ACTA SCIENTIFIC NUTRITIONAL HEALTH (ISSN:2582-1423)

Volume 3 Issue 12 December 2019

Review Article

Review the Effect of Omega 3 Supplementation on Severity and Frequency of Epilepsy

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Received: October 29, 2019; **Published:** November 07, 2019

DOI: 10.31080/ASNH.2019.03.0538

Abstract

Epilepsy (also known as a 'seizure disorder') is a chronic neurological disorder characterized by recurring seizures and occurs when the message delivery system becomes unbalanced and when there is not enough gamma amino butyric acid (GABA) as inhibitory neurotransmitter. Clinical and experimental investigations have demonstrated that the duration and frequency of epileptic seizures can be reduced as a consequence of long-term n-3 PUFA (poly unsaturated fatty acid) supplementation. The aim of the present study was review of the effectiveness of PUFA supplementation especially omega 3 fatty acid as adjunctive treatment for intractable focal or generalized epilepsy in humans studies.

Keywords: Epilepsy; Seizure; Omega 3; EPA; DHA; PUFA

Introduction

Epilepsy is a resulting from sudden bursts of electrical energy in the brain and these electrical discharges produce seizures which vary from one person to another in frequency and form [1]. If the signal goes through all of the brain, the person may shake all over, fall and lose consciousness [2]. Epilepsy (also known as a 'seizure disorder') is a chronic neurological disorder characterized by recurring seizures [3]. A seizure occurs when the message delivery system becomes unbalanced and when there is not enough gamma amino butyric acid (GABA), seizure is occur because of receiving neurons is flooded with signals [4]. Seizures are induced by the influx of sodium and calcium ions mediated by excitatory neurotransmitters such as aspartate and glutamate and also Seizure inhibition is mediated by chloride ions entry and potassium ion outflow mediated by GABAergic neurotransmitter [5] (Figure 1). The seizure causes that divided into two type generalized and partial include high fever, especially in infants, drug use, metabolic disturbances, head trauma, e.g., car accident, brain tumor, infection(meningitis), stroke, Genetic factor and complication of diabetes or pregnancy [6]. The characteristics of seizure are vary greatly and some known characteristics include; uncontrolled movements such as shaking of arms or legs, loss of consciousness, falling, staring into space (absences) mostly in children, appearing dazed, confusing and mumbling [7]. Intractability defined by Berg., *et al*. as failure of two appropriate anti-epilepsy drugs (AEDs) with the occurrence of at least one seizure per month for > 18 months [8]. Approximately one-third of patients with epilepsy do not achieve seizure control with available drugs, and many patients experience troublesome adverse drug effects [9]. Epilepsy is the second most common chronic neurological condition seen by neurologist In children 3-6/1,000 in most country worldwide and higher prevalence rates ranging 14 to 57 per 1000 in some African and South American countries [10,11]. The present study was designed to review the effectiveness of PUFA supplementation especially omega 3 fatty acid as adjunctive treatment for intractable focal or generalized epilepsy in humans studies.

Figure 1: Cellular mechanism of seizure generation.

Role of PUFA and Omega 3 in epilepsy

Clinical and experimental investigations have demonstrated that the duration and frequency of epileptic seizures can be reduced as

a consequence of long-term n-3 PUFA (poly unsaturated fatty acid) supplementation [12,13]. PUFAs (docosahexaenoic acid, 22: 6n-3) are major components of membrane phospholipids in brain tissue [14]. The PUFA role in the body cells is ant- inflammatory (reduced expressions of TNF-α, IL-6, and cyclo-oxygenase-2), reduction of oxidative damage and inflammation, protection against ischemic injury and, neuro-protective bioactivity [15].

Several studies have been shown that omega-3 fatty acids reduce neuronal excitability and may be useful in the non-pharmacological treatment of patients with epilepsy [16].

In the present review in overall, most clinical trial studies have shown an inverse association between omega-3 supplementation and frequency and severity of seizure [12,17-19], however, in some studies these effects were not observed [20,21] (Table 1). In the non-randomized open labeled trial EPA and omega 3 supplementation in 10 patients with chronic epilepsy has not significant effect on epilepsy [22].

