Review / Derleme

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Turkish Society of Pediatric Emergency and Intensive Care Medicine Neurocritical Care Study Group Stroke in Critically Ill Children

Türk Çocuk Acil Tıp ve Yoğun Bakım Derneği Nörokritik Bakım Çalışma Grubu Kritik Çocuk Hastada İnme

Feyza İnceköy Girgin[1], Mutlu Uysal Yazıcı[2], Serhan Özcan[3], Fulya Kamit[4], Pınar Yazıcı Özkaya[5], Çelebi Kocaoğlu[6], Resul Yılmaz[7], Eylem Ulaş Saz[8], Agop Çıtak[9]

[1]Marmara University, Pendik Training and Research Hospital, Department of Pediatric Intensive Care, İstanbul, Türkiye
[2]Gazi University Faculty of Medicine, Department of Pediatric Intensive Care, Ankara, Türkiye
[3]Ankara Bilkent City Hospital, Clinic of Pediatric Intensive Care, Ankara, Türkiye
[4]Memorial Bahçelievler Hospital, Clinic of Pediatric Intensive Care, İstanbul, Türkiye
[5]Ege University Faculty of Medicine, Department of Pediatric Intensive Care, İzmir, Türkiye
[6]Konya City Hospital, Clinic of Pediatric Intensive Care, Konya, Türkiye
[7]Selçuk University Faculty of Medicine, Department of Pediatric Intensive Care, Konya, Türkiye
[8]Ege University Faculty of Medicine, Department of Pediatric Emergency, İzmir, Türkiye
[9]Acıbadem Mehmet Ali Aydınlar University Faculty of Medicine, Department of Pediatric Intensive Care, İstanbul, Türkiye

Abstract

Stroke is a disease whose differential diagnosis is not easy because its symptoms and signs can be seen in many neurologic diseases. When neurological examination, clinical findings and radiological imaging are evaluated together, neurological complications can be minimized with early diagnosis and treatment. Our aim is to increase stroke awareness by emphasizing the importance of time in pediatric acute stroke management and to remind the role of stroke team formation and multidisciplinary approach in early diagnosis and treatment.

Keywords: Child, stroke, pediatric intensive care

Öz

İnme; semptom ve bulgularının birçok nörolojik hastalıkta görülebilmesi nedeniyle ayırıcı tanısı kolay olmayan bir hastalıktır. Nörolojik muayene, klinik bulgular ve radyolojik görüntüleme birlikte değerlendirildiğinde erken tanı ve tedavi ile mortalite ve morbidite en aza indirilebilir. Amacımız, pediyatrik akut inme yönetiminde zamanın önemini vurgulayarak inme farkındalığını artırmak, inme ekibi oluşturulmasının ve multidisipliner yaklaşımın erken tanı ve tedavideki rolünü hatırlatmaktır.

Anahtar Kelimeler: Çocuk, inme, çocuk yoğun bakım

Introduction

Pediatric stroke is a sudden decrease or interruption in blood flow to the brain. Ischemic stroke occurs due to impaired blood flow to the brain as a result of blockage in the arteries, while hemorrhagic stroke occurs as a result of bleeding. Although there are some differences in approach, the supply of oxygen to the brain is disrupted in both cases; therefore, stroke is an emergency situation that requires rapid diagnosis and intervention. The fact that acute neurological changes can

Address for Correspondence/Yazışma Adresi: Feyza İnceköy Girgin, MD, Marmara University, Pendik Training and Research Hospital, Department of Pediatric Intensive Care, İstanbul, Türkiye
E-mail: feyzagirgin@hotmail.com **ORCID ID:** orcid.org/0000-0003-4324-0488
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be seen in many clinical presentations delays early diagnosis and initiation of treatment, which increases morbidity and mortality.[1] Our aim is to raise awareness of the critical importance of time in this situation, to establish a pediatric stroke team, and to emphasize the stages and importance of a multidisciplinary approach.

