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SHORT COMMUNICATION

Supplementation of omega-3 acids reduces the risk of aggression

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ABSTRACT

Aggression is the growing problem in society. Therefore it is important to identify potential factors preventing aggression. In recent years scientists have observed decreased concentrations of omega-3 acids in people prone to aggression. This discovery suggested that the key to reducing aggression could be omega-3 acids supplementation. The aim of this study is to describe whether omega-3 acids consumption may result in reduction of aggressive behavior. Standard up-to-date criteria were followed for review of the literature data. A search for English-language articles in PubMed database was performed. Papers published between 2014 and 2017 were reviewed. In randomized study scientist discovered that omega-3 acids supplementation results in 42-68% reduction of parental complaints about aggressive behaviors in children. The improvement of behavior persisted for six months after cessation of treatment. Scientists in 2015 found out that in the prison population low levels of omega-3 acids in the blood correlate with more aggressive behavior. Patients in treatment group were characterized by more than 30% reduction in aggressive behaviors comparing to placebo group. In another review study we can notice the same conclusions. Aggression against

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others and impulsivity were lower in the group receiving omega-3 acids. A greater susceptibility to aggression has been observed among patients who have lower levels of omega-3 acids in their blood. Scientists have demonstrated positive omega-3 effects on the reduction of aggressive behavior. Omega-3 supplementation is safe and well tolerated and it can be used in combination with other methods of aggression treatment.

***Keywords*:** aggression, omega-3 fatty acids, 3n-PUFAs

1. INTRODUCTION

Human aggression is defined as conscious and intentional behaviour which leads to do someone or something injury, pain or loss [1]. Additionally, the perpetrator knows that his behavior will harm the victim and that the victim will want to defend himself against it. Therefore, the intention of harm is a necessary element of aggression [2].

For years, researchers have been focused on studying what biological, psychological, social, and environmental factors predispose to aggressive behavior and they have been looking for factors that prevent and control this phenomenon. [2, 3].

Recently, scientists found out that low levels of omega-3 acids in the blood and central nervous system correlate with more aggressive behavior like high impulsivity and hostility [4, 5]. After this discovery, interest in the role of omega-3 fatty acids supplementation as a key to reduce aggression increased dramatically [4].

Omega-3 fatty acids (3n-PUFAs) are polyunsaturated fatty acids with a double bond at the third carbon atom from the end of the carbon chain [6]. The human organism can synthesize omega-3 acids only in small amounts, and that is why their level depends on food intake or supplementation [7]. Omega-3 acids are eicosapentaenoic acid (EPA) and docosahexaenoic acid (DHA), which have a main source in seafood such as crustaceans, lobsters, molluscs, oysters, squid and sea fish [8, 9] and alpha linolenic acid (ALA), which are derived from plants oils like perilla seed oil, soybean oil and from linseed or walnuts [10]. Another main source of omega-3 fatty acids are dietary supplements [7]. Therefore, they are one of the main components of the Mediterranean diet, recognized by their content as very healthy [11].

Omega-3 fatty acids bring many health benefits. Many positive features of omega-3 fatty acids have been reported. Those features are reduction of inflammation, oxidative stress, platelet aggregation, thrombus formation, plaque rupture or foam cell formation, which contains pathological diseases. They are also connected with reduction of triglycerides without raising low-density lipoprotein cholesterol, what is important in treatment of atherogenic dyslipidemia. [12] Among other things, they have been shown to increase the synthesis of substances like nitric oxide (NO) or prostacyclin in endothelial cells, which gives them functions like vessels vasodilation, anti-aggregatory and anti-inflammatory effects. [13]. One of omega-3 fatty acids, EPA improved the balance between NO and ONOO −1, which is one of the reactive oxygen species [14]. It also suppressed generation of reactive oxygen species induced by palmitic acid, expression of cytokines, activation of apoptosis-related proteins, and apoptosis in human umbilical vein endothelial cells [15, 16]. EPA inhibited lipid peroxidation in membrane vesicles with normal or elevated cholesterol levels [17]. Glucose contributes to lipid peroxidation, by causing the pathological changes in lipid

structural organization. EPA inhibited lipid peroxidation and cholesterol crystalline domain formation in membrane lipid vesicles caused by glucose [h-18] Intercalation of EPA to the lipid bilayer of the membrane, where it disturbs the propagation of reactive oxygen species gives it an antioxidant effect [18].

