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Jacobs Journal of Physical Rehabilitation Medicine

Research Article

Early Intervention Vs Vojta Therapy for Neurological Development Of Infants With Hypoxic Ischemic Encephalopathy

Angélica García-Pérez[1,4], Blanca Rivera-García[2], Gerardo Alvarado-Ruiz[3], María del Carmen Rojas-Sosa[4],Verónica Ramírez-Alvarado[4], Margarita Rojano-Rodríguez[4], Israel Grijalva[*1]

[1]*Unidad de Investigación Médica en Enfermedades Neurológicas, UMAE Hospital de Especialidades, Centro Médico Nacional Siglo XXI. Instituto Mexicano del Seguro Social. México, D. F.*

[2]*Hospital General de Zona No. 24, Instituto Mexicano del Seguro Social. México, D. F.*

[3]*Instituto Nacional de Pediatría. México, D. F.*

[4]*Unidad de Medicina Física y Rehabilitación Siglo XXI. Instituto Mexicano del Seguro Social. México, D. F.*

**Corresponding author: Dr. Israel Grijalva, UMAE Hospital de Especialidades, CMN Siglo XXI, Planta Baja, Avenida Cuauhtémoc 330, Col. Doctores, CP 06025, México, D. F. México, Tel: 011 52 5555780240; Email: igrijalvao@yahoo.com*

Received: 07-07-2015

Accepted: 09-24-2015

Published: 10-16-2015

Abstract

Background

Grade II hypoxic ischemic encephalopathy (GII-HIE) in newborns produces neurological sequelae in approximately 50% of patients. Neuro-rehabilitation offers rational therapeutic approaches in patients at risk of neurological damage; however, there is little information on comparison of different rehabilitation therapies.

Objective

Evaluate and compare results of Vojta therapy versus an early intervention program on the neurological and electrophysiological development of infants diagnosed with GII-HIE.

Methods

Controlled, randomized, simple blinded trial with term newborn patients diagnosed with GII-HIE, based on Sarnat-Sarnat criteria, aged 1-4 months. Thirty patients were recruited from the neonatology departments of two general hospitals in Mexico City. All patients underwent: Gesell Development Coefficient and evoked auditory, visual and somatosensorial potentials before therapy, and at 3 and 6 months of treatment. Therapy was applied by a therapist trained in the specific procedure for 30-40 minutes twice a week, for 6 months. The early intervention program includes proprioceptive and exteroceptive techniques that cover tactile stimulation (sucking, massage), vestibular stimulation, auditory stimulation (music, etc.), and visual stimulation (environment decoration, mobile elements).

Results

Twenty-seven patients finished the study, 13 girls and 14 boys, with an average age of 1.6 months; 12 had Vojta therapy and 15 early intervention. The Vojta therapy group had significantly higher scores in the Gesell test and its four neurological development areas (Mann-Whitney U, Gesell global, p=0.032; motor, p=0.04, language, p=0.01, adaptive, p= 0.01 and personal social, p= 0.02); in addition, there was also significant shortening (0.08 milliseconds) of the I-V interval in evoked auditory potential of the brain stem (p=0.05).

Conclusions

Patients submitted to both therapies showed clinical and electrophysiological improvement, but the Vojta group had greater improvement in both the four areas of neurological development and in the I-V interval of evoked auditory potential.

Keywords: Infantile Cerebral Paralysis; Handicap; Neurophysiological Development; Rehabilitation Therapies

Introduction

Hypoxic Ischemic Encephalopathy (HIE) in the perinatal period is the most frequent cause of neonatal mortality and chronic neurological handicap in infancy [1,2], and causes serious neurological sequelae in 20-50% of cases [3,4]. HIE is classified according to severity in 3 degrees. The majority of patients with Grade I do not present neurological sequelae [5]. Grade II (GII) is customarily associated with encephalopathy and between 25 and 50% show neurological sequelae in the long term, including: fine motor problems in the absence of cerebral paralysis, neuropsychological and memory disorders, behavior problems with repercussions in daily life (especially problems with attention and social integration) [6], as well as special education needs (patients with Grade II HIE can benefit from rehabilitation strategies) [3,4,7]. Finally, patients with Grade III HIE present severe sequelae or die [8].

Much has been discussed about which is the best strategy to reduce or prevent long-term disorders and improve motor and cognitive results for children with HIE. Except for hypothermia as a neuroprotector strategy in patients with moderate or severe neonatal encephalopathy after perinatal asphyxia or in pre-term children with HIE, no efficient pharmacological treatment has been described for this kind of patients [9,10].

