The Neurotrophic Effect of Piracetam And Omega-3 Fatty Acids Based On EEG And EMG Parameters In Children Sufferring From Cerebral Palsy

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الخلاصة:

الشلل الولادي هو أحد المشاكل الصحة المألوفة لدى الأطفال، حدث صدب 2\١٠٠٠ من الأطفال المولودن و سبب اضطرابات دهنة وحركة وأخلاقة. والآن فإنّ ثمة اعداد واسع النطاق لمحاولات تنمة الأعصاب. وقد أعددنا هذ الدراسة لتقم الأثر المنمي للعصب لكل من البراسيتام والأحماض الشحمة أومكا-٣، وقد تم تقم الإستجابة وفقاً للمراقبة السررية وتخطط أعصاب الدماغ والعضلات كأدوات مراقبة معتدة.

لقد أظهرت نتائج تخطط الأعصاب فوق المنطقة المتضررة للمخ إستجابات معتدة للبراسيتام والاومكا-٣ عند P<0.05 بعد مراقبة تخطط الدماغ أسبوعاً واعطاء الدواء ومناً لمدة شهرن بالمقارنة مع المجموعة التي لم تأخذ العلاج. فقد تحسن شكل التخطط من نمط موجة الضمور العصبي ثتا قبل العلاج إلى النمط الفعال الفا. وكانت الإستجابة أكثر فاعلة عند الأطفال الذن تعاطون البراسيتام والأومكا-٣ سوة. كما أظهرت نتائج التخطط العصبي إستجابة مناظرة بتقلل شدة المنعكس العضلي لعضلة الرباط الإكلي للساق، حث خفض الاتحاد بنهما شدة المنعكس من ١٠.٥ ملفولت إلى ٦.٥ ملفولت بعد العلاج بمعامل ارتباط r معتد به عند P< 0.05. ونستنتج من ذلك أنّ البراسيتام وأحماض الأومكا-٣ تعتبر علاجات قمة للأطفال الذن عانون من تحطم وضمور الأعصاب.

Abstract:

Cerebral palsy is a common pediatric problem encountered in about 2 per 1000 born children and causing variable mental, motor and behavioral sequalaes. Newly introdued trials of neurogenesis with different agents are now extensively evaluated. Our study was conducted to evaluate the neurotrophic response to piracetam and omega-3 fatty acids in children suffering from variable forms of cerebral palsy. The response was monitorred both clinically and with EEG and EMG patterns as being a highly predictve tools for assessing cerebral palsy. The damaged brain sites under the skull showed progressive improval in response to piracetam and omega-3 fatty acids upon daily supplement throughout 2 month in comparism with the controlled EEG pattern of the untreated children at P< 0.05 as a right axis EEG wave shift from neurodegenerative theta wave (4-5 Hz) to the active alpha wave. However combining these 2 drug showed additve synergestic effects. Similar reciprocal EMG response of the gastrocnemous tendon reflex amplitude had been obtained with a synergistic decrease by combining piracetam with

omega-3 fatty acids from 10.5 mV before treatment to 6.5 mV after 2months of treatment with significant correlation coefficient r at $P < 0.05$. In conclusion piracetam and omega-3 fatty acids are valuable therapy for children with neurodegenerative disorder especially when being combined.

Introduction:

Cerebral palsy is one of the most important causes of neurodegenerative diseases in infants. Incidence of children born with cerebral palsy was around 2 per 1000 in separate survey studies.(1,2)

Those patients could be presented with sequalaes of neurodegenartion for example epilepsy had a prevalence of 36.1%.(3) in addition to
learning difficulties or mental retardation in 73 and 76 per cent.(4,5)
Pathophysiology and complications: Cerebral palsy is associated with EEG abnormalities and development quotient. Seventy-six per cent patients had spastic cerebral palsy. Hypotonic cerebral palsy was the next common type (14%). Athetosis and ataxic forms were found to be rare (2% each). Epilepsy was associated with 56% patients. Sixty per cent of patients had abnormal EEG, out of these hypotonic patients had maximum (70%) chances of EEG abnormality followed by spastic patients (55%). Developmental retardation was more severe statistically in the patients with abnormal EEG than normal EEG.(6,7,8)