Stroke Epidemiology

Stroke is difficult to diagnose due to the variability of its symptoms and findings. The incidence of childhood stroke varies widely in the literature, but is estimated to range from 2.5 to 13 per 100.000 each year.[2,3] Male children and the black people are known to be at higher risk.[4] Ischemic stroke is more common than hemorrhagic stroke. The mortality rate in children is approximately 10-25%, but hemorrhagic stroke has a significantly higher mortality rate than ischemic stroke.[1,5]

The Etiology of Stroke and Risk Factors

Common risk factors associated with pediatric stroke include vascular disorders, infections, cardiac causes, and coagulopathies.[6] Other risk factors include hematological disorders, renal disorders, child abuse, autoimmune disorders, metabolic disorders, and head trauma.[7] These risk factors increase the likelihood of cardiac-related embolic events, which are responsible for most ischemic strokes in children.[6] Congenital heart disease, bacterial and other thrombotic endocarditis, cardiomyopathies, rheumatic heart disease, and valvular disease are other cardiac-related risk factors.

Sickle-cell anemia is a hematological disease in which stroke occurs due to the obstruction of blood flow by cells that take on a sickle shape as a result of abnormal hemoglobin.[8] Antiphospholipid antibodies associated with venous thrombosis, protein C deficiency, factor V Leiden mutations, *MTHFR* gene mutations, and antithrombin III deficiency are some congenital or acquired prothrombotic conditions that are other important causes of stroke. These conditions can lead to ischemic or hemorrhagic strokes. Obtaining a detailed family history and reviewing the medications used by the patient can be helpful in determining the underlying etiology. Valproic acid, an antiepileptic drug, has been associated with acquired protein C deficiency.[9]

Hemorrhagic strokes can often be caused by congenital conditions such as arteriovenous malformations. Dissections usually occur as a result of tearing of the artery wall due to trauma. In conditions such as Marfan syndrome, pseudoxanthoma elasticum, moyamoya disease, and fibromuscular dysplasia, they may occur due to coughing, sneezing, or arteriosclerosis. Dissections can lead to strokes through obstruction of the vascular lumen due to the development of intramural hematomas or through thromboembolism. The onset of symptoms can range from one day to one week. Intracranial dissections are a more common cause of stroke in children than in adults.[10]

Cerebral venous thrombosis (CVT) may occur in adolescents with cancer, inflammatory or hematological diseases, and in those using oral contraceptives.[10] Craniofacial infections such as otitis, sinusitis, periorbital infections, meningitis, and encephalitis can lead to CVT.[9] Direct invasion, the presence of a prothrombotic state, and increased platelet aggregation are contributing factors. In the presence of prothrombotic risk factors, dehydration can act as a facilitating factor in triggering a stroke. Viruses such as varicella-zoster virus, human immunodeficiency virus, herpes virus, human parvovirus B19, enterovirus, and influenza A and other bacterial, fungal and parasitic agents such as *Mycobacterium tuberculosis*, *Treponema pallidum*, *Chlamydia pneumoniae*, aspergillus, and *Trypanosoma* cruzi are inflammatory causes that can lead to this condition.[11,12]

Oncological strokes can occur as a result of the cancer itself or the treatments used to treat it. The group at highest risk is leukemia patients and those undergoing radiation therapy.[12,13] Most cases occur during the first 5 months of treatment.[14] It is known that radiation exposure in these patients increases the risk of stroke in a dose-dependent manner.[15] Cytarabine and L-arginase are two important agents known to cause this effect.[16]

Genetic disorders are important risk factors for strokes in the pediatric population. Family history and a detailed physical examination are important in identifying the underlying genetic disorder. Neurofibromatosis type 1, hereditary hemorrhagic telangiectasia, homocysteinemia, cyanocobalamin, pyridoxine, and folate deficiencies can lead to stroke by causing early atherosclerosis and vascular wall damage.[17-19]

Moyamoya disease is a non-inflammatory vasculopathy associated with stenosis of intracranial arteries, particularly the distal internal carotid artery and its branches. These patients are at high risk of stroke due to occlusion or narrowing of the vessels. Collateral vessels formed at the base of the brain may delay the onset of symptoms. Symptoms may be related to ischemia or intracranial hemorrhages that arise as a complication of the collateral blood vessel network. Although hemorrhagic stroke is more common in adults, most children present with ischemia. It is associated with both genetic and environmental factors. It can be confirmed by radiographic studies.[20]

Clinical Findings in Stroke

Although the brain anatomy of children is similar to that of adults, there are many physiological differences. This situation leads to the emergence of different clinical pictures. The

brain of children is more metabolically active. The amount of glucose used by the brain of a five-year-old child is up to 200% higher than that of an adult brain.

