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Clinical Study

Treatment Challenges in Pediatric Stroke Patients

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Aim. In this study we presented our experience of 18 years on the etiology, risk factors, prophylactic and acute treatment, the effect of treatment to recurrence rate of patients with stroke. *Methods*. The population included 108 patients who had been treated for stroke at Pediatric Neurology Department of Ankara University with the diagnosis of arterial ischemic stroke and sinovenous thrombosis between January 1992 and August 2010. Forty-one girls (38%) and 67 boys (62%) with mean symptom age 3.1 ± 4.04 years, (0–18 years old) were followed up with a mean period of 4.9 ± 3.78 years (0–17 years). *Results*. 30 patients had no risk factors, 34 patients had only one risk factor and 44 patients had multiple risk factors. Recurrence was seen in three patients. There was no any statistical correlation between the recurrence of stroke and the existence of risk factors ($P = .961$). Seventeen patients received prophylactic treatment; 2 of them without any risk factors, 3 had one risk factor, 12 patients, who constituted the majority of our patients, had multiple risk factors ($P = .024$). *Conclusion*. With this study we showed that the right prophylaxis for right patients reduces the rate of recurrence.

1. Introduction

In recent years, the incidence for paediatric stroke has reached up to 8 per 100,000 children per year and is attributed to the increase in the sensitivity and the specificity of noninvasive imaging methods (i.e., CT, MRI, MRA, and cranial ultrasound studies) and the increased survival rate due to more effective treatments for diseases like prematurity, congenital heart disease, and leukemia that predispose to stroke [1–4]. Stroke in children and adolescents has different presentation compared to that in adults. The 80–85% of adult stroke cases is reported to be ischemic while it is around 55% in children. The rest is hemorrhagic strokes for both age groups [5]. Ischemic strokes are thought to be underdiagnosed in infancy and childhood. It is very important to increase our knowledge about stroke in children, especially regarding etiology, outcome, and also possible treatments to reduce morbidity, mortality, and recurrence [6–13].

One fourth of "stroke in the young" is seen in children. The incidence of childhood AIS (acute ischemic stroke) is at least 2.6 per 100,000 children per year [14]. Neonates make up 25% of paediatric AIS patients and are therefore at considerably increased risk. In newborns with seizures, 12 to 14% are diagnosed with underlying cerebral infarction. There is a slight male predominance (60%) in childhood AIS [15, 16].

In paediatric cases, the diagnosis may be delayed or even missed. In neonates, AIS often presents only with lethargy or seizures. In children, the diagnosis of cerebral infarction is frequently delayed. Compared with adults, acute hemiparesis in children is more likely to be attributed to migraine headache, seizure, or focal encephalitis than stroke [17].

Subtle symptoms are less likely to be reported by the child or to be attributed to stroke. In the Canadian Registry, children with AIS presented most frequently with hemiparesis (51%), speech disorder (17%), and seizures (48%). However, the neurological presentations of AIS are age related. In infants with in utero AIS, the diagnosis usually becomes apparent only when pathological early hand dominance develops between 6 and 12 months of age and leads to a CT scan [13, 18]. Neonates with acute stroke present with seizures or lethargy in the first few days after birth, and hemiparesis is present in less than 25% at diagnosis, although it may develop later [7, 14, 19]. Older infants with AIS

typically present with an acute focal neurological deficit, usually hemiparesis. In school-age children, speech deficit or other subtle signs including sensory or visual deficits can be recognized. More than 50% of children experience diffuse symptoms accompanying AIS, including headache, lethargy, or confusion. These symptoms are more common in younger children [14, 20]. It is important to differentiate a postictal hemiparesis from the typically brief Todd's paresis, as seizures can be due to AIS [20].

