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Research Article

Outcome at Age Five Years or Older for Children with Perinatal Brain Injury Treated With Neurohabilitation or Neurodevelopmental Therapy

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Abstract

Background: To evaluate the outcome at age five years or older for children with perinatal brain injury who received Katona neurohabilitation therapy or neurodevelopmental therapy (Bobath therapy) at birth, a blinded evaluation of the infant groups was performed by an expert neuropediatrician.

Methods: Twenty-two infants with a gestational age (GA) ranging from 25 to 40 weeks were treated with neurohabilitation (n = 11) or with neurodevelopmental therapy (n = 11), with both procedures initiated before three months of corrected age. The groups were matched by sex and GA. Treatments were intensive, were sustained for at least 24 months, and required family participation. At birth, neuropediatric examinations and MRI were performed. Children were followed up, and at three-year-old Bayley-II scales were administered; the follow-up continued up to the present age.

Results: Abnormal MRI findings were observed in 21 (95%) infants. At three years old, among children treated with Katona's method, the Bayley-II score was slightly abnormal in one patient for both indices, another child had a lower performance on the mental index, and a third patient showed a very low psychomotor index; four patients treated with the Bobath procedure had very abnormal results on both indices. The outcome of a blind evaluation of the group showed that eight of 11 children treated with Katona had a normal evaluation, and only four of the children treated with the Bobath method were normal; the risk ratio (RR) was 37% (0.73 - 0.36 = 0.37).

Conclusion: The resulting outcomes after five years or more using Katona's neurohabilitation in newborns with perinatal brain damage were better than the outcomes for children treated with the Bobath procedure, even if the latter was initiated early and with great intensity.

Keywords: *Perinatal Brain Injury; Neurohabilitation; Neurodevelopmental Therapy; Katona; Bobath; MRI*

Introduction

The survival rate of premature newborns has increased due to better follow-up of high-risk pregnancies in maternal fetal medicine, advances in neonatal medicine, improved hospital equipment and pharmacological treatment for newborns, among others. Approximately 11% of infants are delivered prematurely [1,2]. In particular, infants at risk for perinatal brain injury (PBI) are those born before 36 weeks gestation [3]. Survivors born before 28 weeks gestation with a low birth weight (less than 1000 grams) have at least a 20 - 50% risk of morbidity [4]. The neurodevelopmental prognosis for premature infants is difficult to establish since it vastly varies between in-

dividuals and may produce different injury patterns that are tied to the initial time, duration, topography and severity of the lesion [5]. In relation to term infants, the incidence of PBI due to hypoxic ischemic encephalopathy (HIE) is estimated to be 3.0 per 1000 live births and is associated with prolonged labor and delivery [6]. PBI is a lesion that mainly alters the structure of the nervous tissue and involves deficits in sensory [7], motor [8] and cognitive functions such as attention [9] and language [10]. The most common pathologic findings in preterm newborns are White matter lesions [5,11], which can trigger outcomes that have different degrees of severity. The preterm population affected by a severe injury is relatively small (~10%), while the percentage of infants with a moderate injury is considerably higher, approximately 30 - 50% [6,11].

Neurohabilitation is a therapeutic treatment that promotes the psychomotor and cognitive capabilities that newborns and nursing infants have not yet developed.

These capabilities are potentially modifiable if they result in alterations during the developmental process, due to the plasticity of the immature brain [12]. Interventions immediately after hospital discharge, intense practice of the elementary sensorimotor patterns (ESP) and active participation of newborns and their families [13,14] are the main bases of neurohabilitation. ESP is a group of congenital motor functions [12,14] characterized by a high degree of organization, persistence and stereotyping that can be activated by placing the head in specific positions to stimulate the vestibular receptors and trigger motor responses. The procedure also involves improvement in precognitive functions such as auditory and visual attention. This therapy has demonstrated that it has a better outcome if it is initiated before three months of age [12].

