Oral linolenic acid dietary supplementation in posterior blepharitis and meibomian gland dysfunction

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Aim
The aim of this research is to study the role of oral linolenic acid (omega-3 fatty acids) dietary supplementation in posterior blepharitis and meibomian gland dysfunction (MGD) in patients attending the Outpatient Clinic at Fayoum University Hospital.
Patients and methods
Fifty patients with moderate to severe chronic blepharitis and simple obstructive MGD were included in the study. Patients received oral omega-3 dietary supplementation consisting of one 1000-mg capsule once daily and were examined every 6 weeks for 3 months. Objective clinical measures included tear production (Schirmer *I* with anesthesia), tear film stability (fluorescein tear break-up time), ocular surface health (fluorescein surface staining), tear meniscus height, plugged meibomian gland orifices, and eyelid telangiectasia.
Results
Twenty-four (48%) patients had an age between 45 and 60 years, 20 (40%) patients were more than 60 years old, and six (12%) patients were less than 45 years old. The male to female ratio was 1 : 2. Twelve (24%) male patients were smokers, whereas four (8%) female patients were using oral contraceptive pills. Twenty-two (44%) patients were hypertensive, whereas eight (16%) patients were diabetic. There was a significant improvement of dry-eye symptoms, signs, tear break-up time, Schirmer test, and meibomian gland orifices after 3 months of oral linolenic acid use.
Conclusion
The results after 3 months of treatment and follow-up were very satisfactory for the efficacy. Oral linolenic acid (omega-3 fatty acids) is effective in the treatment of moderate to severe chronic blepharitis and MGD.

Keywords:
blepharitis, meibomian gland dysfunction, omega-3 fatty acids, oral linolenic acid, Schirmer test, tear break-up time

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Introduction

About 20% of adults above the age of 45 years have some discomfort from blepharitis and meibomian gland dysfunction (MGD) [1].

Healthy meibum is essential for a healthy ocular surface, as the functions of the lipid layer include slowing evaporation of the aqueous tear components, enhancing tear film spreading and stability, preventing spillover of tears from the lid margin, preventing contamination of the tear film by sebum, and sealing the apposed lid margins during sleep. In addition, meibum contributes to providing a smooth optical surface at the air–tear interface, allowing for optimal vision [2].

In MGD, meibum is often abnormal, progressively changing in color from clear to yellow and in consistency from liquid to toothpaste-like. In addition, ductal hyperkeratinization may result in blockage of the duct orifice, deterioration of acini clusters, and stagnation of the meibum within the gland [3].

Obstructive MGD results in an unstable tear film, increased evaporation, meibomian gland dropout, thickened lipid secretions, and low lipid volume. Simple obstructive MGD is typified by plugged meibomian gland orifices and cloudy or thickened secretions. Cicatricial MGD is characterized by scarred marginal and tarsal mucosa, which causes exposure and retraction of the meibomian ductules. The patients often present with posterior displacement and/or elongation of the orifices into the marginal or tarsal conjunctiva. In patients with MGD, it is known that warm compresses will improve the tear

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stability. Evidence of alteration in the meibum melting point demonstrates that changes in the meibum content occur with MGD and result in the production of toxic tear film destabilizing components such as fatty acids (FAs) [4].

The inherent lid-margin inflammation, which is defined as part of blepharitis, affects the meibomian glands over time. MGD may be defined as progressive meibomian gland obstruction due to ductal hyperkeratinization or inspissation of secretions. MGD is synonymous with posterior blepharitis, particularly when chronic inflammation occurs, and may be obstructive, simple, or cicatricial in nature [5].

Although MGD rarely threatens sight, it is a troublesome and symptomatic condition. Many patients move from doctor to doctor, seeking relief from their symptoms. There is a general agreement that MGD is age-related, increasing in prevalence from nearly 0% in patients in the first decade of life to nearly 68% in patients over 60 years of age [5].

Patients with blepharitis typically present with symptoms of eye irritation, itching, erythema of the lids, and/or changes in the eyelashes [6,7].

