Original Article

Effect of Omega-3 Fatty Acid in Dry Eye Syndrome

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ABSTRACT

Introduction: Dry eye syndrome (DES) is a multifactorial disease of the ocular surface. It is accompanied by increased osmolarity of tear film and inflammation of the ocular surface.

Objective: To evaluate the impact of Omega-3 fatty acids in patients with DES and compare their effectiveness with topical lubricating agents in relieving subjective symptoms and improving clinical signs.

Methodology: A prospective interventional study involving patients diagnosed as 'moderate' to 'severe' Dry Eye Syndrome were included by convenience sampling. The inclusion criteria were patients above 20 years who were diagnosed as dry eye in the Outpatient Department in Nepal Eye Hospital. All the samples underwent detailed comprehensive eye examination, followed by a detailed dry eye evaluation. The severity of the dry eye was assessed both objectively based on 'Schirmer's-II test' and 'Tear Film Break Up Time (TBUT)', and subjectively by Ocular Surface Disease Index (OSDI) questionnaire. Each patient was prescribed Omega-3 fatty acid for three months and were followed up after one month and three months.

Result: The baseline Schirmers-II, TBUT and OSDI Score was 5.85 + 5.38 mm, 4.00 + 2.077 seconds, and 38.61 + 8.35 respectively. No significant change in the Schirmer's score was noted after the end of treatment period, but the TBUT and OSDI Score improved significantly.

Conclusion: This study shows that omega-3 fatty acid has significant role in improving TBUT and subjective symptoms in patients with dry eye syndrome but has no effect on the Schirmer's test.

Key words : Dry eye syndrome; omega-3 fatty acid; Schirmer's test; tear break up time.

Financial Interest : Nil
Conflict of Interest : Nil

Received : 10.09.2024
Accepted : 24.10.2025

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Access this article online
Website: www.nepjol.info/index.php/NEPJOPH
DOI: https://doi.org/10.3126/nepjoph.v17i1.69713

ISSN: 2072-6805, **E-ISSN:** 2091-0320

INTRODUCTION

Dry eye syndrome (DES) is a multifactorial disease of ocular surface. It is accompanied by inflammation and increased osmolarity of tear film (Messmer et al., 2015; Manish et al., 2020; AAO, 2013). Studies show different prevalence rates ranging from 14.6-57.5% (Kangari et al., 2013). Common symptoms of dry eye include reduced vision, difficulty reading, and increased discomfort during prolonged screen time or digital device use (Al-Mohtaseb et al., 2021). These DES symptoms can seriously affect patients' quality of life (Wróbel-Dudzińska et al., 2023; Benítez-Del-Castillo et al., 2017; Morthen et al., 2021).

The DES has been an important and interesting research over past few decades. Therapeutic regimens like extracellular Uridine-triphosphate (Wang et al., 2023), androgen hormones (Gorimanipali et al., 2023; Wang et al., 2021), and tear replacements containing recombinant forms of cytokines growth factors are currently under evaluation (Bhargava et al., 2013). Essential fatty acids in diet have shown to improve DES. Omega-6 and omega-3 fatty acids are among essential fatty acids that cannot be synthesised in the body and must be obtained from diet. Omega-3 fatty acids include alpha linolenic acid (ALA), eicosapentaenoic acid (EPA), and docosahexaenoic acid (DHA) (Swanson et al., 2012). Eicosapentaenoic acid and docosahexaenoic acid are derived from fish oil and have more potent immunomodulatory activity than ALA, which is derived from vegetable oils (Institute of Medicine (US), 2011). Omega-3 fatty acid seems to influence DES via restoring lipid layer in tear film by clearing meibomitis and increasing tear secretin from lacrimal gland (Lin et al., 2014). Dry eye symptoms are known to improve when omega-3 was used as adjunct therapy with other dry eye treatments.

This study aimed to evaluate the impact of Omega-3 fatty acids in patients with DES and compare their effectiveness with topical lubricating agents in relieving subjective symptoms and improving clinical signs.

METHODOLOGY

This was a prospective interventional study, conducted in accordance with the principles of the Declaration of Helsinki. Approval was obtained from the institutional review board of National Academy of Medical Sciences, Mahabouddha, Kathmandu, Nepal (Reference number: 649/2079/080). The possible consequences of the study were explained and all participants agreed to participate voluntarily. Written and oral informed consent was obtained from each participant.

