

Children and Cerebral Palsy: The Hopeful Clinical and Neuro-Imaging Impacts of Joint Therapy

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Abstract

Background: Cerebral palsy is a common pediatric problem encountered in about 1:3 per 1000 born children and causing variable mental, motor and behavioral dilemmas. Newly introduced trials of neurogenesis with different agents are now extensively evaluated.

Objective: Our study was conducted to evaluate the neurotrophic response to vitamin B₁₂ vitamin and omega-3 fatty acids in children diagnosed early with variable forms of cerebral palsy. The response was monitored both clinically and with C.T Scan as being a highly predictive tool for assessing cerebral palsy.

Design: The study was carried out on 40 cerebral palsy patients; 26 (65%) out of them were girls, and 14 of them were boys, aged from 0 to 5 years old; from outpatient clinic at Zakho/Duhok General Hospital in Kurdistan Region-Iraq. Patients were treated by oral omega -3 and vitamin B₁₂ and followed up for 6 months to one year. They were represented and adjusted by full history taking and clinical examination. Brain C.T scans were done for every patient to assess the degree of brain atrophy before and starting this combined therapy, and every month for six months to one year.

Results: The study revealed that early supplement of combined both omega 3 and B₁₂ vitamin in children under 5 with cerebral palsy (CP) shows great response based on clinical examination and CT scan findings. Almost, 80% of children with delayed speech, 77% of children with delayed milestone and hypertonia, and 87% with delayed walking. The response to the treatment was equal in both sexes. In addition, Neuro-radiological improvement in CT scan results was obtained in 70% of treated children from moderate/severe forms of cortical brain atrophy to a mild form after 6 months to one year of combined therapy of omega 3 and vitamin B₁₂.

Conclusions: The study showed progressive clinical and Neuro-radiological improvement in response to weekly supplement of B₁₂ and daily omega-3 fatty acids throughout 6 months to one year. The greatest improvement, particularly in speech and motor development was significantly observed.

Keywords: Cerebral Palsy; B₁₂ and Omega 3; Brain; Motor and Speech Development; C.T Scan; Clinical Improvement

Introduction

Cerebral palsy is the most common and costly form of chronic motor disability that commence in childhood; the incidence is 1:3 per 1000 children with male: female ratio of 1.4:1 [1]. The escalating prevalence of cerebral palsy occurs as a result of enhanced survival of

very premature infant weighing less than 1000 grams who grow and later develop cerebral palsy at a rate of 15 per 100, and the major lesions that contribute to cerebral palsy in preterm infant are intracerebral hemorrhage periventricular leukomalacia [1]. Substantial evidence suggests that cognitive impairment can be influenced by a number of environmental factors such as nutrition [9]. Nutrition plays a key role in maintaining optimal brain health throughout the lifespan of an individual [10]. In view of this, the studies examining the link between nutrition and mental health have gained widespread attention in recent years. Boys with intrauterine growth retardation and birth weight less than the third percentile is 16 times more likely to have CP than males with optimal growth, and infants with weights above the 97th percentile are 4 times more likely to have CP [1].

Omega-3 fatty acids

Are micronutrients that play key roles usually in the regulation of specific biological processes that can be linked to maintain optimal neuronal function and they are associated with various health benefits such as cardiovascular protection and cognitive functions, while B-group vitamins that are vital for extracting energy out of fuel nutrients and for making red blood cells. Therefore, those specific biological roles cannot be considered isolated anymore. This recent study in nutritional science focusses and take into account the potential synergistic results of these micronutrients in brain health and oxidative stress. The concept here is that what one micronutrient mostly will have a powerful impact on what another is doing, even more if they are related to the same metabolic pathway [29].

As a result, B vitamin may play vital role in brain atrophy, particularly in people with high levels of omega-3 fatty acids. In the same way, the beneficial effect of omega-3 fatty acids on brain atrophy may be restricted to subjects with good B vitamin status [29,30]. This might explain why some B vitamin trials on brain function have failed.

Furthermore, the role of omega-3 fatty acids, especially DHA in brain development is gaining worldwide attention [11]. The dietary sources of omega-3 fatty acids are fish and sea foods only [12] which are the rich sources of DHA. Further, over the past two centuries, the western diet has altered such that the ratio of omega-3 to omega-6 fatty acids has changed from 1:1 to 1:20 - 25 indicating that this diet is deficient in omega-3 fatty acids and is rich in omega-6 fatty acids [13]. Thus, the deficiency of omega-3 fatty acids and consumption of western diet has been suggested to be associated with cognitive impairment [14, 15].