On the other hand, neuro-rehabilitation continues to be an alternative method to handle these children as it offers rational therapeutic approaches in patients at risk of neurological damage [11,12].

Among the intervention modalities there are some with a neurophysiological focus, such as Bobath or "neurodevelopment" therapy widely used in the United Kingdom and United States, and Vojta therapy (VT), widely used in Scandinavian countries and the rest of Europe [13]. Other intervention models based on early multiple stimulation are used in many rehabilitation services in various parts of the world, including our country [13,14]. Unfortunately, there are no comparative studies among them to test their differential benefits.

Follow-up of neurological development can be done through clinical and electrophysiological evaluation. The Gesell Scale allows assessment of maturity and the organization of the neuromotor system that offers objective information [15], and includes four areas of neurodevelopment: motor, adaptation, language, and social-personal, to obtain the Gesell Coefficient of Development (GCD). The multi-modal potentials evoked evaluate the electric responses provoked by auditory, visual and somatosensorial stimuli to determine the dysfunction or maturity of the corresponding pathway. The visual potentials have a sensitivity of 0.90 (0.74 – 0, 97); and specificity 0.92 (0.68 – 0.98) to detect and predict neurological deficit [16-27].

The objective of the present study was to evaluate and compare the result obtained in neurological development, both in the VT program and a program of early intervention (EI) in children 1-4 months old with a diagnosis of GII HIE through the clinical (Gesell scale) and electro-physiological (multi-modal evoked potentials) tests.

Patients and Methods

The present study was carried out in the Unidad de Medicina Física y Rehabilitación Sur Siglo XXI of the Instituto Mexicano del Seguro Social (IMSS, a national health institute), in Mexico City following approval by the Research and Ethic Committee of Hospital General de Zona 32. All the parents were informed of the protocol procedures and approved the participation of their children by signing an informed consent.

A controlled randomized, simple blind study was carried out. Inclusion criteria were: diagnosis of GII HIE based on the criteria of Sarnat-Sarnat; [4] both sexes and aged between 1 and 4 months of extra-uterine life. Not included were children with chromosomal disorders malformations and/or congenital or metabolic diseases, sepsis or meningitis. Patients were sent from the Neonatology departments of Hospital General de Zona number 32 and from Hospital General del Centro Médico Nacional "La Raza". Therapy was assigned randomly through the closed envelope technique by staff outside the protocol. Two therapy sessions per week, lasting approximately 40 minutes, were given in the EI group [29,30], and for 30 minutes in the VT group [31,33], for 6 consecutive months. Each therapy was applied by a therapist trained in the specific technique. In each session the therapist verified that the parents executed the exercises; if the execution was satisfactory the therapist labeled it as complied (positive adherence to treatment) and vice versa. The setting in which the therapeutic sessions took

place met the necessary hygienic conditions: free of noise, adequate temperature and all materials necessary to carry out the treatment.

The EI program consists, briefly, in a set of actions which are based on proprioceptive and exteroceptive techniques that cover tactile stimulation (sucking, massage), vestibular stimulation, auditory stimulation (music, etc.), visual stimulation (environment decoration, mobile elements), and special exercises for the neuromotor alterations presented [30].

If the child presented fever or another acute inflammatory process (such as vaccination), he was allowed to suspend therapy for 5 days. In all other general diseases, the time of each session was shortened without suspending the therapy.

Evaluation of Patients

During the period of the study 3 clinical and electrophysiological measurements were taken: at the onset (pre-treatment), and at 3 and 6 months during treatment.

Neuro-development evaluation. This considered the Gesell scale as applied and scored by a single psychologist to determine the Gesell Development Coefficient (GDC) [15], and the multi-modal evoked potentials: (auditory, visual and somatosensory) interpreted by the same rehabilitation physician responsible for the neurophysiology laboratory. Evaluators were blinded to the therapy used.

Electrophysiological studies were performed with a Nicolet Viking D (USA) equipment. Electrodes were placed according to the international ten-twenty system.

Statistical Analysis

Descriptive statistics were used, expressed in tables, as well as the Shapiro-Wilk test to analyze for data normality; and Student T and Mann-Whitney U were used to establish statistical differences as appropriate, considering $p \leq 0.05$ as significant.

Results

Thirty patients were recruited; 3 were eliminated because the parents refused to continue in the trial after 1 or 2 weeks of treatment. The study ended with 27 patients, 13 girls and 14 boys, with initial average age of 1.63 (± 0.5) months, with no differences between the study groups. VT had 12 patients, and there were 15 in the EI group (Figure 1).

