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REVIEW ARTICLE

Mechanical thrombectomy in children: A little known and scarcely utilized resource

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Abstract

Mechanical thrombectomy (MT) in children with acute ischemic stroke (AIS) and large vessel occlusion is a feasible treatment modality. However, the published experience is limited to case reports and small case series that yield a low grade of evidence. In this narrative review, we summarize the published literature regarding the topic of MT in pediatric patients with AIS. We conclude that MT is a powerful tool that all clinicians need to keep in mind when treating pediatric patients under suspicion of AIS. We hope that the present manuscript aids in increasing awareness about this critical topic.

Keywords: *Stroke. Mechanical thrombectomy. Pediatric. Review.*

Trombectomía mecánica en niños: un recurso poco conocido y raramente utilizado

Resumen

La trombectomía mecánica (TM) es una modalidad de tratamiento factible en niños con infarto cerebral agudo (ICA) y oclusión de gran vaso. Sin embargo, la experiencia publicada se limita a reportes de caso y pequeñas series de casos que proveen un bajo grado de evidencia. En esta revisión narrativa, resumimos la literatura publicada en el tema de la TM en pacientes pediátricos con ICA. Concluimos que la TM es una herramienta ponderosa que todos los clínicos necesitan tener en mente cuando tratan pacientes con sospecha de ICA. Deseamos que el presente manuscrito ayude a incrementar la conciencia acerca de este importante tema.

Palabras clave: *Enfermedad vascular cerebral. Trombectomía mecánica. Pediatría. Revisión.*

Introduction

Acute ischemic stroke (AIS) constitutes a rare entity in the pediatric population. Nevertheless, it carries a significant diagnostic delay due to a low index of clinical suspicion when it occurs. In adults, acute recanalization therapies, whether be with intravenous (IV)/intra-arterial (IA) thrombolysis with recombinant tissue plasminogen activator (rTPA) or with mechanical thrombectomy (MT), are the current standards of treatment. In those presenting within the 4.5 h, time windows IV rTPA is still the angular stone for treatment. Nevertheless, patients with occlusions affecting the internal carotid artery or the proximal segments of the major cerebral arteries within 6 h from onset of symptoms are candidates to MT[1]. Since 2018 and mainly due to the results of the DAWN

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and DEFUSE 3 trials, patients with up to 24 h from symptom onset are also candidates to MT in what is currently known as extended time window MT[2].

However, trials that provide evidence for the current treatment guidelines selectively excluded patients younger than 18 years. However, MT in children with AIS and large vessel occlusion (LVO) is a feasible treatment modality[3]. Still, the published experience of MT in pediatric AIS is limited to case reports and small case series that yield a Grade IV level of evidence[4].

In this narrative review, we summarize the published literature regarding the topic of MT in pediatric patients with AIS, a matter of great interest for all pediatric and adult neurologists.

Epidemiology

AIS during the pediatric ages (0-16 years) has an incidence of 2-8 per 100,000 children. It is a rare event that carries a devastating prognosis due to its long-term economic and social impacts. Reported mortality was 5% in the Canadian Pediatric Ischemic Stroke Registry. Among survivors, 67% exhibit some degree of neurological disability (52% moderate to severe)[5].

Clinical presentation

The clinical presentation differs from that in adults, and it varies depending on the patient's age, clinical context, and etiology of the infarct. One of its main manifestations is irritability, but seizures, conscience impairment, and hemiplegia can all be present. The symptoms above can thus be erroneously attributed to migraine, focal seizures, post-ictal hemiparesis (Todd's paralysis), central nervous system demyelination, or brain tumors. AIS is initially suspected only in about 38% of all cases, leading to a substantial delay in the diagnosis[6].

Etiology

Data from multicentric hospital registries have confirmed that the disorders leading to AIS are different in children than in adults. The most common cause is non-atherosclerotic vasculopathy in up to 49% of the cases, congenital cardiac disease (30%), and thrombophilias (30%)[5].

Focal cerebral arteriopathy characterizes by an irregularity in the arterial inner wall in the absence of acute inflammation of autoimmune or infectious origin[7]. The arterial occlusion without visible abnormalities of the arterial wall is associated with embolic sources, mainly cardiac[8]. Focal cerebral arteriopathy has a reversible course in 68% of the patients and is progressive in 20%. The self-limited inflammatory process present in focal cerebral arteriopathy has a reversible course in 68% of the patients lasting 1-3 months, but can have a progressive course in 20% of the patients[9].