After taking detailed history, patients were asked to fill a 12-point Ocular Surface Disease Index (OSDI) Dry Eye Questionnaire. The dry eye symptoms included itching, redness, burning, watering, discomfort, foreign body sensation and photophobia. After ascertaining the responses to each of the questions, the OSDI score were calculated. Patients who were found to have dry eye on this questionnaire with OSDI Score >23 were subjected to objective tests of tear function under room temperature conditions which included Tear film break up time (TBUT), Schirmers test and Blink rate. The TBUT of less than 10 seconds was considered abnormal. Schirmers test was performed by

using a Whatmann filter paper number 41 and the amount of wetting of the paper strip after five minutes was recorded. Blink rate was also determined by using corneal analyser CA800.

A total of 93 patients diagnosed as Dry Eye Syndrome based on OSDI Score >23 were enrolled in this study using convenience sampling technique. The exclusion criteria included: Patients under medications such as antihistamines, tricyclic, anti-depressants, oral contraceptives and diuretics, or an active contact lens wearer. Patients with active ocular infections, systemic illness and patients with previous history of ocular surgery were also excluded.

Patients were divided into two groups Group I and Group II. In Group I, Dry Eye was treated with artificial teardrops four times a day for three months and in Group II, patients were treated with omega-3 supplementation one tablet (500mg) per day. Patients were followed up at baseline, one month, and three months after treatment initiation. In each follow-up, all the study procedures were re-examined and the findings from consecutive follow-ups were recorded. Any patients lost during follow-up were discarded from the study.

IBM SPSS Statistics version 22 (IBM Corp., Armonk, NY, USA) was used in all statistical analyses. In the evaluation of the compliance of data with normal distribution, the Kolmogorov-Smirnov test was used. Values from groups that complied with normal distribution were evaluated with the paired samples t-test, and values that did not comply with normal distribution were evaluated with the Wilcoxon test. Differences between measurements were evaluated with independent t-tests and Mann-Whitney U tests between groups. Values of $p < 0.05$ were accepted as statistically significant.

RESULT

Out of 93 enrolled subjects, only 68 patients completed the first follow-up examination; all the examinations were completed by 60 patients (30 each in Group I and II). The mean age of the enrolled cohort in Group I and II was 32.46 ± 9.98 and 31.20 ± 9.94 years respectively. In Group I, thirteen patients were female and seventeen patients were male, while in Group II, fifteen patients were male and fifteen were female. The symptoms of dry eye among the enrolled subjects are charted (Figure 1). In Group I, foreign body sensation was the most common symptom, whereas in Group II, burning and stinging sensation was more prevalent.

In the clinical examination, Meibomian gland dysfunction was observed in eleven patients (three in Group I and eight in Group II). The baseline characteristics of dry eye examination of the enrolled patients is tabulated (Table 1). There was no statistically significant difference between two groups in terms of their baseline characteristics.

The dry eye parameters in the first and final follow-up are tabulated (Tables 2, 3). There was no statistically significant difference between the dry eye parameters in two groups following one month of treatment and following completion of the treatment.

The change in dry eye parameters from baseline to completion of study duration are tabulated (Table 4). In both groups, there was no significant change in Schirmers and TBUT score between

Baseline and first follow-up and baseline and final follow-up. A significant difference was observed in both groups in OSDI Score between baseline and first follow-up (p = 0.048; 0.031) and between baseline and final follow-up (p = <0.01; <0.01). In Group I, the OSDI score significantly decreased from 37.58 ± 8.19 at baseline to 30.13 ± 10.80 at the completion of the treatment (p = <0.01). Similarly, In Group II, the OSDI score lowered, from 36.79 ± 8.34 at baseline to 25.18 ± 7.61 at the completion of the study (p ≤0.01).

At the baseline, in Group I 63.33% patients had severe dry eye based on OSDI Score. At the end of the treatment, 66.67% and 33.33% patients had moderate and mild dry eyes respectively (Figure 2). Similar to Group I, in Group II as well at the end of the treatment, 66.67% and 33.33% patients had moderate and mild dry eyes (Figure 3).