The integrated scores obtained in the GDC before and after 3 months of treatment showed no significant differences between groups (Mann-Whitney U, p = 0.8 and p = 0.5, respectively). At the end of follow-up (6 months) there were significantly higher global scores in favor of the VT group (Mann-Whitney U, p= 0.032); upon separately comparing the four areas of development of the same scale, there was also statistical significance in favor of the VT group (Motor p=0.04, Language p=0.01, Adaptation p= 0.01 and Personal Social p= 0.02) (Table 1).

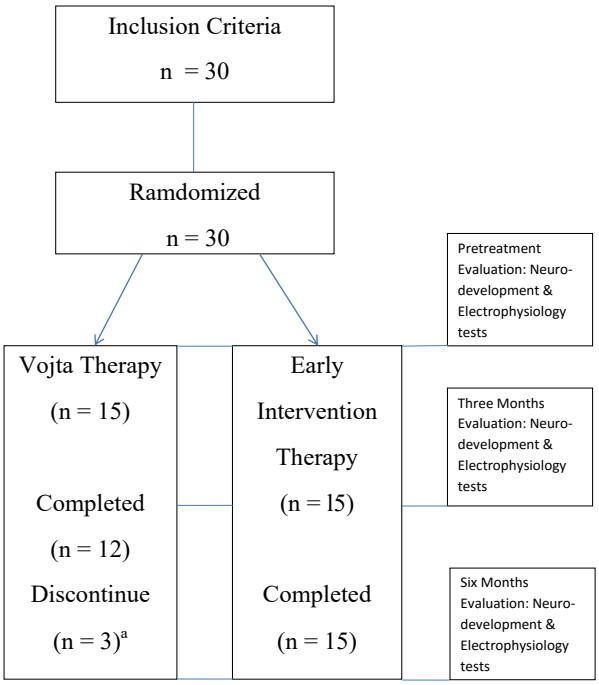

Figure 1. Design of the clinical trial.

a. The parents of three patients refused to continue in the trial after 1 or 2 weeks of treatment.

Regarding neurophysiological studies, auditory evoked potentials (AEP) showed differences in: a) significant increase in the amplitude of Wave I in the EI group ($p< 0.05$); and b) significant shortening of the interval of central I-V neuro-conduction (0.08 milliseconds) in the VT group ($p< 0.05$). As for visual evoked potentials (VEP), only the amplitude of potential P100 was significantly greater in the EI group ($p< 0.05$). There were no significant differences in latencies, amplitudes, or neuro-conduction intervals in the somatosensory evoked potentials (SSEP) (Table 2).

No adverse events that warranted interrupting the treatment were presented during the performance of the program.

Discussion

Patients subjected to both therapies showed clinical and electrophysiological improvement; however, VT proved to be superior to EI in favoring significantly greater neurological recuperation in the four areas of neurodevelopment: motor, language, adaptation and personal social. From the neurophysiological point of view, VT was also superior to EI in demonstrating significant shortening of the central neuro-conduction of the AEP, related to an increase in myelination. On the other hand the

Table 1. Neurodevelopment characteristics of infants with Grade II hypoxic ischemic encephalopathy (GII-HIE) subjected to Vojta or Early Intervention rehabilitation therapy evaluated with Gesell scale.

	Vojta Therapy (n = 12)					Early Intervention Therapy (n = 15)					
	Basal	Three months	Within-group p value	Six months	Within-group p value	Basal	Three Months	Within-group p value	Six Months	Within-groups p value	Between group p value
Gesell scale											
Motor	1.33±0.88	4.25±1.76	0.24	9.58±4.54	0.04	1.00±0.85	3.20±1.82	0.15	6.33±3.54	0.05	p=0.04
Language	1.42±0.99	4.42 ±2.35	0.31	10.17±4.20	0.01	1.13±0.83	3.60±1.84	0.18	6.27±3.45	0.01	p=0.01
Adaptative	1.33±0.88	4.05±1.73	0.37	10.08±4.33	0.01	1.07±0.80	3.27±1.92	0.08	6.13±3.48	0.01	p=0.01
Personnel-social	1.42±0.90	4.58±1.83	0.27	10.25±4.39	0.01	1.07±0.88	3.33±2.06	0.06	6.33±3.38	0.01	p=0.02
GDC	59.17±43.00	92.0±26.5	0.11	96.75±33.8	0.03	63.3±0.12	75±36.14	0.14	82±27.04	0.02	p=0.03

GDC: Gesell development coefficient
Within-group p value: compares basal versus three or six month scores.
Between group p value: compares final scores of both therapy groups.
All scores are mean ± standard deviation.

