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Exploring the Efficacy of Omega-3 Fatty Acid Supplementation in Dry Eye Disease: A Comprehensive Review

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ABSTRACT

Introduction

Dry eye syndrome, as defined by TFOS, is a multifactorial ocular surface disease with tear film instability, hyperosmolarity, inflammation, and neuro-sensory abnormalities. With a prevalence between 6.5% and 52.4%, it poses a substantial public health challenge, significantly affecting patients' quality of life. Omega-3 fatty acid supplementation is often suggested by clinicians as an adjunctive treatment, offering potential benefits across various levels.

Aim of the study

The purpose of the study was to investigate the effect of oral supplementation of omega-3 fatty acids on the treatment of dry eye syndrome.

Materials and methods

Literature selections of PubMed and Google Scholar databases from the last seven years (2016-2023) were performed. Articles were searched in English using the following keywords: dry eye disease; omega-3; fatty acid.

Results

Omega-3 fatty acids may have benefits in the treatment of dry eye syndrome, as argued by a number of potential mechanisms of action. However, the literature does not agree on the efficacy of their use in the treatment of dry eye syndrome, and thus there is insufficient evidence to bring omega-3 acids into the standard of treatment for dry eye syndrome.

Conclusion

Studies on the effect of oral supplementation of omega-3 fatty acids on the treatment of dry eye syndrome are at an early stage and need to be continued to improve knowledge. There is a need for further long-term studies to standardize conclusions about the efficacy of these acids in reducing dry eye symptoms.

Keywords: dry eye disease; omega-3; fatty acid.

I. Introduction

Dry eye syndrome (also known as dry keratoconjunctivitis) is defined by the Tear Film & Ocular Surface Society (TFOS) as "a multifactorial disease of the ocular surface characterized by loss of homeostasis of the tear film, and accompanied by ocular symptoms, in which tear film instability and hyperosmolarity, ocular surface inflammation and damage, and neuro-sensory abnormalities play etiological roles" [1]. Dry eye syndrome is common, with a prevalence oscillating between 6.5 and 52.4%, depending on different sources. In the United States, symptoms of the condition occur in about 14% of adults, more often in the elderly population, making it one of the most common reasons for ophthalmology consultations [2]. The increased incidence in the elderly is associated with atrophy of the lacrimal gland and gradual dysfunction that occurs after age 40. Other risk factors include female gender, history of estrogen therapy after menopause, use of antihistamines, adverse environmental conditions, complications from prolonged and frequent use of eye drops, stress, and complications of contact lens use [3].

Surgery on the surface of the eye, whether for commercial purposes or therapeutic indications (such as laser vision correction or cataract surgery), can also leads to dry eye syndrome. Postoperatively, this occurs through a number of mechanisms including the overuse of medicated eye drops containing preservatives, disruption of corneal innervation through corneal incisions, and inflammation caused by the surgery [4,5].

The use of electronic devices equipped with monitors is also a significant etiological factor, especially in today's context. The implementation of restrictions related to the coronavirus pandemic in 2019 has resulted in a widespread increase in computer usage for entertainment, education, and work. This trend has exacerbated the issue of dry eye syndrome among patients and provided an opportunity for further exploration of the relationship between these factors. Studies have observed that prolonged screen time can have adverse effects on the anterior surface of the eye. Extended use of a computer monitor reduces the frequency, amplitude and quality of blinks. The blink rate during screen work decreases from 18.4 blinks/min to 3.6 blinks/min, leading to a deterioration tear film quality and the potential chronic inflammation [6,7].

The occurrence of dry eye syndrome or its increased severity can also be associated with certain systemic diseases, including rosacea, Sjögren's Syndrome, RA, rheumatoid arthritis (RA), nicotine use or peripheral arterial disease. Therefore, it may manifest as a secondary condition [8, 9].

Dry eye syndrome is a chronic condition that significantly impacts the quality of patients' lives. It is marked by discomfort in the eye, a sensation of 'sand under the eyelids' or a foreign body, itching, burning, redness of the eyeball, swelling of the eyelids, fatigue and impaired vision, affecting various aspects of daily functioning [4]. The severity of dry eye symptoms varies among individuals, and the commonly used subjective Ocular Surface Disease Index (OSDI) questionnaire is often employed for assessment. Evaluation using the OSDI is conducted on a scale from 0 to 100, with values increasing directly in proportion to the severity of the disorder. The OSDI questionnaire is known for its high sensitivity and specificity, enabling the differentiation between healthy individuals and those affected by dry eye syndrome. It also allows for the assessment of severity categorized as normal, mild, moderate, or severe results [10,11].