Common complaints are burning, watering, foreign-body (FB) sensation, crusting and mattering of the lashes and medial canthus, red lids, red eyes, photophobia, pain, and decreased vision. The condition most typically has a chronic course with intermittent exacerbations and eruptions of symptomatic disease. In most types of blepharitis, there is some involvement of the meibomian glands [5,8,9].

Omega-3 FAs and omega-6 FAs are essential for normal growth and development. Omega-3 FAs and omega-6 FAs compete for the same enzyme to eventually be converted into anti-inflammatory prostaglandins 3 and less inflammatory leukotrienes and into proinflammatory prostaglandins 2 and more inflammatory leukotrienes, respectively [10,11].

There are two hypotheses as to why dietary supplementation of omega-3 FAs may alleviate blepharitis and the resulting MGD and dry-eye symptoms. The first hypothesis relies on the fact that the breakdown of omega-3 FAs results in the production of molecules that suppress inflammation, whereas the breakdown of omega-6 FAs results in the production of molecules that can lead to inflammation. The second hypothesis regards the composition of the tear film. It has been suggested that an unstable tear film results from abnormal meibomian gland secretions and can result in evaporative dry eye. Supplementing the diet with high amounts of omega-3 FAs is likely to change the FA 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 [10–12].

This study was designed to study the role of oral linolenic acid (omega-3 FAs) dietary supplementation in posterior blepharitis and MGD in patients attending the Outpatient Clinic at Fayoum University Hospital.

Patients and methods

This is a prospective observational study. The study was conducted in accordance with the principles of the Declaration of Helsinki and was approved by the Institutional Review Board of Fayoum University. All participants signed an informed consent before being enrolled in the study.

Fifty patients with moderate to severe chronic blepharitis and simple obstructive MGD were included in the study.

Inclusion criteria

The inclusion criteria were as follows:

(1) Patients with moderate to severe chronic blepharitis and simple obstructive MGD with onset of ocular symptoms (consistent with blepharitis, dry eye, and MGD) of more than a 3-month duration were included.
(2) The use of artificial tears was allowed during study participation.

Exclusion criteria

The exclusion criteria were as follows:

(1) Pregnant and nursing women.
(2) Patients on oral tetracycline drugs (including doxycycline and minocycline), oral corticosteroids, or any topical medications for at least 1 month before study enrollment.
(3) Young patients for whom oral linolenic acid is difficult to swallow or administer.

Patients received oral omega-3 dietary supplementation consisting of one 1000-mg capsule once daily and were examined every 6 weeks for 3 months.

Clinical examination

All patients had a detailed full medical history including age, sex, residency, occupation, menstrual history, history of hormonal therapy, hirsutism, oral vitamin A treatment, topical retinoic acid treatment, and history of systemic diseases – for example, diabetes mellitus, hypertension, or hyperthyroidism.

At the initial and final visit, patients had a complete eye examination including visual acuity, intraocular pressure measurement, and fundus examination.

Patients were asked about symptoms of ocular irritation, itching, lid hyperemia, ocular mucous secretion, photophobia, FB sensation, and dry-eye sensation.

Objective clinical measures included tear production (Schirmer I with anesthesia), tear film stability [fluorescein tear break-up time (TBUT)], ocular surface health (fluorescein surface staining), tear meniscus height, plugged meibomian gland orifices, and eyelid telangiectasia.

The Schirmer *I* test was performed with anesthesia. At least three drops of topical anesthetic eye drops were administered to the conjunctiva and both lid margins, to obtain the anesthesia of all the ocular structures. The strip was placed in the conjunctival sac at the junction of the lateral third to the medial two-thirds. Patients sat in the dark with both eyes closed for 5 min. The strips were removed and a measurement (mm) of the wet area of the strip was made.

Fluorescein TBUT was performed by damping a fluorescein strip with a drop of nonpreserved saline solution, and the strip was touched to the inferior palpebral conjunctiva. Patients were asked to blink several times to mix the fluorescein with the tear film. They were asked to open their eyes and not to blink, and the time between the opening of the eyes and the appearance of the first dry spot was measured in seconds. The test was repeated three times and the average of the three measurements was recorded as the final TBUT.

