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Dry Eye Changes After Phacoemulsification After Using Oral Linoleinic Acid (Omega 3 Fatty Acids)

Abd Elrahman Shaban Ahmed Abd Elaleem [a], *Doaa Mohamed Ahmed Ahmed* [a] *and Mohamed Yasser Sayed Saif* [a]

a Ophthalmology department, Faculty of Medicine, Beni-Seuf University, Egypt

Abstract:

The current study was designed to evaluate the effect of oral linoleinec acid (omega 3 fatty acid) on patients who complained from dryness after Phacoemulsification. It was a Cross-Sectional study conducted first of April 2020 to end of February 2021 in the ophthalmology department at Beni-Suef University Hospital, and included 107 participants that had Phacoemulsification surgery, (60.7% males and 39.3% females), their age ranged from (48) to (71) with an average age of (62.07 ±6.03) years old. All participants were subjected to full clinical and laboratory investigations and received oral linoleinic acid capsules 1000 mg for 3 months after operation. Dry-eye markers including the ocular surface disease index (OSDI) and subjective symptom questionnaire, tear-film assessment using Schirmer testing 2, and break–up time test was sequentially evaluated preoperatively and postoperatively at 1st day,1st week, 1st month, 2nd month and 3rd month .Written Informed consent had been taken from all studied participants prior to beginning of the study. OSDI scores decreased significantly between baseline and three months post-operatively, YBUT scores increased significantly between baseline and three months post-operatively and Schirmer test scores increased significantly between baseline and three months post-operatively. Based on our results, oral omega-3 supplements could be safely added to the postoperative protocols following phacoemulsification to reduce the incidence of postoperative dry eye syndrome.

Keywords: Cataract, Phacoemulsification, (omega 3 fatty acid).

1. Introduction:

Cataract is currently the main cause of avoidable blindness especially in the developing world accounting for about three quarters of blindness. In developed world phacoemulsification is the primary method of performing cataract surgery. However, in many developing countries involving the majority of cataract blindness in the world today, phacoemulsification is not viable due to density of cataract involved and high cost of the equipment [1].

Phacoemulsification has become the preferred method of cataract extraction over the last 15 years [2], [3]. Phacoemulsification affect tear production post operatively in cataract patient, whose schirmer 1 test had decreased, causing a risk for the cornea to be damage and dry eye symptoms [4].

Dry eye symptoms were characterized by burning, stinging, redness, sensation of a foreign body, photophobia and blurred vision and scored by the grades of 0, 0.5, 1 or 2.

- Grade 0: no dry eye symptoms.
- Grade 0.5: trace or seldom of dry eye symptoms.
- Grade 1: sometimes or mild dry eye symptoms.
- Grade 2: frequent or moderate dry eye symptoms [5].

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 (PGE3) and less inflammatory leukotrienes and into proinflammatory prostaglandins (PGE2) and more inflammatory leukotrienes, respectively [6]. It is the ratio of omega-6 to omega-3 FAs that is important in influencing the overall inflammatory state of the body. demonstrated that overproduction of proinflammatory PGE2 and underproduction of anti-inflammatory PGE1 and PGE3 occur when the omega-6 to omega-3 FA ratio is high [6].

The pathogenesis of DES includes the presence of inflammatory cytokines such as IL-6, IL-8, IL-12, TNF-α e IFN-γ on the ocular surface triggered by the dryness that would change the tear film osmolarity producing more inflammation and perpetuating the phenomenon in a positive feedback process [7].

Nowadays, DES is interpreted as chronic inflammation in ocular surface that starts with tear hyperosmolarity and promotes ocular changes increasing dry eye symptoms

and severity [8]. According to these findings, oral supplementation with omega-3 and omega-6 fatty acids could improve inflammation on the ocular surface and relieve symptoms of DES [9]. Given this new therapeutic alternative, we designed the current study with an objective to evaluate the effect of oral linoleinec acid (omega 3 fatty acid) on patients who complained from dryness after Phacoemulsification.

2. Patients and Methods:

2.1. Study design & patient population:

This present was a cross sectional study conducted on participants who had been selected conveniently from attendants of the ophthalmology outpatient clinic in Beni-Suef Insurance hospital during the period from first of April 2020 to end of February 2021.

