Original Article

Early Intensive Inpatient Rehabilitation for Children Undergoing Hemispherotomy

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Abstract

Background: Hemispherotomy is the treatment of choice for children with refractory epilepsy. Although hemiplegia, sensory and motor impairments result from this surgical procedure, seizure control is effective as well as anticonvulsant dose reduction. Description of functional gains after rehabilitation of these children are still incomplete. **Aims:** To evaluate the effects of an early intensive rehabilitation program in the gross motor function of lower limbs after 30, 90, 180 and 360 days of surgery for the treatment of epilepsy (hemispherotomy), and compare to historic controls. **Materials and Methods:** prospective and longitudinal case series, with historic controls. Fourteen out of sixteen children who underwent hemispherotomy from January 2012 to February 2013 received an early rehabilitation protocol (ERP). Functional assessment included the Berg Balance Scale (BBS), Fugl-Meyer Scale (FMS) lower limb subscale, and Gross Motor Function System of Classification (GMFCS), as well as the need of wheelchairs and walking aids. A historical group of 13 children who received a conventional rehabilitation protocol (CRP) was used as control. **Results:** FMS and BBS improved in ERP subjects until 6 months after surgery and reached a plateau. One year after hemispherotomy, all children in the ERP group could walk independently and had mild limitations to mobility whereas, among those in the CRP subjects, there was a higher prevalence of musculoskeletal deformities and severe gait restrictions. **Conclusions:** ERP promotes rapid functional recovery during one-year follow-up and, as compared to the CRP group, the average functional capacity of the ERP group was considerably higher. These data support the beneficial effects of a specific, individualized and early rehabilitation approach for such patients.

Keywords: Epilepsy, gait, hemispherotomy, mobility, rehabilitation

Introduction

Approximately 20%–30% of patients with epilepsy do not respond to conventional treatments[1] (antiepileptic medications) and are considered refractory to pharmacological therapy; also, they usually show features of disease progression due to the diffuse location of the seizure onset zone or network.[1-4] In such cases, the most effective treatment option is surgery; for refractory hemispheric epilepsy, functional hemispherectomies, and hemispherotomies are most often the surgical strategy of choice, aiming for the total disconnection between the affected cerebral hemisphere and the unaffected side.[5,6] However, after this surgical procedure, children develop an impairment of motor control contralateral to the disconnected hemisphere, in both proximal and distal segments.[7]

Individuals who have undergone hemispherotomy are likely to improve brain reorganization if they receive specific rehabilitation.[8,9] Studies on cortical reorganization after functional hemispherotomy have shown that even years after surgical resection there is an optimal reorganization of the cortical networks to favor motor control.[7,10] Therefore, interventions for motor recovery based on cortical plasticity and neurodevelopmental standpoints could be able to promote optimal functional conditions.[7,10-12]

The medical literature has only a few studies about the implications of early intensive motor rehabilitation protocols in

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children and adolescents submitted to hemispheric disconnective surgery.[7,10] Most studies in this age group are related to traumatic brain and spine injury in the context of intensive care.[13-15] Furthermore, research studies that investigate the specific role of inpatient motor rehabilitation techniques are scarce.[16]

Considering this lack of knowledge in the field and the importance of rehabilitation in the postoperative period, we developed the present study about the results of our institutional protocol of early intensive postoperative inpatient rehabilitation after hemispherotomy for children with refractory epilepsy.

Subjects and Methods

Design

This study is a prospective, longitudinal case series with historical controls. Institutional Review Board authorization (Case No. 6382/2011) was obtained and both participants and their parents were requested to sign an informed consent form.

Sample

The recruitment group consisted of children under 18 years old with refractory hemispheric epilepsy that received surgical treatment (hemispherotomy) at our Pediatric Neurosurgery Unit from January 2012 to February 2013. All patients underwent a thorough pre-surgical workup to establish the surgical strategy, including video-electroencephalographic monitoring, 3-Tesla magnetic resonance imaging, single-photon emission computed tomography, neuropsychological and psychiatric assessments, and social evaluation. Children were not included if any other clinical or orthopedic condition would prevent them from receiving the rehabilitation care, or if signed consent could not be obtained. After enrollment, patients and primary caregivers were required to remain in hospital for 1 month after the surgical procedure.

Sixteen participants were initially selected, but two were further excluded, and the study group ultimately included 14 participants receiving early and intensive rehabilitation [Figure 1].