The duration of a neurological deficit in children with AIS is frequently brief. The classical criteria for stroke in adults include focal neurological deficit persisting for at least 24 hours. Using these criteria, many AIS events in children would be missed. In infants focal signs are rare and in children a very rapid return of neurological function (less than 1 hour) can be associated with an infarct on the CT or MRI scan. In the absence of finding arterial stenosis on vascular imaging, the differentiation of transient ischemic attack (TIA) from migraine or seizure can be difficult. Recognition of TIAs in children is important, however, because appropriate antithrombotic therapy can prevent subsequent AIS [21].

Approximately one half of acute ischemic stroke cases occur in children with no known risk factors [22]. The most frequent causes for AIS in childhood are arteriopathies (fibromuscular dysplasia, moya-moya syndrome), vasospastic disorders (migraine), hemoglobinopathies, leukemia, acquired prothrombotic states, congenital heart disease, and acquired heart diseases [21]. Although risk factors in children with AIS are strikingly different from those in adults, in whom atherosclerosis is the overwhelming etiology, many of the risk factors being discovered in children with stroke also play an important contributory role in adults with stroke [15, 23].

The childhood stroke is underdiagnosed due to its challenging nature. It is in most cases not included in the differential diagnosis of acutely ill children. Acute hemiparesis in children is more likely to be attributed to other causes. It is of critical value to have accurate diagnosis and to identify patient-specific risk factors. As a result, an appropriate treatment can be initiated fast, systemic complications may be minimized and a secondary stroke may be prevented [23].

Although the role of laboratory screening in childhood stroke is not clear, complete blood cell count, iron studies, PT, PTT sedimentation rate, and antinuclear antibody are often sent. Hb electrophoresis and urine drug screens, particularly for sympathomimetics, may be indicated [24]. A full evaluation for thrombophilia is reasonable in all children and should include protein C and protein S, antithrombin III, heparin cofactor II, plasminogen, von Willebrand antigen, factor VIII, factor XII, factor V Leiden, activated protein C resistance, prothrombin 20210 gene, serum homocysteine, methylene-tetra-hydro-folatereductase, lipoprotein (a), and antiphospholipid antibodies. Apart from the gene studies, the blood samples should be taken at least 4–6 months after the insult [25–27].

The optimal method for diagnosis of stroke is MRI with diffusion- and perfusion-weighted imaging. Being a noninvasive procedure MR angiography (MRA) detects large vascular abnormalities. It is proven to be as effective as cerebral angiography in detecting large lesions. MR spectroscopy and diffusion-weighted imaging with MRA increase the sensitivity of MRI detecting ischemia and infarction [24–26, 28–30].

As there is no randomized controlled treatment trials in children with AIS, many of the treatment approaches increasingly used in children have been adapted from studies in adults. However, there are age-related differences in the hemostatic, vascular, and neurological systems compared with adults. This must be taken into account while applying antithrombotic and neuroprotective therapies to children with AIS. Children with stroke are primarily treated for the underlying risk factors and prevention of recurrent cerebral ischemic events [21].

Due to having a negligible risk of recurrence, neonates with AIS do not require routine antithrombotic treatment. However, recurrent TIAs and strokes occur in 7 to 20% in older infants and children with AIS. For these patients, long-term therapy with ASA is needed to prevent the risk. In children with cardiogenic AIS, dissection, high-grade stenosis of a cerebral artery, severe prothrombotic conditions, or failure of ASA therapy in preventing recurrence, LMWH or coumadin is frequently continued for several months. The risk of recurrent cerebral thrombotic events must be balanced against the risks of treatment, particularly bleeding risk [21, 31].

Thrombolytic agents should only be used in the setting of a clinical trial until safety and feasibility data are available as they carry an unknown but potentially very significant risk of hemorrhage in children with AIS [32, 33].

Clinical presentation, underlying cause, size of infarct, and stroke subtype appear to be influential factors on the outcome. Infarct volume greater than 10% of intracranial volume is associated with worse outcome. Although mortality among children is lower than in adults, stroke in children is associated with long-term sequelae. According to the studies, 55% of children develop sensory or motor problems, seizure, developmental delay, or cognitive disorders; 15% die and 35% are neurologically normal [4, 5, 34].