Diagnosis

Due to its low sensitivity in children, the utilization of computed tomography (CT) scans as the initial diagnostic approach for pediatric AIS constitutes one of the causes for diagnostic delay[6]. Only 10% of the patients receive a confirmatory diagnosis of AIS during their first 3 h hospitalized; this figure reaches 20% at 6 h from symptoms onset. When the initial neuroimaging modality does not identify the diagnosis of AIS, the mean time to diagnosis is 44 h. Magnetic resonance imaging (MRI) is conclusive in 100% of the cases and must be the first choice in the pediatric population[10].

Treatment

Up to this date, there are no randomized controlled trials to sustain the recommendations for the treatment of AIS in pediatric patients. The current guidelines are loosely derived from the evidence obtained from adults and based mainly on expert consensus[11]. Acute reperfusion interventions such as IV rTPA and MT are recommended only as a rescue maneuver in selected patients[2]. Recanalization of LVO is pursued to improve neurological outcomes. Despite the lack of data regarding safety and efficacy in children, rTPA employment in the USA is ≤ 2%[12]. The consensus group for the Thrombolysis in Pediatric Stroke (TIPS) suggests applying the standard dose (0.9 mg/kg) when rTPA is considered for the treatment of pediatric stroke.

Regarding MT, the Guidelines from the American Heart Association published in 2015 state that benefits from this procedure have not been established for patients younger than 18 years; therefore, MT with stent retriever might be reasonable in selected patients under 18 years with AIS due to LVO in whom treatment can be initiated within 6 h from symptom onset[1]. In 2018, after the publication of the DAWN and DEFUSE 3 trials, a revision of the same guideline extended the therapeutic window for MT up to 16-24 h from symptom onset. Nevertheless, the modification did not address the possibility of extrapolating the extension in the therapeutic window to pediatric patients[2].

Notwithstanding the facts mentioned earlier, MT appears as a feasible and attractive option for the treatment of pediatric AIS[3]. This is because the low rate of early diagnosis excludes most patients from receiving other acute reperfusion interventions such as IV rTPA. According to current diagnostic delays, even a 6 h time window MT is challenging to perform, leaving the only treatment option the extended window time MT. Still, it is worth noting that this therapeutic conduct is supported by Class IV evidence[4].

The published evidence suggests that the safety profile of MT in children does not differ from that in adults. Most of the children that receive MT achieve favorable neurological outcomes. Special cautions are warranted in those younger than 5 years and those weighing <15 kg because the narrower arteries predispose them to complications from the use of endovascular devices[13]. Another concern is the execution of MT in patients with focal cerebral arteriopathy, Moya-Moya disease, and arterial dissections in whom the contact of foreign materials with the damaged arterial wall has the potential to aggravate the primary injury. In this regard, data from the Save ChildS Study did not show a higher complication rate in the 14 patients treated with MT[3].

Standard window time MT

The Save Childs Study is a cohort that registered data from 27 European and American centers; it recruited 73 pediatric patients that underwent MT within the 6 h time window. The results showed 87% of successful recanalization and neurologic outcome improvement, a median PedNIHSS score of 10 points. The complication rate was 1.37, with only one event of post-interventional bleeding[3]. There are other published case series that describe 100% rates of at least partial endovascular recanalization and a favorable clinical outcome in 91%[14]. In an analysis of 12 patients that underwent MT with stent retrievers, 50% were treated within 6 h from symptom onset; there were no procedure-related complications, and the clinical outcome at 3 months was 1 point in the modified Rankin scale[15].

A sub-analysis of the Multicenter Randomized Clinical Trial of Endovascular Treatment for AIS in the Netherlands attempted to show efficacy and safety data by prospectively following nine children with AIS secondary to LVO treated with 6 h time window MT. Outcomes demonstrated functional independence at 6-month follow-up in all the patients without cardiac disease. In four patients with ventricular assist devices, the clinical outcome was not optimal due to the base cardiac pathology complications[16].

Extended window time MT

The extended window time MT in pediatric stroke does not count with evidence from prospective studies, and due to its rare nature and low incidence, the prospects of ever acquiring such data are limited[16]. After considering this fact, it is crucial to generate practical strategies that allow clinicians to adequately identify those children prone to benefit from MT after the standard window for treatment. Image-guided protocols that include some form of perfusion neuroimaging can determine the existence of penumbral tissue potentially salvageable regardless of the time from onset of symptoms. Such protocols have been tested with good results in adults and allow the treatment of patients well beyond the standard window of treatment[17].