Early intensive inpatient rehabilitation program

The early rehabilitation protocol (ERP) was applied immediately after surgery as soon as the patient was clinically stable, and continued for 30 consecutive days in an inpatient regimen. It consisted of 2 h of physical therapy per day, performed by the same physical therapist [Table 1]. Cognitive impairments secondary to hemispherotomy are common, thus the amount physical stimulation was carefully controlled.

Due to the great variability of the motor and cognitive impairment, the rehabilitation program was developed in phases defined by acquisition of motor goals and not based on the number of sessions. Therapeutic strategies were individualized according to the condition of each child and focused on their unique functional requirements. Physical therapy interventions aimed to maintain range of motion, muscle flexibility, balance and gait training, in order to maximize functional capacity and prevent secondary complications. During this period, parents were systematically oriented about the phases and objectives of rehabilitation and informed about the need for continuation of the therapeutic interventions. There were special efforts to warrant the continuation of therapeutic approach after discharge, so rehabilitation services close to the children home were contacted to discuss the case and offer some advice on the therapeutic goals and use of orthosis or walking aids.

Historical control group

Ethical restrictions would impede a parallel control arm without rehabilitation interventions, so a historical group (conventional rehabilitation program [CRP]) was chosen as control. It included 13 children who underwent the same surgical procedure with the same medical team and similar clinical indications, but whose neuromotor rehabilitation took place in their hometown prior to 2012. The standard rehabilitation until that year consisted of postoperatory physical therapy once a day for 1–5 days until hospital discharge. After this, parents would receive a letter of referral to be given to the rehabilitations teams in their hometowns – mostly only the physical therapist. There were no efforts to maintain the contact with local rehabilitation services.

For this group, all clinical evaluations related to the study were performed 2–3 years after discharge from hospital. Figure 1 shows the flowchart used for the patient recruitment.

Assessment

Information regarding rehabilitation activities of patients in their hometown such as technical and therapeutic interventions, professionals involved, stimulation frequency and use of equipment and orthotics was retrieved by interviews with parents of both ERP and CRP groups. The same physiotherapist performed all the assessments. ERP children were evaluated prospectively in five different time points: Preoperative, 30 (PO30), 90 (PO90), 180 (PO180), and 360 days' (PO360) postoperatively. 6 years after their surgeries, these children were reassessed to collect data on control of seizures, walking ability, therapeutic sessions, and participation in education and leisure. Conversely, the CRP group was evaluated only once, all the evaluations related to the study, for this group was performed 2–3 years after surgery.

Motor function

Motor function was assessed using the Gross Motor Function Classification System,[17] which was designed originally to classify children with cerebral palsy into five levels, according to their performance in self-initiated abilities in sitting, walking, and wheeled mobility. Children classified in levels I e II were considered Mild; level III was Moderate and levels IV or V were considered Severe.[18]

Fugl-Meyer Assessment was used to evaluate motor function. The Fugl-Meyer Assessment was modified to include only the motor portion of the lower extremity (maximum 34 points).[19]