The general rate of stroke recurrence is between 26% and 30%, particularly during the first 6 months poststroke [28]. It is higher among children with identified risk factors. Because of unidentified risk factors for recurrence or lack of adequate treatment, idiopathic stroke may have a higher recurrence than previously believed [1, 35].

There is limited evidence regarding the efficacy of secondary prevention strategies in childhood stroke; however, ASA (acetyl salicylic ascit) is widely used. ASA is indicated for secondary prevention of AIS in children except in patients with SCD and those with high risk of recurrence and severe hypercoagulable state. Although the ideal prophylactic dose is undefined, doses between 1–5 mg/kg body weight per/day have been effective so far. Platelet antiaggregants are sometimes also used in patients with MMD (Moya Moya Disease). When the patient is a poor candidate for surgery or has a relatively mild disease clopidogrel may be an alternative treatment when long-term therapy with ASA is contraindicated or not tolerated. Clopidogrel should not

be used in combination with ASA in patients with multiple risk factors for intracranial hemorrhage and intracranial vasculopathies [36].

Long-term anticoagulation with heparin or warfarin may be indicated in patients with congenital or acquired heart disease, arterial dissection, selected hypercoagulable states, or recurrence of AIS despite ASA treatment. Some probable risk factors are modifiable [37]. Hyperhomocysteinemia may respond to supplements of folate, vitamin B6, and vitamin B12. Patients with lipid abnormalities can be managed with weight control, dietary modifications, and/or drug therapy. Patients with known inflammatory disorders or lupus should receive disease-specific treatment [28, 38].

In this study, we presented our experience in the etiology, risk factors, prophylactic and acute treatment, and the effect of treatment on recurrence rate in patients who had been treated for stroke at Pediatric Neurology Department of Ankara University for 18 years.

2. Methods

The study was designed on retrospective data. The population included 108 patients who had been treated for stroke at Pediatric Neurology Department of Ankara University with the diagnosis of arterial ischemic stroke between January 1992 and August 2010, and who were younger than 18 years at the time of the stroke. Forty-one girls (38%) and 67 boys (62 %) with mean symptom age of 3.1 ± 4.04 years (0–18 years old) were followed up in our institution for a mean period of 4.9 ± 3.78 years (0–17 years).

The definition of stroke included the presence of an acute thrombotic cerebrovascular event that manifested as hemiplegia, aphasia, visual or balance disturbance, or seizures. In all patients, the clinical diagnosis of ischemic stroke was confirmed with CT, MRI, and magnetic resonance angiography. Only pediatric stroke cases objectively confirmed by suitable imaging methods were included. Written informed consent was obtained from the parents of all patients.

Inclusion criteria were

(1) age 0 days through 18 years,

(2) sudden-onset focal neurological deficit, convulsion and loss of consciousness,

(3) neuroimaging (CT, MRI) demonstrating recent ischemia/infarct of arterial or venous distribution,

(4) cerebral/cervical arterial stenosis demonstrated on MR angiography using a 1.5- or 3-T magnet, CT angiography, or conventional angiography.

All patients underwent echocardiography and hematologic investigation (PT, PTT, fibrinogen, protein C, protein S, antithrombin III, lipoprotein(a), factor VIIIC, factor IX, homocysteine, and prothrombotic gene mutations (FV G1691A, PT G20210A, MTHFR C677T)).

The study was approved by the Ankara University Local Ethics Committee, and informed consent for all blood samples was obtained from parents of patients before the procedures. Blood samples were taken by peripheral venipuncture into plastic tubes without any additives and into plastic tubes containing 1/10 by volume of 3.8% trisodium citrate. After centrifugation, it is stored at −70°C. For genetic analysis, venous blood was obtained in EDTA-treated sample tubes. The FV G1691A, PT G20210A, and MTHFR C677T genotypes were determined by polymerase chain reaction and analysis of restriction fragments as previously reported [39].