The Bobath procedure or Neurodevelopment Treatment (NDT) is also based on the neuroplasticity of the nervous system, postural control mechanisms and motor learning, along with the continuous practice of postural patterns and normal movements of functional activities in daily life [15,16]. According to [17], "The framework utilized in the Bobath concept for the analysis of movement and movement dysfunction focuses on postural control for task performance, the ability to move selectively, the ability to produce coordinated sequences of movement and vary movement patterns to fit a task, and the role of sensory input in motor behaviour and learning." Even in the new concept of the Bobath therapy, the integration of posture and movement according to the quality of task performance and the use of facilitation by sensory stimulation to promote motor control and motor learning remain to be main aspects. A review of 36 selected studies on the effect of early intervention from the newborn period to 18 months [18] concluded that an intervention following the principles of neurodevelopment therapy (NDT) does not have a beneficial effect on motor development. In the studies reviewed, general sensory stimulation and general stimulation of motor development were used after discharge from the NICU but consisted only of the participation of therapists for a few hours a week. In the review of [19], which included 24 studies of infants with CP, only four of the 16 results favoring NDT were clinically significant. In another review of 367 patients in nine studies, the mean age of the participating infants was 17 months, and the overall mean effect was 0·31, which is a small treatment effect according to Cohen rules [20].

In previous papers, we have reported the results of the neurohabilitatory treatment described by Katona in children with risk factors for brain damage and perinatal brain injury [21,22]. However, as this procedure is little known, we decide to use some of its main characteristics (early beginning and intensive treatment) with the NDT described by Bobath [15,16], which is mainly used in rehabilitation and is well known among many physiotherapists. Although there are few references using the Bobath therapy in infants and although the results are contradictory, we considered that perhaps following these characteristics of Katona's approach (very early and very intense intervention) may improve the results obtained using the Bobath procedure.

In this work, we were especially interested in comparing the efficacy of the Bobath and Katona procedures as early treatments to prevent motor and cognitive sequelae in infants with PBI, beginning the treatment at the first three months and with a careful follow-up of their neurodevelopment. The objective of this work was to compare the Katona vs. Bobath treatments applied to infants with PBI, using a blinded infant group evaluation of the outcome, at the age of five years or older. To our knowledge, the Bobath procedure has not been used in the way we describe in this report.

Methods

The Ethics Committee of the Instituto de Neurobiología of the Universidad Nacional Autónoma de México approved this study, which also complies with the Ethical Principles for Medical Research Involving Human Subjects established by the Helsinki Declaration. Informed written parental consent for participation in this study was obtained for all subjects.

Patients

Inclusion criteria: A total of 22 children who were five years or older with perinatal brain damage and whose treatment was initiated in the first three months of age with neurohabilitation or neurodevelopmental therapies were included in this study. The diagnosis of perinatal brain damage was made consistent with neuropediatric and MRI standards. The groups were formed and matched for sex and gestational age (GA). Table 1 shows the characteristics of the infants in each group and their gestational age, sex, perinatal diagnosis and the results of the blind group psychomotor development evaluations at three years old using the Bayley Scales of Infant Development.

Exclusion criteria: The presence of genetic factors associated with brain damage, cardiovascular pathology, brain malformations and/or chromosomal aberrations excluded patients from this study.

Procedure

After the infants were discharged from the hospital where they were born, their parents were invited to participate in a special project of the Unit for Neurodevelopmental Research (UDR) at the Universidad Nacional Autónoma de México in Querétaro.

Before three months of age, infants begin the therapies. As previously described [12-14,21,22], a neurohabilitation session consists of several maneuvers with each one repeated four or five times with a duration of 40 - 45 minutes per session and the application of three to four sessions each day that are intermixed with the regular activities of an infant: feeding, resting periods, bathing, and playing. For the application of the neurodevelopmental procedure described by Bobath [15,16], the treatment followed the same duration and frequency of sessions. The treatment of neurohabilitation is complex and considers various aspects of infant development while the evaluation and therapy, such as eye tracking, hearing following, language and attention are performed. Another characteristic of this type of treatment is that it requires persistent contact between the family (responsible for home therapy) and the group of professionals taking care of the infant. Special attention to the parents is essential as they are a fundamental part of the therapy. These characteristics were also used in the group of infants treated with the neurodevelopmental method.