2.2. Ethical Consideration:

Informed written consent was obtained from all participants before recruitment in the study, after explaining the objectives of the work**.** Confidentiality was guaranteed on handling the data base.

2.3. Inclusion criteria:

(Patients did phacoemulsification, Bothe males and females from any age group, Non- diabetic, Non-smoker patients who had phacoemulsification).

2.4. Exclusion criteria:

(Patients Refusal, Diabetics, Rheumatoid and smokers)

2.5.

2.6.

Methods:

Consecutive patients who had phacoemulsification cataract surgery were assessed and received oral linoleinic acid capsules 1000 mg for 3 months after operation. Dry-eye markers including the ocular surface disease index (OSDI) and subjective symptom questionnaire, tear-film assessment using Schirmer testing 2, and break–up time test were sequentially evaluated preoperatively and postoperatively at 1^{st} day,1^{st} week , 1^{st} month, 2^{nd} month and 3^{rd} month. All patients received pre-operatively eye drops of 1% cyclopentolate and 1% tropicamide for mydriasis. Peribulbar anesthesia was used for all patients. A standard coaxial phacoemulsification technique was done with insertion of foldable PCIOL in the bag. All patients had a full ophthalmic examination including visual acuity, slit lamp examination, fundus examination, intraocular pressure (IOP) measurement and ultrasonography if the fundus is not seen. Post operatively, patients received topical 0.3% ofloxacin eye drops and 0.1% fluorometholone plus diclofenac sodium eye

drops to prevent infection and inflammation after the surgery.

The Ocular Examinations Included:

(1) Tear film break up time (TFBUT) measurement, (TFBUT ≤ 5 seconds = dry eye; TFBUT > 5 seconds = normal).

(2) Schirmer's 2 test: (The Schirmer's-2 test was considered abnormal if the length of the wetting was <6mm at the end of 5 min).

(3) Ocular surface disease index (OSDI) score:

- The OSDI is assessed on a scale of 0 to 100, with higher scores representing greater disability.
- The index demonstrates sensitivity and specificity in distinguishing between normal subjects and patients with dry eye disease. The OSDI is a valid and reliable instrument for measuring dry eye disease severity (normal, mild to moderate, and severe) and effect on vision-related function.
- Assessment of Patient's Dry Eye Disease by use answers D and E from the previous section to compare the sum of scores for all questions answered (D) and the number of questions answered (E) with the chart below.
- Find where patient's score would fall.
- Match the corresponding shade of red to the key below to determine whether the patient's score indicates normal, mild, moderate, or severe dry eye disease **(Figure -1).**