F VIII and F IX were studied with one-stage clotting assay, and vWf was studied with immunoturbidimetric assay. Factor VIII and factor IX levels were accepted as high if the value was higher than the cutoff value of 150 IU/dl. Protein C and S were measured with commercially available enzyme-linked immunosorbent assay kits.

Lipoprotein A was studied by "particle enhanced" immunonephelometric assay; the reference range was 0–30 ng/mL. For homocysteine, after 12 hours fasting, blood specimens with EDTA were drawn and measured using AxSYM homocystein assay(Abbot, Wiesbaden, Germany).

Table 1: Initial symptoms.

Initial Symptom	*n*/total	Percent (%)
hemiparesis or hemiplegoia	70/108	64.8
seizures	37/108	34.2
cranial nerve involvement	2/108	1.8
Postoperative period	1/108	0.9
Headache	5/108	4.6
Fever	3/108	2.7
Intracranial hypertension	3/108	2.7
Dystonia	2/108	1.8
Altered state of consciousness	2/108	1.8

3. Statistical Analysis

Statistical analysis of the study was performed using Statistical Package for Social Sciences (SPSS/PC 13.00). The data are presented as the mean ± standard deviation (SD). All categorical data were analyzed with a Chisquare test or Fisher's exact test. A P value of equal to, or less than.05, was considered to indicate statistical significance.

4. Results

Hemiparesis or hemiplegia occurred in 54 (50%), hemiparesis and seizure in 12 (13%), hemiparesis and cranial nerve involvement in 2 (1.9%), and seizures in 23 (21.3%) patients. Five patients presented with headache. Initial symptoms are shown in Table 1.

The overall distribution of prothrombotic risk factors and underlying clinical diagnosis are shown in Table 2.

Eleven patients received acute treatment: 7/93 acute arterial ischemic stroke, 2/8 sinovenous thrombosis, and 2/7 hemorrhagic stroke received acute treatment. Table 3 shows the drugs that were used in acute treatment.

Table 2: Prothrombotic risk factors and underlying clinical diagnosis.

	Cholesterol°	Triglyceride°	High-CRP	Fibrinogen°	Homocysteine°	Lipoprotein A°	Factor VIIIμ	Factor IXμ	Protein Sα	Protein Cα	Antithrombin IIIα	APCR	Factor V Leidenβ	MTHFRβ	Prothrombinβ	Total
Idiopathic	2	3	1	—	4	5	11	5	7	5	1	7	6	9	2	59
Encephalitis	—	—	—	1	1	1	5	—	—	1	—	—	1	—	1	9
Malignancy	—	—	—	—	2	1	3	—	1	—	—	—	1	1	—	4
Trauma	—	—	—	—	—	—	—	—	—	1	—	1	1	—	—	2
Congenital heart disease	—	—	—	—	3	1	4	3	1	5	1	1	—	2	—	9
Hypernatremic dehydration	—	—	—	—	—	—	—	—	—	—	—	—	—	1	1	3
Moya Moya disease	—	—	—	—	1	—	—	—	—	—	—	—	—	1	—	3
Perinatal hypoxia	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	1
Antiphospholipid antibody	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	1
Undergone varicella	1	1	—	—	—	—	—	—	—	—	—	—	—	—	—	2
Isolated glucocorticoid	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	1
Congenital adrenal hyperplasia	—	—	—	—	1	1	1	1	1	1	—	—	1	1	—	3
Arterio-venous malformation	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	1
Cyclosporin toxicity	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	1
Purulent meningitis	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	2
Phenylketonuria	—	—	—	—	—	1	1	—	—	1	—	—	—	—	—	1
Rheumatic heart disease	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	1
Thalassemia major and BMT*	—	—	—	—	1	—	—	—	—	—	—	—	—	1	—	1
Behçet's disease	—	—	—	2	1	1	1	—	—	—	—	1	—	—	—	2
Late-onset hemorrhagic disease of newborn	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	1
Megaloblastic anemia	—	—	—	1	1	—	1	—	—	—	—	—	1	1	—	1
Total								—								108

*= bone marrow transplantation, °=hyper, μ=increased, α=deficiency, β=mutation.

