

Dry Eye and Ocular Surface Disease

# Essential fatty acids in the treatment of dry eye syndrome A myth or reality?



Ammar M. Al Mahmood, MD, FRCS(Glasg.)<sup>a</sup>; Samar A. Al-Swailem, MD<sup>b,\*</sup>

## Abstract

Dry eye is a common condition that can severely impair the quality of life. Systemic and topical omega-3 fatty acids and omega-6 fatty acids have been used as treatment for patients with dry eye disease and showed promising results. Further multicenter randomized controlled trials are required in order to establish a standardized protocol for the treatment of dry eye syndrome with those essential fatty acids.

**Keywords:** Dry eye syndrome, Ocular surface tissues, Essential fatty acid

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## Introduction

Dry eye syndrome (DES) is a frequent cause of office visits due to ocular discomfort and commonly leads to problems with sustained visual activities.<sup>1</sup> These include problems during reading, using a computer, driving at night and carrying out professional work.<sup>2–3</sup> DES manifests more in elderly people.<sup>4–6</sup> Moreover, it affects women more selectively.<sup>7</sup>

DES is a complex condition involving the lacrimal glands, eyelids, and tear film, as well as a variety of ocular surface tissues including epithelial, inflammatory, immune, and goblet cells.<sup>8</sup>

Essential fatty acids (EFAs) have been of interest in the area of dry eye disease treatment. Both topical and systemic EFAs have been evaluated in regard to alleviation of DES manifestations. In this paper we try to review the literature in regard to efficacy of using EFAs to treat DES.

## Source of EFAs

EFAs are fatty acids that humans and other animals must ingest because the body requires them for good health but cannot synthesize them.<sup>9</sup> These are polyunsaturated fats.<sup>10</sup>

The EFAs omega-3 and omega-6 play pivotal functions and display a wide spectrum of positive effects in the body, such as: helping to lower cholesterol and triglyceride levels; giving energy to the body; helping to reduce acute and chronic inflammation; reducing respiratory and asthma-like symptoms; enhancing appropriate pre- and postnatal development mainly of the central and peripheral nervous systems; helping in the regulation of blood pressure; reducing the odds of developing cancer, heart disease, and stroke; managing emotional distress and depression; and benefiting patients with neurodegenerative disorders.<sup>11–16</sup>

Some of the food sources of omega-3 and omega-6 fatty acids are fish and shellfish,<sup>17,18</sup> flaxseed (linseed, (hemp oil,

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<sup>a</sup> Division of Anterior Segment, Dhahran Eye Specialist Hospital, Dhahran, Saudi Arabia

<sup>b</sup> Division of Anterior Segment, King Khaled Eye Specialist Hospital, Riyadh, Saudi Arabia

\* Corresponding author. Address: Division of Anterior Segment, King Khaled Eye Specialist Hospital, P.O. Box 7191, Riyadh 11462, Saudi Arabia. Tel.: +966 1 4821234x2044; fax: +966 1 4821234x3727.

e-mail address: [angelofsa@yahoo.com](mailto:angelofsa@yahoo.com) (S.A. Al-Swailem).

soya oil, canola (rapeseed) oil, chia seeds, pumpkin seeds, sunflower seeds, leafy vegetables and walnuts.<sup>10</sup>

### *Role of EFAs in the management of DES – pathogenesis*

Many hypothesize that the cause of dry eye is inflammatory. The omega-3 fatty acid eicosapentaenoic acid (EPA) and the omega-6 fatty acid arachidonic acid (AA) act competitively as substrate for both enzymes cyclooxygenase and 5-lipoxygenase. The anti-inflammatory action is believed to result from the synthesis of prostaglandin E3 (PGE3) and of leukotriene B5 (LTB5) (from EPA that inhibits the conversion of AA to potentially harmful inflammatory mediators prostaglandin E2 (PGE2) and leukotriene B4 (LTB4)).<sup>19</sup>

### *Role of systemic EFAs in the management of DES – clinical trials*

Multiple trials looked at the effect of oral supplement of omega-3 and omega-6 in the treatment of DES. A large cross sectional study by Miljanović et al.<sup>20</sup> has suggested that a higher dietary intake of omega-3 fatty acids is associated with a decreased presence of DES in women.

Barabino et al.<sup>21</sup> evaluated the effect of linoleic acid and gammalinolenic acid, on chronic ocular inflammation in 26 patients with aqueous-deficient keratoconjunctivitis sicca. Statistically significant changes in symptoms ( $P < 0.005$ ), lissamine green staining ( $P < 0.005$ ), and ocular surface inflammation ( $P < 0.05$ ) occurred in the study group compared with controls.