There is increasing evidence which indicates the importance of omega-3 fatty acids in brain health across the lifespan [16]. DHA, which is the core member of omega-3 fatty acids, is highly concentrated in the brain and the outer segments of retinal rods and cones, constituting around 50 % of the total polyunsaturated fatty acids [17]. DHA participates in a number of neuronal processes, including neurogenesis, neuroplasticity, neuronal differentiation and survival, membrane integrity and fluidity [18]. A large body of evidence in animals has shown that maternal supplementation of DHA during gestation has neuroprotective effects against prenatal stress-induced brain dysfunction [19], hyperoxic injury, and hypoxic ischemic injury [20].

Mechanism of action: For omega-3 fatty acids and B vitamins, the so-called **one-carbon cycle**, is the linked point. A complex series of chemical reactions, in which the one carbon cycle is vitally included, during which a carbon unit is transferred from folate compounds to other metabolic pathways. Carbon units are the building blocks that our body needs for the synthesis of new cellular components. They are extracted from dietary sugars and proteins. Consequently, inputs in the form of glucose (mainly extracted from dietary sugars) and amino acids (mainly extracted from dietary proteins) enter the pathway, are processed through chemical reactions, and are then provided for diverse biological functions. This one-carbon metabolism can be considered an Integrator of nutrient status [28].

Vitamin B₁₂

Is a key micronutrient required for proper brain development and is associated with one carbon metabolism that plays a pivotal role in transmethylation reactions. It is involved in the formation of S-adenosylmethionine (SAM), which is an important substrate for epigenetic mechanisms [21]. Vitamin B₁₂ is known to have fundamental roles in the brain function at all ages and also in the prevention of disorders of CNS development, mood disorders and dementias including Alzheimer's disease and vascular dementia in elderly people [22]. Elevated

methylmalonic acid and total homocysteine concentrations are important sensitive metabolic markers for vitamin B₁₂ deficiency [23]. Vitamin B₁₂ deficiency is mainly clinically presented with myelopathy and neuropathy [24]. Megaloblastic anemia, tingling and numbness of the extremities, gait abnormalities, visual disturbances, memory loss and dementia are considered the main symptoms of vitamin B₁₂ deficiency [25].

Studies indicate a need for supplementation of vitamin B₁₂ to improve pregnancy outcome and reduce the risk of neurodevelopment disorders [26]. Reports indicate a positive association between maternal vitamin B₁₂ status and cognition in the offspring [27]

Cerebral palsy

Is a diagnostic term belongs to a group of brain diseases known as encephalopathy and various symptomatology including posture and movement resulting in activity limitation that is contributed to static disturbances in the developing infant brain [1]. Cerebral palsy is one of the most important causes of neurodegenerative diseases in infants [31].

Types and etiology of cerebral palsy

Cerebral palsy can present in various clinical signs, impairment in cognition, sensation, perception and behavior. Furthermore, it can present as a global mental and physical disturbance or isolated depletion in gait and cognition, however, many children with cerebral palsy are at higher education and vocational level, without any sign of cognitive dysfunction [1,5,6]. The etiology of cerebral palsy is multifactorial as it is caused by various genetic, environmental, metabolic, ischemic, infectious and other acquired reasons that result in common group of neurologic disorder [1].

The diagnosis of cerebral palsy is mainly based on clinical examination, history taking and Neuroimaging of the brain [2,8]. Neuroimaging such as C T of the brain is of highly significant value to assess the degree of the brain lesion, site, etiology, and even for the prognosis and follow up with cerebral palsy patients [3,7]. The aim of this study is to prove that early combined therapy (omega 3 fatty acids and B₁₂ vitamin) has its clinical value in cerebral palsy children with delayed milestone and speech impairment. The table 1 illustrates the types and etiology of cerebral palsy.

Categorization and major causes of cerebral palsy		
Motor syndromes (% of CP)	Neuropathology/MRI	Major causes
Spastic diaplegia 35%	Periventricular leukomalacia Periventricular cysts or scars in white matter, Enlargement of ventricles, Squared off posterior ventricles	Prematurity Ischemia Infection Endocrine/metabolic as thyroid
Spastic quadriplegia 20%	Periventricular leukomalacia Multicystic encephalomalacia Cortical malformations	Ischemia Infection Endocrine/metabolic Genetic /developmental
Hemiplegia 25%	Stroke: in utero or neonatal Focal infarct or cortical, subcortical damage Cortical malformations	Thrombophilic disorder Infection/genetic/developmental Periventricular hemorrhagic infarction

Table 1: Categorization and major causes of cerebral palsy.