While the pathogenesis of dry eye syndrome is not fully understood, it is recognized as a multifactorial condition. One of its primary causes is the disruption of homeostasis and hyperosmolarity of the tear film, leading to immune-mediated inflammation in the anterior segment of the eye [1,12]. In dry eye syndrome, cells on the ocular surface express pro-inflammatory mediators such as prostaglandins (PGE2), interleukins (IL-1) and leukotrienes. The chronic inflammation of the ocular surface affects the morphology of epithelial cells and results in a reduction in the density of conjunctival cup cells [6].

According to the latest definition of the disease created by TFOS DEWS II, it is crucial to emphasize that dry eye syndrome results in damage to the ocular surface and neurosensory impairment [1]. Among the previously mentioned risk factors, age stands out as one of the most significant. Beyond the age of 40, Meibom's glands become dysfunctional, contributing to the onset of eye syndrome in as many as 38-68% of individuals past this age threshold. Meibom's glands, when functioning properly, secrete meibum, which stabilizes the tear film, protecting the eye surface from drying out. Dysfunction of this glands after the age of 40 impairs this crucial mechanism. Furthermore, alterations in the composition of the tear film lead to chronic inflammation that involves the entire ocular surface. This progressive and self-perpetuating nature of the disease renders it resistant to treatment and may result in permanent damage to the ocular surface [4].

Current treatment strategies for dry eye syndrome encompass several approaches, including the enhancement of tear volume and quality, the reduction of ocular inflammation, adressing underlying eyelid disease, and implementing modifications to diet and lifestyle [4]. Patients commonly turn to preservative-free artificial tears containing moisturizing agents such as hyaluronate, trehalose, and dexpanthenol. Additionally, treatment may involve eyelid scrubs and eye drops with anti-inflammatory properties. Computer hygiene is also emphasized, encouraging frequent blinking and regular breaks to alleviate symptoms [1,13]. In cases where the above methods fail to provide sufficient relief and the dry eye syndrome is severe, second-line treatments involving corticosteroids or cyclosporine may be considered [14].

Numerous clinicians recommend dietary supplements containing omega-3 unsaturated fatty acids, specifically eicosapentaenoic acid (EPA) and docosahexaenoic acid (DHA), due to their promising anti-inflammatory effects. These acids can influence one of the factors contributing to disease symptoms. Moreover, omega-3 acids are generally well-tolerated and do not cause significant side effects [2].

II. Aim of the study

The purpose of the study was to investigate the effect of oral supplementation of omega-3 fatty acids on the treatment of dry eye syndrome.

III. Materials and methods

Literature selections of PubMed and Google Scholar databases from the last seven years (2016-2023) were performed. Articles were searched in English using the following keywords: dry eye disease; omega-3; fatty acid.

IV. Results

The potential supplementation of omega-3 fatty acids in the treatment of dry eye syndrome is grounded in their multi-faceted mechanisms of action. Firstly, their anti-inflammatory effects, both locally and systemically, play a crucial role. Omega-3 fatty acids exhibit anti-inflammatory effects by generating anti-inflammatory molecules through their breakdown and by promoting the synthesis of anti-inflammatory prostaglandins. These actions inhibit the inflammatory pathways associated with this condition. Animal studies have validated the anti-inflammatory effects of omega-3 fatty acids, demonstrating their ability to modify the phospholipid composition of the lacrimal gland and inhibit local inflammation [4]. Secondly, omega-3 fatty acids hinder the synthesis of pro-inflammatory substances and, as indicated by studies, confer a neuroprotective effect on the subbasal plexus of the cornea. This neuroprotective effect contributes to the normalization of tear osmolarity, which tends to be elevated in dry eye syndrome [6].

With these mechanisms of action in mind, many clinicians now recommend omega-3 fatty acid supplementation as an adjunctive treatment for dry eye syndrome. However, conclusions from studies are not entirely consistent. Therefore, a literature analysis covering the period since 2016 was conducted to summarize the current state of knowledge on this issue.