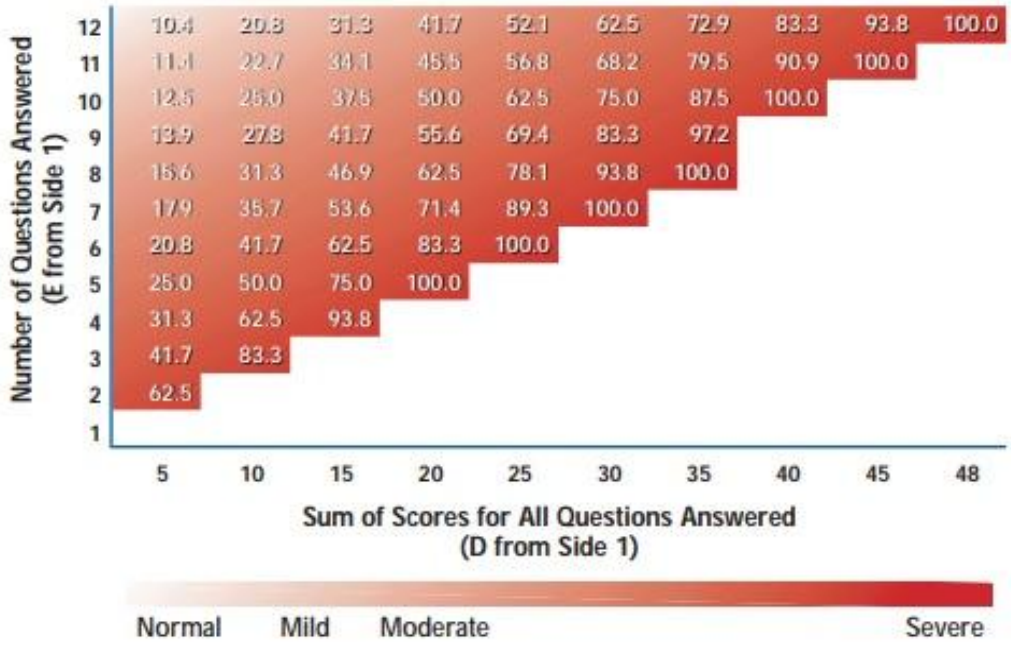

Figure (1): Evaluating the OSDI Score

2.7. Statistical Data Analysis: the collected data was tabulated, coded and analyzed using *SPSS* for Windows, version 23. Continuous variables were presented as mean values ± standard deviation (SD), and categorical variables as percentages. Comparisons among qualitative data were done using chi-squared test and Fisher test. For quantitative data; comparisons between groups was done using independent sample t-test. *P*-values <0.05 was considered as statistically significant.

3. Results:

Table (1) demonstrates the socio-demographic data of the studied population. Age was ranged from (48) to (71) with an average age of (62.07 ±6.03) years old. The studied participants were (60.7%) males and (39.3%) females. Regarding their residence, majority of them were rural residents (68.2%) while (31.8%) were urban residents.

Table (1): socio-demographic data of the studied population; (N= 107):

		Frequency	Percent
Age	**Mean ±SD**	62.07 ±6.03	
	(Minimum – Maximum)	(48 – 71)	
Sex	**Male**	65	60.7%
	Female	42	39.3%
Residence	**Rural**	73	68.2%
	Urban	34	31.8%

Figure (2) demonstrate the description of score of ocular surface disease index (OSDI) at follow-up for dry eye. OSDI scores decreased significantly between baseline and three months post-operatively. At the baseline assessment OSDI mean score was (17.51 ±8.28) that slightly increased at the 1st day post-operative to (17.57 ±8.05) but without a statistically significant difference (p-value= 0.951). At 1st week post-operative, the OSDI score decreased significantly to (14.88 ±7.38) as compared with baseline and 1st day respectively with a statistically significant p-values (p-values= 0.004, 0.001). At 1st month post-operative, the OSDI score decreased significantly to (11.42 ±6.19) as compared with baseline, 1st day and 1st week post-operative respectively with a statistically significant p-values (p-values= 0.001, 0.001, 0.001). At 2nd month post-operative, the OSDI score decreased significantly to (8.16 ±5.05) as compared with baseline, 1st day, 1st week and 1st month respectively with a statistically significant p-

values (p-values= 0.001, 0.001, 0.001, 0.001). At 3rd month post-operative, the OSDI score decreased significantly to (6.30 ±3.98) as compared with baseline, 1st day, 1st week, 1st month and 2nd months respectively with a statistically significant p-values (p-values= 0.001, 0.001, 0.001, 0.001, 0.042).

As illustrated in table (2), according to OSDI assessment, in the 1st day postoperative abut 68 patients (28% mild) and (35.5%) showed dry eye signs.