The treatment schedule was established according to the children's routines and included feeding and resting periods. The caregivers took the infants to the UNR for treatment Monday through Friday during the first six months. In this way, the physiotherapist applied the therapy to the infants and supervised the way parents had applied it, ensuring the accuracy and the correction of any detected flaws. In addition, parents were required to carry out the therapy at home at least two more times a day. After six months, attendance to the NRU was reduced to twice a week, though parents were still required to perform therapy at least twice a day.

Infants in both groups were examined each month during the period of treatment for 24 months. Not only motor performance but also visual and auditory attention were evaluated, as well as the ages at which the infant mastered various developmental milestones. Figure 1 shows the time chart for the different evaluations. Those infants of both groups, who had neurological signs at 24 months continue with rehabilitatory treatment. From 24 to 36 months of age, infants were evaluated each three months by a neuropediatrician and a psychologist who performed the psychomotor development evaluations using the Bayley Scales of Infant Development, Second Edition (BSID-II) [23]. A different psychologist, who did not know which infant belonged to which group performed these Bayley Scales at three-years-old. The Mental Development Index (MDI) and Psychomotor Development Index (PDI) scores were obtained. Children were followed up each six months by neuropediatricians and psychologists until the evaluation at age five years or older. At this age, each child was examined by a different expert neuropediatrician (NG). This specialist performed a blind evaluation of the therapy group and made a diagnosis. The diagnosis was considered normal if the child does not have any neurological sign, on the other hand, the diagnosis was abnormal and a specific diagnosis was made if the child has any symptom or sign of cerebral palsy, epilepsy, visual or auditory deficits, intellectual disability, learning disorder, Attention Deficit Hyperactivity Disorder or Global Developmental Delay.

Results

Table 1 shows the characteristics of each group, the results of the evaluation for each patient at birth and the performance on the BSID-II at three-years-old.