Fluorescein ocular surface staining was performed by evaluating the corneal fluorescein stain 1 min 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).

Meibomian gland health and meibum character were determined by assessing the percentage of gland blockage (orifice visible but no meibum expressible) and stenosis (orifice not visible, no meibum expressible) and by grading gross meibum character (Table 1).

The lid margin, lashes, and meibomian glands were examined with the slit lamp. The presence or absence of collarettes, madarosis, and distichiasis was noted. Lid-margin telangiectasia was graded on a scale of 1–4.

Scoring of meibum character and color is shown in Table 1. A score of greater than 1.5 indicates healthy meibum.

Results

Out of the 50 patients with moderate to severe chronic blepharitis and simple obstructive MGD, it was found that 20 (40%) patients were more than 60 years old, 24 (48%) patients were between 45 and 60 years old, and six (12%) patients were less than 45 years old (Table 2). The male to female ratio was about half (Table 3). Twelve (24%) patients were smokers, and all were male. Only four (8%) female patients were using oral contraceptive pills. Twenty-two (44%) patients were hypertensive, whereas eight (16%) patients were diabetic.

Watering was the presenting symptom in 54% of the patients. Burning and FB sensation were the presenting symptoms in 32% of the cases, whereas red lids and eyes were found in 14% of the cases.

At baseline, 37 (74%) patients had moderate watering of the eye, whereas 13 (26%) patients had severe

Table 1 Meibum character and color

Meibum	Score
Meibum character	
Fluid	0
Thickened	1
Granular	2
Toothpaste-like	3
Meibum color	
Clear	0
Yellowish	0.5
White	1

Table 2 Distribution of chronic blepharitis and simple obstructive meibomian gland dysfunction cases according to age

Age groups	*N* (%)
<45 years	6 (12)
45–60 years	24 (48)
>60 years	20 (40)
Total	50 (100)

watering. At 6 weeks following the use of oral linolenic acid (omega-3 FAs), seven (14%) cases had mild watering, 33 (66%) cases had moderate watering, and 10 (20%) cases had severe watering. At 3 months, 27 (54%) cases had mild watering, 20 (40%) cases had moderate watering, and three (6%) cases had severe watering. There was a statistically significant improvement in watering with treatment compared with baseline (Table 4).

At baseline, 11 (22%) cases had mild burning and FB sensation, 20 (40%) cases had moderate burning and FB sensation, and 19 (38%) cases had severe burning and FB sensation. At 6 weeks after the use of linolenic acid, 27 (54%) cases had mild burning and FB sensation, 14 (28%) cases had moderate burning and FB sensation, and nine (18%) cases had severe burning and FB sensation. At 3 months, 35 (70%) cases had mild burning and FB sensation, 12 (24%) cases had moderate burning and FB sensation, and three (6%) cases had severe burning and FB sensation. There was a significant improvement in burning and FB sensation with treatment (Table 4).

At baseline, 23 (46%) cases had mild itching and hyperemic lids, 19 (38%) cases had moderate itching and hyperemic lids, and eight (16%) cases had severe itching and hyperemic lids. After the oral use of linolenic acid, at 6 weeks, 34 (68%) cases had mild itching and hyperemic lids, 11 (22%) cases had moderate itching and hyperemic lids, and five (10%) cases had severe itching and hyperemic lids. At 3 months, 39 (78%) cases had mild itching and hyperemic lids, seven (14%) cases had moderate itching and hyperemic lids, and four (8%) cases had severe itching and hyperemic lids. There was a significant improvement in itching and lid hyperemia with oral use of linolenic acid (Table 4).