The increased cerebral blood flow requirement in children makes them more susceptible to focal neurological damage during hypoglycemic attacks.[5] Different clinical symptoms may be observed depending on the affected brain regions. While seizures are the most common symptom in young children with stroke, focal impairments such as hemiparesis are more common in older children.[4] Other neurological findings include changes in consciousness, decreased muscle strength, numbness, tingling, difficulty speaking, and brief loss of vision in one or both eyes. Non-spesific clinical symptoms and findings such as headache, nausea, vomiting, and fever may also be present.

Diagnosis and Monitorization of Stroke

Pediatric Stroke Team

A multidisciplinary team approach involving professionals from different fields of expertise is invaluable in the diagnosis, treatment, rehabilitation, and long-term follow-up of stroke patients. This team should include specialists from different fields, such as pediatric neurology, pediatric intensive care, and radiology, as well as physical therapists, speech and language therapists, psychologists, nurses, and social workers.

The Importance and Stages of a Multidisciplinary Approach

In the follow-up of children with stroke, it is critical that the pediatric stroke team works in coordination to ensure rapid and accurate diagnosis of the stroke, prevention of complications, and provision of the best possible support for the child's physical and psychosocial recovery. The stages detailed below may not progress at the same pace for every patient. Factors such as the patient's age, the cause of the stroke, and the extent of neurological damage can result in the process varying from patient to patient.

Emergency Intervention and Diagnosis Period

Intervention during this period is important in terms of eliminating the risk of death and limiting potential damage. Diagnosis is confirmed through symptom recognition, neuroimaging, and laboratory evaluation, and a decision is made regarding the treatment to be administered and when to begin.

Acute Treatment and Follow-up Period

It covers what needs to be done to limit the damage caused. During this period, monitoring in a clinic or pediatric intensive care unit is recommended depending on the patient's clinical condition. At this stage, monitoring of vital signs and neurological findings, evaluation of response to treatment, careful attention to possible complications, and family information are included.

Rehabilitation and Neuropsychiatric Support Period

The aim is to facilitate the child's transition to school and social life by providing physical therapy, speech and language therapy, and psychological support.

Long-term Follow-up

Periodic checkups during this period are performed, including stages for preventing the risk of recurrence, monitoring patients who require long-term anticoagulant use, providing counseling to the family, and planning education.

Family History and Laboratory Tests

Once the patient has been stabilized, family history and laboratory tests are evaluated to identify any underlying bleeding disorders. In cases of acute ischemic stroke, evaluation of underlying thrombophilic abnormalities provides information about the likelihood of recurrence or other at-risk individuals in the family. Protein C, antithrombin, factor V Leiden, lipoprotein a, antiphospholipid antibodies, and homocysteine abnormalities may be associated with venous thrombosis. Antiphospholipid antibodies may also be elevated after viral infection, so it is recommended that the test be repeated 12 weeks after the first positive result. Measurement of protein and homocysteine levels may not be accurate during the acute phase of stroke, and repeat testing after the acute event is recommended.[21]

Pediatric National Institutes of Health Stroke Scale (PedNIHSS)

Clinical symptoms and findings of stroke, especially in young children, can vary widely, including changes in mental status, changes in consciousness, and apnea. The National Institutes of Health has developed scoring systems that motivate young children by asking them questions in a playful manner, thereby enabling accurate assessments. These scoring systems provide convenience for clinicians in terms of screening and follow-up. Adult stroke scales have limited applicability in the pediatric population due to their low sensitivity. The PedNIHSS is one of the most widely used scoring systems for this purpose. It measures the severity of stroke using a child-specific version of the adult NIHSS. The scale, which was introduced in 2011, is used in children aged 2-18 years to measure the severity of pediatric stroke, monitor progress, assess recovery, and predict morbidity and mortality. It consists of 11 categories and 15 headings. It enables a rapid and reliable neurological assessment. A score below 6 is considered mild, while a score above 25 is considered severe neurological deficit. The details of the test are outlined in Table 1.