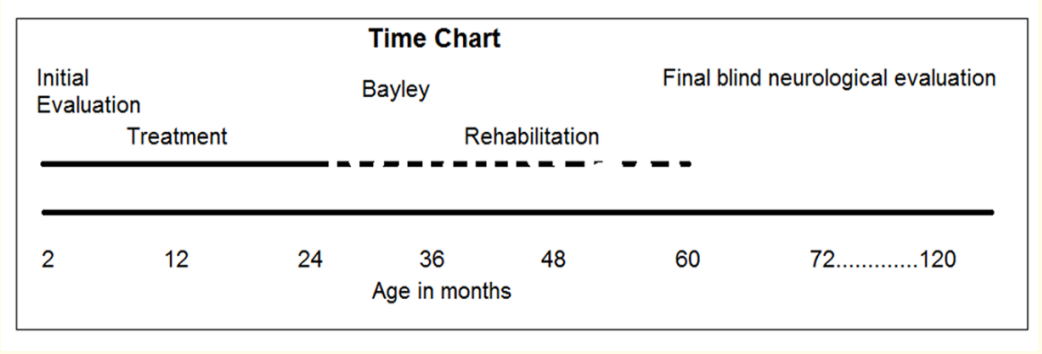

Figure 1: *Time chart of the procedure.*

Group	GA	Sex	Bayley (3 years)		MRI	Diagnosis
			MDI	PDI		
Katona	28	F	114	108	LV[1] > RV[2], WMA[3]	Preterm Enceph
	32	F	118	122	↑LV[1], WMA[3]	Preterm Enceph
	40	F	79	76	↓CC[4]	HIE
	28	M	99	98	Left orbitary cyst, WMA[3]	Preterm Enceph
	32	M	124	113	↑SS[5], WMA[3]	Preterm Enceph
	34	M	91	97	LV[1] > RV[2], WMA[3]	Preterm Enceph
	38	M	104	192	↓CC[4]	HIE
	38	M	105	89	↑SS[5], WMA[3]	Preterm Enceph
	26	M	107	88	↑↑SS[5], ↑↑LV[1], WMA[3]	Preterm Enceph
	36	F	92	55	Right middle cerebral artery infarct	Preterm Enceph
	40	M	70	118	↓CC[4]	HIE
Bobath	32	F	116	125	↓CC[4], ↑SS[5], WMA[3]	Preterm Enceph
	38	F	92	108	LV[1] > RV[2]	HIE
	25	M	106	105	WMA[3]	Preterm Enceph
	34	M	149	101	WMA[3]	Preterm Enceph
	28	F	50	50	Severe WMA[3], CC[4] cysts	Preterm Enceph
	37	F	109	130	Normal MRI	Hypoxic Ischemic Encephalopathy
	32	M	50	50	↓CC[4], ↑LV[1]	Preterm Enceph
	33	M	50	50	↓↓CC[4], ↑↑LV[1], WMA[3]	Preterm Enceph
	38	M	109	113	↑SS[5]	Hyperbilirubinemia
	39	M	82	92	↑LV[1], ↑SS[5], WMA[3]	HIE
	40	M	50	50	Supraventricular small hemorrhages and infarcts	HIE

Table 1*: Characteristics of infants in each group.*

[1]LV: Left Encephalopathy of Prematurity Ventricle; [2]RV: Right Ventricle; [3]WMA: White Mater Abnormality; [4]CC: Corpus Callosum; [5]SS: Subarachnoid Space; Enceph Prem: Encephalopathy of Prematurity; HIE: Hypoxic Ischemic Encephalopathy; ↑: Volume Increase; ↓: Volume Decrease.

In this table 2, we can observe that there was a predominance of the male sex in both groups with perinatal brain injury. According to the WHO classification, taking into account the gestational age (GA), there were two extremely preterm infants (less than 28 weeks gesta-

tion), with one in each group; four very preterm infants (28 to < 32 weeks), with two in each group; four moderate to late preterm infants (32 to 37 weeks), with two in each group; and six term infants, with three in each group. MRI showed mainly white matter abnormalities (WMA) related to Encephalopathy of Prematurity (EP) observed in the preterm newborns and cerebral infarcts related to Hypoxic Ischemic Encephalopathy (HIE) in the term infants. WMA are characterized by an increase in the volume of the lateral ventricles and of the subarachnoid space, as well as by a decrease in the volume of the corpus callosum, which is characterized by one diffuse neuropathological component in the absence of one focal macroscopic component cyst [24]. Figure 2 shows an example of an infant in the Bobath group. In the group treated with Katona's method, one patient with a large hemispheric infarction was observed (Figure 3).

The results of Bayley-II applied at three-years-old showed that from the group that followed Katona's treatment, one patient had both the Mental Development Index (MDI) and the Psychomotor Development Index (PDI) below the normal value, one child had a lower performance on the MDI, and another child had a PDI score below the normal value (The case in figure 2). Four children who followed the Bobath procedure showed extremely low performance on both indices.

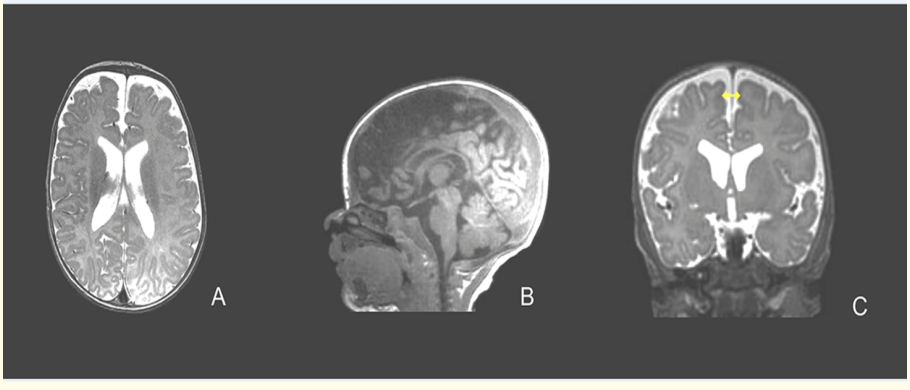

Figure 2: *Diffuse white matter abnormalities (A-B) and gray matter abnormalities by MRI (C). A) T2-weighted images in the axial plane showing dilated lateral ventricles. B) T1-weighted images in the sagittal plane showing thinning of the corpus callosum. C) T2-weighted images in the coronal plane showing augmented subarachnoid space (double direction arrow). Images are in radiological convention.*

