Research Article

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The Positive Clinical Consequence of Early Intervention of Combined Therapy (Omega 3 Fatty Acids and B12 Vitamin) in Children Under 5 with Variable Forms of Cerebral Palsy

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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 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 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 was done for every patient to assess the degree of brain atrophy before starting this combined therapy, and every month for six months to one year. There was an improvement in general health of children after interventional therapy.*

Results: *The study revealed that early intervention of 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, after combined therapy, 80% of children with delayed speech delay have very good response and improvement, 77% of children with delayed milestone and hypertonia, and 87% with delayed walking have positive clinical outcomes. Both sexes have equal response to combined therapy. Such findings were obtained as a result of early treatment and diagnosis of children with (CP). In addition, among the treated children with CP, improvement in CT scan results was obtained. 84% of treated children have great improvement in their neuroimaging results from moderate/severe forms of brain atrophy to mild form of brain atrophy after being treated and followed up for 6 months to 1 year.*

Conclusion: *The damaged brain sites based on CT scan results, showed progressive improvement in response to B12 and omega-3 fatty acids upon daily supplement throughout 6 months to one year. However, combining these 2 drugs showed preservative synergistic consequences. B12 vitamin and omega- 3 fatty acids are valuable therapy for children with various forms of cerebral palsy particularly when being linked. The greatest improvement in speech and motor development was significantly observed in about 32 patients (80%) of treated children with B12 vitamin and omega- 3 fatty acids. Others have less response to combine therapy as being presented and diagnosed beyond 1 year of age (16%).*

Keywords: Cerebral palsy, Early intervention, B12 and omega 3, Brain, Motor and speech development, C.T Scan and clinical improvement, Outpatient clinic

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 gram who grow and later develop cerebral palsy at a rate of 15 per 100 [1]. The major lesions that contribute to cerebral palsy in preterm infant are intracerebral hemorrhage periventricular leukomalasia [1]. Substantial evidence suggests that cognitive impairment can be

influenced by number of environmental factors such as nutrition [2]. Nutrition plays a key role in maintaining optimal brain health throughout the lifespan of an individual [3]. In view of this, the studies examining the link between nutrition and mental health have gained widespread attention in recent years. CP is more common and more severe in boys compared to girls [1]. Boys with intrauterine growth retardation and birth weight less than the third percentile are 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 role usually in the regulation of specific biological processes that can be linked to them. Omega-3 fatty acids are associated to various health benefits such as cardiovascular protection and cognitive functions, and 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, from a systemic approach regarding the organism as a whole, with every part being linked. This recent study in nutritional science focus 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 powerful impact on what another is doing, even more if they are related to the same metabolic pathway [4].

As a result, B vitamin supplementation play vital role 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 [4,5]. 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 [6]. The dietary sources of omega-3 fatty acids are fish and sea foods only [7]. 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 [8]. Thus, the deficiency of omega-3 fatty acids and consumption of western diet has been suggested to be associated with cognitive impairment [9,10].

There is increasing evidence which indicates the importance of omega-3 fatty acids in brain health across the lifespan [11]. 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 [12]. DHA participates in a number of neuronal processes including neurogenesis, neuroplasticity, neuron differentiation and survival, membrane integrity and fluidity [13]. 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, hyperoxic injury, and hypoxic ischemic injury [14,15].

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. Thus one-carbon metabolism can be considered an integrator of nutrient status [16].

Vitamin B_{12}

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 [17]. Vitamin B_{12} 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 [18].

Elevated methylmalonic acid and total homocysteine concentrations are important sensitive metabolic markers for vitamin B12 deficiency [19]. Vitamin B12 deficiency is mainly clinically presented with myelopathy and neuropathy [20]. Megaloblastic anaemia, tingling and numbness of the extremities, gait abnormalities, visual disturbances, memory loss and dementia are considered the main symptoms of vitamin B_{12} deficiency [21].

Studies indicate a need for supplementation of vitamin B12 to improve pregnancy outcome and reduce the risk of neurodevelopment disorders [22]. Reports indicate a positive association between maternal vitamin B12 status and cognition in the offspring [23].

Cerebral palsy is a diagnostic term belongs to a group of brain diseases known as encephalopathy. It is used to describe a group of non-progressive and permanent disorders of posture and movement resulting in activity limitation that is contributed to static disturbances in the developing infant brain [1].

Types and etiology of cerebral palsy is illustrated in Table 1.

Table 1: Categorization and major causes of cerebral palsy

Motor syndrome (% of CP)	Neuropathology/MRI	Major causes
Spastic diaplegia 35%	Periventricular leukomalasia 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 leukomalasia 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 infraction

Cerebral palsy can present in various clinical signs, impairment in cognition, sensation, perception and behavior 5. Furthermore, it can present as a global mental and physical disturbance or isolated depletion in gait and cognition [24,25]. However, many children with cerebral palsy are at high educational and vocational level, without any sign of cognition dysfunction [1]. 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].

Although cerebral palsy has been considered as a static encephalopathy, some of its neurologic signs like movement disorder, hip dislocation and scoliosis might progress overtime [1].

The diagnosis of cerebral palsy is mainly based on clinical examination, history taking and neuroimaging of the brain 2, 8. Also, CT 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 in cerebral palsies patients [26,27]. 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 palsies children with delayed milestone and speech impairment. This truth is approved clinically and with CT scans identification of the brain.

Methods

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

A total of 40 cerebral palsy patients (26 girls, 14 boys) with over all mean age 25.6-months were collected. Data were collected from their parents about age, sex, main clinical presentation, and prenatal, perinatal, postnatal history, history of delayed milestone and speech. They all had complete clinical and neurological examination; head circumference was measured by tape measure. Data were analyzed using percentage. All patients were sent to radiology department at same hospital for CT of the brain. Patients were treated 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 was done for every patient to assess the degree of brain atrophy before starting this combined therapy, and every month for six months to one year.

Results

Among 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).

Table 2

Specific clinical signs of CP children in this study	Total no	Improvement after combined therapy %
Speech delay	40	80%
Delayed milestone and hypertonia	40	77%
Delayed movement and walking	40	87%

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 omega 3 and B12 vitamin was identified (Table 3).

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

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

Discussion

The presented study revealed that females are affected more than males; this finding was purely new and never being 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 all these are considered as contributing factors [1].

In this study, female gender is considered risk factor in children with cerebral palsy. All patients were originally from Iraq and of Kurdish ethnicity. In the present study the majority of patients were 6-59 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 in 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.

The spastic CP was commonest type in the present study followed by hypotonic CP, and among spastic CP diplegic was the commonest type. Children with spastic CP are generally hypotonic in the first 6-9 months, and then gradually become hypertonic [28].

Selected investigations are essential to confirm the diagnosis of children with CP, although the diagnosis of CP is purely made on 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 [27].

The commonest CT finding was cortical brain atrophy with dilatation of 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 [29,30].

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