Omega-3 fatty acids: a potential future treatment for asthma?

“"A number of studies have shown that omega-3 fatty acids may have beneficial effects in a number of asthma phenotypes, by serving as effective inflammatory antagonists and/or pro-resolving agonists.""
Involved in the resolution of inflammation, and also have anti-inflammatory activity. Moreover, it has been recently discovered that EPA and DHA are precursors of important pro-resolving autacoids, resolvins, protectins and maresins, which are powerful bioactive agents involved in the resolution of inflammation, and also have anti-inflammatory and immune regulatory activities, since they inhibit the production of inflammatory cytokines and decrease leukocyte recruitment and diapedesis [2]. Our laboratory has shown that a short-term (3 weeks) high dose of fish oil (3.2 g EPA and 2.2 g DHA) given daily reduces concentrations of proinflammatory mediators (LTC4-LTE4, prostaglandin [PG] D2, IL-1β and TNF-α) in the sputum of asthmatics [3], and that EPA is more effective than DHA in suppressing proinflammatory mediator generation (LTB4, PGD2, TNF-α and IL-1β) from LPS-stimulated cultured human asthmatic alveolar macrophages [4]. In addition, similar high daily doses of fish oil have also been demonstrated to compare favorably with Montelukast (Singular®), a LT receptor antagonist, in attenuating airway inflammation and hyperpnea-induced bronchoconstriction (HIB) in asthmatic patients [5].

Longer duration supplementation with lower doses of omega-3 fatty acids has also been shown to have pro-resolving effects upon airway inflammation. A small but significant improvement in forced expiratory volume in 1 s (FEV1) was observed in asthmatic adults taking a low-dose of fish oil (1 g/day of EPA and DHA) for 12 months [6]. While an intake of 120 mg/day omega-3 fatty acids [7] taken over 10 months, as well as 6 weeks of dietary supplementation with 1 g of triglyceride oil containing 30% EPA/DHA taken daily by children with bronchial asthma resulted in a significant improvement in lung function [8].

Recently, our laboratory [19] examined the therapeutic potential of a different form of marine oil (PCSO-524®; Lyprinol® Omega XL™), a patented extract of stabilized lipids from the New Zealand green lipped mussel, Perna canaliculus, in treating airway inflammation and HIB in asthmatic patients. PCSO-524® given daily (400 mg n-3 PUFA; 72 mg EPA and 48 mg DHA) over 3 weeks significantly reduced airway inflammation and bronchoconstriction following a dry gas airway challenge, bronchodilator use and improved mean asthma symptom scores. Our study [19] supports a number of other studies that have shown PCSO-524® is effective in treating human asthma [16] and allergic inflammation and lung function using a murine model of ovalbumin-induced allergic airway disease [17]. Since the levels of EPA and DHA in our study [15], and the Emelyanov et al. [18] study, using PCSO-524®, were very low, the physiological mechanism(s) behind the attenuation in airway inflammation and improvement in lung function are unclear. The potent anti-inflammatory action of PCSO-524® may be due to the fact that this extract contains up to 91 fatty acid components, and contains furan acids, which have been shown to possess more potent anti-inflammatory activity than EPA [18].

Important to asthma research, a recent study [19] has shown that single-nucleotide polymorphisms (SNPs) within genes involved in the resolution of inflammation, and also have anti-inflammatory activity. Moreover, it has been recently discovered that EPA and DHA are precursors of important pro-resolving autacoids, resolvins, protectins and maresins, which are powerful bioactive agents involved in the resolution of inflammation, and also have anti-inflammatory and immune regulatory activities, since they inhibit the production of inflammatory cytokines and decrease leukocyte recruitment and diapedesis [2]. Our laboratory has shown that a short-term (3 weeks) high dose of fish oil (3.2 g EPA and 2.2 g DHA) given daily reduces concentrations of proinflammatory mediators (LTC4-LTE4, prostaglandin [PG] D2, IL-1β and TNF-α) in the sputum of asthmatics [3], and that EPA is more effective than DHA in suppressing proinflammatory mediator generation (LTB4, PGD2, TNF-α and IL-1β) from LPS-stimulated cultured human asthmatic alveolar macrophages [4]. In addition, similar high daily doses of fish oil have also been demonstrated to compare favorably with Montelukast (Singular®), a LT receptor antagonist, in attenuating airway inflammation and hyperpnea-induced bronchoconstriction (HIB) in asthmatic patients [5].

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involved in de novo lipogenesis may have an impact on the varied plasma TG response following an intake of fish oil, and that these SNP's may affect gene regulation by unknown mechanisms. This varied response to fish oil may possibly be ascribed to genotype determined differences between subjects, and it is quite possible that a gene–diet interaction exists within a subgroup of asthma patients [20]; these particular asthmatic patients may have more than one polymorphism of specific genes in the 5-lipoxygenase (ALOX5) pathway, resulting in an increased production of the AA-derived proinflammatory LTs [20]. Nutraceuticals such as marine oils may play an important role in the treatment of this condition by inhibiting ALOX5, and the resulting proinflammatory mediators.

While a low intake of omega-3 fatty acids does not appear to be a safety issue and pharmaceutical-grade supplements are essentially mercury free, a few side effects of omega-3 fatty acid supplementation can occur, such as a fishy aftertaste, flatulence, acid reflux, bloating, diarrhea, nausea and possibly an increased risk of bleeding and immunosuppression with a high intake of omega-3 fatty acids.

In summary, a number of studies have shown that omega-3 fatty acids may have beneficial effects in a number of asthma phenotypes, by serving as effective inflammatory antagonists and/or pro-resolving agonists. Further large-scale clinical studies in asthmatic patients are required, with the aim to determine the minimum effective dose and duration needed to observe the beneficial effect of omega-3 fatty acid supplementation in asthma, and to determine the prevalence of a number of genotypes in asthma patients which may potentially identify responders and non-responders to therapy, and the existence of a potential gene–diet (omega-3 fatty acids) interaction.

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References
