza contagiousness is considered to be 24 hours before the onset of fever and 24 hours after the normalization of fever.[5-7] The disease has a sudden onset and is characterized by high fever, myalgia, malaise, headache and dry cough. The disease resolves in the majority of patients 3-7 days after the onset of symptoms. Influenza does not usually cause severe illness, but can cause serious and fatal infections in young children, the elderly people and the chronically ill people, who are considered risk groups.[6] There are many laboratory methods available for diagnosis, treatment and surveillance. Antigenic diagnostic methods such as direct immunofluorescence and rapid tests are used in health care institutions where drug use and infection control are in question and therefore rapid diagnosis is important. In these centers, isolation of the virus and detailed antigenic information are not needed, and high sensitivity and specificity of the test are important.[3,6,8,9]

The aim of this study was to evaluate the demographic, clinical and epidemiologic characteristics of patients aged between 1 month and 18 years who presented to the Pediatric Emergency Department of Dokuz Eylül University Hospital with influenza-like symptoms during the 2009 A/H1N1 influenza pandemic that affected the whole world, to obtain information to be used in future pandemics, to determine the points to be considered in the follow-up of patients with this information and to contribute to the epidemiologic data on influenza in our country.

Materials and Methods

Patients aged between 1 month and 18 years who presented to the Pediatric Emergency Department of Dokuz Eylül University Hospital with influenza-like illness (ILI) during the influenza virus 2009 A/H1N1 pandemic were included in the study. The case management guideline of the Centers for Disease Control and Prevention (CDC) was used for the clinical definition of ILI.[3,6] According to this definition, a new-onset axillary temperature above 38 °C and/or sore throat and/or dry cough without any other cause was accepted as ILI and the "pandemic influenza 2009 A/H1N1 follow-up form" was filled out in the pediatric emergency department. In this form, demographic and clinical characteristics, examination and laboratory findings, risk groups, whether they received antiviral treatment, hospitalization, complications and vaccination status were recorded. Patients with complete data on the follow-up form were included in the study. Clinical findings such as body temperature, nasal discharge, cough, sore throat, headache, myalgia, vomiting-diarrhea and respiratory distress were evaluated in all patients. Risk groups for the development of complications were identified as children younger than two years of age, patients with chronic lung, kidney and liver diseases, neurologic, cardiovascular, metabolic and endocrine diseases, chronic aspirin use, immunodeficiency and obesity.[3,6,7] Signs of severe disease were considered as general condition disorder, extreme restlessness, altered consciousness, moderate to severe dehydration, respiratory distress, convulsions, persistent high fever and clinical deterioration after resolution of influenza symptoms.[3,6,7]

Laboratory findings, reasons for hospitalization, treatments administered, length of hospitalization, complications, morbidity and mortality of hospitalized patients were evaluated.

Influenza A/B rapid antigen test was performed from nasal aspiration specimens of patients who were in risk groups for the development of complications or who had signs of severe disease. Laboratory findings included complete blood count, C-reactive protein (CRP), influenza rapid antigen test, and real time-polymerase chain reaction (RT-PCR) test results.

Ethics committee approval for the study was obtained from the Dokuz Eylül University Non-interventional Clinical Research Evaluation Commission (decision no: 2010/06-06, date: 30.06.2010). Consent for the study was obtained from the legal guardians of all patients.

Statistical Analysis

SPSS 15.0 program was used for statistical evaluation. Quantitative variables were expressed as mean ± standard deviation and median (minimum-maximum), and qualitative variables were expressed as percentages. Chi-square test was used to compare categorical data. The significance level of the findings was accepted as $p<0.05$.

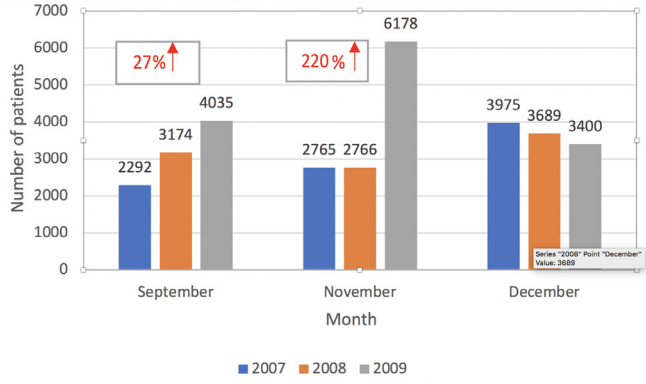
Results

A total of 3,646 patients were admitted to our clinic with ILI symptoms between September 2009 and March 2010. Of these cases, 902 patients with complete data were included in the study. During this period, it was found that the number of patients admitted to the pediatric emergency department increased by 27% in October compared to the previous year and by 220% in November, when the cases were most common, compared to the previous year. It was observed that the number of patients started to increase as of the first week of September, peaked in the third and fourth weeks of November and decreased rapidly in December (Graph 1).

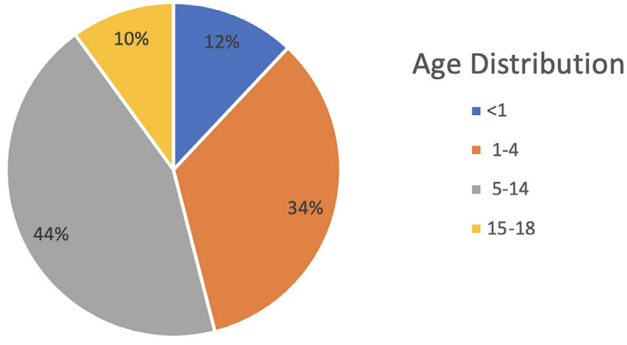
Of the patients admitted to the study, 501 (55%) were boys, 401 (45%) were girls, the mean age was 73.4±56.1 months (median: 60.0 months) (1 month - 204 months), and patients aged 5-14 years were mostly affected by the pandemic (Graph 2). The duration of symptoms before presentation varied between 1-10 days, with a mean symptom duration of 2.03±1.55 days. It was observed that 75% of the patients presented to the emergency department within the first 48 hours of symptoms.

In all cases we evaluated, at least one of the clinical definitions of influenza disease such as fever, cough, sore throat, headache, myalgia, runny nose, vomiting and diarrhea was present. The most common findings in patients admitted to the emergency department with ILI were as follows: fever (92%), cough (89%), runny nose (64%), sore throat (40%), myalgia (26%), headache (26%), vomiting-diarrhea (26%) and respiratory distress (3%) (Graph 3).

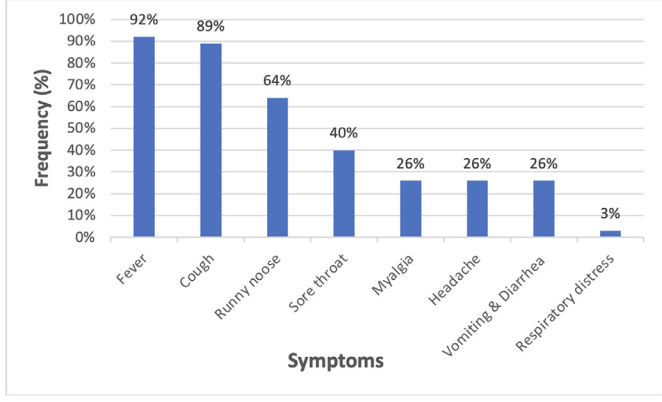
In the emergency department, 132 (14%) patients had a temperature ≤37.9 °C, 486 (54%) had a temperature 38-38.9 °C and 284 (32%) had a temperature ≥39 °C. Four hundred and fifty-one (50%) of the patients had risk factors for



Graph 1. The impact of pandemic influenza on emergency room patient load
*Percentage rates indicate the increase in the number of patients presenting to the emergency room in October-November 2009 compared to 2008



Graph 2. Age distribution of cases (%)



Graph 3. Patients' presenting symptoms

influenza-related complications. The most common risk factor was age less than two years (50.1%). Other risk factors were chronic lung disease (35.5%), neurologic disease (5.1%), cardiovascular disease (2.7%), metabolic disease (2.2%), renal-hepatic disease (1.8%), immunodeficiency (1.3%), hematologic disease (0.9%) and chronic aspirin use (0.4%). Treatment was given to 85% of patients with risk factors.

Signs of influenza-related serious illness were present in 27 (3%) patients. Respiratory distress was detected in 24 (89%) patients and was the most common serious illness finding. Febrile convulsion was detected in one of the other three patients, moderate to severe dehydration in one patient and altered consciousness in one patient. Risk factors were not present in 33% of the patients with serious illness. All patients with signs of severe illness were hospitalized and followed up and antiviral treatment was initiated.

Laboratory evaluation was performed in 111 (12%) of the patients. The mean leukocyte count was 10,000±5,000 (1,700-22,400) mm^3. Leukocytosis was found in 24% and leukopenia in 8% of the patients. CRP was found to be elevated in 50 (45%) patients and the mean CRP value was 22.1±42.4 (median: 8.4) (0.2-314). Chest radiography was performed in all patients with lung auscultation findings on examination. Radiologic findings were detected in 44 (75%) of the patients. Consolidation was found in 23 (52%) patients and peribronchial prominence and increased ventilation were found in 21 (48%) patients.

In the study, 487 (54%) patients underwent influenza rapid antigen test and 203 (42%) were positive. Twenty-four (3%) patients underwent pandemic influenza A/H1N1 RT-PCR test and 16 (67%) were positive. Influenza rapid antigen test was performed in 59 (44%) of 132 patients with fever ≤37.9 °C, and it was found positive in only 2 (3%) patients. Of 486 (54%) patients with a body temperature between 38-38.9 °C, 257 (52%) underwent influenza rapid antigen test and 82 (32%) were positive; 171 (60%) of 284 (32%) patients with a body temperature ≥39 °C underwent influenza rapid antigen test and 119 (70%) of these patients were positive. The positive rate of rapid antigen test was statistically significant in patients with a body temperature ≥39 °C compared to patients with a body temperature of 38-38.9 °C ($p<0.001$).

Antiviral treatment (oseltamivir) was initiated in 395 (44%) patients. Treatment was initiated in 357 (90.4%) patients because of risk factors for influenza-related complications, in 27 (6.8%) patients because of evidence of severe disease and in 11 (2.8%) patients for prophylactic purposes. Antiviral treatment was started in 80% of patients within the first 48 hours after the onset of symptoms. Of the 395 patients who started antiviral treatment, 22 (5.5%) had drug side effects in the form of nausea and vomiting after drug intake.

Thirty-three (3.6%) of the patients were hospitalized, the mean age of these patients was 34.9±41.4 months (median: 18 months) (2-144 months) and 42% of the hospitalized patients were over one year old. The most common reason for hospitalization was pneumonia (n=28; 69.6%). Other reasons for hospitalization were febrile convulsions, dehydration and altered consciousness. Influenza-related risk factors were present in 27 (82%) of the hospitalized patients. The most common risk factor was being younger than two years of age (n=18, 54%). There were no deaths due to pandemic influenza 2009 A/H1N1 during the study period.

Of the 902 patients in the study, 15 (1.7%) received seasonal influenza vaccine and pandemic influenza vaccine together, while 22 (2.4%) received only seasonal influenza vaccine. Three of the patients who received pandemic influenza vaccine presented to the emergency department within 48 hours after vaccination. Two of these patients presented with pain and redness in the vaccinated arm and one presented with a fever of >37.9 °C. The other 12 patients presented to the emergency department with symptoms of ILI within 2-7 days after vaccination.

Discussion

The influenza A/H1N1 pandemic, declared by the WHO as the first pandemic of the 21st century, first started in Mexico in March 2009 and spread rapidly around the world. The pandemic virus is a subtype of influenza that has never been encountered before and therefore people are generally susceptible.[4] The attack rate of pandemic virus infection has been reported to be 20%.[9]

With the pandemic, there has been a significant increase in the patient load admitted to emergency departments with ILI clinic all over the world. In the northern hemisphere, the number of patients affected by the pandemic virus and admitted to the emergency department reached the highest level on the third and fourth patient of November.[6] Similar findings have been obtained in other studies and it has been shown that the patient load in pediatric emergency departments increases by 150-200% during periods of intense pandemic.[10] In this study, similar findings were found in parallel with the literature (Graph 2). These results clearly show the increase in emergency department workload due to the pandemic. It is thought that the excessive media attention to the pandemic, the sensitivity and anxiety in the society and the daily reporting of death cases were effective in this increase.

Pandemic influenza infection mostly affected school-age children and young adults (5-24 years).[2,3,11] Studies have shown that outbreaks usually occur during periods when

schools are open and that school-age children are most frequently exposed.[11] In addition, it has been shown that the rate of spread of pandemic influenza is highest in school-age children (36%).[11] Epidemiologic data have shown that children and young adults are more susceptible to pandemic influenza infection than older people.[3,6,7,12,13] In our study, similar to the data in the literature, it was found that school-age children were most frequently affected by pandemic influenza (Graph 2).

In studies, the most common symptoms in patients with pandemic influenza A/H1N1 were reported to be fever (94%) and cough (92%).[14,15] Clinical findings are similar in seasonal and pandemic influenza. However, vomiting and diarrhea complaints, especially in children, have been reported to be higher in pandemic influenza (approximately 25%), whereas this rate is much lower in seasonal influenza.[2,6,7] In our study, both the most common symptoms of pandemic influenza and the rate of nausea and vomiting symptoms were similar to the literature (Graph 3).