Radiological Imaging Methods

Early and accurate diagnosis of stroke and stroke type is important for emergency stabilization and resuscitation. Magnetic resonance imaging (MRI) is the first imaging method of choice due to its high sensitivity in detecting early ischemia. Techniques such as diffusion, perfusion, susceptibility weighted imaging, and flair examination are helpful in diagnosis. However, its application may be challenging due to factors such as limited availability and the need for sedation to obtain adequate images. For evaluating arteries, magnetic resonance angiography is the most appropriate technique, while MRI and magnetic resonance venography are the most suitable techniques for diagnosing venous sinus thrombosis. Computed tomography (CT) remains the imaging method of choice in cases of acute focal neurological deficits due to its ease of access and application. CT may be preferred in emergency cases involving unconscious, unstable patients. It has been observed that only 50% of non-contrast CT scans show findings consistent with ischemic changes.[22,23] Brain CT may be normal in ischemic stroke cases within the first 24 hours. It can be helpful in the differential diagnosis of acute hemorrhage and in the evaluation of early ischemic infarction, gray-white matter distinction, and edema.[24] While CT is an important parameter in scoring systems and decision-making for mechanical thrombectomy in adults, it may be considered a diagnostic tool in children due to its high radiation dose and the varying hemodynamics of patients under 8 years of age.[25] If there is suspicion of large vessel occlusion, CT angiography may be indicative.

Pediatric Stroke Algorithm

In the recognition and assessment of pediatric stroke, it is important to have practical guidelines and manuals that are easy to use and guide physicians in rapid diagnosis and treatment. The algorithm shown in Figure 1 has been prepared for ease of use in cases of suspected stroke.

Stroke Treatment

Acute and Protective Treatment

There are very few clinicians with extensive experience in mechanical thrombectomy and intra-arterial treatment in pediatric acute ischemic stroke. When large vessel occlusion is detected, it should be evaluated on a case-by-case basis, and if deemed necessary, the patient should be referred to a center with a neuroendovascular specialist who is an expert in endovascular techniques. In cases of hemorrhagic stroke, it is important to correct coagulopathy, if present, and to manage blood pressure by setting age-appropriate blood pressure targets.

The main goals of stroke treatment are to control the size of the infarct, prevent complications, and minimize the risk of permanent damage. Supportive treatment is administered during the acute phase. It is important to ensure airway patency, respiration, and circulation. Patients are evaluated for the need for oxygen therapy and non-invasive or invasive mechanical ventilation. Blood pressure, blood sugar, electrolytes, and body temperature should be maintained at normal levels. Adequate hydration is important. The first choice of fluid may be 0.9% saline solution or Ringer's lactate solution. Hypoosmolar solutions such as 5-10% dextrose should not be used as they may increase cerebral edema.

If the patient has increased intracranial pressure (ICP) or is suspected of having it, the patient is monitored and treated according to traumatic brain injury (TBI) protocol recommendations. Intravenous hypertonic saline is used to control ICP elevation in children with severe TBI. The recommended bolus dose to maintain ICP below 20 mmHg is 2-5 mL/kg administered as an intravenous infusion over 10-20 minutes. A continuous infusion dose of 0.1-1 mL/kg/hour is recommended. Another treatment that can be administered for this purpose is mannitol. The initial dose of 0.25-1.0 g/kg can be titrated as needed to maintain plasma osmolality ≤310 mOsm/L. In recent guidelines, 3% hypertonic saline has become an increasingly important and recommended treatment for cerebral edema.[26]

Seizures, if present, should be controlled. The use of prophylactic anticonvulsants is controversial in cases where seizures are not observed. Since young children have lower seizure thresholds and are at high risk for seizures, anticonvulsant treatment is recommended in the early stages (within the first 7 days) for children with intracranial hemorrhage. Levetiracetam or phenytoin may be selected for this purpose in children.[27] Continuous electroencephalographic monitoring is recommended for the diagnosis of non-convulsive status epilepticus.