The above activities find a number of applications. Scientists not only noticed the positive effect of 3n-PUFAs on behavior and central nervous system function [19], but also on the cardiovascular system by reducing major cardiovascular events and reducing risk of death after an acute myocardial infarction [8, 20]. Omega-3 fatty acids intake is associated with the prevention of cognitive functions loss in people with Alzheimer's disease and reduced risk of development of this disease [8, 21, 22]. It has also been proven that supplementation of fish oil in pregnancy reduces the risk of asthma and autoimmune diseases in offspring [23-25]. New randomized study suggest that supplementation with omega-3 may play a role in treatment of disorders such as hyperactivity and depression [26]. There are reports that in people with depression who eat Mediterranean diet the acids consequently contribute to the improvement of mental health [11]. Another study shows correlation between omega-3 fatty acids supplementation and reduced symptoms of chronic fatigue syndrome [27]. There are studies reporting the possibility of Omega 3 acid interference with the development of insulin resistance [28]. Mitochondial dysfunction results with lipid accumulation and reactive oxygen species production (ROS), which are considered to be important components of cellular insulin resistance[28]. Dietary omega 3 polyunsaturated fatty acids (PUFA) can prevent organism from development of insulin resistance by modulating cellulary metabolism [28]. It has been reported that omega 3 acids may have a beneficial effect on prevention of nonalcoholic fatty liver disease (NAFLD) development. Most meta-analyzes suggest a beneficial effect of these acids on the development of this disease, however, recent randomized studies have reported that omega-3 fatty acids might be beneficial in decreasing liver triglyceride, but not in decreasing other features of steatohepatitis (or liver fibrosis), which does not give complete prevention before the development of the NAFLD [29].

There are also studies showing the effect of supplementation of omega-3 acids in nursing mothers on the development of immune systems in infants[30]. Additionally, there have been reports of the use of acids in cancer prevention, for example, there is a study suggesting the possibility of the influence of omega-3 acids on the growth rate of glioblastoma multiforme. [31] The high level of fat-binding protein in the brain (B-FABP) is associated with increased migration / infiltration in gliblastoma multiforme cells, with a high ratio of arachidonic acid (AA) to docosahexaenoic acid (DHA) and several proteins C (PKC) kinases are overexpressed in glibolastoma multiforme. In the research AA and DHA modulated both conventional and atypical PKC activities in a B-FABP-dependent manner, but had no effect on novel PKC activity. It suggests that conventional and atypical PKCs are potential acceptors of B-FABP/fatty acid-mediated alterations in glioblastoma multiforme growth properties, and glioblastoma multiforme growth can be regulated by omega 3 acids [31]. Another property of omega 3 acids is the ability to use them in the dry eye syndrome as many researches says. Notwithstanding, there is a new research from 2018 which showed no significant improvement in patients taking omega 3 acids after 12 months of treatment compared to the placebo group [32]. In addition to widely known positive properties, there are new reports of the possibility of adverse effects of taking a large amount of omega-3 acids preparations. There is a review by Cheng-Ho Chang et al. based on twenty-one included

randomized controlled trials. Results showed that omega-3 acids were associated with more treatment-related dysgeusia, because of fishy taste and skin abnormalities like eruption, itching, exanthema, or eczema [33]. Omega-3 fatty acid products had small adverse effects upon some laboratory measurements like elevated fasting blood sugar, elevated alanine transaminase, elevated blood urea nitrogen, decreased hemoglobin and decreased hematocrit [33]. Researchers also analyzed subgroups and they revealed that EPA/ DHA combination products were associated with more treatment-related gastrointestinal adverse events, for example, eructation, nausea and low-density lipoprotein cholesterol elevation [33].