The Dry Eye Assessment and Management (DREAM) study was a multicenter, randomized, double-blind clinical trial investigating the effects of omega-3 fatty acid supplementation on symptoms of dry eye syndrome. The study enrolled 535 participants with moderate to severe dry eye disease, who were orally supplemented with 2g of eicosapentaenoic acid (EPA) and 1g of docosahexaenoic acid (DHA), or received a placebo (5g of olive oil) for a duration of 12 months. The extended supplementation period aimed to mitigate the impact of seasonal factors on dry eye syndrome symptoms and assess the safety of long-term use of these fatty acids. The study's unique design allowed for supplementation to be evaluated in a real-world setting, with conclusions applicable to clinical practice. The primary endpoint was the global Ocular Surface Disease Index (OSDI) questionnaire score compared to baseline. Additional parameters, such as tear film break-up time (BUT), Schirmer's Test, corneal examination using fluorescein (following the National Eye Institute [NEI] protocol), and conjunctival staining with lysamine green (according to NEI), among others, were also assessed and compared. However, the results after one year of omega-3 fatty acids and placebo showed no statistically significant difference between the groups, indicating a lack of efficacy of omega-3 fatty acids as an adjunctive treatment for dry eye syndrome [2, 8, 15-22].

In 2016, a randomized, placebo-controlled trial aimed to assess the efficacy of two oral forms of long-chain omega-3 fatty acids in patients with mild to moderate dry eye disease. Participants were assigned to one of three groups daily for 3 months: placebo, eicosapentaenoic acid (EPA) and docosahexaenoic acid (DHA) in two different oral forms. Outcome measures, assessed between days 1 and 90, included tear osmolarity score, Ocular Surface Disease Index (OSDI) questionnaire, mean changes in key clinical symptoms, and tear inflammatory cytokine levels. The study results revealed that moderate doses of both forms of long-chain unsaturated omega-3 fatty acids (1000mg EPA, 500 mg DHA) significantly reduced tear hyperosmolarity and improved tear film stability. Given the crucial role of these factors in the condition's pathogenesis, these improvements resulted in a clinically significant reduction in dry eye syndrome symptoms. On day 90, improvements in tear breakup time and eyeball redness were observed compared to the placebo for both forms of omega-3 fatty acids. Additionally, the use of omega-3 fatty acids led to a reduction in pro-inflammatory cytokine levels in tears. Considering these findings, the study demonstrated the multifaceted benefits of supplementation with both forms of these acids in the adjunctive treatment of dry eye syndrome [23].

A multicenter study conducted by Epitropoulos in 2016 assessed the effects of orally supplemented fatty acids on measures used in the treatment of dry eye syndrome. The study spanned a total of 12 weeks, during which patients were supplemented with either a placebo or omega-3 fatty acids. Throughout and after the 12-week period, the omega-3 treatment group exhibited a statistically significant decrease in tear osmolarity and an increase in omega-3 index levels. Moreover, global Ocular Surface Disease Index (OSDI) questionnaire scores significantly decreased in the omega-3 group, indicating an improvement in patients' symptom perception and the efficacy of omega-3 fatty acids [24].

In 2022, a study was conducted to assess the impact of orally administered polyphenols, including those found in omega-3 and omega-6 acids, on symptoms exhibited by patients with dry eye syndrome. The use of polyphenols for a duration of 12 weeks showed a statistically significant difference between baseline and endpoint values on both the Ocular Surface Disease Index (OSDI) questionnaire and tear film breakup time (BUT). Data from the study suggest that oral supplementation of polyphenols improves symptoms of ocular fatigue and enhances tear film stability, ultimately resulting in a reduction of symptoms in patients with mild to moderate dry eye syndrome [25].

V. Conclusion

Omega-3 fatty acids may have benefits in the treatment of dry eye syndrome, which is argued by a number of potential mechanisms of action and numerous studies conducted. However, the literature does not agree on the efficacy of their use in the treatment of dry eye syndrome, as there are studies showing no benefit. Therefore, there is no conclusive evidence to establish the efficacy and introduce guidelines for omega-3 fatty acid supplementation in dry eye syndrome. As highlighted, the prevalence of the condition is increasing affecting an already extensive portion of the population, which underscores the value of interventions in the area of relieving dry eye syndrome symptoms and improving patients' quality of life. The need for further research in this regard seems crucial and necessary, as contemporary work leaves no clear answer.

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