

Role of Omega-3 fatty acids in meibomian gland dysfunction

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Abstract

Objective: To evaluate the role of omega-3 fatty acids in meibomian gland dysfunction (MGD). **Design:** This was a prospective randomized control study that included patients with MGD attending outpatient Department of Ophthalmology, Subharti Medical College, Meerut. **Subjects:** 40 patients of both sex above 40 years of age with MGD were included in the study. **Methods:** Age matched randomization of patients was done in two groups of 20 each. Patients in group A were given 2 capsules of 300 mg omega-3 fatty acids for 12 weeks while patients in group B were given a placebo oral supplement. Patients were examined at one-month interval for 3 months after the initial visit. At each visit Ocular Surface Disease Index (OSDI), Schirmer test, Tear film break up time (TBUT), Fluroscein staining and meibum quality score was evaluated. **Results:** After 3 months we found statistically significant improvement in subjective as well as objective parameters of group A patients (p value < .05) as compared to group B patients. **Conclusion:** Thus, dietary supplementation with omega-3 fatty acids is an effective treatment modality in meibomian gland dysfunction (MGD).

Key words: Meibum quality score, Meibomian gland dysfunction (MGD), Omega-3 fatty acids, Ocular Surface Disease Index.

Introduction

Meibomian gland dysfunction (MGD) is one of the most common causes of patient complaints in a comprehensive ophthalmology practice [1]. It is often difficult to distinguish the cause as there is a considerable overlap between blepharitis, MGD and dry eye [2].

Generally, the prevalence of MGD is higher in Asian population ranging from 46% to 70%, whereas in Caucasian population it ranges from 3.5% to 20% [3]. According to the International workshop on MGD, MGD is a chronic diffuse abnormality of the meibomian gland characterized by terminal duct obstruction and/or qualitative/quantitative changes in the glandular secretion [3]. It may result in alteration of the tear film, symptoms of irritation, clinically apparent inflammation and ocular surface disease [4].

Healthy meibum is essential for a healthy ocular surface as it constitutes to tear film stability and also provides a smooth optical surface at the air-tear interface [5].

In MGD, meibum is often abnormal progressively changing in colour from clear to yellow and in consistency from liquid to toothpaste like.

Studies have demonstrated that alteration in meibum in MGD results in production of toxic tear film destabilizing components such as fatty acids [6,7].

Additionally, ductal hyperkeratinization may result in blockage of the duct orifice and stagnation of meibum.

Inflammation is also an integral component of MGD. Increased expression of conjunctival markers of inflammation and proinflammatory mediators like cytokines and interleukins have been demonstrated in tear film of dry eye and MGD patients [8,9].

This inflammatory process ultimately disrupts the normal homeostatic functional unit responsible for normal tear production. Omega-3 and omega polyunsaturated essential fatty acids are precursors of lipid mediators known as eicosanoids that play an important role in regulating inflammation [10].

Omega-3 fatty acid eicosapentaenoic acid (EPA) and omega-6 fatty acid arachidonic acid compete for the same enzyme at the level of cyclooxygenase and lipoxygenase pathway [11].

The anti-inflammatory action is believed to result from the synthesis of prostaglandin E3 and leukotriene B5 from EPA that inhibits the conversion of arachidonic acid to potentially harmful mediators prostaglandin E2 and leukotriene B4. The two best sources of omega-3 fatty acids are flaxseed and cold water dark fish (salmon, tuna etc).

There are two hypothesis as to why dietary supplementation of omega-3 fatty acids may alleviate blepharitis and the resulting MGD and dry eye symptoms. The first hypothesis relies on the fact that the breakdown of omega-3 fatty acids results in the production of molecules that suppress inflammation, whereas the breakdown of omega-6 fatty acids result in the molecules that can lead to inflammation [10].

The second hypothesis regards the composition of tear. It has been suggested that an unstable tear film results from abnormal meibomian gland secretions and can in

evaporative dry eye. Supplementing the diet with high amounts of omega-3 fatty acids is likely to change the fatty acid composition and therefore the properties of meibomian gland secretions.

This change may be beneficial in tear stabilization and may prevent the inflammation from blocking the meibomian gland ducts and meibum stagnation [11].