The number of reports of undesirable effects is small, and research into this issue should be continued, but they appear to be safe for the human body. Also, many of the abovementioned applications require further verification.

As research indicates, omega-3 supplementation may be an auxiliary solution for treatment of patients suffering from aggression [5, 34-36].

2. MATERIALS AND METHODS

This review study presents data from systematic reviews and clinical trials. Standard up-to-date criteria were followed for review of the literature data. A search for English-language articles in PubMed and Google Scholar database was performed. Papers published between 2014 and 2017 were reviewed.

3. RESULTS

In randomized, stratified, single-blind, factorial trial published in 2016 in Journal of Child Psychology and Psychiatry scientist studied the effectiveness of the omega-3 supplementation and therapy in the treatment of aggression. 290 prone to aggression children aged 11-12 were included in the study and divided into 4 groups. The first group was a nutrition group and their diet included omega-3 fatty acids, multivitamin and calcium. The dose of omega-3 fatty acids was 1000 mg per day. The second group was a cognitive behavioral therapy group (CBT), the third included a combination of nutrition with CBT and the last one was a control group. The treatment duration was 3 months, but children were observed 9 months after. The screening was performed by using aggression questionnaire filled out by parents and children and a computer program NIMH-DISC-IV diagnosing the occurrence of mental illness, including ADHD. The scientists discovered that after 3 months patients in nutrition group were characterized by reduced externalizing aggressive behavior compared to another 3 groups. After 6 months patients from the Nutrition + CBT group had significantly reduced level of aggressive behavior compared to patients from control and a CBT group. There were no significant differences between groups in the 9 months of follow-up. Throughout the study no major side effects of omega-3 oral fatty acid supplementation were observed. Moreover, omega-3 fatty acids treatment was well tolerated by children [34].

In the next randomized, double blind trial the number of patients was 200. 50% of them were classified in the treatment group consuming 1 gram omega-3 fatty acids daily. The remaining 100 children were assigned to the placebo group. The primary outcome included problems in externalizing behavior like aggression, and the secondary outcome measured

internalizing behavior problems and aggressive behavior in parents. The screening was performed by using report of aggression symptoms sourced from parents and children. In order to exclude the influence of behavioral changes in parents on the results of treatment in children, parents were asked to complete questionnaires about their behavior. Scientists used SPSS (version 20) for data analysis. At the beginning of the study both groups did not significantly differ in the level of omega-3 in the blood. After 6 months of treatment the omega-3 fatty acids level was definitely higher in the study group compared to the control group. This study demonstrated that supplementation of omega-3 fatty acids in children was associated with a 42% decrease in externalizing behavior and 68% in internalizing behavior reported by parents. The study noted a difference in the behaviors observed by parents and children themselves. Children demonstrated only temporary reduction of reactive (58.9%) and proactive (49.7%) aggression. In addition, the amelioration in caregivers' behavior accounted for 61% improvement in children's behavior. This study did not show any dangerous side effects of omega-3 fatty acids intake [35]. The next study involved by 136 adult male prisoners from South Coast Correctional Centre (SCCC), NSW Australia. The level of omega-3 fatty acids was measured and the omega-3 index was calculated in blood samples collected from the convicts. More than half of prisoners had an omega index- 3 lower than 5 (Fig. 1). The study showed a negative correlation between the level of aggression and the omega-3 index. The lower level of omega-3 fatty acids in blood was associated with the increase of aggressive behavior as well as attention deficit disorders. The strongest relationship was observed between omega-3 index and enmity [5].