It has been shown that influenza infection is more severe in patients with risk factors for influenza-associated complications.[3,6] CDC reported that approximately 70% of patients hospitalized for pandemic influenza had at least one risk factor for influenza complications.[6] In our study, similar to the literature, 82% of patients with severe disease findings and hospitalized had at least one of the risk factors for influenza-associated complications. It is an expected result that patients with risk factors will have a more severe course. Therefore, it is considered vital that patients who have risk factors for influenza-related complications during the pandemic period and who show symptoms of ILI should be admitted to a healthcare institution early and antiviral treatment should be started within the first 48 hours of symptoms. Recent data show that 25% of hospitalized pediatric patients, 42% of high-risk outpatients and 75% of children younger than two years with influenza did not receive antiviral treatment based on evidence and guidelines.[16-18]

It has been reported that CRP and white blood cell counts of children with pandemic influenza are generally within normal limits for the patient's age.[19] In our study, the proportion of patients with leukocytosis, leukopenia or elevated CRP was found to be higher compared to the literature. The reason for this is that only cases with severe disease findings were examined and it is thought that bacterial coinfection may be present in these cases. In the literature, the rate of bacterial coinfection in pandemic influenza cases with complications was reported to be between 23-39%.[20,21]

It has been reported that the initial chest radiographs of children with mild symptoms of pandemic influenza are often normal, abnormal radiologic findings are detected in a very small number of children, and the most common finding is excessive ventilation in the lungs with peribronchial prominence.[22] The most common abnormal findings on chest radiographs of children hospitalized due to pandemic influenza have been reported as bilateral, symmetric and multifocal consolidation areas and ground-glass opacities frequently accompanying them.[22] Similar to the literature, the most common radiologic finding in this study was lung parenchymal consolidation, and peribronchial prominence and increased ventilation followed it in the second frequency.

It has been stated that rapid antigen tests with high sensitivity and specificity can be used in the pandemic period for diagnosis due to the rapid spread of influenza, short incubation period, prevention of unnecessary antibiotic use and the necessity to start antiviral treatment within the first 48 hours.[23,24] Influenza rapid antigen tests detect influenza A, but cannot detect influenza A subtypes. Since 99.4% of the influenza A subtype circulating during the pandemic period was pandemic influenza, it was announced by WHO that the positivity detected could be accepted as pandemic influenza.[6,24] In our study, a significant correlation was found between the degree of fever and rapid antigen test positivity. In the literature, it has been reported that the amount of virus excreted by inhalation in influenza infection correlates with fever and is highest in the first 2-3 days of the disease.[6,9] Since approximately 75% of the patients in our study were evaluated within the first 48 hours after the onset of symptoms, the test reliability was considered to be high.

WHO and CDC have recommended pandemic influenza A/H1N1 treatment for children with a high risk of complication-mortality or with signs of severe disease. It has been reported that starting neuraminidase inhibitors (oseltamivir or zanamivir) as soon as possible, especially within the first 48 hours of symptoms, will provide the most benefit.[6,25,26] In this study, it was observed that treatment was started within the first 48 hours in 80% of patients with risk factors and severe disease findings. Early initiation of treatment in appropriate cases is thought to have prevented death or serious complications in any patient. Many studies have reported nausea and vomiting as the main side effect of oseltamivir in children, with vomiting occurring in approximately 15% of children receiving oseltamivir.[25-27] In this study, nausea and vomiting after oseltamivir intake was less common than reported in the literature.

In our study, it was found that the rates of vaccination against both seasonal and pandemic influenza were quite low during the pandemic influenza period. Similarly, in many studies, it has been reported that the rate of vaccination acceptance is lower than expected.[28,29] In studies, the reasons for not being vaccinated in the population have been stated as not

trusting the vaccine, thinking that they will not get pandemic influenza, believing that the disease is mild and insignificant, and not being in the risk group for vaccination.[28,30] Studies have also shown that the rate of pandemic influenza vaccination was significantly higher in patients who received seasonal influenza vaccine.[29,30] In this study, in parallel with the global data, all patients who received pandemic influenza vaccine also received seasonal influenza vaccine. Three of our patients who received pandemic influenza vaccine had mild vaccine side effects, but none of them developed a serious vaccine-related reaction. In our country, the rate of post-vaccine adverse reactions has been reported as 3.62 (100,000).[31]

Study Limitations

The limitation of our study is that it is a single-center study. In order to see the effect of the pandemic period more clearly in our country, multicenter epidemiological studies with a larger number of patients are needed. In this way, it will be possible to prepare for future pandemics at the national level. Our study will contribute to national pandemic data.

Conclusion

In our study, it was found that school-age children were mostly affected by pandemic influenza, and the majority of patients hospitalized with severe disease findings were under two years of age. It is thought that early treatment initiation in patients at risk for the development of influenza-related complications and close follow-up of patients with severe disease findings are important in terms of complications, morbidity, and mortality.

Ethics

Ethics Committee Approval: Ethics committee approval for the study was obtained from the Dokuz Eylül University Non-interventional Clinical Research Evaluation Commission (decision no: 2010/06-06, date: 30.06.2010).

Informed Consent: Consent for the study was obtained from the legal guardians of all patients.

Footnotes

Authorship Contributions

Concept: Ö.Ö., M.D., Design: Ö.Ö., M.D., Data Collection or Processing: Ö.Ö., M.D., Analysis or Interpretation: Ö.Ö., M.D., P.G., Ş.Ç.S., D.Y., Literature Search: Ö.Ö., M.D., P.G., Ş.Ç.S., D.Y., Writing: Ö.Ö., M.D., P.G., Ş.Ç.S., D.Y.

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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Research Article / Özgün Araştırma

DOI: 10.4274/cayd.galenos.2025.48344
J Pediatr Emerg Intensive Care Med 2025;12:29-34

The Value of Serum Ischemia Modified Albumin Levels on Diagnosing Pediatric Testicular Torsion and Predicting Testicular Atrophy After Operation

Pediatrik Testis Torsiyonunun Tanısında ve Ameliyat Sonrası Testis Atrofisinin Öngörülmesinde Serum İskemi Modifiye Albümin Düzeylerinin Değeri

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Abstract

Introduction: To clinically investigate the value of serum ischemia modified albumin (IMA) levels on diagnosing pediatric testicular torsion (TT) and predicting testicular atrophy after operation.

Methods: This prospective case control study was conducted between June 2021 and January 2023. Patients aged 1-18 years who were evaluated for acute scrotum and diagnosed as TT based on clinical and radiological evaluations were included in the study. Demographic data, clinical features, radiological findings, serum IMA levels, operative findings, short and long-term complications, follow-up were recorded.

Results: The serum IMA levels of patients who underwent operation due to TT were statistically significantly higher compared with the control group (p<0.001). Receiver operating characteristic analysis revealed an optimal cut-off point at 18.90 ng/mL for separating the TT group from the control group. When patients who underwent orchiectomy during surgery were compared with those who developed testicular atrophy after detorsion, no statistically significant difference was found in terms of serum IMA levels (p=0.857). Serum IMA levels in patients who underwent orchiectomy during surgery and in patients who developed testicular atrophy after detorsion were significantly higher than in patients without complications (p=0.013 and p=0.012, respectively).

Öz

Giriş: Pediatrik testis torsiyonu (TT) tanısında ve operasyondan sonra testis atrofisini tahmin etmede serum iskemi modifiye albümin (IMA) düzeylerinin değerini klinik olarak araştırmak.

Yöntemler: Bu prospektif olgu kontrol çalışması Haziran 2021 ile Ocak 2023 arasında yürütülmüştür. Akut skrotum açısından değerlendirilen, klinik ve radyolojik değerlendirmelere dayanarak TT tanısı konulan 1-18 yaş arası hastalar çalışmaya dahil edilmiştir. Demografik veriler, klinik özellikler, radyolojik bulgular, serum IMA düzeyleri, operasyon bulguları, kısa ve uzun dönem komplikasyonlar, takip kaydedildi.

Bulgular: TT nedeniyle operasyon geçiren hastaların serum IMA düzeyleri kontrol grubuna kıyasla istatistiksel olarak anlamlı derecede yüksekti (p<0,001). İşaret karakteristiği eğrisi analizi, TT grubunu kontrol grubundan ayırmak için optimum cut-off noktasının 18,90 ng/mL olduğunu ortaya koymuştur. Ameliyat sırasında orşiektomi uygulanan hastalar detorsiyondan sonra testis atrofisi gelişen hastalarla karşılaştırıldığında serum IMA düzeyleri açısından istatistiksel olarak anlamlı bir fark bulunmamıştır (p=0,857). Ameliyat sırasında orşiektomi uygulanan hastalarda ve detorsiyondan sonra testis atrofisi gelişen hastalarda serum IMA düzeyleri komplikasyonsuz hastalara göre anlamlı derecede yüksek bulunmuştur (sırasıyla p=0,013 ve p=0,012).

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Received/Geliş Tarihi: 17.01.2025 **Accepted/Kabul Tarihi:** 18.02.2025 **Epub:** 05.03.2025 **Publication Date/Yayınlanma Tarihi:** 21.04.2025
Cite this article as: Ulusoy O, Şencan M, Bilen A, Ulusoy E, Küme T, et al. The value of serum ischemia modified albumin levels on diagnosing pediatric testicular torsion and predicting testicular atrophy after operation. J Pediatr Emerg Intensive Care Med. 2025;12:29-34

Abstract

Conclusion: In the present clinical study, we found that serum IMA levels are a valuable molecule in the diagnosis of childhood TT, in predicting testicular atrophy, and therefore in the decision for intraoperative orchiectomy.

Keywords: Pediatric, testicular torsion, ischemia modified albumin

Öz

Sonuç: Mevcut klinik çalışma sonucunda serum IMA düzeylerinin çocukluk çağı testis torsiyonunun tanısında, testis atrofisini tahmin etmede ve dolayısıyla intraoperatif orşiektomi kararında değerli bir molekül olduğu sonucuna vardık.

Anahtar Kelimeler: Pediatrik, testis torsiyonu, iskemi modifiye albümin

Introduction

The most common cause of acute scrotum requiring operative treatment is testicular torsion (TT). TT results from twisting of the spermatic cord around its longitudinal axis, causing impairment of blood flow to the testis that may cause testicular necrosis.[1] If detorsion is performed within the first 6 hours after onset of pain, 90-100% testes may be saved. However, if detorsion is performed within 12-24 hours after onset of the pain, the chance of saving the testis has been shown to decrease below 10%.[2] Operative intervention must be performed promptly to avoid loss of function of the ipsilateral testis.[3]

Several biomarkers to determine the permanent testicular ischemic damage after TT have been studied.[4-6] Ischemia modified albumin (IMA) has become a prominent biomarker in recent years regarding the role of ischemia especially for pediatric appendicitis.[7,8] IMA is a useful and well-known biomarker for ischemia. The last amino-terminal end of albumin is the region where the transitional metals such as cobalt, copper, and nickel are bound. Hypoxia, acidosis, free radical damage, and membrane deterioration reduce the binding capacity of the transitional metals and result in a change in the structure of albumin.[9] Experimental studies have shown that serum IMA levels increase after TT.[10-12] To the best of our knowledge serum IMA levels after TT has not been studied clinically. We hypothesized that IMA may be useful during diagnosing pediatric TT, decision making for intraoperative orchiectomy and for predicting postoperative testicular atrophy in pediatric TT.

In current study, we aimed to clinically investigate the value of serum IMA levels on diagnosing pediatric TT and predicting testicular atrophy after operation.

Materials and Methods

This prospective case control study was conducted between June 2021 and January 2023. The study protocol was designed in compliance with the Declaration of Helsinki. Informed consent was obtained from parents or legal guardians before enrollment in the study. The study was approved by the Dokuz Eylül University Non-Interventional Research Ethical Committee (decision no: 2022/03-11, date: 19.01.2022). Patients aged 1-18 years who were evaluated for acute scrotum with diagnosed as TT based on clinical and radiological evaluations were included in the study. Patients with an acute scrotum and presence of decreased and/or absent blood flow on Doppler ultrasonography (US) but no torsion detected during surgery were excluded from the study as this exclusion may change the IMA results. Demographic data, clinical features, radiological findings, serum IMA levels, operative findings, short and long-term complications, and follow-up were recorded.

TT was diagnosed based on medical history, physical examination, gray scale and Doppler US findings. General electric (GE) Logiq S7 (GE Healthcare, Milwaukee, WI) US equipment were used in present study. All gray scale and Doppler US examinations were performed by radiologists with pediatric radiology experience. Redundant spermatic cord, testicular swelling, testicular parenchymal anatomy and hydrocele were evaluated with gray scale US. The Doppler signal (decrease or absence) of the testis and rotation of the spermatic cord were evaluated. In presence of decreased and/or absent blood flow on Doppler US i.e., consistent with TT, an immediate operative intervention was performed.

The patients were divided into 2 groups.

Control group (n=31): Comprised of healthy patients undergoing circumcision under general anesthesia.

TT group (n=21): Patients who underwent operation due to TT.

The TT group was divided into three subgroups based on the surgical outcomes and follow-up results;

TT requiring orchiectomy (n=4): Refers to patients who underwent intraoperative orchiectomy.

No testicular atrophy after operative detorsion (n=14): Patients who underwent operative detorsion and had no testicular atrophy during follow-up.

Testicular atrophy after operative detorsion (n=3): Patients who developed testicular atrophy during follow-up after operative detorsion.

Operative Technique

The inguinal approach was preferred as standard in all patients. Testicular detorsion and testicular fixation were performed in patients in whom testicular blood flow improved after wrapping the testes with warm moist swabs. Orchiectomy was performed in patients in whom no testicular blood flow improvement was observed after wrapping testes with warm moist swabs.

Biochemical Analysis

Blood samples and IMA were collected on admission to pediatric emergency department. Serum IMA levels were measured before surgery. Serum samples for IMA analysis were stored at -80 °C until analysis. Serum IMA levels (cat no: CSB E09594h, Elabscience Biotechnology Co, Wuhan, China) were measured using an enzyme-linked immunosorbent assay (ELISA) kit based on the principle of sandwich enzyme immunoassay. Since the ELISA test gives results in a minimum of two days, IMA values were not used for surgical indication in any patient. Informed consent was obtained from all patients before blood samples were taken.

Statistical Analysis

Statistical analysis was performed using SPSS 24.0 (IBM Corp. Armonk NY, USA). Data are presented as median with interquartile range and 25^{th}-75^{th} percentiles. Histograms were used to assess the normality of sample distributions. The Kruskal-Wallis test was used for analyzing plasma IMA levels among different groups. The Mann-Whitney U test was used for post-hoc comparisons. All t-tests were two-tailed, and group differences or correlations with $p<0.05$ were considered to be statistically significant. Receiver operating characteristic (ROC) analysis was used to detect the optimal cut-off points for separating the TT group from the control group and TT with orchiectomy from TT without orchiectomy. Spearman's ρ test was used to assess the correlation between IMA and the duration of symptoms.