Conflicting results in some of studies probably due to Improper selection of control groups (For example, the soybean [Containing omega 3] or mineral oil[not specified combination]), small sample

Author (year), Country	Age(year) / Sex	N (Intervention/ control)	Intervention type		Duration (week)	Outcome measures	Result	Note
			Intervention	Control				
Alan Yuen W.C., *et al*. UK (2005)	19-65 M/F	57 (29/27)	1g of fish oils (171 mg EPA , 112 mg DHA), and <100 IU vitamin A and <40 IU vitamin D	Mixed oils (palm olein 70%, rapeseed oil 15%, sunflower oil 15%)	12	Seizure frequency	Transiently reduced seizure frequency 24/22/24 (int) 31/25/28 (con)	
Eduardo J., *et al*. Mexico (2011)	4-16 M/F	13	Combination of omega 3 and omega 6: (558 mg EPA, 174mg DHA and 60mg GLA	no treatment	4	Seizure frequency	Decrease seizures of 26.61 to 5.92 per day	
Al Khayat., *et al*. Egypt (2010)	3-10 M/F	40 (20/20)	PUFA: (700 mg DHA, 300 mg EPA)	no treatment	24	Seizure frequenc, seizure severity	Significant decrease in seizure frequency F:3-50 per/month 1-35per/m S:67-134 to 37-68	Age, sex, weight, height adjusted
Bromfield E., *et al*. USA (2007)	22-62 M/F	21 (12/9)	1.32 g EPA, 0.88 g DHA (EPA and DHA 2.2 mg/day in a 3:2 ratio)	2.2 mineral oil	12	Seizure frequency	No effect on seizure frequency Int: 15 to 11 Con: 23 to 5	-
DeGiorgio Ch., *et al*. USA (2008)	18–65 M/F	11 (cross over)	1.7 g EPA 1.2 g DHA and	8 capsules/ day of soybean oil placebo	12	Seizure severity, seizure frequency	S.S: 8.55to7.57(Int) 8.55to7(con) S.F: 11% increased in Int and 14% increase in Control	No effect on seizure frequency and severity
Schlanger S., *et al*. Israel (2002)	12-26 M/F	5	0.9 g EPA, 2.3 g DHA	No treatment	24	Seizure frequency	Reduced seizure frequency 5.25 per/Wk to 1 per/Wk	-

Table 1: Effects of n-3 PUFA on epilepsy in clinical trial studies.

size and Short duration of the study, neglecting other criterion for measurement of epilepsy Lack of attention to participant diets and levels of DHA and eicosapentaenoic acid (EPA) in the blood before and after intervention.

The probable mechanisms of the n-3 PUFAs act are 1-antagonizing neuro- inflammation (decrease the production of pro-inflammatory prostaglandin E2 (PGE2) 2-DHA acts by modulating voltage-dependent and 3-ion channels and particularly the voltage-dependent sodium channel (VDSC) and improvement of mitochondrial energy production are other proposed mechanisms [23,24]. The anticonvulsant actions of n-3 PUFA are shown in figure 2.

Figure 2: Anticonvulsant actions of n-3 PUFA.

ALA: Alpha-Linolenic Acid; LA: Linolenic Acid; PG: Prostaglandin; COX: Cyclooxygenase; AA: Arachidonic Acid.

Conclusion

We conclude that nutrition is one of the factors affecting of epilepsy, in particular deficiency of DHA and EPA omega 3 fatty acids. We suggest that omega 3 fatty acids, as an essential nutrient is worthwhile trying as adjunctive therapy for patient with epilepsy especially in children. Additional well-designed and larger randomized controlled trials are required to establish optimal doses and to quantify the benefit of n-3 PUFA therapy in patients with epilepsy. The advantages of n-3 PUFA in epilepsy treatment are inexpensive and readily available that they have few side effects and n-3 PUFA–enriched diet might serve as an adjunct to the drugs in patients with resistant seizures or as a first-line treatment in idiopathic epilepsy.

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