At baseline, the TBUT was greater than 10 s in seven (14%) cases, 6–10 s in 20 (40%) cases, and less than 6 s in 23 (46%) cases. At 6 weeks after the oral use of linolenic acid, 15 (30%) cases had TBUT greater than 10 s, 18 (36%) cases had TBUT of 6–10 s, and 17 (34%) cases had TBUT of less than 6 s. At 3 months, 24 (48%) cases had TBUT greater than 10 s, 16 (32%) cases had TBUT of 6–10 s, and 10 (20%) cases had TBUT less than 6 s. The mean TBUT was 4.8±3.0 s at baseline and improved to 8.3±4.8 s at 3 months after treatment, which is a statistically significant difference (Table 5).

In the Schirmer test, at baseline, 13 (26%) cases had wetting of greater than10 mm of Schirmer strip, 29 (58%) cases had wetting of 6–10 mm of Schirmer strip, and eight (16%) cases had wetting of less than 6 mm of Schirmer strip. After the use of linolenic acid, at 6 weeks, 15 (30%) cases had wetting of greater than 10 mm of Schirmer strip, 27 (54%) cases had wetting of 6–10 mm of Schirmer strip, and eight (16%) cases had wetting of less than 6 mm of Schirmer strip. At 3 months, 28 (56%) cases had

Table 3 Male/female ratio

Male/female	*N* (%)
Male	18 (36)
Female	32 (64)
Total	50 (100)

Table 4 The difference in symptoms at baseline, 6 weeks, and 3 months following oral linolenic acid (omega-3 fatty acids)

Symptoms	Baseline [*N* (%)]	6-week [*N* (%)]	3-month [*N* (%)]	*P*-value
Watering				
Mild	– (0)	7 (14)	27 (54)	0.049
Moderate	37 (74)	33 (66)	20 (40)	
Severe	13 (26)	10 (20)	3 (6)	
Total	50 (100)	50 (100)	50 (100)	
Burning and foreign-body sensation				
Mild	11 (22)	27 (54)	35 (70)	0.038
Moderate	20 (40)	14 (28)	12 (24)	
Severe	19 (38)	9 (18)	3 (6)	
Total	50 (100)	50 (100)	50 (100)	
Itching and redness in lids				
Mild	23 (46)	34 (68)	39 (78)	0.045
Moderate	19 (38)	11 (22)	7 (14)	
Severe	8 (16)	5 (10)	4 (8)	
Total	50 (100)	50 (100)	50 (100)	

Table 5 The difference in signs at baseline, 6 weeks, and 3 months following oral linolenic acid (omega-3 fatty acids)

Signs	Baseline [*N* (%)]	6-week [*N* (%)]	3-month [*N* (%)]
TBUT (s)			
>10	7 (14)	15 (30)	24 (48)
6–10	20 (40)	18 (36)	16 (32)
<6	23 (46)	17 (34)	10 (20)
Total	50 (100)	50 (100)	50 (100)
Mean	4.8±3.0	6.6±3.2	8.3±4.8
P-value		0.052	0.003
Schirmer *I* test (mm)			
>10	13 (26)	15 (30)	28 (56)
6–10	29 (58)	27 (54)	15 (30)
<6	8 (16)	8 (16)	7 (14)
Total	50 (100)	50 (100)	50 (100)
Mean	10.0±6.7	12.8±8.1	11.6±6.5
P-value		0.577	0.138
Corneal staining grades 0–5			
Mean	1.2±1.2	0.7±0.8	0.6±0.7
P-value		0.006	0.025

TBUT, tear break-up time.

wetting of greater than 10 mm of Schirmer strip, 15 (30%) cases had wetting of 6–10 mm of Schirmer strip, and seven (14%) cases had wetting of less than 6 mm of Schirmer strip. However, there was no statistically significant difference in the mean value of Schirmer's test between the baseline and 6-week and 3-month visits (Table 5).

In addition, there was a significant improvement in mean corneal staining grade at 6 weeks and 3 months following treatment compared with baseline (Table 5).