Although MGD rarely threatens sight, it is a troublesome and symptomatic condition. Patients usually present with burning, watering, foreign body sensation, itching, erythema of lids and changes in eyelashes. The condition most typically has a chronic course with intermittent exacerbations of symptomatic disease. Many patients move from one doctor to another seeking relief from their symptoms.

Purpose of this study- The current treatment modalities for MGD include lid hygiene, warm compresses, artificial tears, topical antibiotic/steroid combination and systemic antibiotics which provide only temporary symptomatic relief. So, the present study has been undertaken to evaluate the role of omega-3 fatty acids in meibomian gland disease.

Material Methods

Study Design- This prospective randomized control study was conducted in Department of Ophthalmology, Subharti Medical College, Meerut between January 2018 and June 2018. It was performed after the approval of the institutional committee and an informed consent was taken from all the patients prior to the study.

A total of 40 patients of either sex above 40 years of age diagnosed with MGD and fulfilling the inclusion criteria were included in the study.

Sampling Method- Age matched randomization of patients was done in two groups of 20 each.

Group A- Patients were given Omega-3 fatty acids in recommended dose (2 capsules of 300 mg Omega-3 fatty acids twice a day for 12 weeks).

Group B- Patients were given a placebo oral supplement for 12 weeks.

Inclusion criteria- Patients above 40 years diagnosed with MGD according to criteria identified at 2011 International workshop on MGD [12].

Exclusion criteria

1. Active ocular infection or other allergic disorders.
2. Contact lens wearers
3. Ophthalmic laser treatment
4. Previous history of herpetic keratitis
5. Degenerative corneal disease.
6. Pregnant and lactating females.
7. Patients on systemic drugs like beta blockers, anti-cholinergics, anticoagulants etc.
8. Patients with other systemic diseases like increase bleeding tendency.

Clinical Examination- A detailed clinical history including age, sex, occupation, hormonal therapy, oral vitamin A treatment as well as history of systemic diseases like diabetes; hypertension or hyperthyroidism was taken from all the patients. At each visit, subjects were asked to complete the Ocular Surface Disease Index OSDI, an established measure of patient dry eye symptoms [12].

A score of 0 to 12 indicates a normal eye, 13 to 22 mild dry eye, 23 to 32 moderate dry eye and over 33 indicates severe dry eye. Thus, a decrease in OSDI score indicates improvement. At each visit complete ocular examination including visual acuity, intraocular pressure measurement and fundus examination was done. Objective clinical measures included tear production (Schirmer I with anesthesia), tear film stability (fluorescein Tear film break up time TBUT), ocular surface health (fluorescein staining) and meibomian gland health (meibum quality).

The Schirmer I test was performed with anesthesia. After instillation of topical anesthetic drops, Schirmer strip was placed in the lower fornix at the junction of lateral third and medial two thirds. The strip was removed after 5 min and a measurement of wet area of the strip was done.

Fluorescein TBUT was performed by touching a fluorescein strip to the inferior palpebral conjunctiva. Patients were asked to blink several times to mix the fluorescein with the tear film. They were then asked to open their eyes and not to blink and the time between the opening of the eyes and the appearance of first dry spot was measured in seconds. It was repeated three times and the average was taken as final TBUT.

Fluorescein ocular staining was performed by evaluating the corneal fluorescein stain 1 minute after fluorescein instillation by observing the cornea through a cobalt blue light. Corneal staining was graded using a scale of 0-3 (absent to diffuse) for 5 corneal regions. The final score was determined by totaling all individual scores for each eye.

The lid margin, lashes and meibomian glands were examined on slit lamp. Scoring of meibum character and colour was done as shown in table 1. A score of greater than 1.5 indicates healthy meibum.

Table-1: Meibum Character and Color Scores

Character Score	Description
0	Fluid
1	Thickened
2	Granular(particulates visible)
3	Toothpaste like
Color Score	Description
0	Clear
0.5	Yellow
1	White

Follow Up- Follow up of patients was done at 1,2 and 3 months after the initial visit. At each visit complete ocular examination was done including Ocular Surface Disease Index (OSDI), Schirmer 1 Test, Tear film break up time (TBUT), Corneal fluorescein staining and Meibum quality score.