EI group was better neuro-physiologically upon demonstrating significant improve of some aspects of AEP and VEP, both probably related with the increase in the number of functional axons.

Gesell [34] established that neurological development is influenced by two main factors: the biological (hereditary) and environmental, which interact reciprocally. The term maturation, he defined as the process of development that is ruled by innate factors [35], and stimulated or modified by environmental factors [34]. On the other hand, he proposed that all normal children go through the same development sequences in the same order [35]. Nevertheless, there are some individual differences in the rhythm of development, with initial potential conditioned by genetic factors. Gesell argued that society and the family should provide an adequate environment so the child could develop his potentials optimally through established patterns and standards [36,37].

The plasticity of the nervous structures is the basis that supports early intervention with early care programs. There is evidence about the influence on cerebral plasticity of stimulation in experimental animals, but exactly what occurs in the human brain is still unknown [38,41].

The present study compared two rehabilitation strategies that have been reported in the literature as efficient, although evidence is limited and contradictory. In this case, an EI program whose sustainment in the literature from the scientific point of view is apparently adequate but not conclusive was compared against the Vojta method, which has only been described in uncontrolled clinical trials.

The literature mentions that the VT improved motor function; however, in the present study it was found that patients subjected to VT improved not only in the motor aspect, as previous authors have indicated [42-45], but also in other areas of neurodevelopment (language, adaptation and personal social), quantified through the Gesell Scale, obtaining individual values of normality or near-normality after finishing the therapy.

It is worth mentioning that there are no articles that support the physiological mechanism through which VT acts; however, it has been noted that VT works through the pre-distension of muscle groups, favoring the global pattern of reflex locomotion always reproducible, that acts at the level of the central nervous system (CNS) from the lowest to the highest circuits (according to the phylogeny and motor ontogenesis). The patterns are innate and are pre-programmed throughout the CNS, and are susceptible to being unleashed at any age [31].

It has been noted that the functions related to VT are the activation of cerebral motor areas and the spinal cord circuits that act on the strengthening of the body, balance, intentional

Table 2. Electrophysiological characteristics of infants with Grade II hypoxic ischemic encephalopathy (GII-HIE) subjected to Vojta or Early Intervention rehabilitation therapy evaluated with multimodal evoked potentials.

	Vojta Therapy n = 12			Early Intervention Therapy n = 15			
	Baseline	Change	Within-group p value	Baseline	Change	Within-group p value	Between- groups p value
Auditory evoked potentials							
Latency wave I	1.85±.20	1.67±12	0.10	2.02±.26	1.67±.15	0.10	0.10
Amplitude wave I	0 .161±.12	0 .168±.12	0.14	0.166±.14	0.198±.13	0.05	0.52
Latency wave V	6.6±.36	6.1±.28	0.14	6.6±.44	6.2±.22	0.15	0.14
Interval I-V	4.86±.34	4.52±22	0 .00	4.85±.48	4.60±21	0 .39	0.05
Visual evoked potentials							
Latency wave P 100	190±.53.5	132±12.9	0.75	172±.31	130±7.28	0.56	0.55
Amplitude wave P 100	0.714±.52	1.215±.74	0.56	0.618±.69	1.509±69	0.05	0.05
Somatosensory evoked potentials							
Latency wave N20	22.6±.1.3	19.7±1.70	0.42	24 ±1.54	19.9±1.14	0 .37	0.49
Amplitude wave N20	0.721±.73	0.994±.45	0.38	0.662 ±.46	0.908±.90	0.38	0.39
Interpeak latencies N9-N13	3.34±1.02	2.87±.59	0.64	3.55 ±1.03	2.75±.39	0 .64	0.29

movements, and activate gastrointestinal and urinary smooth muscle. On the other hand, it has been said that it favors normalization of the inadequate growth of extremities (for example, hypoplasia associated with cerebral palsy in infancy, (and improves language in children with dysarthria and increases stereognosis (even without performing tactile sensitivity exercises) [31].