Results

Twenty-one patients with TT and 31 control patients were enrolled. For of TT patients at the time of operation was 13 years (13.10-14.75 years), the median age of the control group was 11 years (9-15 years). There is no statistically significant difference regarding age between the groups (p=0.482).

Left TT was present in 12 (57.1%) patients. The median duration of symptoms was 14 hours (6-42 hours). The most common clinical features were scrotal pain, followed by scrotal swelling, with edema and absence of cremasteric reflex, which were equally common. The clinical features are summarized in Table 1. Gray scale and Doppler US were performed in all cases. With US; increased ipsilateral testis size was detected in 18 patients (85.7%), and ipsilateral reactive hydrocele was detected in 16 (76.2%) patients. Doppler US showed decreased and/or absent ipsilateral testicular blood flow in all patients.

While 4 of 21 patients underwent intraoperative orchiectomy, operative detorsion was performed in 17 patients. Testicular atrophy was detected within the postoperative first year in three patients out of 17 patients treated with operative detorsion. Orchiectomy was performed for these three atrophic testes.

We have summarized serum IMA levels of the patients in Table 2. The serum IMA levels of patients who underwent operation due to TT were statistically significantly higher compared with the control group [34.50 (22.65-61.45) and 13.50 (6.10-24.30); respectively] ($p<0.001$). No statistical difference was detected between the serum IMA levels of intraoperative orchiectomy and testicular atrophy after detorsion groups (p=0.857). Serum IMA levels of intraoperative orchiectomy and testicular atrophy after detorsion groups were significantly higher compared with no testicular atrophy after detorsion group (p=0.013 and p=0.012, respectively).

ROC curve analyses of IMA were also performed. ROC analysis revealed an optimal cut-off point at 18.90 ng/mL for separating the TT group (n=21) from the control group (n=31). The sensitivity and specificity were 90.5% and 61.3%, respectively. The area under the curve for IMA was 0.885 ($p<0.001$). And also, ROC analysis revealed an optimal

Table 1. Clinical features of TT patients

	n (%)
Scrotal pain scrotal pain	20 (95.2)
Nausea and/or vomiting	7 (33.3)
Scrotal hyperemia	15 (71.4)
Scrotal swelling and edema	17 (81.0)
Absence of cremasteric reflex	17 (81.0)

TT: Testicular torsion

Table 2. Serum IMA levels of the patients

Groups	IMA levels (ng/mL)
Control (n=31)	13.50 (6.10- 24.30)*
TT requiring orchiectomy (n=4)	69.30 (55.25-82.97)†
No testicular atrophy after operative detorsion (n=14)	25.20 (20.90-35.15)
Testicular atrophy after operative detorsion (n=3)	66.40 (50.30-66.40)‡

Data presented as median and interquartile range
*: Control group compared with TT requiring orchiectomy, no testicular atrophy after detorsion and testicular atrophy after detorsion groups ($p<0.001$), †: TT requiring orchiectomy group compared with no testicular atrophy after detorsion group (p=0.013), ‡: Testicular atrophy after detorsion group compared with no testicular atrophy after detorsion group (p=0.012), TT: Testicular torsion

Table 3. Duration of symptom and torsion degrees of the patients

Groups	Duration of symptom (hours)	Torsion degrees
TT requiring orchiectomy (n=4)	72.00 (54.00-108.00)	630 (540-720)†
No testicular atrophy after operative detorsion (n=14)	6.30 (5.75-14.75)*	360 (360-540)
Testicular atrophy after operative detorsion (n=3)	36.00 (24.00-60.00)	360 (360-600)

Data presented as median and interquartile range, *: No testicular atrophy after detorsion group compared with TT requiring orchiectomy and testicular atrophy after detorsion groups (p=0.004 and p=0.006),
†: TT requiring orchiectomy group compared with no testicular atrophy after detorsion group (p=0.008),
TT: Testicular torsion

cut-off point at 43.70 ng/mL for separating TT with orchiectomy (n=7) from TT without orchiectomy (n=14). The sensitivity and specificity were 100.0% and 85.7%, respectively (the area under the curve was 0.959, p=0.001).

Duration of symptoms was notably prolonged in both TT requiring intraoperative orchiectomy group and testicular atrophy after detorsion group compared with no testicular atrophy after detorsion group (p=0.001 and p=0.006, respectively) (Table 3). There was a positive correlation between IMA values and the duration of symptoms (r=0.744, p<0.001) but we couldn't find any association between the clinical features of TT patients and IMA values (p>0.05). Degree of TT was more in intraoperative orchiectomy group compared with detorsion groups (p=0.008) (Table 3).

According to the duration from admission to surgery, there was no difference between TT requiring orchiectomy [30.0 min (22.5-30.0 min)], no testicular atrophy after operative detorsion [35.0 min (30.0-42.5 min)] and testicular atrophy after operative detorsion [40.0 min (30.0-40.0 min)] (p=0.195). The median duration of operation was 60 minutes (47.5-75.0 minutes). Postoperative scrotal hematoma developed in three patients and resolved during follow-up without need for any intervention.

Discussion

Twisting of the spermatic cord along the longitudinal axis, causes obstruction of blood vessels supplying the testis. Severity of blood flow obstruction directly correlates with the degree of ischemic testicular injury, possible functional loss of testis and infertility. One of the notable debates in TT, which can lead to serious consequences, is the decision making for intraoperative orchiectomy.[13] In the literature, 6-hour cut-off value is widely used to define early and late presentations for TT. Saxena et al.[14] showed that intraoperative orchiectomy rate in TT increased from 9.1% to 56% after the 6-hour mark. Similarly, Bayne et al.[15] reported that the most important factor affecting intraoperative orchiectomy rate in TT was time from onset of symptoms to patient presentation. They emphasized that 76.7% of the TT patients presenting 24 hours after onset of symptoms underwent intraoperative orchiectomy as opposed to 10% of patients presenting with in the first 6 hours after onset of symptoms. Duration of symptoms stands out as an important parameter during decision making for intraoperative orchiectomy. Another important parameter in terms of testicular viability is the degree of TT. Castañeda-Sánchez et al.[16] reported that testicular damage increases as the degree of TT increases. The degree of TT was more in patients who underwent intraoperative orchiectomy compared with patients who underwent operative detorsion. In the present study, duration of symptoms was statistically significantly longer in patients who underwent intraoperative orchiectomy and in patients who developed atrophy after operative detorsion. However, duration of symptoms seemed important predicting surgical outcomes, factors such as torsion degree and torsion type may also have an impact. The need to objectively and measurably evaluate the severity of testicular ischemia, which is the common result of all these factors, still continues.

Overall, 38% of TT has been shown to result in intraoperative orchiectomy.[17,18] Several experimental and clinical studies investigated the value of different biochemical parameters in assessing permanent testicular damage after TT.[4-6,10-12,19] One of the markers that can be used for this purpose is IMA. IMA is a sensitive marker that increases with ischemia and oxidative stress.[7,12] Testicular tissue is highly sensitive to oxidative free radicals and exposure to oxidative free radicals damages the germinal cells.[20] Experimental studies shown that serum IMA levels increase after TT.[10-12] Kutlu et al.[12] experimentally showed that serum IMA levels were increased after the 4th hour of TT. They reported that although no significant correlation between histopathologic damage and serum IMA levels, significantly high histopathologic damage in present 4 hour torsion group. Although this study does not evaluate IMA values over 4 hours, it is also valuable in that it shows the increase in IMA values as the duration of symptoms increases. They also suggested that IMA is the potential diagnostic value for TT and that IMA levels in TT should be investigated concerning prognosis. Kutluhan et al.[11] experimentally showed that low serum IMA levels in the early hours of TT may indicate preservation of high spermatogenesis capacity.[11] Mentese et al. [21] has shown that the elevation in serum IMA levels persists for as long as experimental testicular ischemia continues. To the best of our knowledge, there is no clinical

study in the literature regarding the usefulness of serum IMA in patients operated for TT. In our study, the IMA value increased and was positively correlated with ischemia and symptom duration. It was found that an IMA value of 18.90 ng/mL (90.5% sensitivity, 61.3% specificity) helped in the diagnosis of TT. When this value was taken as 43.70 ng/mL (100% sensitivity, 85.7% specificity), it served as a prognostic indicator.

The main controversies in TT are which patients will undergo intraoperative orchiectomy and whether testicular viability be predicted in the postoperative period. Considering the aforementioned discussions, it is obvious that intraoperative orchiectomy or operative detorsion will have vital effects on the ipsilateral testis and therefore on a child's reproductive capacity. We conducted a prospective case-controlled study on the value of serum IMA levels on the decision making for intraoperative orchiectomy and during predicting postoperative testicular atrophy after operative detorsion. As a result of our study, IMA was shown to be a useful parameter in terms of indicating testicular ischemia and testicular atrophy which may develop in the future, consistent with our findings. The present study has shown that, serum IMA values in cases who underwent intraoperative orchiectomy were found to be statistically significantly higher compared with control and no testicular atrophy after detorsion groups. Serum IMA values of patients who developed testicular atrophy after operative detorsion were statistically significantly higher compared to those of the control group and the no testicular atrophy group after operative detorsion. Serum IMA levels of the patients who underwent intraoperative orchiectomy and those of patients who developed testicular atrophy after detorsion were similar. Intraoperative visual evaluation of testicular blood flow is subjective. Serum IMA levels may be used in decision-making during intraoperative orchiectomy and in predicting testicular atrophy after operative detorsion.

Conduction of the present study in a single center and on limited number of patients was the main limitations that may limit the generalization of the results. Another limitation is that serum IMA does increase in several other ischemic conditions other than TT.

Conclusion

IMA has become a prominent biomarker in recent years regarding the role of ischemia in several diseases and studies are currently ongoing. In the present clinical study, we found that serum IMA levels are a valuable biomarker for the diagnosis of childhood TT, in predicting testicular atrophy, and therefore, deciding on intraoperative orchiectomy.

Ethics

Ethics Committee Approval: The study was approved by the Dokuz Eylül University Non-Interventional Research Ethical Committee (decision no: 2022/03-11, date: 19.01.2022).

Informed Consent: Informed consent was obtained from parents or legal guardians before enrollment in the study.

Footnotes

Authorship Contributions

Surgical and Medical Practices: O.U., A.B., E.U., Concept: O.U., M.Ş., A.B., E.U., Design: O.U., M.Ş., E.U., Data Collecting or Processing: O.U., A.B., E.U., T.K., Analysis or Interpretation: O.U., E.U., O.A., G.H., M.O., M.F.A., Literature Search: O.U., E.U., O.A., G.H., M.O., M.F.A., Writing: O.U., E.U., O.A., G.H., M.O., M.F.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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DOI: 10.4274/cayd.galenos.2025.88156
J Pediatr Emerg Intensive Care Med 2025;12:35-8

Use of Hyperbaric Oxygen Therapy for Preventing Amputation in Severe Crush Injury due to Earthquake in a Pediatric Patient: A Case Report

Deprem Kaynaklı Şiddetli Ezilme Yaralanmasında Ampütasyonu Önlemek için Hiperbarik Oksijen Tedavisi Kullanımı: Bir Olgu Sunumu

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Abstract

Hyperbaric oxygen therapy (HBOT) is a treatment modality whose indications expand over time. Although its use is not as widespread in children as in adults, HBOT can also be applied in pediatric patients with similar indications. This case presentation discusses the application of HBOT in a pediatric patient with an upper extremity crush injury. A 3-year-old female patient was stuck under rubble in the February 6, 2023, Türkiye earthquake. After the patient was rescued, a fasciotomy was performed, and a few days later, an amputation was indicated and he was referred to our hospital. In the evaluation made after the transfer to our hospital, amputation was postponed and HBOT was applied. The patient underwent 21 sessions of HBOT. Amputation was prevented after recovery of the extremity with HBOT. In conclusion, HBOT can be used safely and effectively in pediatric patients with extensive damage to the extremities due to crush injuries.

Keywords: Hyperbaric oxygenation, crush injuries, earthquakes, forearm injuries, fasciotomy

Öz

Hiperbarik oksijen tedavisi (HBOT), endikasyonları zamanla genişleyen bir tedavi yöntemidir. Çocuklarda kullanımı yetişkinler kadar yaygın olmasa da, HBOT benzer endikasyonlarla pediatrik hastalara da uygulanabilir. Bu olgu sunumu, üst ekstremite ezilme yaralanması olan bir pediatrik hastada HBOT uygulanmasını tartışmaktadır. 6 Şubat 2023 tarihli Türkiye depreminde enkaz altında kalan 3 yaşında hastaya kurtarıldıktan sonra fasyotomi yapılmış ve birkaç gün sonra hastada amputasyon endikasyonu oluşmuş ve hasta hastanemize sevk edildi. Hastanemize nakil olduktan sonra yapılan değerlendirme sonucunda ampütasyon ertelendi ve HBOT uygulandı. Hastaya 21 seans HBOT uygulandı. HBOT ile ekstremitedeki iyileşme sonrasında ampütasyon önlendi. Sonuç olarak, ezilme yaralanmalarına bağlı ekstremite hasarları olan pediatrik hastalarda HBOT güvenli ve etkili bir şekilde kullanılabilir.

Anahtar Kelimeler: Hiperbarik oksijenasyon, ezilme yaralanmaları, depremler, ön kol yaralanmaları, fasyotomi

Introduction

Hyperbaric oxygen therapy (HBOT) is a treatment method in which a hyperoxygenic environment is provided to tissues by inhaling 100% oxygen within specially designed high-pressure chambers. At pressures higher than atmospheric pressure, the solubility of oxygen in blood and body fluids increases. Increased arterial oxygen pressure enhances the capillary oxygen gradient, leading to an elevation in tissue oxygen pressure. Oxygen suppresses nitric oxide synthesis in endothelial

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Received/Geliş Tarihi: 30.03.2024 **Accepted/Kabul Tarihi:** 25.02.2025 **Epub:** 05.03.2025 **Publication Date/Yayınlanma Tarihi:** 21.04.2025
Cite this article as: Döndü M, Erdal AI, Azapağası E, Karakaş NM. Use of hyperbaric oxygen therapy for preventing amputation in severe crush injury due to earthquake in a pediatric patient: a case report. J Pediatr Emerg Intensive Care Med. 2025;12:35-8

cells, causing vasoconstriction and reducing extravasation, consequently decreasing tissue edema. Studies have shown that HBOT stimulates growth factors and increases fibroblast proliferation, migration, granulation, and angiogenesis, thereby accelerating wound healing.[1,2] Neutrophils and macrophages exhibit oxygen-dependent antibacterial effects. Additionally, oxygen directly exerts antibacterial effects through reactive oxygen species. Since its introduction, the indications for HBOT have expanded. Initially used for decompression sickness and carbon monoxide poisoning, HBOT is now involved in the treatment of conditions such as soft tissue infections, chronic wounds, gangrenous lesions, arterial emboli, compartment syndrome, and limb ischemia.[3,4] While not as widespread as in adults, HBOT is also used in pediatric patients with several indications.[5-13] Pediatric patients can undergo HBOT in chambers with equipment suitable for their age, accompanied by an appropriate companion. In this case report, we present a pediatric patient with a severe crush injury due to the February 6, 2023, Türkiye earthquake and discuss the effect of HBOT in preventing amputation.