Statistical Analysis- Statistical analysis was done using Microsoft Access database. Comparison between randomized groups was done using paired t test and p value < 0.05 was taken as statistically significant.

Results

Out of 40 patients recruited in the study, 38 patients completed the study. The mean age of patients was 49.36 years and majority of them were females (25 out of 38). Disease was bilateral in all patients. There was no significant difference in baseline symptoms and signs in the two groups. Throughout the study, the investigators and patients were blinded to the treatment assignments.

Table-2: Patient characteristics at baseline

Variable	Group A(Omega-3 FA)	Group B (Placebo)
OSDI Score (0-100)	36.3 ± 16.1	35.8 ± 22.5
Schirmer Score (mm)	5.84 ± 2.3	5.92 ± 1.7
TBUT (sec)	5.95 ± 0.76	5.88 ± 0.94
Fluorescein Staining (0-15)	2.2 ± 2.6	2.3 ± 1.5
Meibum Quality Score (0-4)	2.7 ± 0.9	2.5 ± 0.79

Table-3: Patient Characteristics At 3 months

Variable	Group A (Omega-3 FA)	P value	Group B (Placebo)	p value
OSDI Score (0-100)	15.7 ± 13.6	0.005	30.6 ± 12.8	0.4
Schirmer Score (mm)	10.94 ± 3.6	0.02	6.10 ± 1.3	0.5
TBUT (sec)	8.8 ± 1.2	0.007	6.7 ± 0.14	0.2
Fluorescein Staining (0-15)	2.04 ± 1.4	0.3	2.01 ± 0.48	0.6
Meibum Quality Score (0-4)	1.1 ± 0.46	0.02	2.1 ± 1.2	0.2

In our study, the patients supplemented with Omega-3 fatty acid noted a marked decrease in their symptoms at every visit. At 3 months the overall OSDI scores significantly improved in Group A patients ($p = 0.005$) as compared to Group B patients ($p = 0.4$).

Group A patients also showed a marked improvement in Schirmer score ($p = 0.02$) and TBUT ($p = 0.007$) at 3 months. On the contrary no significant improvement was seen in Group B patients ($p > 0.05$). However, fluorescein staining showed no significant change in both the groups at 3 months (p value > 0.05). The health of the meibomian glands and their secretions also showed a marked improvement in Group A. At 3 months, the average meibum quality significantly improved from granular at baseline to thickened or fluid and colour from white or yellow to clear in Group A ($p = 0.02$). No significant improvement was seen in Group B patients ($p = 0.2$).

Discussion

There has been great interest over the past decade in the role of dietary supplements in the management of meibomian gland dysfunction and the resulting dry eye. Current drug therapies have many side effects and do not offer a long-term satisfactory treatment. Thus, many patients move fruitlessly from doctor to doctor to seek a satisfactory solution to the problem.

Recently experimental studies have provided evidence that dietary supplementation of Omega-3 fatty acid modifies inflammatory and immune reactions making them potential therapeutic agents for inflammatory and autoimmune diseases. Omega-3 FA results in competitive inhibition of Omega-6 FA reducing the levels of inflammatory arachidonic acid oxidation products with formation of less active prostanoids [10]. Thus, Omega-3 fatty acids reduce overall inflammatory state of eyelid margin and meibomian glands.

To determine the effect of dietary supplementation with omega-3 fatty acids on MGD, we conducted a prospective randomized control study where 40 patients with MGD were randomly assigned to either the omega-3 or placebo group.

In our study, we evaluated subjective symptoms as well as objective signs in order to define the possible role of Omega-3 fatty acids in MGD. We found that Omega-3 FA's not only alleviates the patients symptoms but also improves the clinical markers of MGD as evidenced by positive drift in OSDI score, Schirmer score, TBUT and meibum quality score. None of the patients in our study reported any adverse effect of Omega-3 FA.

The only demerit is that that the drug is costly due to which some patients cannot afford it for long time.

Pinna et al. conducted a similar study in fifty seven patients with MGD and found that oral therapy with linoleic and linolenic acid along with eyelid hygiene improves symptoms and reduces eyelid margin inflammation in MGD more than either omega-6 FAs or eyelid hygiene alone [11].