Anticoagulant Therapy

After ruling out hemorrhagic stroke, if the patient has arterial dissection, prothrombotic disorders, dural sinus thrombosis, and risk of embolism due to heart disease, anticoagulation therapy with unfractionated heparin or antiplatelet therapy with aspirin should be used in the acute phase.[28,29] Other important contraindications for anticoagulation include moyamoya disease, thrombocytopenia, surgery within the past 24 hours, active bleeding, platelet count below 50.000/mm^3, and a history of heparin-induced thrombocytopenia. Unlike in adults, studies on the use of anticoagulants in children with stroke are limited.

Table 1. PedNIHSS application and scoring

1A. Level of consciousness (0-3)
0: Alert, highly responsive.
1: Not alert but obeys, responds, or reacts to minor stimuli.
2: Not alert, requires repeated stimuli, indifferent to environmental stimuli, has slowed psychomotor responses, drowsy state, requires strong or painful stimuli to move.
3: Responds only with reflex motor or autonomic effects or totally unresponsive, flaccid, areflexic.

1B. Assessment of age and family members (0-2)
a) Ask about age.
b) Ask to point to a family member.
0: Answers both questions correctly.
1: Answers one question correctly.
2: Does not answer either question correctly.

1C. Blinking and touching the nose command (0-2)
0: Performs both tasks correctly.
1: Performs one task correctly.
2: Does not perform either task correctly.

2. Horizontal extraocular movements (0-2)
Only horizontal eye movements are evaluated.
0: Normal
1: Partial gaze palsy: abnormal gaze in one or both eyes, but no forced deviation or complete gaze paresis.
2: Forced deviation or total gaze paresis that cannot be overcome by the oculocerebral maneuver.

3. Visual field (0-3)
In children over 6 years of age, visual field is assessed by finger counting, and in children between 2 and 6 years of age, visual field is assessed using visual threats.
0: No vision loss.
1: Partial hemianopia.
2: Complete hemianopia.
3: Bilateral hemianopia (blindness, including cortical blindness).

4. Facial palsy (0-3)
0: Normal symmetrical movement.
1: Minor paralysis (total or near-total paralysis of the lower part of the face).
3: Complete paralysis of one or both sides (no movement in the upper and lower face).

5 and 6. Assessment of arm and leg motor strength (separate scores for each limb)
The limb being assessed is placed in the appropriate position. For the arms, this position is 45 degrees when lying on the back with the palms facing down, and 90 degrees when sitting. The legs are always assessed in a supine position at 30 degrees. Points are awarded if the arm falls before 10 seconds and the leg falls before 5 seconds. For children who are too young or uncooperative to follow precise instructions, strength is assessed by observing spontaneous or emerging movements.
5A. Left arm (0-9)
5B. Right arm (0-9)
0: No slippage, arm maintains 90 (or 45) degrees for exactly 10 seconds.
1: Slippage, arm maintains 90 (or 45) degrees, but slips down before 10 seconds are up; does not hit the bed or other support.
2: Exerts some effort against gravity, cannot reach or maintain 90 (or 45) degrees (if indicated), slides toward the bed, but exerts some effort against gravity.
3: No effort against gravity, arm falls.
4: No movement.
9: Amputation/joint fusion.

6A. Left leg (0-9) (separate score for each limb)
6B. Right leg (0-9)
0: No slippage, leg maintains 30-degree position for 10 seconds.
1: Slipping, the leg falls before 10 seconds elapse but does not hit the bed.
2: Exerts some effort against gravity but the leg falls onto the bed within 5 seconds.
3: No effort against gravity, the leg falls.
4: No movement.
9: Amputation/joint fusion.

Table 1. Continued

6A. Left leg (0-9) (separate score for each limb)
6B. Right leg (0-9)
0: No slippage, leg maintains 30-degree position for 10 seconds.
1: Slipping, the leg falls before 10 seconds elapse but does not hit the bed.
2: Exerts some effort against gravity but the leg falls onto the bed within 5 seconds.
3: No effort against gravity, the leg falls.
4: No movement.
9: Amputation/joint fusion.

7. Extremity ataxia (0-2)
Ask the child to reach for a toy. For children under 5 years of age or who are unable to cooperate with a standard examination, ask them to kick a toy or the examiner's hand.
0: No ataxia.
1: Present in one extremity.
2: Present in two extremities.

