

Focusing on Omega-3 Fatty Acids for Treatment of Obstructive Sleep Apnea and its Cardiovascular Complications

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ABSTRACT

The aim of this review is to focus on the role of omega-3 fatty acids on OSA and associated CVD risk, as well as provide novel hypotheses on their functional impact. Obstructive sleep apnea (OSA) is associated with increased cardiovascular disease (CVD) morbidity and mortality and is highly prevalent in obesity. The American Academy of Sleep Medicine recommends dietary induced weight-loss as a behavioral treatment option for OSA. Since a complex, rather than linear, relationship exists between weight loss and OSA improvement, dietary intervention studies must focus not only on the direct effects of weight loss, but whether dietary-quality may also affect OSA severity, through potential improvements in neuromuscular function of the upper airway.

Key words: Obstructive sleep apnea; Cardiovascular disease; Omega-3 fatty acids

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OBSTRUCTIVE SLEEP APNEA

Obstructive sleep apnea (OSA) is characterized by recurrent episodes of partial (hypopnea) or complete (apnea) collapse of the upper airway during sleep^[1], which result in oxygen desaturation and arousals despite ongoing inspiratory efforts. These symptoms have dire consequences on cardiovascular health. Indeed, OSA persists in a large proportion of patients with hypertension and other cardiovascular disorders; including coronary artery disease, stroke, and atrial fibrillation^[2]. The prevalence of OSA among the general population is approximately 2 to 7%, and has increased with the obesity epidemic^[3]. Although the precise mechanisms by which obesity increases the risk for OSA are not entirely understood, it is generally believed that increases in central adiposity impose mechanical loads on both the upper airway and respiratory system, predisposing the airway to collapse during sleep^[4]. Thus, weight loss is likely to improve sleep apnea severity through reductions in upper airway mechanical loads.

Weight loss for OSA treatment

The American Academy of Sleep Medicine^[5] recommends behaviorally induced weight loss as a viable treatment option for OSA. This recommendation has been bolstered by findings from large-scale clinical trials that have demonstrated improvement of OSA with interventions that incorporate calorie restricted^[6-7], or very low calorie diets^[8]. Furthermore, others have reported that the magnitude of reduction in apnea-hypopnea index (AHI), a measure of OSA severity, is associated with the degree of weight loss^[9-10]. On the contrary, a recent study found no difference in the change in AHI among OSA patients randomized to surgically induced weight loss or weight loss achieved through very low-energy diet, despite the greater weight loss being achieved in the surgically

treated group^[11]. These findings suggest a complex, rather than simple weight load pathogenesis of OSA. Indeed, central obesity is a source of pro-inflammatory cytokines (IL-6, TNF- α)^[12], known for their somnogenic central nervous system activity that may lead to pharyngeal neuromuscular dysfunction^[13]. Moreover, these cytokines have been found to induce the production of reactive-oxygen species, thereby promoting oxidative stress^[14] that has the ability to impair skeletal muscle force-generating capacity, and adversely affect upper-airway function through myopathic and neuropathic changes^[15]. In this context, it is interesting to consider how altering dietary quality might affect OSA severity beyond simply facilitating weight and fat loss. For example, omega-3 fatty acids are known for their anti-inflammatory and anti-oxidative properties, and therefore may have potential for treatment of OSA and related cardiovascular disease (CVD) complications.

OMEGA-3 FATTY ACIDS AND OSA

Omega-3 fatty acids are classified as polyunsaturated fatty acids; also known as essential fatty acids since they cannot be synthesized in the human body and must be obtained from the diet^[16]. The omega-3 family includes alpha-linolenic acid (ALA), eicosapentaenoic (EPA), and docosahexaenoic acids (DHA). ALA can be found in plant based foods (flaxseeds, canola, soy, perilla, and walnut oils), while EPA and DHA are found in marine foods (seafood and in greatest amounts in ‘fatty’ fish like sardines, herrings, scomber fishes as various mackerel species, salmon)^[16].