Most children with cerebral palsy showed encephalopathic symptomatology, including spastic tetraplegia, extrapyramidal symptoms, and a mental deficit.(9)
Severe hyperbilirubinemia in neonates with prematurity and/or systemic illnesses such as hemolytic disease, acidosis, and hypoxemia enhances their risk for developing cerebral palsy, paralysis of ocular upgaze, and deafness. This neurologic syndrome has been associated with selective neuronal vulnerability in the basal ganglia, certain brainstem nuclei, and Purkinje cells.(10)
Monitorring parameters of cerebral palsy: Electroencephalographic recording is a highly predictive method of assessing cerebral palsy. A study conducted had revealed EEG abnormalities in eight of the 20 subjects tested, consisting mainly of bilateral sharp waves with slower rates.(12,13)

Electromyographic (EMG) kinetic analysis of the gastrocnemius fascia on ankle joint in patients with cerebral palsy (CP) show a decrease in the abnormal energy generated around the ankle in midstance and a statistically significant increase in the energy generated in late stance for push-off.(14)

Relaxant measures such as clonazepam for cerebral palsy was evaluated in another research with restraint of passive knee movements by a dynamic dynamometer and spastic stretch reflexes as EMG activity in muscles stretched which showed a positive effect of low dose clonazepam in reducing spasticity in children when given as a single dose.(15)

Materials and Methods:

EEG recordings are extremely useful to distinguish between acute stage and chronic stage of cerebral abnormalities. The former is characterized by findings of acute depression such as increased discontinuity, decreased faster frequency activities, and lowered amplitudes. The latter mainly includes dysmature patterns and disorganized patterns. The timing of brain insult can be assessed by considering EEG findings in relation to the time of birth. Different modes of brain injury are associated with different types of EEG abnormalities and different types of neurological outcome. Sudden strong brain insults are usually associated with findings of severe depression followed by disorganized pattern and later cerebral palsy, while persistent mild insults are usually associated with prolonged mild depression followed by dysmature pattern and later mental retardation.(11)

Monitorring of cerebral palsy responses with EMG was based on the hypothesis that EMG testing for selective control of the quadriceps and gastrocnemius could differentiate patients with diplegic cerebral palsy from normal controls.(16)

In this study 40 children with cerebral palsy were monitorred for their EEG and EMG both acutely and weakly throughout 63 days of treatment. Diagnosis of cerebral palsy was based on history, clinical examinations, radiological findings and EEG records. Treatment started daily with 10 mg\kg \day of oral equaly mixed eicosopentanoic EPA and decusohexanoic DHA omega-3 fatty acids for group B which includes 10 children with cerebral palsy whereas group C (n=10) was given piracetam 1000mg\day orally daily. The remaining D (n=10) group was given combination of piracetam 1000 mg\day plus omega-3 fatty acids 10 mg\kg\day throughout the 63 days. Wealy assessment of in clinic EEG and EMG of gastrocnemuos tendon reflex were taken along the 2 months of treating them. The results were statistically assessed for treatment correlation with response as a decrease in achillis tendon reflex and increase in EEG frequency from neurodegenerative theta wave to alpha wave.

Results:

Figure (1) Illustrates the neurotrophic effect of piracetam and omega-3 fatty acids as indicated by inreasing the mean EEG frequency after 2 months of treatment.

EEG changes were obvious with statistically significant improvement of the frequency as a response to piracetam, omega-3 FA and their combination as compared with the control untreated group D at $P < 0,05$.