8. Sensory examination (0-2)
Pin-prick test: To determine the degree of sensory loss in small or uncooperative children, any behavioral response to needle pricks is observed.
0: Normal, no sensory loss.
1: Mild to moderate sensory loss; the patient feels that the needle prick is less sharp or dull on the affected side, or there is superficial pain loss with the pinprick, but the patient is aware of being touched.
2: Severe to total sensory loss; the patient is unaware of being touched on the face, arm, or leg.

9. Speech (0-3)
Children with normal language development prior to stroke onset who are ≥6 years of age are asked to describe what is in the picture below, name objects, repeat words from the list, and read sentences from the list (Figures 1, 2, and appendices 1, 2). For children aged 2-6 years, assessment is based on observations of language comprehension and speech during the examination.
0: No aphasia, normal.
1: Mild to moderate aphasia.
2: Severe aphasia.
3: Mute, global aphasia; no usable speech or auditory comprehension.

Figure 1. Picture evaluation test

Figure 2. Object interpretation test

Table 1. Continued

Appendix 1. Repetition test
a. Stop.
b. Stop and go.
c. If it rains, we play inside.
d. The president lives in Washington.

Appendix 2. Reading test
a. Stop.
b. See the dog run.
c. Small children like to play outdoors.

10. Dysarthria assessment (0-9)
Ask the patient to read or repeat the words in Appendix 2.
0: Normal, no dysarthria.
1: Mild to moderate; the patient slurs at least some words, and at worst, can be understood with some difficulty.
2: Severe; the patient's speech is so slow or slurred as to be unintelligible in the absence of or out of proportion to any dysphasia or is mute/anarthric.
9: Intubated or other physical impairment.

11. Inattention or unresponsiveness (0-2)
0: Normal, no unresponsiveness.
1: Inattention or unresponsiveness to simultaneous stimulation from one of the visual, tactile, or auditory modalities.
2: Unidirectional unresponsiveness to more than one modality, failure to recognize one's own hand, or orients to only one side of space.

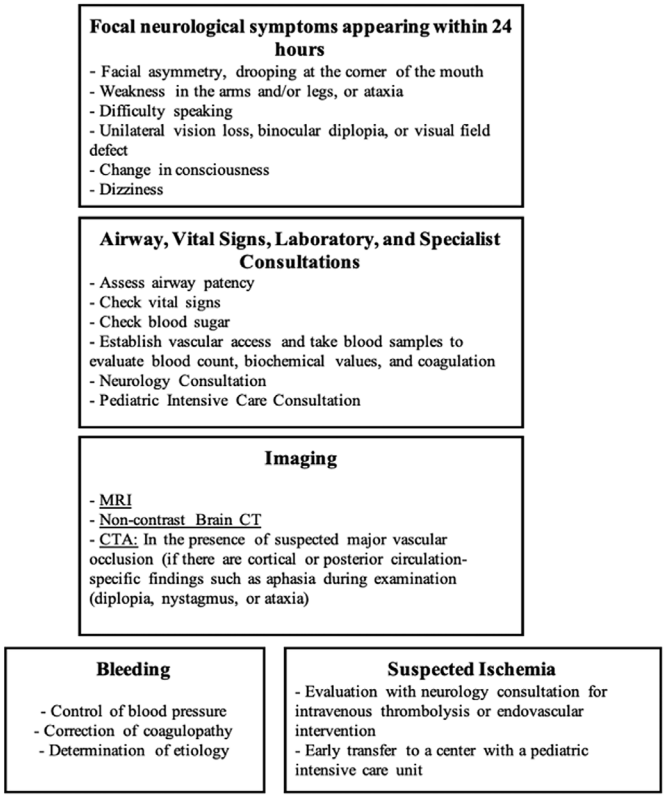

Figure 1. Pediatric stroke algorithm
MRI: Magnetic resonance imaging, CT: Computed tomography, CTA: Computed tomography angiography