Table 3: The medication in acute treatment.

Medication	Acute ischemic stroke *n*(%)	Sinovenous thrombosis *n* (%)	Hemorrhagic stroke *n* (%)
Unfractionated heparin	4 (%4.3)	2 (%25)	—
TPA* + Unfractionated Heparin	2 (%2.2)	—	—
Warfarin	1 (%1.1)	—	—
K-Vitamin	—	—	2 (%28.6)

* =Tissue plasminogen activator.

Table 4: Medication in prophylaxis.

Medication	Acute ischemic stroke *n*(%)	Sinovenous-thrombosis *n*(%)	Hemorrhagic stroke *n*(%)
Aspirin	7 (%7.5)	2 (%25)	—
LMWH*	6 (%6.5)	1 (12.5)	—
Warfarin	1 (%1.1)	—	—

* = low molecular weight heparin.

A total of 7 patients died during the followup: 2 patients died from congenital heart disease (one was receiving aspirin and the other one was receiving LMWH as prophylactic treatment); one patient with antiphospholipid antibody syndrome died at the fourth ischemic stroke attack despite of anticoagulant therapy; the other 4 patients, who were not receiving prophylactic treatment, died from lymphoma, leukemia, encephalitis, and congenital heart disease.

17 patients received prophylaxis: 9 patients aspirin, 7 patients LMWH, and 1 patient coumadin. Table 4 shows the patients on prophylaxis treatment and outcome. Prophylaxis is given to patients especially with congenital heart disease and to children who is carrying prothrombotic risk factors. Table 5 gives the summary of risk factors. Ninetytwo (85%) patients did not received prophylactic treatment. Except from the antiplatelet therapy, 4 patients had folate supplementation for hyperhomocysteinemia.

During the follow-up period (mean, 4.9 ± 3.78 years; range, 0–17 years), recurrence was seen in 4 patients (4.3%). Apart from one patient who died at the fourth ischemic stroke attack (under anticoagulant therapy), one patient with moya moya disease, who had been recruited at the time of the second recurrence, received no prophylactic treatment during the followup and had no other recurrence. Recurrence was observed in another patient with elevated lipoprotein A. However, the patient did not attend the followup. The fourth patient who had recurrence had Thalassemia major and had bone marrow transplantation from his father and his MTHFR mutation was heterozygote. He had no recurrence after prophylaxis.

Table 5 shows prothrombotic risk factors of patients who received prophylaxis; 7 patients had elevated homocysteine, 5 had factor VIII elevation, 4 had MTHFR homozygote mutation, 2 had factor V leiden mutation, 3 had protein C deficiency, and 2 had protein S deficiency.

Table 6 shows the patients on prophylaxis and the outcome of these patients. Prophylaxis is given to patients especially with congenital heart disease and to children who had ongoing underlying prothrombotic tendency like antiphospholipid antibody syndrome and renal transplantation and to the patient who is carrying 6 prothrombotic risk factors. Ninetyone out of 108 (84.3 %) patient did not received prophylactic treatment. Except from the antiplatelet therapy, 4 patients had folate supplementation for hyperhomocysteinemia.

As a result, recurrence was seen in one patient in the group of 17 patients with prophylaxis and no patient had recurrence in the group of 91 patients without prophylaxis. Intracranial bleeding occured in one patient in the prophylaxis group due to aspirin (2 mg/kg/day).

As we can see in Table 7, 30 patients had no risk factors, 34 patients had only one risk factor, and 44 patients had multiple risk factors. Recurrence was seen in three patients; one without any risk factor, one with only one risk factor, and the other patient with multiple risk factors. There was not any statistical correlation between the recurrence of stroke and the existence risk factors ($P = .961$). Seventeen patients received prophylactic treatment: 2 without any risk factors (patients with rheumatic heart disease and antiphospholipid antibody syndrome), 3 had one risk factor, 12 patients had multiple risk factors. The majority of patients who received prophylactic treatment had multiple risk factors (There is statistical correlation. $P = .024$).