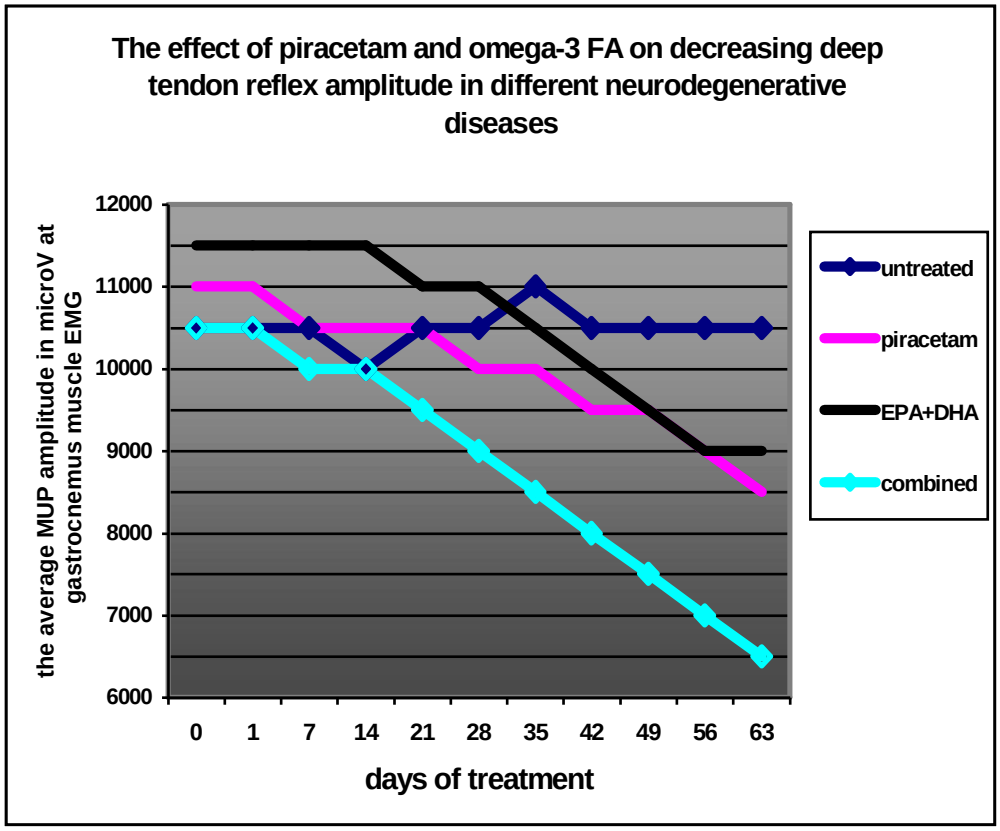

Figure (2): Indirectly correlates piracetam and omega-3 effect with improvement of spastic cerebral palsy as the inverse function of muscle tendon reflex EMG and cerebral neurogenesis along the 2 months of treatment.

There was reciprocal coincidence of decrease in the mean gastrocnemous tendon reflex amplitude from 11 mV to 8 mV after 2 months of daily treatment with piracetam. Statistically significant correlation of decreasing reflex amplitude and treatement was encountered with piracetam, omega-3 FA and their combination.
At $P < 0,05$.

Discussion:

Cerebral palsy is one of the major neurodegenerative pediatric diseases. That affects about 2 per 1000 of born children.(1,2)

It is of critical familial, health and socioeconomic significant so that different therapeutic trials have to be carried out to overcome this problematic disease after occurrence. Our study showed significant improvement of spasticity of cerebral palsy in group B, C and D that were treated with piracetam, C with omega-3 FA and D was treated with combination of them at P, 0.05 as were asssessed with cumulative therapeutic effect by r = correlation coefficient slope. As the neurogenesis is in progress, upper motor neuronal inhibitory pathway will increase to regulate spinal motor units

function. This is reflected as increased EEG frequency centrally from theta wave to alpha wave and decrease in the spastic spinal motor unit activity so that EMG at lower limb muscles will be diminished in amplitude. This improvement of instrumental guided parameters could be attributed to the role of omega-3 fatty acids as a scavengers for the potential neuronal toxic free radicals, in addition to their vital structural activity in neuronal cell membrane and their regulation of prostaglandin series.

On the other hand piracetam is important pyroglutamate compound that have multiple nootropic and neurogenic mechanisms, such as facilitation of neuronal glucose enterance and stimullation of the stimulatory neurotransmisster glutamate, however, piracetam alone (group B) showed more significant neurotrophic effect than omega-3 FA alone. Their combination showed additive synergistic effect (figure 1,2) more potent shift of EEG pattern from neurodegenerative theta wave before treatement to the active EEG alpha wave just 2 months of daily treatment with combination of omega-3 FA and piracetam although each agent alone had revealed a significant similar improvement but of less potency ($P < 0.05$). Similar reciprocal EMG pattern had been obtained by decreasing the gastrocnemous tendon reflex from 10.5 mV to 6.5 mV (normal < 5 mV) after combined treatment course whereas piracetam and EPA+DHA reduced it from 11 mV to 8.5 mV and from 11.5 mV to 9 mV respectively with significant r at $P< 0.05$.

The rationale of using omega-3 as a neurotrophic factor for treating cerebral palsy in our study is supported by the results of many studies revealed that high level of omega-3 fatty acid desaturation is necessary for normal neuronal function(17), in addition to the promising responses had been obtained from using omega-3 as neuroprotector and nootropics in some functional and organic nervous system disorders.(18,19)

On the other hand, results of different comparative studies had agreed with our study in suggesting that the neuroprotective effect of piracetam against oxidative damage and its potential nootropic activity may present a valuable therapeutic combination for the treatment of mental retardation, chronic neurodegenerative disorders and stroke.(20,21)

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