Case Report

In the February 6, 2023, Türkiye earthquake, a 3-year-old female patient, foreign national, was stuck under rubble for 48 hours. After being rescued, the patient was diagnosed with crush injury, and compartment syndrome in the right upper extremity, and a fasciotomy was performed at a hospital near the earthquake zone. Because of compromised circulation in the forearm and hand, the patient was referred to our hospital for potential amputation and subsequent intensive care.

The patient arrived at our hospital 4 days after being rescued from the rubble. The patient's medical history was unremarkable for any known diseases. Upon the first examination after transfer to our hospital, intravenous fluid resuscitation and broad-spectrum antibiotic therapy were started. Upon admission, laboratory evaluation demonstrated a total creatine kinase (CK), level of 19,663 U/L and a lactate dehydrogenase (LDH), level of 1,312 U/L. It was observed that a fasciotomy had been performed on the right hand and forearm, with widespread ecchymosis and blisters. The 3rd, 4th, and 5th fingers were cyanotic (Figures 1, 2). Doppler ultrasound revealed blood flow in the radial and ulnar arteries. It was decided to postpone the amputation and apply HBOT. The patient was started on Iloprost therapy at a dose of 0.5 ng/kg/min and Heparin at a dose of 20 IU/kg/hour. At the end of the 7th day, anticoagulant therapy was continued with subcutaneous enoxaparin. Over the course of a month, the patient underwent 21 sessions of HBOT, with one session per day. Benefiting from these sessions, patients observed a reduction in cyanosis in the fingers and increased blood

Figure 1. Dorsal side view of the forearm in the first evaluation after referral to our hospital

Figure 2. Ventral side view of the forearm in the first evaluation after referral to our hospital

circulation in the forearm. One week following the initiation of treatment, total CK and LDH levels normalized within their respective reference ranges. The plan for amputation was abandoned. Throughout the course of treatment, no indication for the use of any extracorporeal treatment methods was observed in the patient. While continuing HBOT, the patient underwent 10 sessions of debridement of necrotic tissues and 8 sessions of negative pressure wound therapy. After achieving sufficient granulation, the patient's wounds were closed with a partial-thickness skin graft (Figure 3). The patient was discharged three months after admission and transferred to her hometown.

Informed consent for participating in the study was obtained from the parents of the patient.

Discussion

HBOT minimizes the effects of trauma-induced hypoxia and edema through the hyperoxygenation and vasoconstriction it provides. Hyperoxia triggers fibroblast proliferation and neovascularization. Studies have shown that hyperbaric oxygen prevents reperfusion damage and exhibits anti-infective effects by influencing the immune system cells.[1,2]

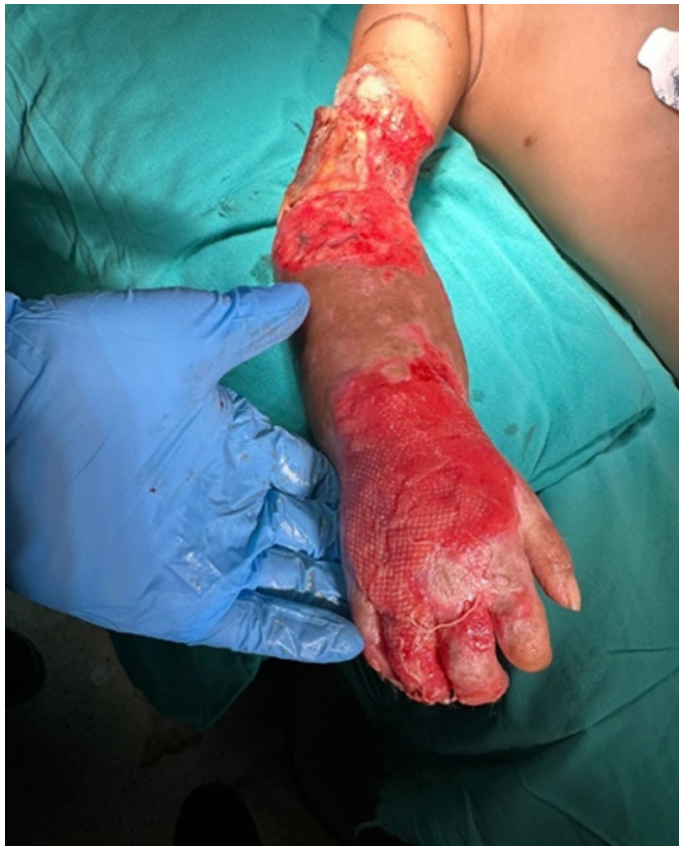

Figure 3. Dorsal side view of the forearm after 21 sessions of HBOT. Circulation appears to be significantly improved. Split-thickness skin grafts were applied to areas with sufficient granulation

HBOT: Hyperbaric oxygen therapy

Considering these effects and the effectiveness observed in this case, it can be stated that HBOT is effective in the management of a patient with crush syndrome.[3]

In the literature, it is observed that in cases of crush syndrome treated with HBOT, amputation rates decrease, wound healing accelerates, and the need for additional surgical procedures decreases.[3] However, studies on the use of HBOT in pediatric crush injuries are limited.[12-15] This case presentation involves a pediatric patient, a victim of an earthquake, referred to our hospital, with a need for amputation. The patient was managed using HBOT without undergoing amputation. Benefiting from these therapies, including the antimicrobial effect of hyperbaric oxygen and increased granulation speed, combined with negative pressure wound therapy, the treatment was completed in a shorter time than expected.

The routine use of hyperbaric oxygen in the pediatric group with crush injuries is not a standard practice. Future clinical studies in the pediatric age group are necessary to establish the benefits of HBOT, expand its indications, assess cost-effectiveness, and integrate it into routine practice during the treatment process. This could lead to a wider adoption of HBOT in pediatric trauma management.

Based on this case report of earthquake-related severe crush injury in a pediatric patient treated successfully with HBOT, we can conclude that HBOT can be used safely and effectively in pediatric patients with extensive damage to the extremities due to crush injuries.

Ethics

Informed Consent: Informed consent for participating in the study was obtained from the parents of the patient.

Footnotes

Authorship Contributions

Surgical and Medical Practices: M.D., A.I.E., E.A., N.M.K., Concept: M.D., A.I.E., E.A., N.M.K., Design: M.D., A.I.E., Data Collection or Processing: M.D., A.I.E., Analysis or Interpretation: M.D., A.I.E., E.A., N.M.K., Literature Search: M.D., A.I.E., Writing: M.D., A.I.E.

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

DOI: 10.4274/cayd.galenos.2025.90277
J Pediatr Emerg Intensive Care Med 2025;12:39-44

Successful Treatment of an 11-Year-Old Boy with Febrile Infection-Related Epilepsy Syndrome

On Bir Yaşında Febril Enfeksiyonla İlişkili Epilepsi Sendromu Tanılı Bir Erkek Çocuğun Başarılı Tedavisi

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Abstract

Febrile infection-related epilepsy syndrome (FIRES) is a subtype of new-onset refractory status epilepticus characterized by refractory status epilepticus following a febrile infection. It is associated with high morbidity and mortality, particularly in children and adults. However, its etiology often remains unclear. The ketogenic diet therapy (KDT), a proven treatment method for drug-resistant epilepsy, continues to be investigated for its mechanisms and efficacy. This case report presents an 11-year-old male diagnosed with FIRES, successfully managed through a multidisciplinary approach and KDT. The patient initially received oral antibiotics for an upper respiratory tract infection but later developed altered consciousness and drowsiness, raising suspicion of encephalitis. He was transferred to the intensive care unit, where refractory status epilepticus occurred 11 days after the onset of fever. Given the clinical presentation, brain magnetic resonance imaging findings, and cerebrospinal fluid analysis consistent with autoimmune encephalitis, the patient was treated with intravenous immunoglobulin, pulse steroid therapy, and plasmapheresis. Despite these interventions, seizure activity persisted, prompting initiation of a classic ketogenic diet at a 3:1 ratio. Seizure activity ceased by the eighth day of KDT. Long-term follow-up revealed that the patient remained seizure-free without antiepileptic drugs, with improved electroencephalography findings. This case highlights the potential role of the ketogenic diet in the early diagnosis and treatment of FIRES. KDT, in combination with immunotherapy, has demonstrated effectiveness in controlling seizures during the acute phase and achieving long-term seizure-free outcomes.

Öz

Febril enfeksiyonla ilişkili epilepsi sendromu (FIRES), yeni başlangıçlı dirençli status epileptikusun bir alt tipi olup, febril enfeksiyon sonrası başlayan refrakter status epileptikus kliniği ile karakterizedir. Bu durum, özellikle çocuklarda ve yetişkinlerde yüksek morbidite ve mortalite ile ilişkilidir. Ancak, etiyolojisi çoğunlukla belirsizdir. İlaca dirençli epilepsi hastalarında ketojenik diyet tedavisi (KDT) patogenezi araştırılmaya devam eden, etkinliği kanıtlanmış bir tedavi yöntemidir. Bu olgu sunumunda, FIRES tanısı almış 11 yaşında bir erkek hastanın, multidisipliner yaklaşım ve KDT ile başarıyla yönetilmesi ele alınmıştır. Hasta, üst solunum yolu enfeksiyonu tanısıyla oral antibiyotik tedavisi almış ancak sonrasında kliniğinde bilinç bulanıklığı, uykuya eğilim gelişmesi nedenilye ensefalit şüphesiyle yoğun bakım ünitesine transfer edilmiştir. Hastada ateşin başlangıcından on bir gün sonra başlayan dirençli status epileptikus kliniği gelişti. Klinik değerlendirme, beyin manyetik rezonans görüntüleme ve beyin omurilik sıvısı analizleri sonucu otoimmün ensefalit ön planda düşünülmüş ve intravenöz immünoglobulin, pulse steroid tedavisi ile plazmaferez uygulanmıştır. İlk tedavilere rağmen nöbet aktivitesi devam eden hastaya klasik ketojenik diyet 3:1 oranında başlatılmıştır. KDT'nin başlamasından sonraki sekizinci günde nöbet aktivitesi durmuştur. Uzun dönem izlemde, hasta antiepileptik tedavi olmaksızın nöbetsiz kalmış ve elektroensefalografi bulgularında düzelme görülmüştür. Bu olgu, FIRES'ın erken tanı ve tedavisinde ketojenik diyetin potansiyel rolünü vurgulamaktadır. KDT'nin, immünoterapilerle birlikte, özellikle akut fazda epileptik nöbetlerin kontrolünde etkili olabileceği ve uzun dönemde nöbetsiz bir seyir sağlayabileceği gösterilmiştir.

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Received/Geliş Tarihi: 13.07.2024 **Accepted/Kabul Tarihi:** 03.03.2025 **Publication Date/Yayınlanma Tarihi:** 21.04.2025
Cite this article as: Karabacak MD, Atakul G, Akıncı G, Coşkun M, Sağlam E, et al. Successful treatment of an 11-year-old boy with febrile infection-related epilepsy syndrome. J Pediatr Emerg Intensive Care Med. 2025;12:39-44

Abstract

Keywords: Status epilepticus, autoimmune encephalitis, limbic encephalitis, new onset refractory status epilepticus, febrile infection related epilepsy syndrome, ketogenic diet

Öz

Anahtar Kelimeler: Status epileptikus, otoimmün ensefalit, limbik ensefalit, yeni başlangıçlı refrakter status epilepticus, ateşli enfeksiyon ilişkili epilepsi sendromu, ketojenik diyet

Introduction

Febrile infection-related epilepsy syndrome (FIRES) is a subcategory of new-onset refractory status epilepticus (NORSE) that requires a febrile infection occurring between 24 hours and 2 weeks before refractory status epilepticus (RSE), with or without fever at the onset of status epilepticus.[1]

In the treatment of patients with RSE, the ketogenic diet therapy (KDT) is gaining popularity, and its efficacy is still under investigation. The ketogenic diet was developed in the 1920s and is a high-fat, low-carbohydrate, moderate-protein diet.[2] In this treatment, the proportions of the ketogenic diet, and the needs for calories and protein are calculated individually and require close monitoring.

FIRES is associated with high morbidity and mortality in children and adults. Despite progress in the clarification of NORSE/FIRES as a clinical syndrome, understanding of the underlying pathogenic mechanisms is limited. A cryptogenic cause accounts for up to 50%[3] of cases, with these cases reported to have worstworse outcomes.[4] Due to the diagnostic challenges and the rarity of this condition, we present this case along with the successful treatment process implemented in the intensive care unit (ICU).

Case Presentation

An 11-year-old male patient presented with a sore throat, a maculopapular rash on the trunk, and axillary temperature exceeding 38 °C. During his initial outpatient clinic visit, he was diagnosed with an upper respiratory tract infection due to fever and sore throat that had started the same day. Oral amoxicillin-clavulanate was prescribed, and the patient was discharged. After three days of antibiotic therapy, the rash resolved, but due to persistent fever and fatigue, the patient returned to our hospital.

On the fourth day of oral amoxicillin-clavulanate therapy, the patient was hospitalized for further evaluation and management due to a refractory febrile state. Physical examination revealed hyperemia in the oropharynx, but the tonsils appeared normal. Other system examinations were unremarkable, with no findings suggestive of central nervous system infection. Intravenous (IV) ampicillin-sulbactam and IV hydration were initiated, and vital signs were closely monitored. Fever did not recur following admission. However, on the second day, the patient developed drowsiness and altered consciousness, raising suspicion of encephalitis. Consequently, he was transferred to the pediatric intensive care unit (PICU) for further management.