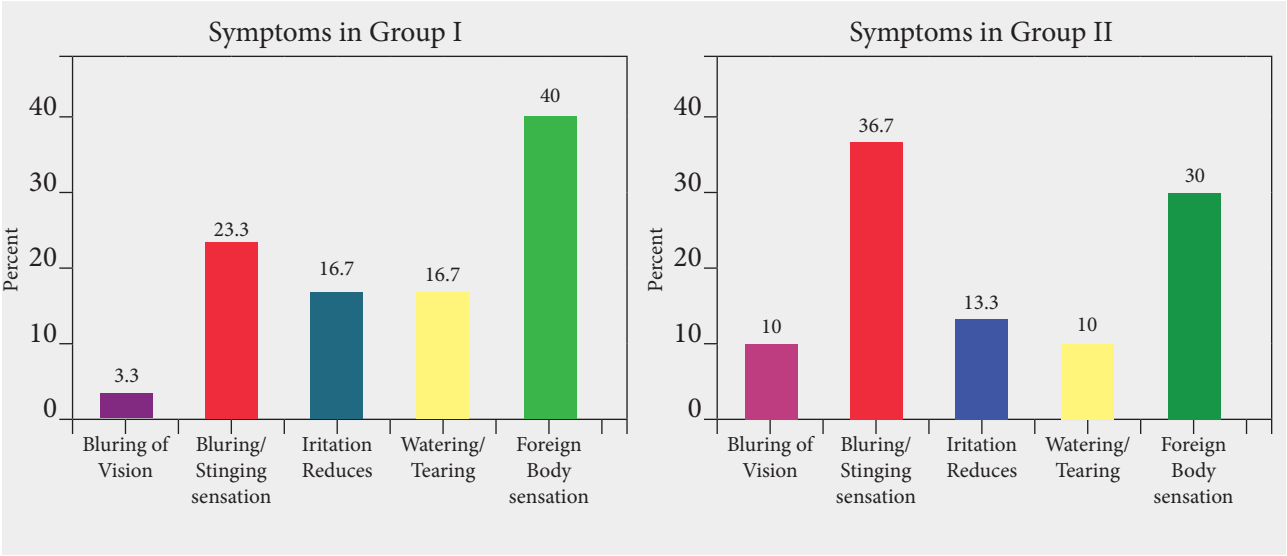

Figure 1: Symptoms of dry eye in the patients.

Table 1: Baseline dry eye parameters of enrolled subjects.

Baseline characteristics	Group I	Group II	p-value (t test)
Schirmers II	8.56 ± 8.32	7.86 ± 6.89	0.698
TBUT	4.26 ± 2.19	6.20 ± 3.61	0.08
OSDI Score	37.58 ± 8.19	36.79 ± 8.34	0.778
Blink Rate	13.6 ± 4.96	14.52 ± 5.23	0.56

Table 2: Follow-up dry eye parameters of enrolled subjects.

First follow-up	Group I	Group II	p-value (t test)
Schirmers II	8.10 ± 8.60	7.80 ± 8.96	0.857
TBUT	4.36 ± 2.18	4.36 ± 1.96	0.440
OSDI Score	34.26 ± 9.12	35.40 ± 8.86	0.625
Blink Rate	15.62 ± 3.26	16.25 ± 4.56	0.752

Table 3: Final dry eye parameters of enrolled subjects.

First follow-up	Group I	Group II	p-value (t test)
Schirmers II	8.76 ± 8.01	7.53 ± 5.00	0.361
TBUT	4.50 ± 2.38	5.03 ± 1.29	0.308
OSDI Score	30.13 ± 10.80	25.18 ± 7.61	0.063
Blink Rate	15.86 ± 4.12	15.36 ± 3.98	0.725

Table 4: Comparison of dry eye parameters between follow-ups.