Methods

Consent was obtained from patients and their parents when this data was collected and entered into the dataset. This is a cross-sectional hospital and private clinic based study, carried at Zakho General Hospital-Kurdistan-Iraq out-patient pediatrics units for the period from October 2015 to November 2016.

A total of 40 cerebral palsy patients (26 girls, 14 boys) with overall mean age 25.6-month was collected. Data were collected from their parents about age, sex, main clinical presentation, and prenatal, perinatal, postnatal history, history of delayed milestone and speech. Diagnosis of cerebral palsy was based on history, clinical examinations, and radiological findings. According to the European Food Safety Authority (EFSA), the patients were treated by combined oral intake of daily 100 - 250 mg\kg\day of oral equally mixed eicosopentanoic EPA and decusohecanoic DHA omega-3 fatty acids [32] and weekly oral vitamin B₁₂ of 1000 - 2000 mcg [33].

Results

Among the total number of patients (40) cases, 80% of children with CP presented with speech delay, 77% of cases presented with delayed milestone and hypertonia, and delayed walking account for 87% of cases with CP in the present study (Table 2).

Specific Clinical Signs of CP Children	Total No.	%
Speech Delay	40	80%
Delayed Milestone and Hypertonia	40	77%
Delayed Movement and Walking	40	87%

Table 2: Specific Clinical Signs of CP Children.

All patients with CP have been followed up clinically and with the aid of CT scan. Great response of children with CP to Interventional combined therapy with daily oral omega 3 and weekly oral B₁₂ vitamin was identified.

All patients have abnormal CT scan abnormalities and brain atrophy was the commonest type of brain pathology finding. Among 40 cases in the present study, there were 28 cases (70%) who had cortical atrophy with dilatation of the ventricles, showed great CT scan improvement. The radiological improvement seen in those children who showed subcortical atrophy had 20% of children (8 cases), whereas only 10% of children (4 cases) with CP had hemi atrophy based on brain CT scan (Table 3).

CT Scan Improvement After Combined Therapy	No	%
Cortical+Ventriculomegally	28	70
Subcortical	8	20
Hemiatrophy	4	10
Normal	Zero	Zero
Total	40	100

Table 3: CT Scan Improvement After Combined Therapy.

Discussion and Conclusion

The presented study revealed that females are affected more than males; this finding was purely new and never been identified in any other study in the past. It has been already mentioned that CP is more common and more severe in boys compared to girls [1]. However, intrauterine growth retardation, birth weight less than the third percentile, and infant with weights above the 97th percentile in all these are considered as contributing factors [1]. In this study, female gender is considered a risk factor in children with cerebral palsy. All patients were originally from Iraq and of Kurdish ethnicity. The range of age was between 6 to 59 months.

Obvious gross motor delay, poor head control, spasticity, exaggerated tendon reflex, hypotonic and decreased reflex were the revealed signs in patients when clinically examined. However, the main clinical presentation of this study was delayed motor milestone with hypertonia (77%). Speech delay was presented in (80%) of the examined children, and delayed walking in 87% of patients.

Selected investigations are essential to confirm the diagnosis of children with CP, although the diagnosis of CP is purely made on a clinical base [2]. Suspected cases of CP must have early Neuroimaging to adjust the degree of brain pathology, to identify the etiology of CP, and to assess the prognosis [3].

The commonest CT finding was cortical brain atrophy with dilatation of the ventricles (70%) followed by sub cortical brain atrophy (20%) and brain hemi atrophy (10%).

Moreover, CT in the present study was abnormal in all cases (40 in number) of both sexes. However, patients with CP might present clinically with normal brain CT scan; an exclusion of metabolic and genetic etiologies is mandatory [4].

Limitations

There are certain limitations of this study that should be acknowledged. A small number of infants participated in this research study; therefore it is not easy to generalize to a larger or broader population. More authors if included in this research study, we might get better results and further understandings of the findings. Also, a pediatric gastroenterologist might be of value and help to share in such study and better conception of the findings would have been achieved as compared to results obtained by two research authors.

Despite of these limitations, the findings generated will have significant reference value for future studies.

Conflict of Interest

Nil.

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Nil.

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