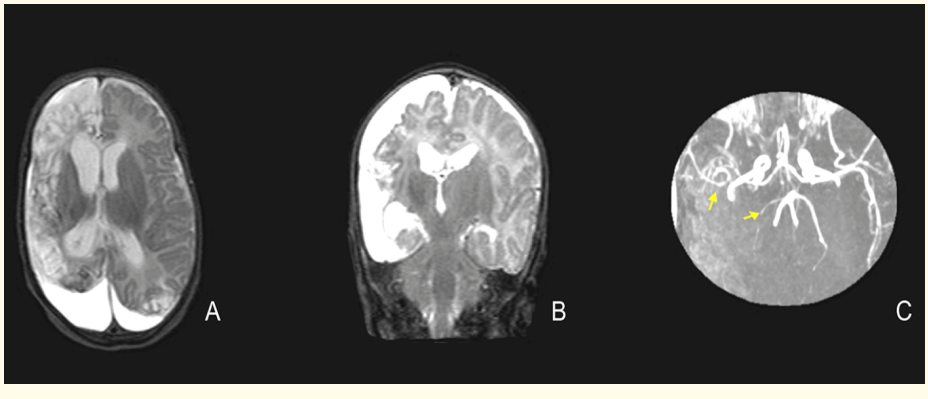

Figure 3: *Arterial ischemic stroke by MRI. A) T2-weighted images in the axial plane showing right extensive arterial ischemic stroke in the middle cerebral and posterior cerebral right arteries territory and subdural hematoma. B) T2-weighted images in the coronal plane showing right subdural hematoma. C) Noncontrast enhanced 3D time of flight magnetic resonance angiography (3D TOF MRA) in the axial plane demonstrates the absence of flow of the middle cerebral and right posterior cerebral arteries (arrows). Images are in radiological convention.*

Group	GA	Sex	Age (years)	Final diagnosis	Sequels
Katona	28	F	5	Normal	None
	32	F	9	Normal	None
	40	F	9	Normal	None
	28	M	7	Normal	None
	32	M	9	Normal	None
	34	M	5	Normal	None
	38	M	7	Normal	None
	38	M	8	Normal	None
	26	F	8	Abnormal	ID[1], CP[2]
	36	F	10	Abnormal	Left arm hemiparesis
	40	M	9	Abnormal	ADHD[3], Learning disorder
Bobath	32	F	8	Normal	
	38	F	7	Normal	
	25	M	5	Normal	
	34	M	8	Normal	
	28	F	7	Abnormal	Spastic CP[2], epilepsy, ID[1]
	37	F	8	Abnormal	Possible ADHD[3]
	32	M	8	Abnormal	Spastic CP[2], ID[1], and focal epilepsy
	33	M	6	Abnormal	CP[2], left hemiparesis, hearing loss
	38	M	7	Abnormal	Possible ADHD[3]
	39	M	9	Abnormal	Learning disorder
	40	M	5	Abnormal	CP[2], GDD[4], epilepsy, hearing loss

Table 2: *Outcome of each child according to blind neurological diagnosis.*
[1]ID: Intellectual Disability; [2]CP: Cerebral Palsy; [3]ADHD: Attention Deficit Hyperactivity Disorder; [4]GDD: Global Developmental Delay.

A comparison of the results of the normal or abnormal outcomes is presented in table 3. Although an analysis using Chi-squared test between groups was not significant ($X^2 = 2.93$, $p < 0.08$), the analysis of the odds ratio Katona/Bobath (4.467; CI 95% = 0.765 – 28.466) was significant and indicates that with Katona's procedure the outcome of normal neurodevelopment is higher (8/4) than with the Bobath treatment and has lower abnormal outcomes (3/7) than the Bobath procedure. The risk ratio (RR) was 37% (0.73 - 0.36 = 0.37) [25].