A treatment plan tailored to each individual should be developed, taking into account the etiology, the condition of the lesion at the time of diagnosis, and its location. When planning anticoagulant therapy, the effects and side effects of the drugs to be administered should be well understood, and the ability to monitor their effects should be kept in mind. Low molecular weight heparin is used as the first choice in acute anticoagulant therapy in children because it does not require dose adjustment and can be administered subcutaneously. For children under 2 months of age, the initial treatment dose is 1.5 mg/kg/dose, and the prophylactic dose is 0.75 mg/kg/dose, administered every 12 hours. For children over 2 months of age, the treatment dose is 1 mg/kg/dose, and the prophylactic dose is 0.5 mg/kg/dose, administered every 12 hours. Monitoring is performed to maintain the anti-factor Xa level within the range of 0.3-0.7 U/mL.[30]

Non-fractionated heparin is used in the treatment and prophylaxis of venous thromboembolism due to its antithrombotic and anticoagulant effects. The initial loading dose is 30 units/kg, administered as an intravenous infusion over 10 minutes (maximum 5000 units). The maintenance dose of heparin therapy is 28 units/kg/h for children under 1 year of age and 20 units/kg/h (maximum 1000 units/hour) for children 1 year of age and older. For level monitoring, it is recommended to check the activated partial thromboplastin time (aPTT) or anti-factor Xa (anti-Xa) 4 hours after the first dose. It is recommended to maintain aPTT between 65-100 seconds or anti-Xa between 0.35-0.7 units/mL.[30]

Aspirin has an antithrombotic effect and is the first choice for arterial lesions. It prevents platelet aggregation by inhibiting the production of thromboxane A2 in platelets. It is recommended to use 3-5 mg/kg/day to prevent recurrences in stroke.[30]

Treatment of Hypertension

High blood pressure may increase the risk of damage because it increases the risk of cerebral edema and hemorrhage after

ischemic stroke. Hypertension detected after stroke may be due to pain or stress response, efforts to maintain perfusion of the infarct area, compensation for increased ICP, or pre-existing hypertension. Knowing the cause is important for determining the direction of treatment. In children with cerebral vascular pathology, perfusion pressure is dependent on cerebral blood flow, and rapid correction of hypertension may cause harmful effects. There is a very delicate balance between regulating blood pressure and maintaining cerebral perfusion pressure. There is no clear consensus guideline on how to manage blood pressure in children after a stroke. Existing guidelines recommend controlling systemic hypertension in children who have had ischemic or hemorrhagic strokes. The drug selected for the emergency treatment of hypertension should be intravenously (IV) administered, act rapidly, be titratable, have a short half-life, and have few side effects. The most commonly used drugs for this purpose are labetalol and nicardipine.[31] Labetalol can be administered IV at a dose of 2 mg/kg within 2-3 minutes. Nicardipine can be administered via IV infusion at a dose of 1 mcg/kg/min.[32] Due to the unavailability of these drugs in our country, esmolol and nitroglycerin are frequently used in the treatment of hypertension. Esmolol is administered IV at a dose of 125-500 mcg/kg over a period longer than 1 minute, followed by an infusion at a rate of 25-150 mcg/kg/min.[33] Depending on the clinical situation, dose titrations of 25-50 mcg/kg/min are recommended every 5-10 minutes as needed. In children, nitroglycerin is recommended to be started at an initial dose of 0.25-0.5 mcg/kg/min, titrated to 1-5 mcg/kg/min IV infusion, and administered at a maximum of 20 mcg/kg/min.[34]

Tissue Plasminogen Activator (tPA)

The most comprehensive study conducted to date on stroke and tPA use in pediatrics is the thrombolysis in pediatric stroke (TIPS) study, published in 2010. The TIPS study was an international, multicenter, dose-escalation, phase 1 trial. In this study, IV tPA therapy was administered over a one-hour period at three different doses (0.75, 0.9, and 1.0 mg/kg) to children aged 2 to 17 years who presented within the first 4.5 hours after the onset of acute ischemic stroke symptoms.[35] The aim of the study was to define safety criteria to guide tPA use in pediatric patients; however, it was terminated due to insufficient enrollment.