In a retrospective review of data from 68 patients younger than 18, the mean time to treatment was 13.7 h, with patients receiving MT up to 72 h after onset of symptoms. Nineteen out of the total received extended time window MT and 79.5% achieved an excellent clinical prognosis; this proportion increased to 87.5% when only considering the patient who underwent MT with FDA approved devices such as the Solitaire and Trevo stents and the Penumbra aspiration system[18].

In a retrospective cohort of 12 pediatric patients with < 18 years of age, eight received MT and five were treated with extended window time MT. Successful recanalization was accomplished in 87.5% and an excellent clinical outcome in 78%. Criteria for MT were image guided; other inclusion criteria included NIHSS > 6 and evidence for LVO[19].

Although MRI is the preferred neuroimaging modality for AIS in children, there might be some situations where it can be contraindicated or unavailable. In these cases, perfusion CT with a Tmax >6 s can be used to determine core/penumbra mismatch[20]. It is important to stress that without some form of perfusion imaging, the estimation of the ischemic core is not possible, and the lack of this data precludes MT. Thus, some children will be excluded from receiving a potentially beneficial procedure.

Conclusions

AIS constitutes a major neurologic emergency. Due to its low incidence and unusual clinical presentation, AIS is a diagnostic entity scarcely recognized in the pediatric population. The 1st h after the onset of symptoms is fundamental for an early diagnosis and better

Table 1. Summary of the published mechanical thrombectomy case reports performed in the pediatric age group

Authors, year	Age	Sex	NIHSS	TTT	Treatment technique	TICI	Clinical outcome
Felker et al.[21], 2010	14	M	NR	9	Merci	0	NR
Taneja et al.[22], 2011	14	F	NR	24	SR	3	NR
Xavier et al.[23], 2012	16	M	11	>72	A + Stent	2A	mRs 1
Stidd et al.[24], 2014	2	M	NR	7	SR	2B	mRs 1
Garnés Sánchez et al.[25], 2016	9	M	35	36	SR	3	NIHSS 3 PSOM 0
Ladner et al.[26], 2014	5	M	22	9	SR	2b	PSOM 0
Rhee et al.[27], 2014	9 9	M M	6 10	7 7	SR SR	3 3	NIHSS 3 NIHSS 3
Sainz de la Maza et al.[28], 2014	12	F	18	8	SR	2B	NIHSS 1
Savastano et al.[29], 2015	22 months	F	NR	16	SR	3	NR
Huded et al.[30], 2015	6	M	15	26	SR	3	NIHSS 0
Weiner et al.[31], 2016	15	M	9	8	SR	2B	NIHSS 0
Lena et al.[32], 2017	NR	NR	NR	>17	A	2B	mRs 1
Nicosia et al.[33], 2017	23 months	NR	NR	18	SR	3	NR
Wilkinson et al.[34], 2017	17 months	F	NR	50	SR	2B	NR
Ghannam et al.[35], 2021	7	F	4	11	SR	2B	NIHSS 1

NIHSS: National Institutes of Health Stroke Scale; TTT: time to treatment; TICI: thrombolysis in cerebral infarction; EVT: endovascular thrombectomy; NR: not reported; SR: stent retriever (Solitaire: Solitaire FR revascularization device by Medtronic, Minneapolis, MN, USA, or Trevo: Trevo Provue Retriever by Stryker, Kalamazoo, MI, USA); A: aspiration (Penumbra reperfusion catheter system, Penumbra Inc., Alameda, CA, USA); RD: Revive: Revive SE clot retrieval device (Codman & Shurtleff Inc., Raynham, MA); mRs: modified Rankin scale; PSOM: pediatric stroke outcome measure; WS: wake-up stroke.

clinical outcome. Whenever there exists a suspicion of AIS, the clinician should promptly order an MRI. In the current absence of evidence-based guidelines for treatment, it is up to the experts in vascular neurology to guide on a case by case basis, table 1 depicts a summary of the published MT cases performed in the pediatric age group. Both the risks of acute recanalization techniques and the potential benefits are to be pondered. Still, MT is a powerful tool that all clinicians need to keep in mind when treating pediatric patients under suspicion of AIS. We hope that the present manuscript aids in increasing awareness about this critical topic.

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Conflicts of interest

The authors declare no conflicts of interest.

Ethical disclosures

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