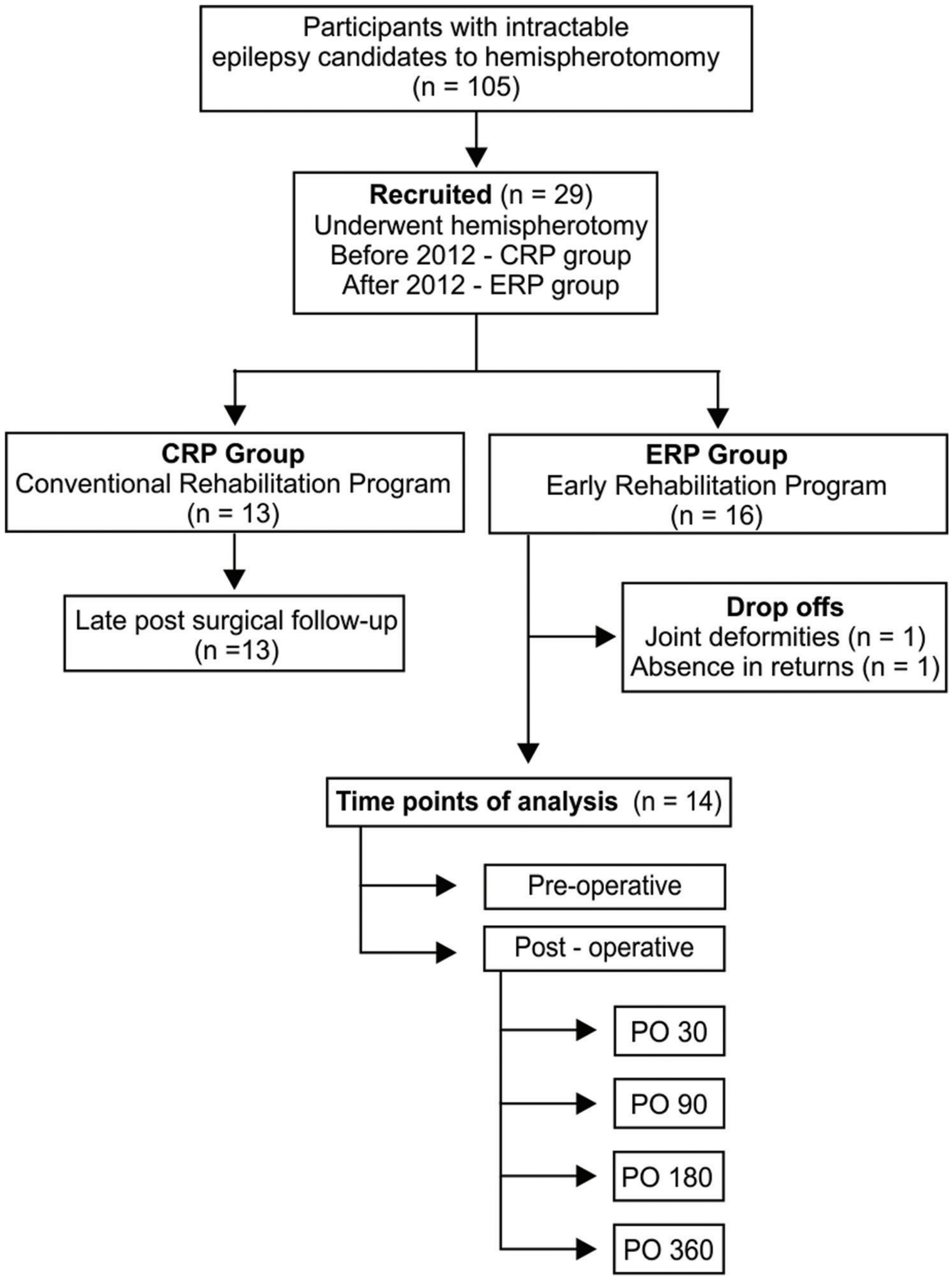

Figure 1: ERP: Early rehabilitation protocol, CRP: Conventional rehabilitation protocol, PO30: 30 days after surgery, PO90: 90 days after surgery, PO180: 180 days after surgery, PO360: 360 days after surgery

The Berg Balance Scale is an instrument for functional assessment of balance, consisting of 14 items, in which performance is scored on a 5-point scale with the maximum score of 56 points.[20]

Statistical analysis

For the statistical analyses, SPSS software (IBM, Armonk, New York, USA) version 22.0 and GraphPad Prism version 5 (GraphPad Software, San Diego California) were used. The Kolmogorov–Smirnov test was used to compare sample distributions. For the comparison of follow-up variables of ERP group, we used repeated measures of ANOVA with Bonferroni *post hoc* test. Comparison between CRP and ERP (PO360) was performed by unpaired *t*-test. Chi-square test was conducted for the Gross Motor Function Classification System analyses. Differences were deemed significant when $P < 0.05$.

Results

Table 2 shows demographic features of the study groups. No significant differences were found between groups in terms of age at surgery, age at seizure onset, etiology, and the side of the brain which was disconnected. However, ERP children were younger at assessment and had a shorter period of epilepsy. 1 month after surgery, 72% of children in the ERP group and 78% of the CRP group became completely seizure free, and

Table 1: Description of physical therapy interventions and phases in early rehabilitation protocol