A previous cross-sectional study found an independent, inverse relation between red blood cell DHA-levels and OSA severity in 350 consecutive patients undergoing sleep studies, independent of age, body mass index, fish intake and fish oil supplements, alcohol consumption and smoking^[17]. Others have found that increasing the levels of marine omega-3 fatty acids in neuronal tissues can stabilize the upper airway innervations, musculature, and feedback control

systems^[18]. Since severe OSA is associated with increased expression of several pro-inflammatory cytokines (especially increased levels of IL-6, TNF- α) and oxidative stress within the muscular compartments of upper airway tissue^[19], the tissue concentration of the anti-inflammatory and anti-oxidative n-3 PUFAs may increase upper-airway muscle-contraction function via an improved upper airway muscle force-generating capacity of dilator muscles (Figure 1).

OMEGA-3 FATTY ACIDS AND OSA RELATED CVD COMPLICATIONS

Marine omega-3 fatty acids may also be able to reduce cardiac dysfunction and even the occurrence of premature death in patients with OSA. Higher blood levels of EPA plus DHA are associated with reduced fatal cardiac events. Both EPA and DHA^[20] have been associated with improving vascular and cardiac hemodynamics, endothelial function, controlled blood pressure, reduced hypertriglyceridemia, and reduced insulin-insensitivity^[21-23]. To what extent marine omega-3 fatty acids improve the OSA-associated cardiovascular-risks, requires further investigation.

CONCLUSION

The 2015 U.S. Dietary Guidelines for Americans^[24] recommends that the general population without established CVD morbidity should consume at least 250 mg/day of EPA+DHA in order to reduce the risk of CVD^[25]. In spite of these recommendations, the intake of marine omega-3 fatty acids is low among the average U.S. adult population (41 mg/day and 72 mg/day of EPA and DHA from foods and supplements, respectively)^[26]. Whether the aforementioned dietary recommendation or other doses of marine omega-3 fatty acids are suitable for OSA patients at high risk of CVD and with suboptimal marine omega-3 intake remains to be established. Future research is needed to examine the effect of marine omega-3 fatty acids on OSA severity and associated cardiovascular risk. Potential improvements in OSA severity may, in turn, lead to improvements in cardiovascular risk.

CONFLICT OF INTERESTS

The authors declare that they do not have conflict of interests.

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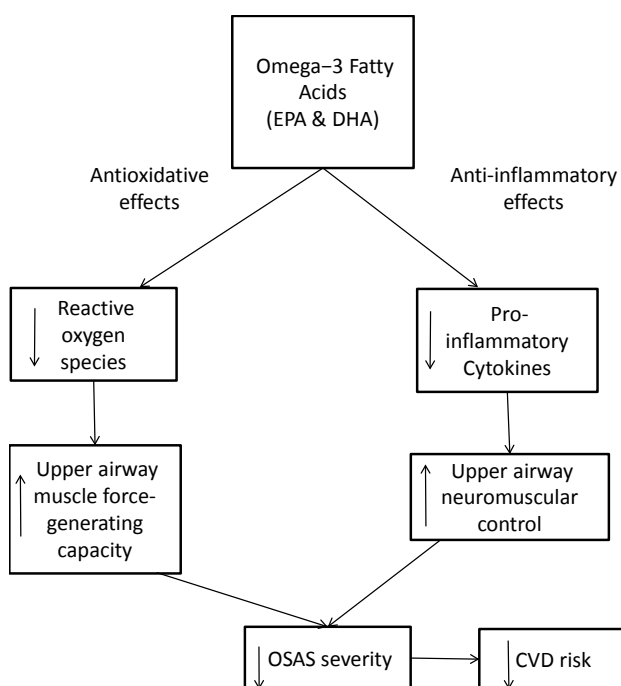


Figure 1 Schematic diagram indicates the possible mechanisms through which the marine omega-3 fatty acids may improve OSA severity and reduce CVD risk. EPA: eicosapentaenoic acid; DHA: docosahexaenoic acid; CVD: cardiovascular disease; OSA: obstructive sleep apnea.

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