The patient's personal and family history revealed no significant findings. During hospitalization, his vital signs were as follows: body temperature, 36.6 °C; heart rate, 96/min; oxygen saturation, 98%; respiratory rate, 22/min; and blood pressure, 115/65 mmHg. Neurological examination findings were mostly normal, including intact eye movements and normal direct/indirect light reflexes, but with a Glasgow Coma Score of 13. No signs of meningeal irritation were noted. Deep tendon reflexes were normal in all extremities, with muscle strength assessed as 5/5. Head and neck examination revealed hyperemia in the oropharynx, but the tonsils appeared normal. No rash or other skin findings were observed. On presentation, biochemical analysis demonstrated normal hepatic and renal function. Electrolyte balance, coagulation status, and ammonia levels were within reference ranges. A mild systemic inflammatory response was suggested by a elevated CRP (15.9 mg/L). Peripheral blood analysis revealed mild leukopenia with a white blood count count of 2.85 x 10^9/L.

Brain magnetic resonance imaging (MRI) and diffusion-weighted imaging without contrast revealed mild T2-fluid-attenuated inversion recovery signal enhancement in the bilateral inferior caudate head, hippocampus, parahippocampal gyrus, and amygdala, consistent with limbic system involvement. The radiologist suggested autoimmune encephalitis or limbic encephalitis as differential diagnoses (Figure 1). Based on these findings, a lumbar puncture was performed to investigate the etiology of encephalitis or meningitis. IV vancomycin, ceftriaxone, and acyclovir were initiated for possible infectious causes. Oral clarithromycin was added as mycoplasma pneumoniae could not be excluded.

Cerebrospinal fluid (CSF) analysis showed no cells on direct examination. Biochemical parameters of CSF were as follows: glucose, 71 mg/dL; protein, 56.6 mg/dL; chloride, 121.1 mmol/L. Simultaneous capillary blood glucose was 116 mg/dL. A meningitis-encephalitis polymerase chain reaction panel analyzed in the CSF sample was negative. Tests for limbic encephalitis panels, anti-neuronal antibodies, and myelin oligodendrocyte glycoprotein antibodies in CSF and serum were also negative (Table 1).

The patient's altered consciousness improved within two days of PICU admission, and fever did not recur during the hospital stay. However, on the fifth day, altered consciousness reappeared, along with orofacial dyskinesia and refractory seizure activity, accompanied by leftward deviation of the head and eyes and tonic contractions of both arms. Treatment for status epilepticus was initiated following the American Epilepsy Society guidelines. After treatment was started, consciousness levels fluctuated over this period, with intermittent psychiatric symptoms, including self-injury and swearing. Anti-convulsant therapy was tailored based on seizure recurrence, clinical progression, and electroencephalography (EEG) findings. During this period of resistant seizures, the patient received infusions of levetiracetam, valproic acid, phenytoin, oxcarbazepine, clobazam, midazolam, and ketamine. EEG findings revealed epileptic activity originating in the bilateral frontocentroparietal regions, more pronounced on the right side. Radiology board reviews of the patient's MRI confirmed bilateral limbic system involvement extending to the caudate nucleus.

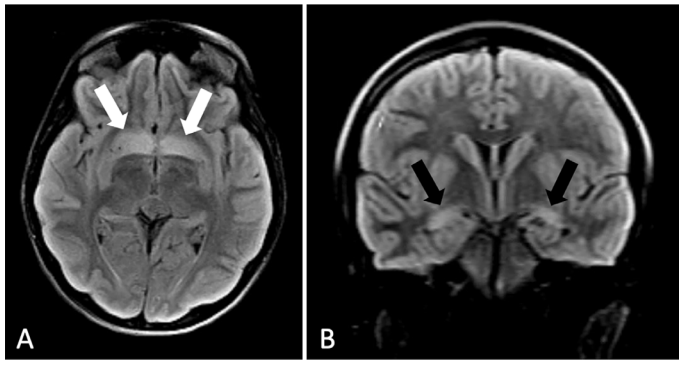

Figure 1. (A) Axial T2-FLAIR shows bilateral symmetric T2 signal enhancement in the globus pallidus (filled white arrows) **(B)** Coronal T2-FLAIR shows cortical swelling and T2 signal enhancement suggestive of bilateral hippocampal involvement (filled black arrows). T2-FLAIR: T2-fluid-attenuated inversion recovery

Based on MRI findings and negative infectious workup, autoimmune encephalitis was considered the leading diagnosis. Intravenous immunoglobulin (IVIG) was administered at 1 g/kg/day for two days. No microorganisms were identified in blood, urine, and CSF cultures. Acyclovir and vancomycin were discontinued, while ceftriaxone was continued for 21 days. Clarithromycin therapy was completed for seven days.

During follow-up, the patient was evaluated by the child and adolescent psychiatry team due to the development of sleep disturbances and delirium. To rule out paraneoplastic limbic encephalitis, abdominal and scrotal ultrasonography, as well as a whole-body contrast-enhanced MRI, were performed. These tests did not reveal any additional pathologies. Thyroid function tests and serum thyroid autoantibodies were unremarkable. Serum aquaporin-4 antibody, and West Nile virus antibody were negative. No pathology was detected in immunologic tests [immunoglobulin G-A-M-E, lymphocyte subset panel, regulatory T cell (Treg) flow cytometry panel, C3, C4, antinuclear antibody] performed in the pretreatment period.

The patient was diagnosed with FIRES following a multidisciplinary evaluation. There was no history of a diagnosed disease. Investigations into the etiology of RSE excluded any identifiable acute or active structural, toxic, or metabolic causes. There was a fever 11 days before the onset of RSE. The patient, whose clinical findings did not improve and whose seizure activity continued, was treated with IVIG, followed by pulse steroid therapy for 11 days, and then 6 cycles

Table 1. Parameters analyzed in the patient's CSF and serum samples

Autoimmune limbic encephalitis panel (CSF/serum)	Anti-neuronal antibodies (CSF)	Meningitis - encephalitis PCR panel (CSF)
AMPA 1 (Glu1) AMPA 2 (Glu2) ANTI-CASPR2 ANTI-DPPX ANTI-GABA B ANTI-LGI 1 NMDAR antibody	Anti-Hu (ANNA-1) Anti-Ri (ANNA-2) Anti-Tr (DNER) Anti-Yo (PCA-1)	*Escherichia coli* *Haemophilus influenzae* *Listeria monocytogenes* *Neisseria meningitidis* *Streptococcus agalactiae* *Streptococcus Pneumoniae* *Herpes Simplex Virus 1* *Herpes Simplex Virus 2* *Human Herpesvirus 6* *Human Parechovirus* *Enterovirus* *Varicella Zoster Virus* *Cryptococcus neoformans/gattii* *Cytomegalovirus*

AMPA: α-amino-3-hydroxy-5-methyl-4-isoxazolepropionic acid, CASPR2: Contactin-associated protein-like 2, DPPX: Dipeptidyl-peptidase-like protein-6, GABA: Gamma-aminobutyric acid, GluR1/2: Glutamate receptors 1 and 2, LGI1: Leucine-rich, glioma-inactivated 1, NMDAR: N-methyl-D-aspartic acid receptor, ANNA: Anti-neuronal nuclear antibody, DNER: Delta and Notch-like epidermal growth factor-related, PCA-1: Purkinje cell cytoplasmic antibody type 1, CSF: Cerebrospinal fluid, PCR: Polymerase chain reaction

of plasmapheresis. Thiamine and biotin supplementation was given for possible thiamine-biotin responsive basal ganglia disease. A repeat EEG showed improved the background rhythm. Follow-up MRI showed regression of limbic system findings, although bilateral external capsule involvement persisted (Figure 2). Since the patient's seizure activities continued, KDT was initiated.

The classic ketogenic diet calculates the ratio of grams of fat to grams of carbohydrates plus protein. The most feasible ratios calculated to date are 3:1 or 4:1, with approximately 80-90% of the energy provided by fats and 10% by carbohydrates and proteins collectively. In our patient, the classic KD was initiated at a 3:1 ratio under the supervision of a dietitian, 18 days after the first seizure activity. During KDT, electrolytes, arterial blood gases, serum ketone bodies, and glucose levels were monitored. Ketosis was assessed through measurements of serum ketone levels. No KDT-related side effects were observed during follow-up.

From the eighth day of KDT onward, no further seizure activity was observed. Follow-up cranial MRI findings revealed normalization, while EEG demonstrated persistent multifocal epileptic abnormalities, albeit with reduced intensity. After resolution of the SE clinical presentation and a notable reduction in seizure frequency, the patient was transferred to the pediatric neurology ward following a one-month stay in the PICU. The patient continued receiving valproate, levetiracetam, and clobazam as anti-convulsant, alongside KDT and oral prednisolone. The treatment plan included gradual tapering and discontinuation of oral prednisolone, and the continuation of IVIG therapy at a dose of 1 g/kg per month.

In the patient's long-term follow-up, anti-convulsant medications were discontinued after the seventh month. Although pathological findings such as the presence of spike-wave activity in the left parietoccipital and frontal areas on EEG persist, he was followed up using KDT without seizures. At this time, second-line immunotherapy has not been started, as the patient, with the current clinical presentation, has responded well to first-line immunotherapy. Informed consent was obtained from the patient's family.

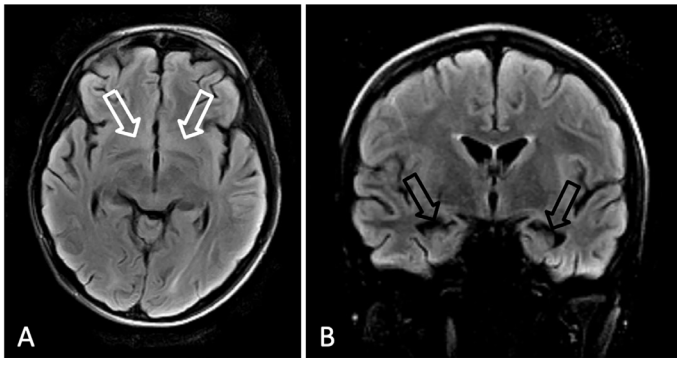

Figure 2. (A) Axial T2-FLAIR shows normalized signal in the globus pallidus (empty white arrows). **(B)** Coronal T2-FLAIR shows ventricular enlargement consistent with bilateral hippocampal atrophy (empty black arrows). T2-FLAIR: T2-fluid-attenuated inversion recovery

Discussion

We present a case of a rare epilepsy syndrome with unclear aetiology in a healthy boy whose seizures were eventually completely controlled after comprehensive treatment, especially first-line immunotherapy and KDT in the acute phase. In the long term, anti-seizure medications were discontinued.

If a previously healthy child presents with severe status epilepticus closely associated with a febrile illness, and after a short period of recovery infectious encephalitis is excluded, FIRES should be considered.[5] Although viral and autoimmune causes are often implicated in the etiology, most cases (up to 50%) remain cryptogenic despite extensive evaluation.[4,6] At this stage, preventing seizure recurrence is of utmost importance. In patients without clinical seizures, imaging, and laboratory evaluations should be performed at frequent intervals, and immunotherapy should be organized during the active phase of the disease to enable discontinuation of antiepileptic drugs.

In cases of seronegative autoimmune encephalitis, brain MRI has an important place in the differential diagnosis. MRI is an imaging modality that demonstrates inflammation-related changes in patients with autoimmune encephalitis. While different specific neuroimaging findings can be observed in various antibody-associated syndromes, as in our case, T2-weighted images typically demonstrate signal hyperintensity restricted to limbic regions.[7]

In addition to brain MRI, CSF examination is important to confirm the diagnosis and exclude infectious causes of encephalitis. Since the sensitivity and specificity of CSF and serum analysis differ between antibodies, it is recommended to perform antibody testing in both samples.[8] However, despite appropriate antibody screening tests, antibodies are reported to be negative in 7% of cases.[9] Comprehensive antibody screening in our patient revealed negative antibody results.

EEG is important in detecting and managing seizures and assessing their frequency in autoimmune encephalitis. although EEG abnormalities are seen in more than 75% of patients, EEG findings may be completely normal.[10] In our case, although the EEG findings were useful for detecting seizure activity and assessing background rhythm, they were not decisive for making a differential diagnosis. In this regard,

a retrospective study published in 2016 by Baysal-Kirac et al.[11] reported that there was no significant difference between the EEG findings of seronegative and anti-neuronal antibody-positive epilepsy patients. Therefore, we considered that EEG findings could be supportive of our diagnosis and treatment.

Various studies and case series have shown that the efficacy of antiepileptic drugs and other therapeutic agents in reducing seizure frequency and shortening the duration of the disease is controversial. Consequently, the epileptic process in FIRES may be considered self-limiting.[12] Nonetheless, the potential benefits of treatments employed during this process should not be underestimated.

In this case, the patient developed RSE 11 days following the onset of fever. Comprehensive investigations failed to reveal any underlying structural, metabolic, acute toxic, or infectious causes that could have precipitated RSE. Therefore, a diagnosis of FIRES was made, and the patient was managed in a multidisciplinary setting. In our patient, it is important to discontinue antiepileptic medication in the acute phase and maintain seizure-free clinical follow-up with KDT alone. The persistence of EEG findings can indicate that the existing autoimmune process continues, but clinical findings are not observed. Whether this is a response to first-line immunotherapy or a self-limitation of the existing autoimmune epileptic process remains controversial.

KDT is a treatment method with proven efficacy in patients with drug-resistant epilepsy, and although research on its mechanism of action is ongoing, its efficacy in the treatment of FIRES is still being studied.[13] Studies by Nabbout et al.[14] involving nine FIRES patients and Peng et al.[15] analyzing retrospective data from seven FIRES cases suggest that KDT is a safe and promising therapeutic option in FIRES, and that early initiation of the KDT provides a favorable prognosis.