Phase	Aim Type intervention	Exercises	Intensity (series - repetitions)	Motor development
I	Muscular recruitment Prevent of deformities Equilibrium reactions (trunk)	1. Exercise passive ROM. U and L limbs	3-8	1st step: Postural control to: get up and down
		2. Passive stretching	3×30 s	
		3. Massage	15 min	
		4. Active/active-assisted exercises. U and L limbs	3-8	
		5. Isometric exercises and active-resisted	3-8	
		6. Sensory Stimulation	2-8	
		7. Mobility	2-8	
		8. Positioning in bed	15 min	
		9. Orthosis (used in all stages)	Intervals of exercises daytime use	
II	Muscle strength Mobility Postural control	1. ROM exercises for U&L limbs	3-10	2st step: Postural adjustment Presence control of static equilibrium Activation of the hip/knee extensors
		2. Passive stretching	3-30s	
		3. Massage joint mobilization	15 min	
		4. Active/assisted exercises – U and L limbs	3-10	
		5. Isometric/resisted active exercises	3-10	
		6. Sensory stimulation	3-10	
		7. Balance (static)	3-10	
		8. Mobility	3-10	
III	Gait Training	1. Phase II	2 h	3 step: Postural adjustment Anticipatory and compensatory postural adjustments Improving muscle response (synergy)
		2. Motor learning (Frenkel's exercises)		
		3. Balance training (static and dinamic)		
		4. Gait (essential components)		
		5. Gait walking (with support)		
IV	Gait training Skill functional	1. Phase II/III (combination)	2 h	
		2. Task. oriented to gait training		
		a. Strategies for changing direction of locomotion		
		b. Strategies for going over obstacles		
		3. Gait training		

65% were classified as IA according to Engel's scale at 1–year follow-up in both groups.

The groups were comparable in terms of etiology. Rasmunssen's encephalitis responded for 50% of both groups, and hemimegalencephaly for the rest of the cases.

Age ranged from 9 to 11 years in both groups, and the left hemisphere was involved more frequently. In the ERP group, the male: female ratio was 1.5:1. All children in this study were attending classes either in regular schools (ERP: 60%, CRP: 30%) or special schools (ERP: 40%, CRP: 70%). Subjects were regularly seen in physical therapy services in their communities [Table 2].

After 6.0 ± 0.5 years from surgery and ERP, one child had died, and 12 (85.7%) were reassessed. Mean age was 10.5 ± 3.1 years, 75.0% were seizure free, 75.0 could walk independently, 83.3% and 58.3% were followed with physical or occupational therapist, respectively. One of them worked full time, 3 practiced sports and 8 were still in school (5 regular, 3 special).

In the CRP group, 31% ($n = 4$) of the participants had equinus deformities and used wheelchairs for locomotion, although their parents reported that none of them used a wheelchair or had musculoskeletal deformities prior to surgery. None of the ERP cases developed fixed deformities within 1 year or in the long-term follow-up. None needed wheelchairs 1 year after surgery, but in the extended follow-up, one was wheelchair bound and another used a walker.

Motor achievements

In the ERP group, 11 children experienced postoperative motor impairment in the contralateral side of the disconnected hemisphere, characterized by worsening of hemiparesis immediately after surgery. Three other children (two with Rasmussen encephalitis, one with hemimegaloencephaly) were heavily medicated for epilepsy before the surgical procedure and could not perform active and functional contractions in both upper limbs and lower limbs. Nevertheless, 3 or 4 days after surgery, despite the new impairment (hemiplegia) caused by hemispherotomy, they were able to perform some active contractions of the lower limbs.

Figure 2 shows the follow-up Gross Motor Function Classification System of the ERP group indicating their motor impairments. There was a progressive shift from the most

Table 2: Demographic and clinical description of subjects

	Early rehabilitation program (*n*=14)		CRP (*n*=13)	
	Mean±SD	Frequency (%)	Mean±SD	Frequency (%)
Sex				
Male		64		46
Age (months)				
At assessment	9.1±3.3	-	12.0±3.9	-
At surgery	9.1±3.3	-	7.0±4.1	-
Epilepsy onset	3.9±2.8	-	2.1±2.2	-
Epilepsy duration	2.7±1.3	-	4.9±3.3	-
Etiology				
Development	-	50	-	64
Progressive	-	50	-	46
Disconnected hemisphere	-		-	
Left	-	57	-	57
GMFCS	-		-	
Mild	-	85.7	-	15.4
Moderate	-	14.3	-	46.2
Severe	-	0.0	-	38.4
Engel (free seizures – IA)	-		-	
1 month	-	72	-	78
12 months	-	65	-	64
Deformities (%)	-		-	
12 months	-	0	-	31

CRP: Conventional rehabilitation program, SD: Standard deviation, GMFCS: Classification of mobily based on the gross motor function classification system