5. Discussion

Given the absence of data from randomized controlled trials, it is important to acknowledge the rather flimsy evidence, which is mainly dependent on consensus. This evidence base can be improved by prospective randomized controlled trials in paediatric stroke. There are various obstacles to this lofty aim, one being the low occurrence of childhood stroke and the need for a large population base in order to provide a sufficient sample size for case-control studies or for trials of interventions predicted to have a small benefit. Another challenge is the wide heterogeneity of childhood stroke aetiologies compared with most adult strokes, in which one overriding mechanism, atherosclerosis, predominates. The patients aetiologies, followed in our clinic, were similar to the literature except sickle cell disease [40, 41].

Table 5: The risk factors and prothrombotic risk factors of patients who received prophylaxis.

Risk Factors	Cholesterol	Triglyceride	High-CRP	Fibrinogen	Homocysteine	Lipoprotein A	Factor VIII	Factor IX	Protein S	Protein C	Antithrombin III	APCR	Factor V Leiden	MTHFR	Prothrombin 20210	Total
Protein S deficiency	—	1	—	—	—	—	1	—	3	—	—	—	1	—	—	3
Congenital heart disease	—	—	—	—	3	1	3	2	—	3	1	—	—	1	—	5
Moyamoya disease	—	—	—	—	1	—	—	—	—	—	—	—	—	1	—	1
Undergone varicella	1	1	—	—	—	—	—	—	—	—	—	—	—	—	—	1
Cyclosporin toxicity	—	—	—	1	—	—	—	—	—	—	—	—	—	—	—	1
Rheumatic heart disease	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	1
Thalassemia major-BMT°	—	—	—	—	1	—	—	—	—	—	—	—	—	1	—	1
other*	—	—	—	1	2	1	2	1	—	—	—	1	2	3	—	4
Total								—								17

*One of the patients had heterozygous factor V Leiden mutation, one had MTHFR homozygote mutation, one had antiphospholipid antibody syndrome, and the other patient had megaloblastic anemia with MTHFR heterozygote mutation. °bone marrow transplantation.

Table 6: Patients who received prophylaxis and outcome.

Basic disease	Anticoagulant therapy	Prothrombotic risk factors	Outcome
Congenital adrenal hyperplasia	Aspirin	FV Leiden gene mutation in heterozygous form, MTHFR gene 677 TT homozygous mutation, elevated FVIII, FIX homocystein, and lipoprotein(a)	Intracranial bleeding was diagnosed and the aspirin prophylaxis was ceased and no recurrence was observed during the follow-up period
Antiphospholipid antibody syndrome	Coumadin, LMWH	FV Leiden gene mutation, elevated FIX	Died at the fourth ischemic stroke attack
Congenital heart disease	Aspirin	Elevated FVIII, FIX homocystein, and lipoprotein(a)	No recurrence
B12 deficiency-related megaloblastic anemia	Aspirin	FV Leiden gene mutation MTHFR gene 677 TT mutation, elevated F VIII, and homocystein	No recurrence
Congenital heart disease	Aspirin	MTHFR gene 677 TT mutation, elevated F VIII, and homocystein	No recurrence
Protein S deficiency-related sinus venous thrombosis	LWMH	Protein S deficiency, elevated triglyceride	No recurrence
Congenital heart disease	Aspirin		No recurrence
Moyamoya	Aspirin	MTHFR gene 677 TT homozygous mutation, elevated homocystein	No recurrence
Protein S deficiency related sinus venous thrombosis	LMWH	Protein S deficiency, elevated F VIII	No recurrence
İdiopathic	LMWH	MTHFR gene 677 TT homozygous mutation, activated protein C resistance	No recurrence
Receiving cyclosporine for renal transplantation	LMWH		No recurrence
Bone marrow transplantation for beta thalassemia major	LMWH	MTHFR gene 677 TT homozygous mutation, elevated homocystein	Recurrence*
İdiopathic	Aspirin	MTHFR gene 677 TT mutation	No recurrence
Congenital heart disease	Aspirin	Protein C deficiency	Died from congenital heart disease
Congenital heart disease	LMWH	Elevated homocystein, protein C, and AT III deficiency	Died from congenital heart disease
Rheumatismal heart disease related prosthetic valve	Coumadin		No recurrence
Down syndrome and congenital heart disease	Coumadin	Elevated homocystein, FVIII, FIX	No recurrence

*prophylaxis was given after recurrence.