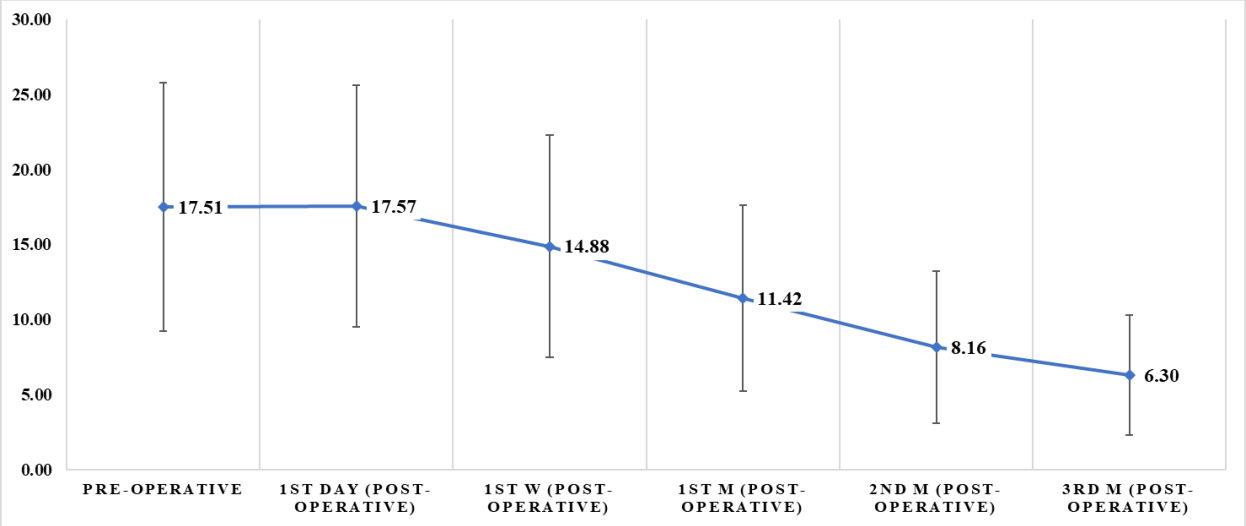

Figure (2): Distribution of Score of OSDI at Follow-Up for Dry Eye.

Table (2): OSDI changes at Follow-Up for Dry Eye among studied population; (N= 107):

		Follow-up					
		Pre-Operative	**1st Day**	**1st Week**	**1st Month**	**2nd Month**	**3rd Month**
OSDI	**Normal**	41 (38.3)	39 (36.4)	43 (40.2)	62 (57.9)	84 (78.5)	103 (96.3)
	Mild	27 (25.2)	30 (28.0)	44 (41.1)	43 (40.2)	23 (21.5)	4 (3.7)
	Moderate	37 (34.6)	38 (35.5)	20 (18.7)	2 (1.9)	0 (0.0)	0 (0.0)
	Severe	2 (1.9)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)

Figure (3) demonstrate the description of score of tear beak up time (TBUT) at follow-up for dry eye. YBUT scores increased significantly between baseline and three months post-operatively. At the baseline assessment YBUT mean score was (6.65 ±2.92) that decreased significantly at the 1st day post-operative to (5.52 ±2.36) with a statistically significant difference (p-value= 0.001). At 1st week post-operative,

the YBUT score decreased significantly to (4.87 ±2.87) as compared with baseline assessment with a statistically significant p-value= 0.001), while as compared with 1st day the difference was statistically non-significant (p-value =with a statistically significant p-values (p-values= 0.004, 0.001). At 1st month post-operative, the YBUT score decreased slightly to (5.90 ±2.76) as compared with baseline, but without a statistically significant (p-value= 0.055), and with 1st day the difference was statistically non-significant (p-value= 0.093), while with the 1st week the score showed a statistically significant p-value= 0.008). At 2nd month post-operative, the YBUT score increased significantly to (7.49 ±3.00) as compared with baseline, 1st day, 1st week and 1st month respectively with a statistically significant p-values (p-values= 0.031, 0.001, 0.001, 0.001). At 3rd month post-operative, the YBUT score increased significantly to (8.91 ±3.51) as compared with baseline, 1st day, 1st week, 1st month and 2nd months respectively with a statistically significant p-values (p-values= 0.001, 0.001, 0.001, 0.001, 0.001). Table (3) illustrates the TBUT changes at Follow-Up for Dry Eye among studied population