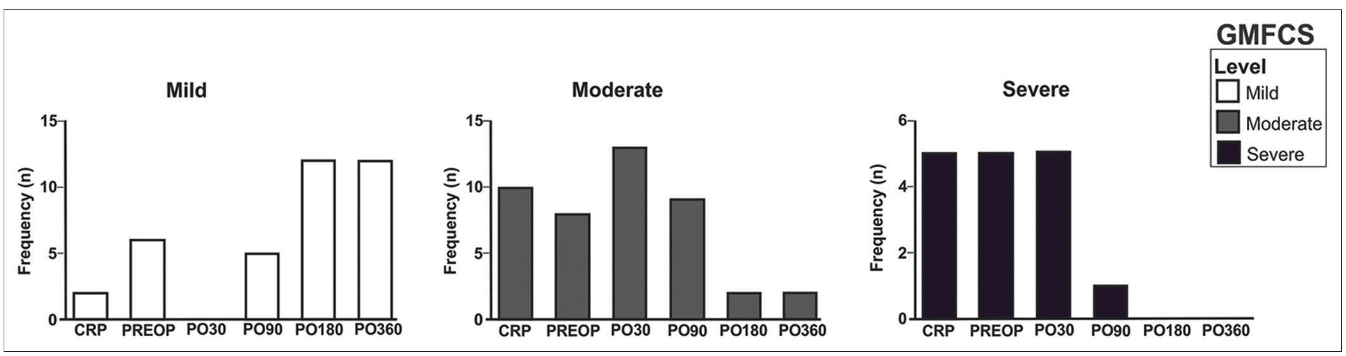

Figure 2: GMFCS: Classification of mobily based on the gross motor function classification system, PREOP: before surgery, PO30: 30 days after surgery, PO90: 90 days after surgery, PO180: 180 days after surgery, PO360: 360 days after surgery

disabled categories in PO30 and PO90 to a larger proportion of children with mild limitations in PO360. The proportion of those classified as mild in the ERP increased while moderate and severe cases reduced (Chi square = 44.23, df = 10, $P = 0.0001$). After the 180–day follow-up, there was no child classified as severe.

Motor function analysis

The Berg Balance Scale and Fugl-Meyer Assessment followed the same patterns across the follow-up: An initial motor deterioration followed by progressive improvement until PO180 and a plateau afterward (Berg Balance Scale: $F = 18.45$, $P < 0.0001$; Fugl-Meyer Assessment: $F = 12.97$, $P < 0.0001$). For Berg Balance Scale, mean CRP values were significantly lower than those on PO360 in the group under early intensive inpatient rehabilitation. For Fugl-Meyer Assessment, although mean CRP values were also lower than PO360, this was not statistically significant [Figure 3].

Discussion

This study successfully demonstrated that ERP improves motor function by the end of the 1st month postoperatively and warrants the understanding and adherence of primary caregivers to the rehabilitation interventions needed to maximize successful functional skills. The most striking results were the improvement of gross motor skills, classified as mild in 75% of children in ERP 1 year after surgery, as opposed to 85% moderate or severely impaired in CRP between 2 and 3 years after surgery. In addition, none of the children under early intensive rehabilitation

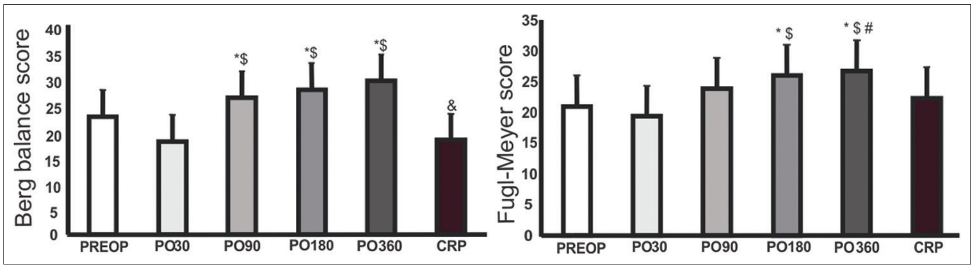

Figure 3: PREOP: before surgery, PO30: 30 days after surgery, PO90: 90 days after surgery, PO180: 180 days after surgery, PO360: 360 days after surgery. CRP: Conventional rehabilitation protocol

developed joint deformities in comparison with the conventional approach which resulted in 31% of equinus.

Regarding the operative aspect, the procedure was always performed by the same senior surgeon for both groups, making it unlikely that progressive learning curve differences may have interfered with outcomes.[21] Thus, despite the modest differences in age of first clinical assessment and surgery it is possible to assume that the only strict difference between the studied groups is the postoperative rehabilitation approach.