Conclusion

In conclusion, the number of FIRES cases reported in the literature is steadily increasing. The majority of FIRES and NORSE cases have an average ICU stay of 20-40 days, and the mortality rate in children is around 12%.[12] The pathogenesis and exact mechanism of this catastrophic type of encephalopathy are not known. The efficacy of current therapies remains uncertain, as many patients exhibit inadequate responses to administered treatments. This case underscores the importance of early recognition of FIRES, timely initiation of immunotherapy, and the potential life-saving impact of KDT in refractory epilepsy syndromes.

Ethics

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

Footnotes

Authorship Contributions

Concept: M.D.K., G.A., H.A., Design: E.S., A.Ü., Data Collection or Processing: M.D.K., S.S.Ç., Analysis or Interpretation: G.Ak., M.C., A.Ü., Literature Search: M.D.K., G.A., G.Ak., Writing: M.D.K., G.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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DOI: 10.4274/cayd.galenos.2025.75688
J Pediatr Emerg Intensive Care Med 2025;12:45-55

Status Epilepticus in Critically Ill Children

Kritik Çocuk Hastada Status Epileptikus

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Abstract

Introduction: Status epilepticus (SE) is a neurological emergency that requires rapid and accurate management. SE is a condition in which the mechanisms that terminate seizures fail or the mechanisms that lead to abnormally prolonged seizures are activated. Refractory SE (RSE) refers to ongoing seizure activity despite adequate treatment with benzodiazepines and at least one non-benzodiazepine anticonvulsant. Super-RSE is defined as SE that continues for 24 hours or longer.

Methods: This review outlines the current clinical definitions, management protocols, and therapeutic strategies for SE, with a focus on pediatric patients. Initial assessment and stabilization should be performed promptly, including mandatory evaluation of the patient's blood glucose and other electrolyte levels. Appropriate dextrose treatment should be administered to patients with hypoglycemia. Following the initial assessment, first-line treatments-such as intravenous diazepam, intramuscular midazolam, or rectal diazepam-should be administered based on vascular access and body weight. If the patient does not respond to first-line treatments and the seizures persist, second-line treatments-such as levetiracetam, phenytoin, valproic acid, or phenobarbital-should be selected and administered by the physician. Patients unresponsive

Öz

Giriş: Status epileptikus (SE); çocuklarda en sık görülen nörolojik acildir. SE, nöbetin sonlandırılmasını sağlayan mekanizmaların başarısızlığı veya anormal derecede uzun süreli nöbetlere yol açan mekanizmaların başlatılması durumudur. Refrakter SE (RSE); yeterli benzodiazepin ve en az bir benzodiazepin olmayan antikonvülzan tedavi uygulamasına rağmen devam eden nöbet aktivitesidir. Süper RSE ise 24 saat veya daha uzun süre devam eden SE olarak tanımlanır.

Yöntemler: Bu çalışma, çocuk hastalarda SE'nin klinik tanımlarını, yönetim protokollerini ve tedavi stratejilerini özetlemektedir. Öncelikle ilk değerlendirme ve stabilizasyon yapılıp, kan şekeri dahil, tüm elektrolitler kontrol edilmelidir. Birincil basamak tedaviler; intravenöz diazepam, intramusküler midazolam veya rektal diazepam olup, hastanın damar yolu varlığına ve vücut ağırlığına göre uygun ilaç tercih edilmelidir. Birincil basamak tedavilere yanıt vermeyen, nöbeti devam eden hastalara ikincil basamak tedaviler olarak; levetirasetam, fenitoin, valproik asit veya fenobarbitalden bir tanesi seçilerek verilebilir. İkincil basamak tedavilere yanıt vermeyen hastalara üçüncül basamak tedaviler midazolam, ketamin, tiyopental veya propofol sürekli infüzyonlarından bir tanesi uygulanabilir.

Bulgular: RSE etiyolojisinde otoenflamatuvar, otoimmün süreçler veya kriptojenik yeni başlangıçlı RSE düşünüldüğü zaman immün

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Received/Geliş Tarihi: 12.10.2024 **Accepted/Kabul Tarihi:** 18.01.2025 **Epub:** 20.03.2025 **Publication Date/Yayınlanma Tarihi:** 21.04.2025
Cite this article as: Özcan S, Uysal Yazıcı M, Kamit F, İnceköy Girgin F, Yazıcı Özkaya P, et al. Status epilepticus in critically ill children. J Pediatr Emerg Intensive Care Med. 2025;12:45-55

Two of the authors of this article (M.U.Y., A.Ç.) are members of the Editorial Board of this journal. They were completely unaware of the peer-review process of the article.

to second-line therapy should be managed in a pediatric intensive care unit in collaboration with a pediatric neurologist. For patients unresponsive to second-line therapies, third-line treatments may include continuous infusions of midazolam, ketamine, thiopental, or propofol. There is no standardized protocol for transitioning from continuous infusion therapy to intermittent therapy.

Results: In cases of RSE where autoinflammatory or autoimmune processes, or cryptogenic new-onset RSE are suspected, immunomodulatory therapies (such as corticosteroids, intravenous immunoglobulin, plasmapheresis, etc.) should be considered. Other therapies like ketogenic diet, hypothermia, and neurosurgery may be applied in selected patients. Continuous electroencephalography monitoring should be used in the management of status epilepticus.

Conclusion: Mortality due to status epilepticus can be as high as 3%, because of these patients to be followed up jointly by pediatric neurologist and pediatric intensivist and to be monitored in the pediatric intensive care unit.

Keywords: Children, status epilepticus, refractory status, pediatric ıntensive care unit

modülatör tedaviler (kortikosteroid, intravenöz immünglobulin, plazmaferez vb.) göz önüne alınmalıdır. Ketojenik diyet, hipotermi ve nörocerrahi gibi diğer tedaviler seçili hastalarda uygulanmaktadır. SE monitörizasyonunda sürekli elektroensefalografi kullanılmalıdır.

Sonuç: SE bağlı mortalite %3'e varan oranda değişmekte, bu nedenle bu hastaların çocuk nöroloji ve çocuk yoğun bakımla ortak takip edilmesi ve yoğun bakımda izlenmesi uygundur.

Anahtar Kelimeler: Çocuk, status epileptikus, refrakter status, çocuk yoğun bakım

Introduction

1.1. Definition

A seizure is a paroxysmal disorder of the central nervous system and consists of abnormal excessive hypersynchronous discharges of cortical neurons and may be accompanied by changes in behavior, movement and/or consciousness. Status epilepticus (SE) is a common pediatric neurological emergency that requires prompt recognition and intervention. SE was described thousands of years ago by the people of that period in Mesopotamian inscriptions as "...his neck turning left, hands and feet are tense, and his eyes wide open and from his mouth froth is flowing without him having any consciousness".[1] SE annually affects 25,000-50,000 children, 40% of whom are children under 2 years of age. In 2015, the International League Against Epilepsy, which published seizure classification and SE reports in 1970 and 1981, defined two operational time dimensions at the meeting to evaluate the definition of SE. Time point "*t1*" indicates when treatment should be initiated, because if the seizure has not stopped after this point, it is characterized by sustained seizure activity. Time point "*t2*" defines the time point at which the risk of long-term consequences increases. In the new definition, SE is defined as seizures that are prolonged as a result of activation of seizure termination mechanisms (after time point *t1*). Depending on the type and duration of the seizure (after time point *t2*), SE can lead to long-term consequences such as neuronal death, neuronal damage and disruption of neuronal connections. The International League Against Epilepsy has determined the duration of abnormally prolonged seizure in convulsive SE to be 5 minutes for *t1* and 30 minutes for *t2* when the risk of long-term effects increases.[2,3] These time points are used to decide when and how to start treatment in SE, to reduce long-term adverse outcomes and to determine clinical effects (Table 1).

Refractory SE (RSE) is seizure activity that persists despite the administration of initial benzodiazepine group (first-line treatments) and non-benzodiazepine group (second-line treatments) therapies, although there is no one hundred percent consensus on the definition.[4] In these patients, clinical and electroconvulsive seizures may continue for hours. These patients should be followed up together with pediatric neurology and pediatric intensive care unit specialists in pediatric intensive care units where continuous electroencephalography (EEG) monitoring can be performed 24 hours a day. Treatment should be titrated to provide seizure suppression or burst-suppression with continuous EEG monitoring.[5]

Super RSE (SRSE) has been defined as SE that persists for

Table 1. Conceptual definition of status epilepticus

SE type	Time point 1 (*t1*) (point at which the seizure is likely to be prolonged)	Time point 2 (*t2*) (the point at which the seizure is likely to cause long-term damage)
Tonic-clonic	5 minutes	30 minutes
Focal seizure with impaired consciousness	10 minutes	>60 minutes
Absence	10-15 minutes	Insufficient data

SE: Status epilepticus

24 hours or longer. Seizures occurring during reduction or withdrawal of anesthesia should also be considered as SRSE.[4]

Non-convulsive SE is an occult, clinical or non-convulsive seizure disorder and is mostly detected during intensive care follow-up of patients with convulsive SE. Without continuous EEG monitoring, it is not possible to distinguish post-ictal stupor or coma due to sedative effects of treatments from non-convulsive seizures. Electroencephalographic seizures have been observed in approximately 15% of patients with controlled seizures.[5]

1.2. Morbidity and Mortality in Status Epilepticus:

Although the mortality rate related to SE varies between countries, it has been reported to be 3% in developed countries. In studies reported from different countries, mortality was found to be between 1% and 28%. In a study conducted in our country, in which 100 SE patients followed up in pediatric intensive care unit were evaluated, mortality was found to be 10%.[6] Although the risk of epilepsy can be observed with a rate of 13-74% in children followed up because of SE, the rate of a new SE may develop up to 20% during the 4 years following SE. The recurrence rate is highest in patients with structural or metabolic disorders.[5]

1.3. Febrile Seizures and Febrile Status Epilepticus:

Febrile seizures are seizures that occur in children between the age of 6 months and 60 months (most commonly between 12-18 months) with a body temperature of 38 °C and higher. Central nervous system infection or metabolic disorders should be excluded especially in children with no previous history of seizures. Simple febrile seizure is a type of febrile seizure that occurs in generalized tonic-clonic form in the patient and does not exceed 15 minutes. Simple febrile seizures usually do not recur in the first 24 hours. Complex febrile seizures are defined as seizures that last longer than 15 minutes and/or have focal findings and/or recur in the first 24 hours. Febrile SE refers to febrile seizures lasting longer than 30 minutes. The postictal period of most simple febrile seizures is short and the child's behavior and consciousness return to normal in a short time.[7]

Table 2. Common causes of convulsive status epilepticus in pediatric patients

Acute pathology
◦ Acute symptomatic • Acute central nervous system infection (meningitis, encephalitis) • Anoxic damage • Metabolic imbalance (hypoglycemia, hyperglycemia, hyponatremia, hypocalcemia) • Traumatic brain injury • Drug-related - Antiepileptic non-compliance or withdrawal - Antiepileptic overdose - Non-antiepileptic overdose ◦ Prolonged febrile seizure
Indirect pathology
Cerebral dysgenesis Perinatal hypoxic ischemic encephalopathy Progressive neurodegenerative diseases Previous brain damage (meningitis, stroke, trauma)
Idiopathic/cryptogenic

2.1. Management of Status Epilepticus:

SE is a neurologic emergency that should be managed rapidly and accurately. It may be observed for various reasons (Table 2).[8] Although the outcome of SE depends on the underlying cause, seizure duration is important. Timely and appropriate intervention is more important than pharmacologic intervention.[8]

The following goals should be achieved in the treatment of acute convulsive SE:

1.Ensuring airway, respiration and circulation

2.Stopping the seizure and prevent its recurrence

3.Management of RSE in patients with RSE

4.Recognizing life-threatening lesions and taking necessary interventions (hypoglycemia, meningitis, intracranial space-occupying lesions, etc.)

Although most seizures (approximately 75%) stop within the first 5 minutes, a patient with an ongoing seizure on admission to the emergency or intensive care unit should be considered to have had a seizure for more than 5 minutes.

2.2. Ensuring Airway, Respiration and Circulation:

In patients admitted to a health center for SE, ABC should be reviewed, vital signs should be checked and the patient should be monitored. Hypoxemia is often present in these patients, and administration of antiepileptics by family members or 112 before hospitalization increases the risk of respiratory depression. Airway patency and respiration should be assessed first, and 100% oxygen therapy with an irreversible mask should be started. The patient should be given an appropriate sniffing position and easily accessible secretions should be aspirated. After aspiration, the patient should be repositioned and the airway should be opened with head tilt-chin lift or jaw-thrust maneuvers if necessary. In patients with acute disturbance of consciousness or severe neuromuscular weakness, the airway may be closed because adequate glossopharyngeal muscle tone cannot be maintained. In these patients, an appropriately sized oropharyngeal or nasopharyngeal airway should be used. If the patient has signs of respiratory depression (decreased air intake and outflow, superficial breathing, inadequate respiratory effort, apnea, central cyanosis) or if oxygen saturation is below 90% despite 100% oxygen therapy, ventilation with a balloon mask should be started and rapid sequential intubation should be considered if the findings

persist or the status is prolonged. Some patients may require neuromuscular muscle blockade during intubation. Short half-life neuromuscular blocking agents should be used in these patients. In patients receiving neuromuscular blocking agents, electroencephalographic seizure activity in the brain persists even if the motor component of the seizure disappears. In cases where continuous infusion of neuromuscular blocking agents is required, the patient should be followed up with continuous EEG monitoring.

Patients with seizures should be monitored tachycardia and hypertension are observed in patients with seizures. After the seizure stops, blood pressure and pulse rate return to the normal range for age. Bradycardia, signs of low perfusion and hypotension are poor signs of impaired tissue perfusion and oxygenation. Findings may be due to hypoxia and therefore ventilation with a balloon mask should be started and the patient should be endotracheally intubated. Blood glucose should be checked rapidly in a patient having a seizure. If the patient's blood sugar is <60 mg/dL, dextrose at 0.5 g/kg should be administered intravenously. If there is a central route, 2 mL/kg of 25% dextrose can be given or 10% dextrose 5 mL/kg should be administered peripherally. Blood glucose should be checked every 5 minutes and if hypoglycemia persists, the bolus dose of dextrose should be repeated.