Dry eye parameters	Baseline vs first follow-up		Baseline vs final follow-up	
	Group I	Group II	Group I	Group II
Schirmers II	0.926	0.841	0.414	0.562
TBUT	0.569	0.661	0.673	0.841
OSDI Score	0.048	0.031	<0.01	<0.01

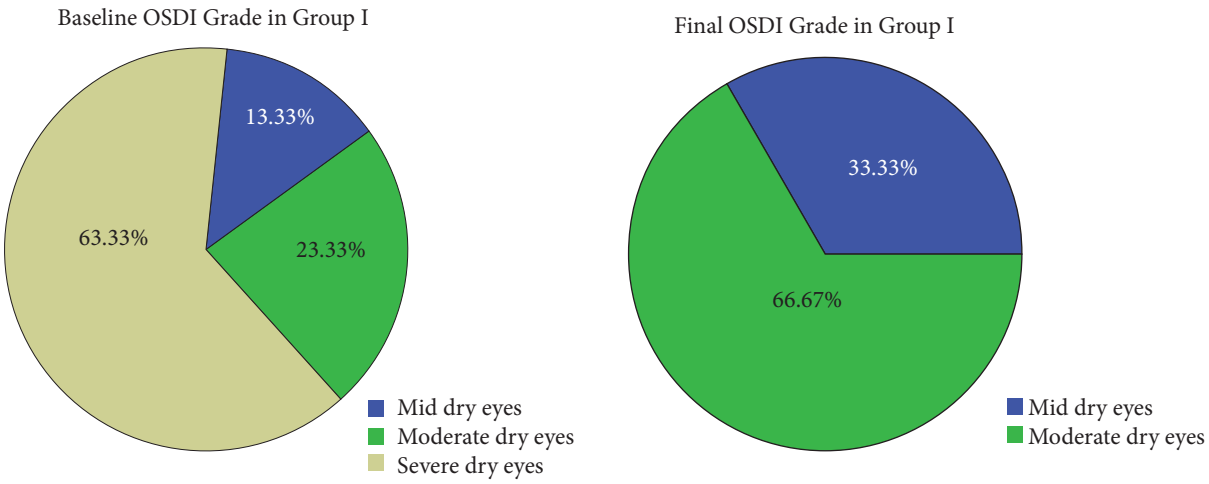

Figure 2: Ocular surface disease index grade in group I.

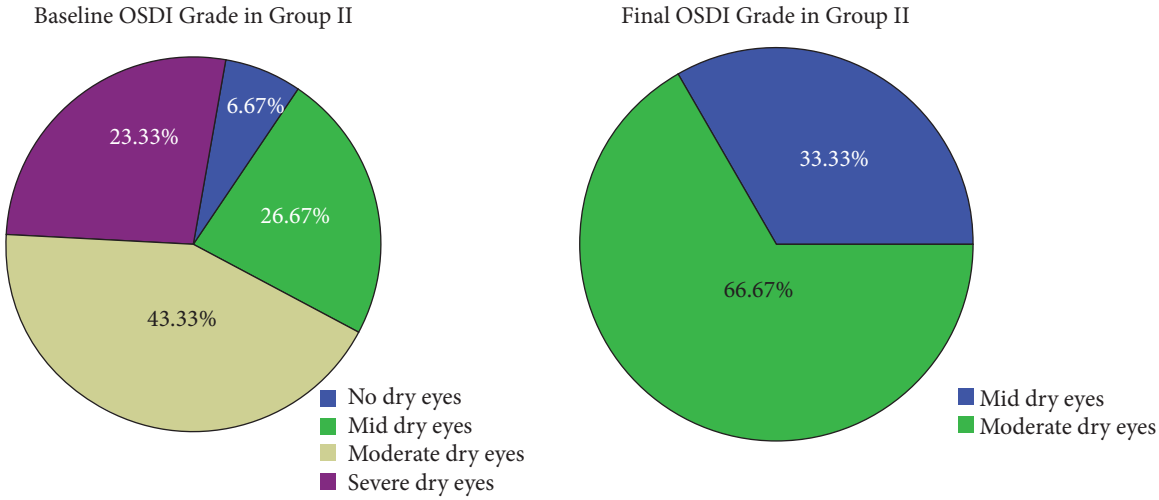

Figure 3: Ocular surface disease index grade in Group II.

DISCUSSION

In this hospital-based study, it was discovered that giving omega-3 fatty acids led to a reduction in OSDI scores in patients with DES. As, there is no universally agreed gold standard diagnostic test for the DES, a pragmatic approach was adopted for all of current study patients at each follow-up. This approach involved by applying standard objective and subjective tests as per the recommendations of the DEWS 2007 subcommittee, considering their practicality in general clinic, cost effectiveness and acceptability (DEWS, 2007).