Aragona et al.<sup>22</sup> evaluated the effect of oral omega-6 essential fatty acids on PGE(1) tear content and signs and symptoms of ocular discomfort in patients with Sjögren's syndrome (SS). This was a randomized, double-masked, controlled, clinical trial involving 40 patients with primary SS. Twenty patients received omega-6 supplements while controls received placebo. In omega-6 treatment group significant changes were noted in the following: increased tear PGE1 levels, reduction of DES symptom score, and improved corneal fluorescein stain.

Wojtowicz et al.<sup>23</sup> investigated the potential effect of dietary supplementation with omega-3 fatty acid on lipid composition of meibum, aqueous tear evaporation, and tear volume in patients with dry eye. Thirty-six patients were included in this case-control trial whom received a daily dose of fish oil, containing 450 mg of eicosapentaenoic acid, 300 mg of docosahexaenoic acid, and 1000 mg of flaxseed oil for 90 days. At the end of the study, 70% of the patients treated with omega-3 supplements became asymptomatic and Schirmer testing together with fluorophotometry suggested that the omega-3 supplement increased tear secretion. A similar improvement was reported by Kokke et al.<sup>24</sup> in 76 patients with contact lens related DES following treatment with omega-6 supplements.

Tear film hyperosmolarity is a focal factor in dry eye. Larmo et al.<sup>25</sup> evaluated in a double-blind, randomized, parallel trial, effect of consumption of 2 g of sea buckthorn (SB) oil, containing omega-3 and omega-6 fatty acids and anti-oxidants daily for 3 months to improve dry eye symptoms. There was a general increase in the osmolarity from baseline to the end of the intervention. Compared with the placebo group,

the increase was significantly less in the SB group when all participants were included ( $P = 0.04$ ) and when only participants consuming the study products for at least 80% of the intervention days were included. This positively affected the dry eye symptoms.

Some reports tried to evaluate the effect of omega-3 deficiency on severity of DES. Viau et al.<sup>26</sup> evaluated whether a dietary deficiency in omega-3 may increase the severity of the pathology in a scopolamine-induced model of dry eye in the rat. Rats of three consecutive generations were bred under a balanced diet or a diet deprived of omega-3. Dry eye was experimentally induced by continuous scopolamine delivery in female animals from the third generation of both groups. Dryness was evaluated in vivo using fluorescein staining. Deficiency in omega-3 supplement does not increase the severity of dry eye in a rat model of dry eye.

Jackson et al.<sup>27</sup> evaluate the effect of a prescription-only medical food supplement containing omega-3 and omega-6 essential fatty acids on dry eye signs and symptoms, with or without concomitant topical cyclosporine. A proper balance of omega-3 and omega-6 essential fatty acids improved tear break up time and relieved patient symptoms. The addition of topical cyclosporine did not show any extra benefit.

### *Role of systemic EFAs in the reducing inflammation of DES – clinical trials*

Pinazo-Durán et al.<sup>28</sup> in a prospective case control study have evaluated clinical outcomes, and expression levels of inflammation and immune response mediators in human reflex tear samples in patients diagnosed with nonsevere DEDs whom received a combination of antioxidants and omega-3 essential fatty acids for three months. Levels of interleukin (IL)-1 $\beta$ , IL6, and IL10 in tears were significantly lower in the treatment versus control group. Subjective symptoms of dry eye significantly improved in the treatment group.

Brignole-Baudouin et al.<sup>29</sup> in a multicentre, double-masked, randomized, controlled trial demonstrated that supplementation with omega-3 and omega-6 fatty acids can reduce expression of HLA-DR conjunctival inflammatory marker and may help improve DES symptoms.

### *Role of topical EFAs in the management of DES – clinical trials*

Rashid et al.<sup>30</sup> used topical drops of ALA and linoleic acid EFAs in different formulations in a mouse model in which dry eye was both pharmacologically and environmentally induced.

Treatment with ALA significantly decreased corneal fluorescein staining compared with both vehicle and untreated controls. Additionally, ALA treatment was associated with a significant decrease in CD11b<sup>+</sup> cell number, expression of corneal Interleukin-1 $\alpha$  and Tumor necrosis factor (TNF) and conjunctival TNF. All these are important inflammatory mediators that are raised in DES patients.

## **Conclusion**

A clear answer exists to our concern: "Essential Fatty Acids in the treatment of Dry Eye Syndrome: A myth or reality?", as most of the studies suggest a beneficial role of

omega-3 and omega-6 supplement in reducing inflammation and improving DES symptoms. We therefore find it a reasonable practice to encourage higher consumption of foods rich with those EFAs initially followed by prescribing oral supplements in patients not satisfied with topical medications alone. Although it should be kept in mind that these supplements need some time to work and commitment from patients to achieve its desired goal. More studies are required in order to consider these supplements as part of an established protocol to treat DES.

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### Conflict of interest

The authors declared that there is no conflict of interest

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