Tachycardia, cold extremities, prolonged capillary refill, weak pulses and decreased urine output are signs of low cardiac output. At least two vascular accesses should be established. In patients with signs of circulatory disorders, appropriate isotonic fluid replacement should be administered intravenously or intraosseously at 20 mL/kg. If the patient's fever is high, intervention should be made. Paracetamol 10-15 mg/kg max: 500 mg intravenous can be administered rectally.[9]

2.3. First-line Treatments:

First-line treatments can be administered in the pre-hospital period and in the emergency department. Benzodiazepines are the first group of drugs to be used in the first step. Benzodiazepines can be administered intravenously, or if there is no vascular access and it will take a long time to open, they can be administered by other routes until the vascular access is opened. Treatment options in patients without intravenous access include intramuscular, intranasal and buccal midazolam and rectal diazepam (Table 3).[8] Intramuscular midazolam is the first-line treatment for a pediatric patient older than one year and/or over 13 kg with convulsions without intravenous access. Rectal diazepam is the first-line treatment for convulsions in a patient younger than one year or weighing less than 13 kg, who has no vascular access. Intravenous diazepam is the first-line treatment option in the patient with an intravenous access. If the seizure does not stop within 5 minutes after benzodiazepine is administered to the patient, a second dose of intravenous diazepam should be administered to the patient with intravenous access.[10]

All benzodiazepines act by potentiating the neuroinhibitory effect of gamma amino butyric acid (GABA). The main difference between midazolam, lorezepam and diazepam is due to their different pharmacokinetic properties. All three benzodiazepines are metabolized via cytochrome p450-dependent isoenzymes. Midazolam, which has a half-life of 1-4 hours, is the most rapidly metabolized one. While enzyme activity is at the lowest level in the newborn, enzyme activity above normal is observed at 2-3 years of age and enzyme activity decreases back to adult level at 4 years of age. Repeated doses should be administered with caution in children in the infant age group.

2.4. Second-line Treatments:

If the first-line treatments are applied twice with 5-minute intervals but seizures do not stop, second-line treatment is started. Phenobarbital therapy for those under 1 year of age and phenytoin therapy for those over 1 year of age, traditionally used in secondary line, have changed with the introduction of new drugs. Levetiracetam, valproic acid and lacosamide are more frequently used new generation drugs.[1] However, in a randomized blind study in the United States, there was

Table 3. Anticonvulsants used in the first-line treatment of status epilepticus

Drug and route of administration	Dose	Maximum dose	Administration rate	Repeated dose	Risks
Midazolam					
Intramuscular	0.2 mg/kg	10 mg		In a seizure that continues 5 minutes after the first dose	Hypotension, respiratory depression, sedation
Buccal	0.5 mg/kg	10 mg			
Intranasal	0.2 mg/kg	10 mg (5 mg for each nostril)			
Diazepam					
IV, IO	0.3 mg/kg	5 mg (<5 years) 10 mg (≥5 years)	Longer than 2 minutes	In a seizure that continues 5 minutes after the first dose	Hypotension, respiratory depression, sedation
Rectal	0.5 mg/kg	20 mg			

IV: Intravenous, IO: Intraosseous

no difference between groups in terms of levetiracetam, phenytoin and valproic acid efficacy levels and side effects in 384 patients with benzodiazepine resistant seizures.[11] In the ConCEPT study published in Australia and New Zealand and the EcLIPSE study published in the United Kingdom, no significant difference was observed in terms of clinical seizure cessation in both groups when two groups treated with phenytoin and levetiracetam were compared in pediatric patients with benzodiazepine-resistant SE. In another multi-centered study comparing levetiracetam, fosphenytoin and valproic acid treatments, which was performed in the United States, similar results were found for all three treatments for the treatment of benzodiazepine resistant SE, and each of the three drugs could be applied as the first option in the second-line treatment of SE.[12,13] Drugs used in the second line treatment of SE are given in Table 4).[8]

Phenytoin is one of the frequently used antiepileptics in the treatment of SE. Phenytoin affects the neuronal membrane by stabilizing it. Therapeutic effect occurs in about 20 minutes. Phenytoin is not effective in stopping drug-related seizures despite its frequent use and increases the risk of arrhythmia in these poisoning.

Phenobarbital is often an antiepileptic used for the seizure of the newborn and SE. Its potential side effects include respiratory depression, hypotension, bradycardia and prolonged sedation. When used with benzodiazepines, it may have an intubation requirement due to respiratory depression. Phenytoin is more in the background because it disrupts neurological evaluation due to prolonged sedation effect. Phenobarbital has no intravenous form in our country. Therefore, its use is limited.

Levetiracetam is a 2nd line agent preferred for its efficacy on all types of seizures, low side effect profile, low protein binding rate and limited metabolism from the liver. Although its oral and intravenous use is common, intramuscular route is applied safely and with high bioavailability. Intramuscular peak effect occurs in 2 hours. In patients with SE, it is thought that the application of levetiracetam may have a role in pre-hospital treatment due to its safe use and effectiveness.

Sodium is effective by regulating valproate sodium channels, potassium channels and GABA activity. Rare but severe side effects of valproic acid use are liver failure due to hepatotoxicity, pancytopenia and hyperammoniemia. It should not be used in patients with mitochondrial disease.

Pyridoxine (Vitamin B6) is the cofactor of glutamic acid decarboxylase and GABA transaminase enzymes, used in GABA synthesis and metabolism in the brain. Pyridoxine deficiency is a rare disease. Although it is mostly seen in the newborn and infant period, it can also be seen in children up to the age of 30 months. In patients with pyridoxine deficiency, seizures

Table 4. Anticonvulsants used in the second-line treatment of status epilepticus

Drug and administration route	Dose	Maximum dose	Administration rate	Repeated dose	Risks	Suggestions
Phenytoin						
IV, IO, IM	20 mg/kg	1000 mg	It should be administered above 1 mg/kg/min dose. (It should be prepared only with 0.9% NaCl)	If the dose is insufficient, repeat at 5 mg/kg	Hypotension, bradycardia, arrhythmia, extravasation injury if developed	Should not be given with fosphenytoin, should not be given in drug-induced seizures
Phenobarbital						
IV, IO	20 mg/kg	1000 mg	It should be administered above a dose of 1 mg/kg/min. (It should be prepared with 0.9% NaCl or 5% dextrose)		Respiratory depression, Hypotension, prolonged sedation	2nd best option in a patient <6 months, with febrile status and maintenance therapy with phenytoin
Levetiracetam						
IV, IO, IM	60 mg/kg	3000 mg	It should be given over 5-15 minutes (it should be prepared with 0.9% NaCl or 5% dextrose and should have a concentration of 15-50 mg/mL)		Psychosis	
Valproic acid						
IV, IO	30 mg/kg	3000 mg	It should be given over 5 min. (It should be prepared with 0.9% NaCl or 5% dextrose)	An additional dose of 10 mg/kg can be administered.	Liver failure, presence of mitochondrial disease, <2 years of age	

IV: Intravenous, IO: Intraosseous, IM: Intramuscular

resistant to other conventional antiepileptics can be seen. These patients respond quickly and dramatically to pyridoxine. After other causes of seizure are ruled out, pyridoxine 100 mg can be administered intravenously. Pyridoxine should be administered by EEG monitoring if possible. The improvement in EEG brings to mind the deficiency of pyridoxine.[14]

2.5. Third-line Treatments:

One definition of RSE implies seizures that have been going on for more than 1 hour despite anticonvulsive treatment. In another definition, it is emphasized as the condition that seizure continues despite the administration of two groups of anticonvulsive treatment-one of which is non-benzodiazepine group. These patients are at risk for complications, long hospitalization and mortality.

Although conventional antiepileptics has a low efficacy in the treatment of RSE, drugs such as topiramate, levetiracetam and carbamazepine should be continued during attacks. Higher doses or more potent agents should be used in RSE treatment. Treatment options are high-dose benzodiazepine, short-acting barbiturates, valproic acid, ketamine, lidocaine and inhalation anesthetic agents. The patients in induced coma may have cardiopulmonary insufficiency and metabolic imbalances. Multidisciplinary study is required here. Pediatric neurology specialist should lead the patient management in a diagnostic sense and should be a guide for the treatment selection and drug interactions. Pediatric intensive care specialist should provide the necessary respiratory and circulatory support treatments, management of metabolic disorders, safe induction of coma and anesthesia.

Nowadays, high-quality studies required to determine optimum RSE management are limited. Therefore, differences occur in management and treatment goals. Partly for this reason, treatment response of 15-35% of patients receiving RSE treatment is not sufficient and SRSE develops in these patients. SRSE is an ongoing seizure activity in which seizure continues more than 24 hours despite the use of anesthetic agent or in the stage of anesthetic agent cessation.[15]

The definition of new-onset RSE (NORSE) is used for the patients with RSE developing without epilepsy or associated neurological disease, and without an identifiable acute structural, toxic and metabolic disorder. Febril infection-related epilepsy syndrome (FIRES), which is defined in a sub-category of the NORSE, is defined in school-age children. These patients usually have a history of feverish infection until 24 hours to 2 weeks before the SE. The SE seen in these patients may occur with fever or without fever. The etiology of these syndromes is unknown.

Its clinical presentation is mostly focal SE with convulsive SE or impaired consciousness. Another presentation is non-convulsive SE. Although the convulsive SE often evolves into non-convulsive SE, it is very important to distinguish the difference between these two phenotypes because the therapeutic approaches have different consequences. The development of non-convulsive SE in the patient is more often associated with resistance to treatment and delayed recognition of the clinic.

Most patients who are monitored due to RSE have structural brain damage, metabolic disorder and/or cerebral hypoxemia. Diagnostic studies during the evaluation of the patient who was followed due to RSE are given in Table 5.

Table 5. Diagnostic studies that should be performed in patients followed up for RSE-FIRES

Clinical evaluation
• Evaluation for pathologies not previously considered; meningoencephalitis, sepsis, FIRES, demyelinating disease, toxicology • Detailed examination for cortical malformations, neurocutaneous syndromes, autoimmune diseases, monogenic epileptic encephalopathies, metabolic diseases, chromosomal anomalies • Ophthalmic evaluation
Laboratory parameters not previously evaluated
• Inflammatory markers: CRP, erythrocyte sedimentation rate, von Willebrand factor antigen • Infectious agents: bacterial, fungal or viral cultures and serology tests • Oligoclonal band • Autoantibody tests, neuronal or ion channel antibodies
Cranial imaging
• Gadolinium-based diffusion cranial magnetic resonance imaging, MR angiography
CSF analysis
• CSF: glucose, protein level and cell count • Bacterial, fungal or viral cultures and serology tests • Oligoclonal band • Autoantibody tests, neuronal or ion channel antibodies
Brain biopsy
• In the detection of microvascular vasculitis findings on MR angiography

CSF: Cerebrospinal fluid, FIRES: Febrile infection-related epilepsy syndrome, RSE: Refractory status epilepticus, CRP: C-reactive protein, MR: Magnetic resonance

Continuous electroencephalographic monitoring (CEEG) is the basis for the diagnosis and management of RSE and SRSE. Continuous EEG monitoring helps to stop non-convulsive seizures and to ensure burst-suppression. It is also useful in the induction of pharmacologic coma and in the detection of unrecognized seizures during drug withdrawal. Although continuous EEG monitoring plays an important role in the initial management and diagnosis of RSE/SRSE, not all pediatric studies have included CEEG monitoring in the management of RSE/SRSE. This situation greatly limits the generalization of clinical results and comparison of study results since CEEG cannot be applied in all pediatric studies on CEEG monitoring.

The therapeutic goal in patients with RSE, SRSE, NORSE and FIRES is to control clinical and electrographic seizures. In this respect, four parallel therapeutic strategies need to be addressed:

1. Is there an indication for immunotherapy? What is the hierarchy of escalation of antiepileptic therapies and anesthetic agents given as infusions?

2. Is there an indication for immunotherapy?

3. Should a ketogenic diet be started?

4. Does the patient have an indication for surgical treatment?

Pharmacotherapy in the treatment of RSE is possible with additional dose boluses of level 2 therapies (phenytoin, levetiracetam, phenobarbital, valproic acid) or medically induced coma with continuous infusion of anesthetic agents with continuous EEG monitoring. Some patients benefit from additional boluses of level 2 drugs while others benefit from continuous infusion of anesthetic agents. In the treatment management of RSE, there are no definite patient criteria to guide treatment. Since no standard treatment protocol has been established, the treatment dose should be titrated until electroencephalographic seizure arrest or burst-suppression is achieved in continuous EEG monitoring and seizure control is achieved for 24-48 hours. After that, the drug dose should be gradually decreased.[15] Drugs to be used in the treatment of RSE and SRSE are shown in Table 6.