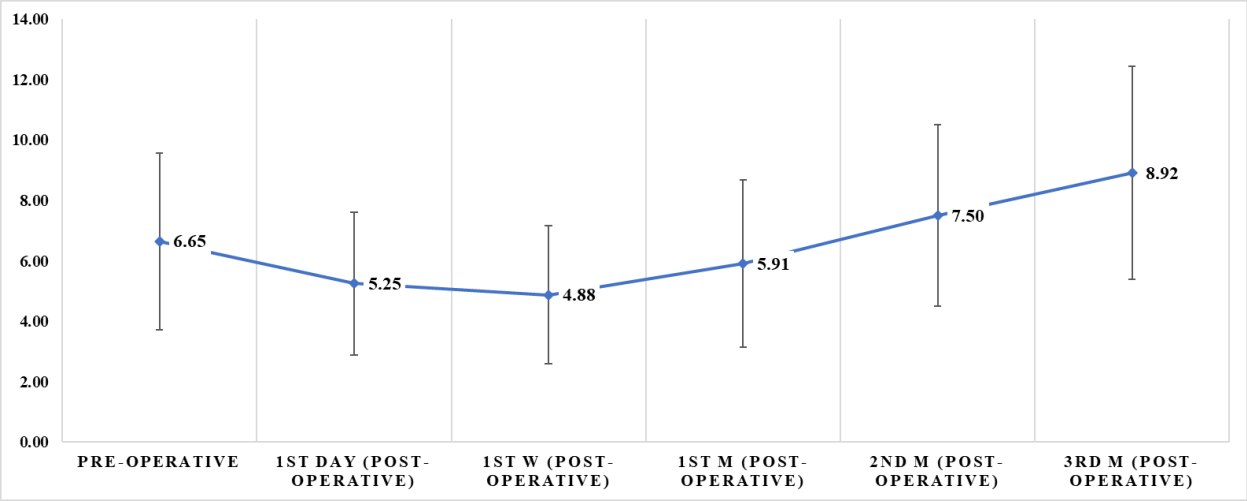

Figure (3): Distribution of Score of TBUT at Follow-Up for Dry Eye.

Table (3): TBUT changes at Follow-Up for Dry Eye among studied population; (N= 107):

		Follow-up					
		Pre-Operative	**1st Day**	**1st Week**	**1st Month**	**2nd Month**	**3rd Month**
YBUT	**Normal (> 5 seconds)**	66 (61.7)	40 (37.4)	25 (23.4)	46 (43.0)	74 (69.2)	82 (76.6)
	Dry eye (≤ 5 seconds)	41 (38.3)	67 (62.6)	82 (76.6)	61 (57.0)	33 (30.8)	25 (23.4)

Figure (4) demonstrate the description of score of Schirmer test at follow-up for dry eye. Schirmer test scores increased significantly between baseline and three months post-operatively. At the baseline assessment Schirmer test mean score was (10.97 ±4.6) that increased significantly at the 1st day post-operative to (12.79 ±6.00) with a statistically significant difference (p-value= 0.019). At 1st week post-operative, the Schirmer test score decreased significantly to (9.15 ±5.3) as compared with baseline and 1st day respectively with a statistically significant p-values (p-values= 0.019, 0.001). At 1st month post-operative, the Schirmer test score decreased insignificantly to (9.54 ±5.7) as compared with 1st week, (p-value= 0.065). While as compared with baseline and 1st day the difference was statistically non-significant (p-value= 0.093), while with the 1st week the score showed a statistically significant p-value= 0.008). At 2nd month post-operative, the Schirmer increased significantly to (7.49 ±3.00) as compared with baseline, 1st day, 1st week and 1st month respectively with a statistically significant p-values (p-values= 0.031, 0.001, 0.001, 0.001). At 3rd month post-operative, the Schirmer score increased significantly to (8.91 ±3.51) as compared with baseline, 1st day, 1st week, 1st month and 2nd months respectively with a statistically significant p-values (p-values= 0.001, 0.001, 0.001, 0.001, 0.001). Table (4) demonstrates the Schirmer-2 Test changes at Follow-Up for Dry Eye among studied population