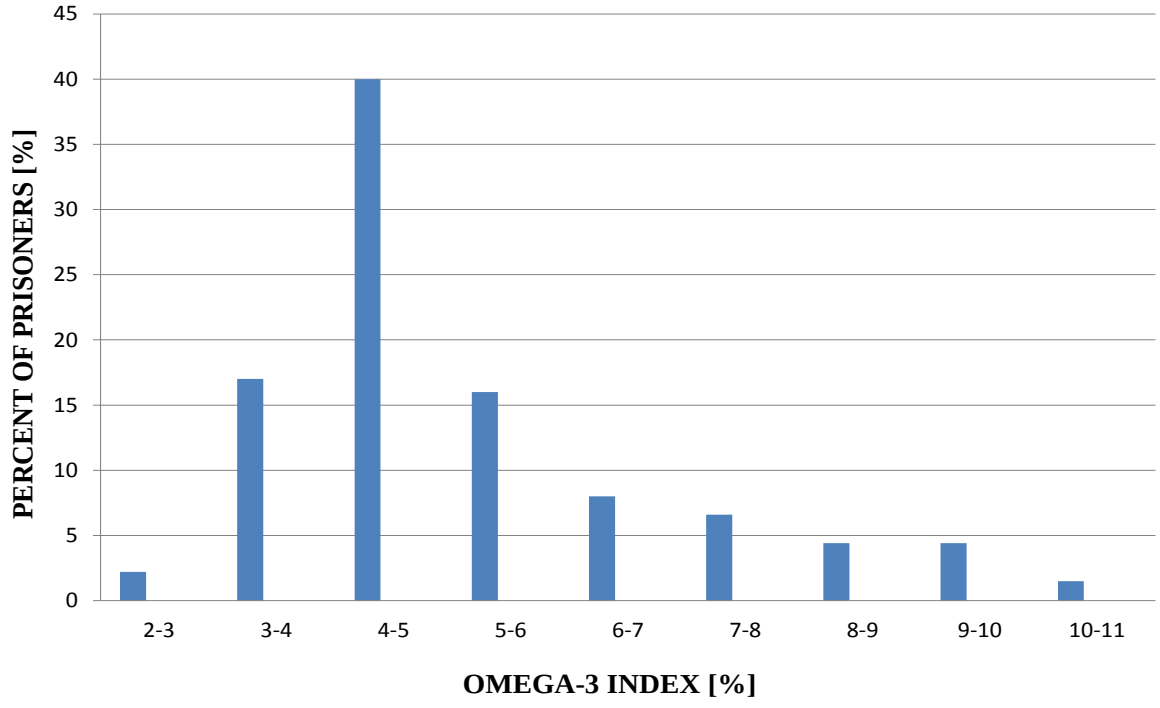

Figure 1. Omega-3 index in female prisoners calculated as a percentage of the sum of EPH and DHA of total fatty acid content in erythrocytes [5].

In meta-analysis research published in 2014 authors mentioned that patients who had received omega-3 fatty acids treatment had significantly reduced violent and antisocial behavior (35-37%) vs. patients receiving placebo (10%). The same conclusion can be found in another randomized controlled trial. Supplementation of 3n-PUFAs among 221 young adult prisoners reduced amount of aggressive behavior leading to incidents by 30%. Additionally, a decreased anger level was observed in prisoners. A study which included 23,020 women and their children showed that a diet rich in products containing omega-3 acids was correlated with a lower risk of both externalizing and internalizing behavioral [36].

Another research was a meta-analysis which included data from clinical trials, meta-analyses and systematic reviews published from 1980 to 2015. Aggression toward others, impulsivity and negative attitude were definitely lower in patients in the study group who were taking omega-3 fatty acids. The results of the study also suggest the possibility of using omega-3 acids to improve mood in patients suffering from depression. Additional omega-3 fatty acids treatment effect was the reduction of stress [4].

4. CONCLUSIONS

Omega-3 supplementation can be an effective complement to the pharmacological treatment of aggression. Researchers have shown a positive effect of omega-3 fatty acid supplementation on reducing aggressive behavior [4, 5, 34-36]. In addition, this method is safe and well tolerated by people and no major side effects were reported in patients receiving omega-3 fatty acids [34, 35]. However, some studies show a possible occurence of adverse effects [33]. The minor side effects observed included gastrointestinal adverse events like vomit, upset stomach, diarrhea, nausea, eructation and a fishy aftertaste [4, 33, 34]. Omega-3 fatty acids also provide many other health benefits. Researches proved good influence of supplementation on the heart, hepatic diseases and autoimmune system disorders [24, 25, 37, 38].

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