In a patient who will receive infusion therapy for SE, midazolam infusion is usually started in the first stage. If midazolam fails, ketamine or pentobarbital infusion is administered. The elimination half-life of midazolam varies between 1.5 and 3.5 hours. This pharmacodynamic allows for repeated bolus administration and aggressive titration of the infusion, leading to relatively faster recovery. Midazolam has anxiolytic, muscle relaxant, hypnotic and anticonvulsant effects like other benzodiazepines. The exact clinical or electroencephalographic target point of midazolam has not been clearly defined. Seizure control and infusion administration time were found to be longer in patients with continuous EEG monitoring

Table 6. Pharmacological agents used in the treatment of RSE/SRSE

Drug	Action mechanism	Dose	Side effects	Clinically important points
Midazolam	Positive allosteric modulation of GABA-A receptors, increased chlorine channel opening frequency	Initial loading dose 0.2 mg/kg, Infusion rate: 0.05-2 mg/kg/h. Existence of sudden seizures under infusion: 0.1-0.2 mg/kg bolus, infusion is increased by 0.05-0.1 mg/kg/h	Hypotension, respiratory depression	Prolonged use tachyphylaxis and drug accumulation
Thiopental	GABA receptor activation, increased chlorine channel opening, NMDA receptor inhibition, variability in chlorine, calcium, potassium ion channel conductivity	2-7 mg/kg, infusion rate ≤50 mg/min. Infusion rate: 0.5-5 mg/kg/h Existence of sudden seizures under infusion: 1-2 mg/kg bolus, infusion is increased by 0.5-1 mg/kg/h	Hypotension, cardiac and respiratory depression	The need for mechanical ventilation, burst-suppression should be provided in infusion EEG.
Propofol	Chlorine canal conductivity, GABA-A receptor activation	Initial loading dose 1-2 mg/kg, Infusion rate: 20 mcg/kg/min. Titrated in 5-10 mcg/kg/min doses. Should be carefully used over the dose of >65 mcg/kg/min. Existence of sudden seizures under infusion: every 5 minutes Infusion is increased by 5-10 mcg/kg/min.	Propofol infusion syndrome, hypotension, cardiac and respiratory depression	The need for mechanical ventilation, In the child, the extended infusion is relative contraindication in the presence of metabolic acidosis, the presence of hypertriglyceridemia, and the presence of mitochondrial disease. ICP decreases, İt should be used carefully with steroid and catecholamine.
Ketamine	Non-competitive NMDA is glutamate receptor antagonist, it decreases neuron inducibility	Bolus: 0.5-3 mg/kg Infusion dose: 1-10 mg/kg/h	Tachycardia, hypertension,	It is relative contraindication in patient with increased ICP. Ketamine is an enzyme stimulant and inhibitor.
Inhaled anesthetic-Isoflurane-	Increases GABA-A receptor activity. Non-competitive NMDA is glutamate receptor antagonist.	Should be applied in the concentration of 1-5%. Burst-suppression should be provided in EEG monitorization.	Hypotension, atelectasis, paralytical ileus, infection, deep vein thrombosis in need of vasopressor	High rate of repeated seizure

ICP: Intracranial pressure, GABA: Gamma amino butyric acid, NMDA: N-methyl D-aspartate, RSE: Refractory status epilepticus, SRSE: Super refractory status epilepticus

compared to patients without continuous EEG monitoring. Early burst-suppression is rarely achieved with midazolam infusion in continuous EEG monitoring, so it should not be a treatment target in patients receiving midazolam infusion. In patients receiving midazolam infusion, the goal should be to achieve 12 hours of seizure-free time followed by dose reduction. Titration of midazolam infusion is shown in Table 7.[5] There are studies in which midazolam infusion was administered up to a dose of 1.92 mg/kg/hour. Midazolam is soluble below pH 4.5 and a patient receiving 1.5 mg/kg/hour infusion receives as much ion as the hydrogen ion present in the whole body. Therefore, unexplained metabolic acidosis may be observed in patients receiving high doses, especially in patients with hepatic and renal insufficiency. Other infusion therapies should be considered in these patients. In the KETASER study, doses above 0.36 mg/kg/h (>6 mcg/kg/min) were defined as midazolam infusion failure. This dose was also defined in other studies.[16]

In patients for whom midazolam infusion has failed, clinicians usually use barbiturates as secondary agents. Pentobarbital and thiopental are barbiturates that, like midazolam, act by increasing GABA activity. In addition, they cause glutamate N-methyl D-aspartate (NMDA) receptor inhibition and restriction of ion conduction in the axonal membrane. Although pentobarbital is commonly used in clinics abroad, thiopental is available in Türkiye. Thiopental can be used as an infusion at a dose of 0.5-5 mg/kg/hour following a bolus of 2-7 mg/kg. In studies, its efficacy in stopping seizures was found to be less than propofol. It takes a long time to be excreted from the body due to its long half-life. It may cause hypotension, cardiopulmonary depression, infection, anemia and prolonged intensive care unit stay. SE cessation rates of barbiturates vary between 64-69%.[15] Since seizures persist despite midazolam infusion in patients who will be started on barbiturate infusion, it should be kept in mind that seizures may recur with barbiturate infusion and a more careful clinical follow-up should be applied in these patients in terms of the risk of SRSE development.

Propofol is a non-barbiturate anesthetic agent (GABA agonist) used for rapid induction and maintenance of anesthesia. It stops seizures within minutes after initiation of administration and provides burst-suppression. Long-term propofol infusion is not recommended in the United States and other countries. Bradycardia, apnea, hypotension and propofol infusion syndrome (metabolic acidosis, rhabdomyolysis and cardiovascular collapse, arrhythmia, renal failure) may occur. Propofol infusion syndrome may occur when the drug is administered in excess of 4 mg/kg/hour or for longer than 48 hours.

Ketamine is a typical NMDA antagonist. It has anti-convulsant and neuroprotective properties. With its unique mechanism of action, it is an alternative treatment alternative in patients

Table 7. High dose midazolam titration in refractory status epilepticus treatment

Time after treatment starts	Midazolam dose	Step
0th min; Initial bolus	0.5 mg/kg	A
0th min; Start continuous infusion	Start 2 mcg/kg/min (0.12 mg/kg/hour)	B
5th min; Seizure continues after the 5th minutes (Step A)	Bolus repeated 0.5 mg/kg Infusion: Increase 4 mcg/kg/min (0.24 mg/kg/hour)	C
10th min; Seizure continues after the 10th minutes following Step C	Bolus 0.1 mg/kg Infusion: Increase 4 mcg/kg/min (0.24 mg/kg/hour)	D
15th min; Seizure continues after the 15th minutes following Step D	Bolus 0.1 mg/kg Infusion: Increase 4 mcg/kg/min (0.24 mg/kg/hour)	E
20th-45th min: If the seizure persists or repeats after step E, the step D is repeated every 5 minutes until the maximum dose is reached	Maximum infusion rate 36 mcg/kg/min (1.92 mg/kg/hour)	F (5 cycle can be repeated from D to E)
45th min: Following the completion of the step F, it should be confirmed that the seizure stops with EEG. If the seizure or seizure activity continues, treatment should be considered as unsuccessful and step into H	After the seizure control is provided with clinical monitorization and EEG, begin step I after 12 hours	G
45th-60th min: Failed treatment	Reducing midazolam infusion and providing general anesthesia with ketamine or pentobarbital	H
Patient without clinical and electrographic seizures for 12 hours, infusion dose is decreased	Decrease by 2 mcg/kg/min every 30 minutes.	I
EEG monitorization is continued for seizure observation of 12 hours	Other antiepileptic treatment plan should be made and infusion should be discontinued. If there is seizure during the reduction, go to the K step. The patient is likely to have a SRSE	J
Failure in decreasing	Bolus repeat 0.1 mg/kg Infusion: Increase 4 mcg/kg/min (0.24 mg/kg/hour) Evaluate alternatives	K

EEG: Electroencephalography, SRSE: Super refractory status epilepticus, min: Minute

receiving high dose midazolam infusion. If ketamine will be administered to patients whose seizures persist while receiving midazolam infusion under the treatment of RSE, the dose of midazolam should be reduced from 0.36 mg/kg/hour to 0.12 mg/kg/hour in patients receiving midazolam for less than 5 days to prevent anesthetic reactions. In patients receiving midazolam infusion for more than five days, the midazolam dose should be reduced from 0.36 mg/kg/hour to 0.24 mg/kg/hour in order to prevent seizures that may develop due to sudden benzodiazepine withdrawal and to prevent reactions that may develop due to sudden discontinuation of benzodiazepine. Recently published adult and pediatric studies have shown that ketamine may cause metabolic acidosis, hemodynamic disorder, sepsis and pneumonia due to prolonged use.[15]

In the ongoing KETASER01 study protocol reported from Italy, which was conducted in pediatric patients followed up due to multicenter RSE, ketamine dose was started at a dose of 10 mcg/kg/min following a bolus at a dose of 2-3 mg/kg, and the infusion dose was increased by 5-10 mcg/kg/min every 10 minutes until the seizure was under control. A bolus of 1-2 mg/kg was repeated before each increase. The maximum dose was set as 100 mcg/kg/min. After the seizure was under control, the infusion was planned to continue for 48 hours-7 days. When the seizure continued and adverse events developed, ketamine was discontinued and defined as failure. Ketamine dose was reduced by 25% every 12 hours at doses of 50-100 mcg/kg/min and by 25% every 6 hours at doses below 50 mcg/kg/min. In patients receiving ketamine infusion, the goal of continuous EEG burst-suppression like midazolam is rarely achieved. The aim is to stop seizures for 48 hours.[16]

As a last-line treatment, inhaled anesthetics can be used in the treatment of RSE. Among inhaled anesthetics, isoflurane is most commonly used in pediatric patients. Since the efficacy of inhaled anesthetics is temporary, it saves time for diagnostic studies to be performed and adjunctive therapies to be arranged. However, since they are short-acting, seizure activity relapses at a high rate as soon as they are discontinued.[15]

If a seizure recurs in a patient who is in the period of tapering continuous anesthetic infusion therapy due to RSE, this is called super-resistant SE. From this point, treatment is continued with higher doses, additional infusions or oral antiepileptics that cannot be given intravenously.

Immune modulatory therapies should be considered when autoinflammatory, autoimmune processes or cryptogenic NORSE are considered in the etiology of RSE. The most commonly used treatments are corticosteroids, intravenous immunoglobulin (IVIG) and plasmapheresis. However, their efficacy is controversial. In a publication reporting the treatment of five young adults followed up for NORSE, early immunomodulatory treatment (steroid, IVIG and azothiopurine) helped to achieve seizure control in 3 patients and reduced anticonvulsive treatment to a reasonable level.[15] In a study in which twenty-one RSE/SRSE patients were evaluated, the treatment response rate with additional immune modulator therapy was only 5%.[15] Immune modulator therapies used in the treatment of RSE are shown in Table 8.

Plasmapheresis is mostly used in parallel with other immune therapies in the presence of FIRES, anti-NMDA encephalitis and RSE/SRSE due to paraneoplastic autoimmune encephalitis. Although there are previous studies showing that patients with FIRES who receive early plasmapheresis treatment have better outcomes, there are also case series in which plasmapheresis is administered for FIRES and no benefit was seen.

Immune therapies targeting inflammatory cytokines thought to be involved in the etiology of refractory epilepsies may

Table 8. Immune modulator agents used in the treatment of RSE/SRSE

Drug/Treatment	Action mechanism	Dose	Side effects	Clinically important points
IVIG	Change in expression and function of Ig-G specific receptors (decrease in cytokine release), decrease in complement-related cell damage	Total dose of 1-2 g/kg is given in 3-5 days	Hypersensitivity reactions, transfusion associated lung damage, thromboembolic events, renal damage due to the concentration of solution, aseptic meningitis	It should be used in the treatment of crypogenic or autoimmune RSE/SRSE.
Methylprednisolone Prednisone	Inhibition of inflammation -related proteins (cytokine, chemokine) and immune -suppressive effect	Methylprednisolone: 1 gr/day, 3-5 days Prednisone: 60 mg/day	Glucose intolerance, psychiatric disorders, reduced immune functions, adrenal insufficiency	
Plasmapheresis	Cleaning of autoantibodies, immune factors and high -weight proteins participating in the possible inflammatory process	5 sessions		

IVIG: Intravenous immune globulin, RSE: Refractory status epilepticus, SRSE: Super refractory status epilepticus

be used instead of conventional immunotherapy. Recently, anakinra has been a treatment of interest in the treatment of FIRES. Anakinra is an Interleukin type 1 receptor antagonist. It prevents the biological activation of IL-1β. In animal experiments for IL-1β-resistant seizures, IL-1β overexpression was observed in microglia and astrocytes of subjects. This suggests anakinra as a potential therapeutic agent.

Ketogenic Diet

Ketogenic diet is a safe and effective form of treatment containing high fat, low carbohydrate and sufficient protein used as a treatment alternative in treatment-resistant epilepsies. Due to its anti-inflammatory and antiepileptic properties, it has gained value as adjunctive therapy in recent years. In pediatric case series, the success rate was found to be 54%. Ketogenic diet is contraindicated in carnitine deficiency, beta oxidation defects, beta carboxylase deficiency and porphyria. Ketogenic diet should be started with a 4:1 or 3:1 ratio (ratio of fat to protein and carbohydrate in grams), with glucose completely excluded from the diet. It may cause hypoglycemia, acidosis, weight loss and gastroesophageal reflux in the early period. Blood glucose should be checked every 3 hours for the first 3 days. If blood glucose falls below <45 mg/dL, glucose should be given. Urine and serum ketones should be checked daily. Steroids should be avoided because they inhibit ketosis.

Hypothermia

Therapeutic hypothermia is mainly used in the treatment of traumatic brain injury. Nowadays, it can also be used in the treatment of RSE and SRSE as adjunctive therapy due to its neuroprotective and antiepileptic properties as shown in animal experiments. It has been reported in case series that RSE was controlled with hypothermia used as adjunctive therapy in the childhood age group. In a multicenter series evaluating 270 patients with convulsive SE, hypothermia did not prevent progression to RSE and did not provide positive results compared to standard treatments.[17]

Epilepsy Surgery

Resistant cases with persistent seizures despite multiple medical treatment may be evaluated for surgical treatment by centers performing epilepsy surgery. When a focal epileptic focus is detected on neuroimaging, it can be evaluated for focal resection. Neuroimaging alone is not sufficient to determine the potential surgical resection site. At least, it should be shown that the ictal and interictal discharges of the region with structural lesion are compatible. In clinically stable patients, flurodeoxyglucose positron emission tomography should be performed to show interictal and ictal hypermettabolism of the epileptogenic focus. Special patient groups such as cortical dysplasia, tuberous sclerosis complex, polymicrogyria, hypothalamic hamartoma, hemispheric syndromes, Sturge-Weber syndrome, Rasmussen syndrome and Landau-Kleffner syndrome can be treated with epilepsy surgery. Surgical procedures may include vagal nerve stimulator, resection of the cortical lesion, temporal lobectomy, hemispherectomy, corpus callosotomy or multiple subpial resection.

Footnotes

Authorship Contributions

Concept: S.Ö., M.U.Y., F.K., F.İ.G., P.Y.Ö., Ç.K., R.Y., E.U.S., A.Ç., Design: S.Ö., M.U.Y., F.K., F.İ.G., P.Y.Ö., Ç.K., R.Y., E.U.S., A.Ç., Data Collection or Processing: S.Ö., M.U.Y., F.K., F.İ.G., P.Y.Ö., Ç.K., R.Y., E.U.S., A.Ç., Analysis or Interpretation: S.Ö., M.U.Y., F.K., F.İ.G., P.Y.Ö., Ç.K., R.Y., E.U.S., A.Ç., Literature Search: S.Ö., M.U.Y., F.K., E.U.S., A.Ç., Writing: S.Ö., M.U.Y., E.U.S., A.Ç.

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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