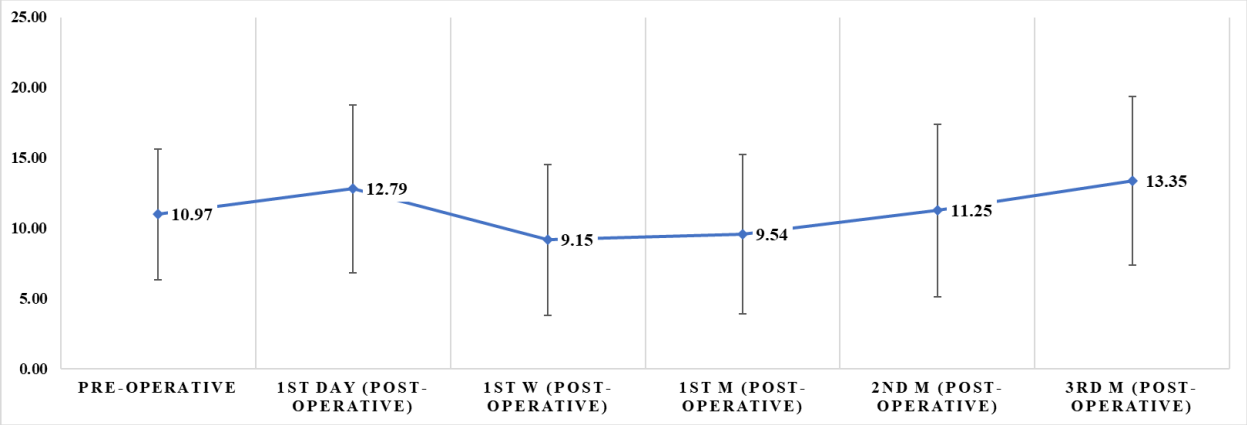

Figure (4): Distribution of Score of Schirmer test at Follow-Up for Dry Eye.

Table (4): Schirmer-2 Test changes at Follow-Up for Dry Eye among studied population; (N= 107):

		Follow-up					
		Pre-Operative	**1st Day**	**1st Week**	**1st Month**	**2nd Month**	**3rd Month**
Schirmer-2 Test	**Normal (> 6mm)**	91 (85.0)	87 (81.3)	50 (46.7)	59 (55.1)	79 (73.8)	92 (86.0)
	Dry Eye (<6mm)	16 (15.0)	20 (18.7)	57 (53.3)	48 (44.9)	28 (26.2)	15 (14.0)

4. Discussion:

Ocular surface dysfunction includes a spectrum of diseases that impair the ocular surface leading to a constellation of clinical signs and patient symptoms [10]. Dry-eye disease is likely the most common subtype of ocular surface dysfunction; however, many others can be present along with dry-eye disease or masqueraded as dry-eye disease [11]. These include blepharitis, epithelial basement dystrophy, Salzmann nodular degeneration, allergic conjunctivitis, conjunctivo-chalasis, floppy eyelid syndrome, and others [11], [12]. The prevalence of dry-eye disease varies in the literature but has been reported to be as high as 35% in some populations [13].

Dry-eye disease and meibomian gland dysfunction are very common diseases, and prevalence significantly increases with age [14]. Cataract surgery is one of the most common procedures performed in Egypt

with a growing annual incidence [15]. The typical age of patients having cataract surgery is over 50 years [10]. As patients who undergo cataract surgery are older than refractive surgery candidates and have more comorbidities, they may experience even more severe post-surgical dry eye [16], [17].

There are many factors that are responsible for the development of dry eye after phacoemulsification, such as the long-term use of antibiotic-steroid eye drops, decreased tear film break-up time owing to surface irregularity at the site of the incision, decreased mucin production from the conjunctiva secondary to incision placement, and decreased corneal sensation owing to the surgical incision, which disrupts the cornea-lacrimal gland loop, leading to reduced tear secretion, poor tear film production and stability due to surgically induced ocular inflammation, and exposure to light from the operating microscope [18]. Dry eye symptoms may temporarily affect the quality of vision and the quality of patient life [19].

Omega-3 fatty acids (FAs) and omega-6 FAs are essential for normal growth and development [20]. 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 pro-inflammatory prostaglandins 2 and more inflammatory leukotrienes, respectively [21], [22].

The current study was designed to evaluate the effect of oral linoleinec acid (omega 3 fatty acid) on patients who complained from dryness after Phacoemulsification. It was a cross-sectional study included follow-up of (107) cataract patients after phacoemulsification surgery.

Previous studies have identified several risk factors associated with cataract, including smoking [23], [24], diabetes [25], [26], sunlight exposure [27], high body mass index [28], steroid use [29], increasing age [30], [31], female gender [32], [33]. In the current study, participants' age was ranged from (48) to (71) with an average age of (62.07 ±6.03) years old, but although many previous studies have shown that females are more susceptible to cataracts, more than two thirds of the respondents in our current studies were males (60.7%), this difference could be explained by the fact that the participants in the current study were recruited from one center only and the study was not-multicenter.

In a study on dry eye following cataract surgery, focused on tear film changes after phacoemulsification and the effect of clear corneal incision location on tear film [34]. 68 eyes of 68 patients without preoperative dry eye and with senile cataract requiring phacoemulsification in a prospective, cohort study. Basic Tear Secretion Test (BTST), Tear Meniscus Height (TMH) measurement, Tear Break Up Time Test (TBUT) and Schirmer's 1 Test (S1T) were performed in all participants before and three months after surgery. Preoperative keratometry was used to determine the steepest meridian and corresponding location of the clear corneal incision. Topical chloramphenicol and betamethasone eye drops were administered on a tapering dose for one month postoperatively. There was no statistically significant difference between the results of preand post- operative S1T, TMH and BTST. These latter tests were not statistically different between incisions at different locations. However, TBUT results differed significantly in preand post-operative examination in both incision location groups [34].