Meibomian gland orifices were visible in 20 (40%) patients at baseline, whereas 25 (50%) patients had stenosed meibomian gland orifices and five (10%) patients had blocked meibomian gland orifices. After the oral use of linolenic acid, at 6 weeks, 31 (62%) patients had visible meibomian gland orifices, 16 (32%) patients had stenosed meibomian gland orifices, and three (6%) patients had blocked meibomian gland orifices. At 3 months, 35 (70%) patients had visible meibomian gland orifices, 12 (24%) patients had stenosed meibomian gland orifices, and three (6%) patients had blocked meibomian gland orifices. However, there was no statistically significant difference between the mean baseline value and the 6-week and 3-month follow-up values (Table 6).

Discussion

The purpose of the present study was to determine the effect of oral linolenic acid (omega-3 FAs) dietary supplementation in blepharitis and MGD. Fifty patients diagnosed as moderate to severe chronic blepharitis and MGD were included in the study.

The present study reported that the male to female ratio was almost 1–2. Although the biochemistry of inflammatory pathways of men and women are the same, the role and levels of androgens are different. As androgens play a role in both the meibomian and lacrimal glands, there may be a difference in the effect of omega-3 dietary supplementation in men versus women. The present study participants' numbers were too low to segregate results based on sex. Therefore, further studies including more patients are recommended.

Table 6 The difference in meibomian gland orifices and stages at baseline, 6 weeks, and 3 months following oral linolenic acid (omega-3 fatty acids)

Meibomian gland	Baseline [*N* (%)]	6-week [*N* (%)]	3-month [*N* (%)]
Orifices			
Visible	20 (40)	31 (62)	35 (70)
Stenosed	25 (50)	16 (32)	12 (24)
Blocked	5 (10)	3 (6)	3 (6)
Total	50 (100)	50 (100)	50 (100)
Stages 0–3	1.9±0.6	1.7±0.7	1.6±0.7
P-value		0.886	0.338

The present study included a comparison of patients presenting symptoms and signs at baseline and after 3 months of intake of oral linolenic acid (omega-3 FAs) – for example, patients' symptoms (watering, itching, hyperemic lids, burning, and FB sensation), TBUT, Schirmer *I* test, and meibomian gland orifices.

Pinna *et al.* [10] found that therapy with linoleic and γ-linolenic acid tablets along with eyelid hygiene improves symptoms and reduces eyelid margin inflammation in MGD more than either omega-6 FAs or eyelid hygiene alone.

Wojtowicz *et al.* [13] concluded that dietary supplementation with omega-3 FAs in dry eye showed no significant effect on meibum lipid composition or aqueous tear evaporation rate. On the other hand, the average tear production and tear volume was increased in the omega-3 group as indicated by both Schirmer testing and fluorophotometry. In the present study, the mean Schirmer *I* score was 8.74 mm, which improved to 9.74 mm after 3 months of oral linolenic acid.Macsai [14] concluded that experimental studies have provided evidence that dietary supplementation of omega-3 FAs modifies inflammatory and immune reactions, making omega-3 FAs potential therapeutic agents for inflammatory and autoimmune diseases and stated that there is a clear need for more carefully designed and controlled clinical trials in the therapeutic application of omega-3 FAs in blepharitis and MGD.

In the present study, results revealed that there was significant improvement in TBUT. The mean TBUT was 4.8±3.0 s and improved to 8.3±4.8 s after 3 months of oral linolenic acid.

Epitropoulos *et al.* [15] demonstrated a significant improvement in dry-eye signs and 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 was seen as early as 6 weeks, suggesting a rapid response to nutritional therapy [15].

Opitz *et al.* [16] suggested that if older patients were identified and treated before they became symptomatic, end-stage disease or MG atrophy may not occur.

Summerton [17] 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.

Conclusion

In the present study, patients with MGD were given oral linolenic acid (omega-3 FAs). The results after 3 months of treatment and follow-up were very satisfactory for efficacy. Therefore, oral linolenic acid (omega-3 FAs) is effective in the treatment of moderate to severe chronic blepharitis and MGD.

More studies are recommended to include more patients with long-term follow-up.

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Nil.

Conflicts of interest

There are no conflicts of interest.

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