In a retrospective, multicenter study conducted in France between 2012 and 2015, 11 pediatric patients (mean age 11.8 years) with arterial ischemic stroke received IV recombinant-tPA treatment. The most common clinical findings in the patients were acute hemiplegia, hemiparesis, and dysphagia. The average time from symptom onset to MRI was 165 minutes, and the average time to treatment was 240 minutes. In most patients, the affected region was the middle cerebral artery territory. No post-treatment intracranial or peripheral bleeding was reported.[36]

These two studies demonstrate the challenges in treating pediatric stroke. Although the process of initiating treatment may vary among centers due to uncertainty and concerns regarding the initiation of tPA, the general consensus is that the diagnosis and treatment of stroke should be performed according to a specific standard. Although the TIPS study could not be continued, it plays an important role in optimizing the diagnosis and treatment of acute pediatric stroke.

There is no consensus on the determination of the patient group in which IV thrombolytic therapy should be administered in pediatric patients. The optimal time for thrombolytic therapy is generally accepted to be between 3 and 4.5 hours from the onset of stroke symptoms. The 2019 American Heart Association/American Stroke Association guidelines recommend a 4.5-hour window for thrombolytic therapy in children, with individual assessment based on clinical conditions.[21] Recommendations exist regarding the initiation time and dose based on coagulation factors and fibrinogen levels.[37] Since there are no pediatric randomized controlled trials on this topic, recommendations are generally based on adult guidelines and expert opinions; and a dose range of 0.3 mg/kg to 1.0 mg/kg is recommended.[35]

Mechanical Thrombectomy

Like the use of tPA in pediatric stroke, mechanical thrombectomy is not yet a fully established practice. There are a few retrospective studies conducted on small groups of pediatric patients that examine long-term neurological outcomes in this regard.

Satti et al.[38] reviewed 29 pediatric patients treated for ischemic stroke using modern devices (excluding older techniques such as wire manipulation and balloon angioplasty) between 2008 and 2015 in the literature, and found that the average time to treatment was 8.8 hours. Of the 29 patients included in the study, 23 reported positive clinical outcomes; compared to adults, the delay in initiating treatment was attributed to delays in diagnosis in children, as well as a lack of standardization in neurointerventional diagnosis and treatment.[38]

Bhatia et al.[39], along with Fragata and colleagues, investigated the efficacy of mechanical thrombectomy for pediatric ischemic stroke associated with large vessel occlusion using meta-analyses. They demonstrated that mechanical thrombectomy resulted in good long-term neurological outcomes in 87 of 96 cases, good short-term outcomes in 55 of 79 cases, and successful recanalization in 86 of 98 cases. The study reported two deaths and one case of symptomatic intracranial hemorrhage.[39]

Similar to adult applications, the use of modern devices for mechanical thrombectomy in pediatric populations appears to be associated with low complication rates and good clinical outcomes. While the current literature is still limited to small cohort studies, case series, and case reports in pediatrics, pediatric case applications and related publications have been increasing in recent years.

Supportive Treatment

After the patient with stroke has been stabilized, it is important to provide general care and supportive treatment. A multidisciplinary approach in accordance with the algorithm should be implemented by the stroke team. Appropriate supportive measures include maintaining metabolic balance, controlling seizures, correcting dehydration and anemia, early nutrition, and treating underlying infections.[40] Good care is important for minimizing potential complications and evaluating the patient for physical therapy.

Conclusion

Awareness of pediatric strokes is important, and more education is needed in this area. Due to the wide range of signs and symptoms in children and other diseases that can interfere with differential diagnosis, misdiagnosis or failure to diagnose is common. For this reason, it is often difficult to diagnose early. The diagnosis of stroke in children requires a combined assessment of neurological examination, clinical findings, and radiological imaging. Stroke is an emergency situation that requires rapid diagnosis and treatment. In centers with limited resources, it is important to refer the patient to the nearest center where treatment and follow-up can be provided. Serious neurological defects may result from poorly managed stroke, but early diagnosis and treatment minimize this and ensure long-term positive outcomes. In order to rule out conditions that may be confused with stroke in children and to make a quick diagnosis, MRI is recommended as the first imaging method, if possible. In cases where bleeding is suspected and MRI cannot be performed; CT may be performed. While tPA is a powerful thrombolytic agent commonly used in adults for early treatment, its use in infants and young children is limited to specific cases due to the lack of sufficient clinical studies. Given the challenges involved in the early diagnosis, decision-making, and management of stroke, the importance of having a multidisciplinary pediatric stroke algorithm to support clinicians is clear.

Footnotes

Authorship Contributions

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

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