Refractory epilepsy in children represents a functional and/or structural brain impairments, which potentially leads to limitations in activities and restrictions in participation, mostly because of fear of new seizures, falls or sedative effect of antiepileptic drugs. After hemispherotomy, the disabling features secondary to epilepsy may be worsened by impairments brought through by the surgical disconnection of neural pathways, such as hemiplegia, visual and somatosensory deficits, cognitive and behavior modifications[21-25] surgical treatment, conversely, compensates for the lack of interaction with the environment seen in children with frequent tonic–clonic seizures or motor paroxysms. We have documented this reduced performance in motor skills at PO30 with all the assessment measures.

Progressive mobility gains from PO30 to PO180 were documented in ERP subjects. Lower limbs strengthening warranted appropriate muscle tone and improvement in coordination and executive motor functions, coupled with prevention of deformities. After hospital discharge at PO30, these motor skills were exercised by parents or physical therapists in primary care facilities in their cities according to detailed recommendations provided by our rehabilitation team. The improvement of balance and lower limb motor function was demonstrated for as much as 6 months, which allows individuals to isolate the control of different segments of the lower limb, develop anticipatory strategies of motor control and provide adequate conditions for activities such as gait, transfer, and stair climbing. The first 3 months after brain injury are known to carry the biggest potential for rehabilitation in stroke subjects.[26,27] Jørgensen and colleagues observed that global functional recovery occurs within 3–6 months after injury, and reestablishment of gait function usually occurs within 3 months after the onset of stroke.[28] Rehabilitation strategies, including repetition of motor tasks and strengthening exercises can induce new neurological pathways and functional reorganization of intact cortical and subcortical motor areas.[11,29,30]

Studies with hemispherectomy children demonstrated that mobility training with body weight–supported treadmill therapy improved walking and induced adaptations of cortical representational. Thus, children who undergo functional hemispherectomy and do not receive proper rehabilitation should receive task-specific training to enhance brain reorganization.[7,31,32]

Although is not possible to quantify the difference of rehabilitation interventions after all these children returned home, the impact of very acute therapy and orientation lasted at least 1 year and ensured the condition for further functional improvements. The lack of professional guidelines and parental orientations may have contributed the presence of deformities in the CRP group which was multifactorial and involved incorrect positioning while seating and lying down, or use of orthotic devices. In addition, the development of spasticity contributes to this problem and started after 2 weeks in the ERP group. It could be controlled with stretching and passive mobilization of joints and only one ERP child required botulinum toxin type A injections to manage spasticity.

Limitation of the methods

Although it may be stated that this classification was not developed or validated for children with refractory epilepsy, which is not a stable brain injury, this assessment tool has already been used for this group.[33,34] In this study, it became clear that ERP children evolved from highly dependent in mobility to very functional levels, in keeping with the current medical literature,[35] while CRP had more individuals in levels with reduced gross motor skills. Some similar criticism may refer to the use of FMA, which was also originally developed to assess post stroke neurologic impairments, but it has been widely used for a variety of other neurologic conditions.

One can also argue that because historic controls were older on first clinical assessment and had a longer epilepsy duration by the time they were operated, they would have longer lasting diseases and more musculoskeletal deformities. It happens, though, that children with intractable epilepsy do not show deformities or spasticity before surgery. The effect of medication is rather opposite, and they are usually hypotonic or sleepy. Another problem is that ERP children were followed for 1 year after surgery, but CRP children were evaluated after a mean period of 5 years after surgery. We have made contact with 85.7% of ERP children and the functional differences concerning walking abilities and social participation continued the same.

Limitations of this study also include sample size which was limited by the frequency of the disease and low rate of follow-up appointments of patients who live in distant parts of the country.

The use of historical controls is prone to patient selection bias, outcome evaluation bias and different treatments once the therapeutic team and knowledge may change. However, in our study, both the experimental and historical control groups had similar demographic and clinical profiles compared to those in the literature.[11,13,24] The surgical team, technique and perspective, indications for hemispherotomy were the same for both the groups.

Because we considered it unethical to randomize children not to receive the early rehabilitation, we used historical controls.

Implications for rehabilitation

Although the findings of this study support the well-known practice of early rehabilitation intervention that produces significant effects on clinical outcomes, favoring neural reorganization at critical moments of recovery, this is an innovative proposal in Brazil, where such this kind of treatment is not routine.

In addition, there are countries where managed care restricts the access of these children to early intensive rehabilitation, based on the absence of medical literature documenting the effect of this treatment.

We consider this protocol a safe, efficient, and beneficial intervention to the patient, favoring levels of functional independence.

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Nil.

Conflicts of interest

There are no conflicts of interest.

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