

Omega-3 Supplementation And Exercise-Induced Asthma: Not All Fish Oils Are Created Equal

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Citation

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Abstract

EDITORIAL

In the Paleolithic era 40,000 years ago (1), the hunter-gatherers foods were rich in long chain Omega-3 fatty acids with an estimated ratio of 1:1 of Omega-6 to Omega-3 fatty acids (2). In the Neolithic era 10,000 years ago animals were domesticated and farms grew various crops rich in Omega-6 fatty acids relative to Omega-3 fatty acids. This changed the intake of Omega-6/Omega-3 fatty acid ratio from 1:1 to anywhere from 15:1 to 50:1 in the modern era. Currently, the mortality rate from cardiovascular disease is estimated to be about 45/1000 population in Europe and the U.S. (2). In contrast, the Inuit from Greenland and Alaska have an estimated cardiovascular mortality of about 7/1000 population and still maintain a diet with an Omega-6 to Omega-3 ratio of 1:1 (2). The high Omega-3 level in the Inuit diet is felt to be secondary to a high fish and seafood intake. This striking data has spawned many studies to try to explain the fatty acid content of the diet in relation to cardiovascular disease and health. It appears that as a general concept the Western diet that is high in Omega-6 fatty acids and low in Omega-3 fatty acids promotes inflammation, atherosclerosis, and subsequent cardiovascular disease (2,3). Moving back to a diet rich in Omega-3 fatty acids with less Omega-6 fatty acids with a reduction in Omega-6 to Omega-3 ratio closer to one appears to lower secondary (4,5) and primary cardiovascular events in subjects at high risk (6).

Similar to cardiovascular disease, the Inuit have shown a low prevalence of asthma (7) and inflammatory markers as measured by C-reactive protein (low) and high red blood cell markers for the presence of long chain Omega-3 fatty acids (8,9). This has prompted study of the possible effects of Omega-3 fatty acids in asthma, a chronic inflammatory disease of the airways. An association between low dietary

intake of long chain Omega-3 fatty acids (OR 1.65, 95% C.I.; 1.18 to 2.39) versus higher intake and asthma in adolescents has been suggested in a cross-sectional study, although causality cannot be determined (10,11). When comparing Omega-3/Omega-6 ratios of polyunsaturated fatty acids (PUFA) in plasma and erythrocyte membranes as a surrogate for intake, PUFA ratios were significantly lower in asthmatics relative to healthy controls (12). Subdividing asthmatics by Omega-3/Omega-6 ratios of PUFA revealed higher exhaled nitric oxide (eNO) in asthmatics with low versus high ratios (12). When feeding house dust mite allergen sensitive asthmatics 0.7 gms/day of Omega-3 PUFA versus placebo for 5 weeks, there was a significant drop in eNO and in vitro cysteinyl leukotriene release in the Omega-3 PUFA diet group of asthmatics relative to regular diet asthmatics (13). Finally, one prospective cohort study followed those from age 18-30 at baseline and found an inverse association between intake of Omega-3 fatty acids and incident asthma (14). The adjusted hazard ratio for the highest versus lowest quintile of Omega-3 fatty acid intake was 0.46 (95% C.I.; 0.33 to 0.64). This protective effect was slightly attenuated in those on a high Omega-6 fatty acid diet (14).

Exercise challenge to precipitate c in relation to dietary fish oil supplements (long chain Omega-3 fatty acids) has been evaluated in at least three studies (15,16,17). The first study evaluated elite athletes who only had asthma secondary to exercise (15). The three week diet consisted of 3.2 g of eicosapentaenoic acid (EPA) and 2.2 g of docosahexaenoic acid (DHA) compared to a regular diet for three weeks. The results clearly showed less of a reduction in 15 minute post-exercise FEV1 back to the normal range with Omega-3 supplements compared to the placebo or normal diet. In addition, leukotrienes E4 and B4, tumour necrosis factor, interleukin-1beta, and 9 alpha, 11Beta prostaglandin F2 were

all reduced after exercise on the Omega-3 diet (15). Finally, the neutrophil lipid content of EPA increased in the Omega-3 diet and the arachidonic acid (AA) and linoleic content significantly decreased, relative to the normal diet. This provided evidence of compliance with diet, the speed with which lipid membranes can be changed with diet (3 weeks) and manifest a change in clinical response from baseline (3 weeks), and reveal rapid interactions with other lipids (15). A second study by the same authors found similar findings with subjects who were both known asthmatics and also had exercise-induced asthma (16). A third study in primarily mild asthmatics with exercise-induced asthma compared montelukast 10 mg daily versus a fish oil diet of EPA 3.2 g daily and DHA 2 g daily for 3 weeks (17). The outcome was prevention of exercise-induced bronchospasm as measured by eucapnic voluntary hyperventilation (EVH) after 3 weeks of treatment. Both the montelukast and a fish oil diet improved EVH-induced bronchospasm to a similar extent from baseline. Combining both treatments for 3 weeks gave no additive benefits compared with each individual treatment. In addition, all three treatments reduced eNO compared to baseline and the fish oil diet reduced urinary markers of inflammation after EVH stimulation. Finally, compared to baseline, bronchodilator use was reduced in all subjects on any treatment.