Table 7: Recurrence and risk factor relation.

Risk factor	No. of recurrences	recurrence	Total
None	29	1	30
One risk factor	33	1	34
multiple risk factors	43	1	44
Total	105	3	108

Aetiologies can predict treatment effect to a large extent; hence, subgroups of more homogenous patients will need to be studied in some cases. An important issue is the difficulty in recognizing vascular pathologies in children with diverse presentations, such as coma, seizures, and hemiparesis. One of the most effective interventions to improve outcomes in adults who had stroke is the reorganization of services into specialist stroke units. However, the small number of patients with stroke in most paediatric centres creates a challenge for building up such specialized units [42].

As acute treatment recommendations in the guidelines are restricted, 11 patients received acute treatment: 7/93 acute ischemic infarct, 2/8 sinovenous thrombosis, and 2/7 hemorrhagic stroke received acute treatment. Only one patient with antiphospholipid antibody syndrome died at the fourth ischemic stroke attack despite of anticoagulant therapy.

The role of antiplatelet therapy is well established in adult arteriovascular disease. The prevalence of these diseases has prompted the search for "a Better aspirin", and new targets for antiplatelet therapy are being actively sought.

Currently, the use of antiplatelet therapy in paediatric disease is significantly limited.

Neonates with AIS do not require routine antithrombotic treatment because they have a negligible risk of recurrence. However, in older infants and children with AIS, long-term therapy with ASA is needed to prevent recurrent TIAs and strokes, which occur in 7 to 20% of patients. In children with cardiogenic AIS, dissection, high-grade stenosis of a cerebral artery, severe prothrombotic conditions, or failure of ASA therapy in preventing recurrence, LMWH, or coumadin is frequently continued for several months. The risk of recurrent cerebral thrombotic events must be balanced against the risks of treatment, particularly bleeding risk. Thrombolytic agents carry an unknown but potentially very significant risk of hemorrhage in children with AIS, and should only be used in the setting of a clinical trial until safety and feasibility data are available. And in our study Intracranial bleeding was occured in one patient in the prophylaxis group due to aspirin.

Related literature (Lynch, Fullerton, Lanthier, and others) points to a varying rate of stroke recurrence which is between 26% and 30%, particularly during the first 6 months after stroke and is higher among children with identified risk factors [21, 22, 43]. While following our patients, we utilize the guidelines and the majority of the patients who received prophylactic treatment had multiple risk factors [37]. We had seen 3 recurrences, one without any risk factor. There has not been any recurrence in the group of patients who received prophylactic medication since we always consider to provide prophylaxis for eligible patients. However, the physicians who are following stroke in pediatric age must pay attention to the stroke patients who had no risk factors for recurrence.

Long-term followup for children is better than for adults. Most of our patients achieved an age-appropriate independency. The use of antithrombotic therapy appears to be increasing in pediatric AIS, as almost all children were independent at followup.

6. Conclusion

Stroke among children is a rare disease. However, significant morbidity and mortality have been identified. Stroke should be included in the differential diagnosis of any child presenting new-onset focal deficits, altered speech, or disequilibrium and be thoroughly investigated. Advanced imaging techniques have improved the diagnosis and understanding of paediatric stroke. Studies to determine the optimal acute treatment of childhood stroke and secondary prevention and risk factor modification are of critical importance and urgently needed. Until prospective randomized data on chronic anticoagulation in pediatric patients are available, pediatric patients should be treated on an individual basis.

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