Imamura et al. reported significant improvement in the psychomotor development of 713 children, from newborns to 12 months of age, who had shown delayed psychomotor development, managed with VT, who showed normal development at the end of treatment [43]. Likewise, Hayasi and Arizona [42] reported two cases of children with severe hypoxic encephalopathy at birth. Rehabilitation management was begun at one and two months of age, respectively, using VT, with monitoring of spontaneous movements, postural reflexes and neurological manifestations. The patients evolved favorably without presenting any kind of paresis or mental retardation. The authors of both papers concluded that a program of VT applied at an early stage can improve neurological development [42,43]. Kanda et al. also published results on the clinical use of VT initiated at an early stage and with long-term effects on 10 premature children with 33 weeks of gestation (WG) and weight under 2000 grams, clinically diagnosed with spastic diplegia, who had magnetic resonance image studies that showed peri-ventricular lesions of the white matter; the cohort was followed for 62 months, after which they found that children were able to walk or stand for 5 seconds, concluding that VT implemented improvement in the motor development of this kind of child [45].

Martinez-Fuentes et al. performed a study with the objective of analyzing the mental and motor development progress of premature children using VT before other interventions, which included 21 premature children (6 boys and 15 girls), with average age of 32 WG; 6 received VT and 15 other interventions. The results showed significantly greater mental and motor progress in children subjected to the Vojta technique [46].

The above studies are uncontrolled clinical trials, so in spite of the reported benefits, the results are questionable, since the positive effect described so far might be due to the natural history of the ailment in each patient. Therefore, the beneficial effect of VT should be tested with a more adequate methodological design, such as the present work.

On the other hand, studies have also been published that evaluate the effect of EI programs, concentrating on premature neonates, with the same objective of improving motor and cognitive aspects. There are 16 controlled and uncontrolled clinical trials, of which 3 showed conclusive data in favor of EI, considered in the meta-analysis of Spittle et al. [47], which qualified the usefulness of EI; the 3 conclusive publications are: the I.H.D.P. study, which is a multi-centric trial that investigated the effects of EI in pre-term neonates compared with the standard follow-up; the second study is by Bao, who performed a controlled, quasi-randomized multi-centric study of an intervention package that centered on child development, in comparison with the standard follow-up; the third work is by Melnyk, who performed a quasi-randomized pilot project that compared the "Creating Opportunities for Parent Empowerment" (COPE) program with the customary handling. These three studies showed statistically significant differences in favor of the EI group. The other 13 studies did not produce conclusive results.

In addition to the methodology design problem of the studies mentioned above, and due to the fact that EI has multiple strategies to stimulate neuro-development, the grouping of the studies for global analysis is complicated.

The program used for the present study was published by Dr. Torres Góngora and is used as the standard treatment in the Physical Medicine and Rehabilitation Units of the IMSS in Mexico City [30]; nevertheless, to date this intervention has not been subjected to an efficacy study.

In spite of the fact that in the present study VT showed higher scores in the patients using it, it is important to stress that the patients that received EI also improved.

The somatosensory and visual potentials evoked are sensitive to identifying functional alterations in the Central Nervous System during asphyxia and after, and are indicators of long-term prognostic value [17-20]. The incidence of abnormalities in the SSEP of asphyxiated term newborns is 33 to 65% [5]. Around 65% of newborns with abnormalities of SSEP at 3 months have neurological abnormalities in the future [5,24]. If the abnormalities persist, they are associated with neurological deficit [26]. The present study sought the association of the two rehabilitation programs implemented in the therapeutic management of these children with GII-HIE, with electrophysiological changes in the multi-modal potentials evoked. In relation to the AEP, there was an increase in the amplitude of the I wave in both groups, but significantly higher in the EI group; a greater amplitude of P wave in VEP was also observed, but significantly greater in the EI group. In both cases, the findings express axonal activation in the auditory and visual pathways [27,28]. This might be explained by the increase in external stimuli, which upon increasing in frequency may reinforce already-established axonal connections to different levels [27, 28]. Another possibility is the facilitation of plastic phenomena that favors new connections [27,28]. In the VT group significant shortening was found in the I-V interval of the AEP of 0.08 milliseconds, which indicates improvement of the pathway myelination [12,23,27,28].

Conclusions

Neuro-rehabilitation therapies are important to improve functionality of GII HIE infants. VT is better than EI in clinical neurodevelopment and in central neuro-conduction of the AEP, although EI group was better neuro-physiologically on some aspects of AEP and VEP. These results should lead to continuation of this kind of study with longer term follow-up, and in collaboration with other centers that care for this type of patients.

Acknowledgment

This study was supported by IMSS. The first author was CONACYT and IMSS scholarship.

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