The current study compared the long chain Omega-3 fatty acid DHA 4 g daily versus placebo for three weeks to determine the effect of DHA without EPA (18). No effects were found compared to placebo in relation to improvement in EVH induced bronchospasm, expired breath condensate (EBC) pH, or EBC 8-isoprostane or protectin D1 concentrations. This is in contrast to the same authors previous studies using both EPA and DHA combined (15,16,17). Using the combination long chain fish oils resulted in a clear reduction in bronchospasm as measured by exercise (15,16) or EVH (used as a proxy for exercise,17) compared to a regular diet without fish oils.

One weakness of the current study was related to having no objective evidence that the subjects actually took the fish oil (18). Food frequency questionnaires, although validated, are not as certain as biochemical measurements of compliance. Pill counts to determine compliance do not prove that subjects actually ingested what was prescribed. In addition, EBC values were not different between groups which could simply reflect that DHA does not change values and EPA is also needed. It could also mean that subjects were not compliant with the treatment prescribed. Another weakness

of the study was the very small sample size. Based on previous studies the authors did calculate the sample size needed to find a difference if one was present and they evidently had an 80% power to detect a difference. However, the sample size was very small making individual variation between subjects a possible reason for not detecting a difference if one was present. A third weakness of the study might be the length of the study, only three weeks. The time course of DHA concentrations in different cell compartments can vary up to 1-6 months which might mean even if there were effects, treatment might need to be extended a bit longer (19). Therefore, there is some uncertainty related to the findings of this study (18). Conversely, the authors in previous studies have had objective evidence of ingestion of fish oil which was convincing (15,16,17). The previous studies also demonstrated a reduction in inflammatory markers and resolution of exercise-induced asthma with the combination of the two major long chain Omega-3 fish oils used, both EPA and DHA (15,16,17). These previous studies give the authors credibility in carrying out these studies and a sense this study may be correct.

Assuming the subjects were compliant with the DHA fish oil and the lack of benefit of DHA is present, this clearly shows in a short study that all fish oils are not created equal in relation to exercise-induced asthma. Although the conversion rate of DHA to EPA is up to 12% (20), this evidently was not enough to replenish EPA stores to act to improve exercise-induced asthma (18). Either EPA alone or EPA with DHA appears to be needed to improve exercise-induced asthma. If EPA alone is given, there is negligible conversion of EPA to DHA when given as a supplement (19,21). This means EPA supplements, if effective in preventing exercise-induced asthma would be without DHA influence. However, since there are many other beneficial effects of DHA it would still be prudent to give both EPA and DHA together if taken as a supplement.

If one believes that Omega-3 fatty acids are healthy and should be in one's diet, what would be some recommended minimal requirement? It is generally felt that the long chain Omega-3 fatty acids EPA and DHA cannot be synthesized effectively from dietary alpha-linolenic acid, with a rate of conversion of 5-10% and 2-5% in humans, respectively (22). Therefore, exogenous intake is required. A NIH working group suggested a minimal intake of a combination of EPA and DHA of at least 650 mg/day (22), which can be easily obtained from only 1200 mg fish oil tablet daily. If one is eating fish, a reasonable dose of nonfried fish intake would

be eating fish approximately twice per week to increase EPA and DHA to desired levels (23). Since frying fish may reduce the content of Omega-3 fatty acids, nonfried fish is preferred (23).

The NIH has listed at least three conditions where long chain Omega-3 fatty acids (fish or fish oil tablets) are highly recommended to improve health: high blood pressure reduction, secondary cardiovascular disease, and hypertriglyceridemia. There are more than 20 other conditions that have suggestive evidence to improve one's health. In addition, new studies continue to pour out of the literature suggesting improvements in health when taking the long chain Omega-3 combination EPA and DHA (24). When it comes to fatty acid intake and nutrition, it appears that moving back in time to the Paleolithic era would be reasonable.

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