In this study, the OSDI questionnaire was used as it is consider reliable and help to assess the severity, natural history and effects of dry eye. Compared to the Short Form 12- Health Survey, the National Eye Institute Visual Functioning Questionnaire, and the Mc Monnies Dry Eye Questionnaire, the OSDI questionnaire has a sensitivity of 60% and specificity of 79% (Schiffman et al., 2000).

Schirmer's test is used as the most common objective test for dry eye. This test is inaccurate and unrepeatable because of the reflex secretion produced by its invasive nature (Wright et al., 1962). The low cost of the strips, their case in application and the lack of availability of a more acceptable diagnostic test, has led to the schirmer test being the most commonly applied test for dry eye diagnosis.

TBUT measurement with fluorescein is another widely used method for diagnosis of dry eye by ophthalmologists. The TBUT test is considered more reliable than the Schirmer test, as it is repeatable and minimally invasive (Nivhols et al., 2004). However, the instillation of fluorescein can destabilise the tear film (Wang et al., 2007). The measurement of break up time in the absence of fluorescein can overcome this

problem and give a more accurate assessment of tear stability.

Omega-3 fatty acids cannot be produced by the body and need to be supplemented by diet. In diseases situations, polyunsaturated fatty acids control the arachidonic acid pathway and the inflammatory response. Animal experiments and clinical intervention studies indicate that omega-3 fatty acids have anti-inflammatory properties and, therefore, might be useful in the management of inflammatory and autoimmune diseases (Simopoulos et al., 2002).

In present study, subjects were divided in two groups: Group I treated with artificial tear and Group II treated with Omega-3 supplement for three months followed up for two consecutive months (Baseline, 1st and last follow-up) at the interval of 1 month each from day of enrollment where the changes over follow-ups of both Schirmer's test and TBUT scores did not significantly differ between baseline, the first and last follow-up in either group. However, in a study by Bhargava et al., (2013) which consists of placebo or control and interventional group, showed the significant difference regarding Schirmer's value. This may suggest that the treatment did not have a significant impact on tear production or tear stability.

Schirmer test at baseline value was 8.56 ± 8.32 for Group I whereas 7.86 ± 6.89 for group II which was observed 8.10 ± 8.60 mm and 7.80 ± 8.96 for Group I and II respectively in 1st follow-up and for final follow-up it increased to 8.76 ± 8.01 and 7.53 ± 5.00 for respective group. This change in Schirmer's test does not follow a clear cut trend and is therefore insignificant. No studies has shown such results. In a study by Kangari Het et al (2013) reported that the Schirmer's scores were significantly better in the treatment group by omega where the schirmer value increased from 6.0 ± 2.6 mm (baseline) to 6.8 ± 2.8 mm after intervention.

However, a significant difference was observed in the OSDI score between baseline and the first follow-up ($p = 0.048$; 0.031) and between baseline and the final follow-up ($p < 0.01$; < 0.01) in both groups. This indicates that the treatment had a positive effect on the subjective symptoms of dry eye. The OSDI score is a validated questionnaire that assesses the severity of dry eye symptoms, including ocular discomfort, visual disturbances, and impact on daily activities. The decrease in OSDI score suggests an improvement in the overall ocular surface health and reduction in dry eye symptoms.

In Group I, the OSDI score significantly decreased from 37.58 ± 8.19 at baseline to 30.13 ± 10.80 at the completion of the treatment ($p <0.01$). Similarly, in Group II, the OSDI score decreased from 36.79 ± 8.34 at baseline to 25.18 ± 7.61 at the completion of the study ($p <0.01$). These findings indicate that the treatment was effective in reducing dry eye symptoms in both groups. The improvement in OSDI scores suggests that the treatment modality used in this study effectively alleviated the subjective symptoms of dry eye. This finding is similar to the study by Kangari et al., (2013) and his colleagues.

However, it is important to note that the lack of significant changes in Schirmer's test and TBUT scores indicates that the treatment may not have directly influenced tear production or tear

stability. Further research is needed to explore the underlying mechanisms of the treatment and its impact on objective dry eye parameters.

CONCLUSION

Omega-3 fatty acid does not improve the clinical signs of dry eye, but significantly improves the subjective symptoms. Further studies are warranted to elucidate the long-term effects and mechanisms of action of the treatment modality used in this study.

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