Wojtowicz et al. concluded that dietary supplementation with Omega-3 FAs in MGD and dry eye showed no significant effect on meibum lipid composition or aqueous tear evaporation rate [13].

On the other hand, the average tear production and tear volume was increased in the omega-3 group as indicated by Schirmer test and fluorophotometry.

Olenik A et al. conducted a randomized double mask trial to evaluate the effect of Omega-3 FAs supplementation in MGD and found that oral Omega-3 FAs, 1.5 grams per day are beneficial as an adjunctive treatment of MGD, mainly by improving tear stability [14].

Macasai et al conducted a prospective randomized placebo controlled masked trial to evaluate the role of Omega-3 dietary supplementation in patients with blepharitis and MGD [15]. This trial demonstrated a decrease in the RBC and plasma ratios of Omega-6 to Omega-3 in patients taking Omega-3 dietary supplementation, as compared to controls, and improvement in their overall OSDI score, TBUT and meibum score. This study was the first to demonstrate an induced change in the fatty acid saturation content in meibum as a result of dietary supplementation with Omega-3 fatty acids.

Epitropoulos et al. demonstrated a significant improvement in dry eye symptoms from baseline with the oral ingestion of re-esterified omega-3 supplements for 12 weeks compared with those taking a control. The improvement of many of the signs were seen as early as 6 weeks suggesting a rapid response to nutritional therapy [16].

Opitz et al. suggested that if older patients were identified and treated before they became symptomatic, end-stage disease or MG atrophy may not occur [17]. Summerton suggested that Omega-3 dietary supplementation for blepharitis and MGD may decrease the red blood cell and plasma ratios of omega-6 to omega-3 and improve the overall ocular surface index score, TBUT and meibum score [18].

Nagpal et al. conducted a randomized control study to study the effects of Omega-3 fatty acids in patients with meibomian gland dysfunction. After 3 months, they found statistically significant improvement in mean OSDI, TBUT, Rose Bengal staining and Schirmer test. Thus they concluded that oral omega-3 fatty acids 1g per day is beneficial in the treatment of MGD [19].

Saif AT studied the role of oral linolenic acid dietary supplementation in posterior blepharitis and meibomian gland dysfunction. He found significant improvement in dry eye symptoms, TBUT, Schirmer test and meibomian gland orifices after 3 months and concluded

that oral linolenic acid (omega-3 fatty acids) is effective in treatment of moderate to severe chronic blepharitis and MGD [20].

In our study also we found statistically significant improvement in OSDI score, TBUT, Fluorescein staining and meibum quality score 3 months after oral omega-3 fatty acids. Thus, this study supports the role of inflammation in etiology of MGD and suggests that Omega-3 FA's may improve tear film stability and prevent the inflammation of lid margin, meibomian gland ducts and meibum stagnation.

Despite affecting millions and altering the quality of life the current treatment modalities for MGD are palliative and provide only temporary symptomatic relief. But with the better understanding of underlying pathophysiological process of disease, systemic omega-3 fatty acids have been found to have a positive effect on MGD by subsiding vicious cycle of ocular inflammation

Conclusion

We conclude that dietary supplementation with Omega-3 FA's either as an alternative or as an adjunct therapy holds great promise in the treatment of meibomian gland dysfunction and the resulting evaporative dry eye disease. Although the results of our study are encouraging but our study has certain limitations. The sample size is relatively small and follow up period is also short. So further work with a larger sample size and long term follow up is warranted to access the efficacy and safety of oral Omega-3 FA's in patients with meibomian gland dysfunction.

Contributions

- Dr. Charu Jain– central idea behind the study, main author of this study, workup and complete evaluation of all patients.
- Dr. V.K. Malik– arranged free medications for the patients included in study and also guided at each step during the study process.
- Dr. Rohan Bowry– helped in workup of patients, along with compilation of data and its statistical analysis

Funding: Nil, **Conflict of interest:** Nil

Permission from IRB: Yes

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How to cite this article?

Jain C., Malik V.K., Bowry R. Role of Omega-3 fatty acids in meibomian gland dysfunction. *Ophthal Rev: Trop J Ophthalmol Otolaryngol.* 2018;3(4):79-84. doi: 10.17511/joo.2018.i04.04

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