In the current study, all the studied patients received oral linoleinic acid capsules 1000 mg/day for three months after operation. We evaluated all the studied patients pre-operative, and then we followed up them for a period of three months after the phacoemulsification. Evaluation included dry-eye markers (the ocular surface disease index (OSDI), tear film break up time (TFBUT) and schirmer II test).

Several studies have investigated the role of oral supplement of omega-3 fatty acids in the treatment of dry eye syn-drome as an anti-inflammatory agent. Adding omega-3 has shown to increase tear production [35], [36].

In this current study, OSDI and TFBUT showed significant improvement in the studied cases during follow-up, this improvement was significantly highest in the first month post-operative.

These results illustrated that supplementing the diet withhigh amounts of omega-3 polyunsaturated fatty acids de-creases dry eye symptoms after cataract surgery and increasestear film stability.

In our study, tear film osmolarity and consequently Schirmer's test results improved significantly in the over the period of the three months follow-up. Those findings were comparable with many previous studies reported significant improvement in dry eye symptoms.

Over the past five years, several systematic reviews have consideredthe efficacy and/or safety of nutritional supplements containingomega-3 and/or omega-6 fatty acids for treating dry eye disease [37], [38].

Kangari et al., showed that adding omega-3 supplements to standard treatment of non-surgically induced dry eye syndrome would significantly improve OSDI, TBUT, and Schirmer's test results [39]. Similarly, a recent study that conducted to evaluate the efficacy of omega-3 fatty acids on dry eye after phacoemulsification, found that the OSDI and TBUT showed significant improvement in both the control and treatment groups, but this improvement was significantly higher in the treatment group in comparison with the control group. These results illustrated that supplementing the diet with high amounts of omega-3 polyunsaturated FAs decreased the dry eye symptoms after phacoemulsification and increased the tear film stability. However, there was no statistically significant difference between the treatment and control groups according to the Schirmer test results [40].

On the contrary, Mohammadpour et al., [17] reported similar results in post-cataract surgery dry eye syndrome for OSDI and TBUT, but there was not any statistically significant improvement in the Schirmer's test, which is a quantitative tear film index (P=0.155).

Ong et al., studied the effect of omega-3 fatty acids in the treatment of dry eye syndrome after photorefractive keratectomy concluded that adding omega-3 to standard treatment can lead to a significant higher improvement in epithelial healing, TBUT, and visual acuity. In their study, all patients in the treatment group reached visual acuity of 20/20, but only 4 patients in the control group reached this level of visual acuity [41]. Our study also demonstrated significant improvement in tear osmolarity, and alleviation of symptoms measured by OSDI, in addition to improve TBUT, with oral supplement ofomega-3 combined with conventional therapy.

In contrast to the results of our current study and many similar studies, a clinical trial was carried out on 349 patients allocated to the omega-3 FA supplementation group and 186 to the placebo group, for treatment of dry eye condition. The mean difference between the omega-3 FA supplement group and the placebo group in the OSDI score did not differ significantly group (−13.9 points and −12.5 points, respectively, the mean

baseline changes in the conjunctival stain score, corneal stain score, TBUT, and Schirmer's test result have been non-significantly differences between the omega-3 FA supplemental group and the placebo group. The treatment adhesion rate for the active supplementary group at 12 months was 85% which implies that n-3 FA additives did not benefit patients with dry eye condition as compared with placebo supplements [42].

In contrast to our study, the Zhu et al., [37] analysis pooled data from RCTs that evaluated any form of PUFA supplement. These authors identified a total of nine relevant studies and reported that PUFA supplementation appeared to provide no benefit about tear volume (measured via the Schirmer test) nor tear stability (quantified via fluorescein TBUT) but imparted a significant improvement (relative to placebo) for each of dry eye symptoms (measured via the OSDI questionnaire), [37]. However, to accept or deny these and other results, we recommend larger RCTs studies on a larger number of patients.

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