Group	Normal	Abnormal	Total
Katona	8 (73%)	3 (27%)	11
Bobath	4 (36%)	7 (64%)	11
Total	12	10	22

Table 3: *Odds ratio of the outcome of patients according to the treatment received.*
Katona/Bobath OR (4.467; CI 95% = 0.765 - 28.466).

Another important aspect is the severity of the sequelae. Two cases treated with the Bobath method had as sequelae cerebral palsy, intellectual disability and epilepsy, and another child had a global developmental delay, cerebral palsy and epilepsy. Only one of the children treated with Katona's method had cerebral palsy and intellectual disability. In a girl with a right extensive arterial ischemic stroke in middle cerebral and posterior cerebral right artery territory and subdural hematoma who was treated with Katona's method, the sequela at 10 years-old was a slight paresis of the left arm (Figure 2).

Discussion

First, it is important to state that we did not have a control group of children who did not receive early treatment because professor Katona has a huge database with more than 2000 infants, demonstrating the benefits of neurohabilitation.

Furthermore, according to The Declaration of Helsinki [26], the use of placebo or no intervention is acceptable "where no proven intervention exists" and "the patients who receive any intervention less effective than the best proven one, placebo, or no intervention will not be subject to additional risks of serious or irreversible harm as a result of not receiving the best proven intervention". However, we did publish a paper that compared a small sample of children who abandoned the treatment with a group treated very early with neurohabilitation [21] and another paper with a large sample of treated infants [22]. In both papers, we demonstrate that Katona's procedure was a very good treatment for children with prenatal and perinatal risk factors.

The dominance of the male sex in the sample is in agreement with other observations [27,28]. All children with one exception had abnormal MRI findings, which corroborated that the initial diagnosis also had a structural basis; thus, the effectiveness of treatments was evaluated in infants with proven perinatal brain damage.

As neurohabilitation training triggers the initiation of a series of movements, increasing independent involuntary movements may be considered a very active process. Stimulation of the vestibular receptors produces activation of the vestibular nuclei and their projections to the spinal cord, brain stem, reticular formation, cerebellum and basal ganglia. The continuous repetition of this stimulation after some weeks also results in the activation of the motor cerebral cortex and its pyramidal and extrapyramidal tracts giving rise to voluntary movements required for the verticalization of the body axis and synchronous movements needed to crawl and later to walk [12].

The results of the application of Bayley-II at three-years-old indicate that at this age, there are clear differences between both treatments that are in favor of Katona's group; using the Bobath neurodevelopmental therapy, four cases had very low values on the mental (MDI) and the psychomotor (PDI) indices, while with Katona's procedure, one child had low values on both indices, one child had a lower performance on the MDI, and another child performed lower on the PDI.

The results of the blind group evaluation of the outcomes showed that for the extremely preterm infants, one infant with Encephalopathy of prematurity (EP) treated with Katona had an abnormal outcome, and in the Bobath group, two very preterm infants and two moderate or late preterm infants had abnormal outcomes.

A comparison of a normal and abnormal outcome after five years or more using the odds ratio clearly indicates that with Katona's procedure, the outcome of normal neurodevelopment is higher (8/4) than with the Bobath treatment, and there are fewer abnormal outcomes (3/7) than with the Bobath procedure. Other very important results are in relation to the severity of the sequelae in each group. It was evident that more children with severe sequelae were observed with the Bobath than with Katona's procedure. However, these results were obtained with a small sample. Nonetheless, it should be considered that samples with continuous longitudinal evaluations for 5 or more years are difficult.

Conclusion

Katona's neurohabilitation is a better procedure than the Bobath neurodevelopmental method for achieving a superior outcome for infants with perinatal brain injury. However, this result should be viewed with reservations since it was obtained with a small sample.

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