

Omega-3 Supplement; A Comparison of Recommendations

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Abstract

Purpose: Research has shown Omega-3 supplementation can benefit dry eye patients. Our objective is to aid optometrists in the treatment of dry eye syndrome by summarizing the recommendations for oral Omega-3 supplements.

Methods: We sent an online survey consisting of ten questions to optometrists affiliated with the Oklahoma Association of Optometric Physicians (OAOP) and the Facebook groups ODs on Facebook and Corporate Optometry to see if they are recommending Omega-3 supplements, which specific products, and at what dosage.

Results: Ninety-five optometrists responded. 43.16% stated that their dry eye patients number between 26-50% of their practice. 60% responded they recommend Omega-3 supplements, and 37.89% said they tell their patients to increase their dietary fish intake and take Omega-3 supplements. 50% of eye care physicians responded that they sell dry eye supplements. When asked about how familiar optometrists are with the different forms of Omega-3 fatty acids, 30.85% stated they are very familiar, while 54.26% stated they are somewhat familiar and 14.89% stated they are not familiar at all with the different types.

Conclusion: We found that the majority of optometrists who responded to our survey are recommending their patients consume between 1500-2000 milligrams of Omega-3's per day for dry eye. Many health professionals uphold that at least 1,000 mg/day of EPA and DHA should be consumed to aid in improving systemic health. In the absence of standards specifically for dry eye it is reasonable to base Omega-3 supplement recommendations on those for systemic health.

Keywords: Dry eye, Omega-3, Omega-6, Supplements.

Dry eye is a significant problem in today's world. It is hard to come across a single patient a dry eye complaint, whether it is tear film instability leading to fluctuating vision or the grainy foreign body sensation that accompanies a dry ocular surface. Fatty acid supplementation has been shown to improve objective and subjective dry eye symptoms [1]. Dry eye disease or keratoconjunctivitis sicca is a diagnosis that is often encountered in most optometric practices [2-4]. Women and the elderly are more likely than other populations to experience dry eye and the number of dry eye patients is increasing yearly in association with the aging of society and the increase in personal computers and digital devices [5-8]. It is difficult to treat as clinical signs do not always correlate with patient symptoms [5]. Dry eye syndrome (DES) is a multifactorial disease of the ocular surface [9]. Rapid evaporation of tear and inadequate production of tears and ocular surface inflammation are among the causes of this syndrome. Prolonged dry eye can lead to ocular symptoms of foreign body sensation, redness, and discomfort, also surface damage on the cornea and conjunctiva, all

of which degrade visual performance [10]. The tear layer maintains a smooth surface for optical clarity, lubricates the eye, and offers protection against ocular infection. Blinking serves to periodically distribute tears evenly over the ocular surface and encourages both secretion and mechanical drainage of tears through the lacrimal drainage system [11]. Increased use of digital devices reduces the blink rate and contributes to dry eye signs and symptoms. Some of the most common patient symptoms include decreased vision and difficulty with everyday tasks like reading, working on a computer and driving at night [9].

DES can be divided into two broad categories: evaporative and aqueous deficient. Both types have an increased tear osmolarity. Evaporative dry eye may result from inadequate secretion of oil from the Meibomian glands or may be due to partial blinking. Aqueous deficient dry eye syndrome can be caused by a systemic deficiency in vitamin A. This reduces the overall health of epithelial tissues. Aqueous deficient dry eye can be further divided into Sjogren's and non-Sjogren's categories [12]. Evaporative dry eye or Meibomian Gland Dysfunction (MGD) is one of the main

causes of dry eye that optometrists encounter on a regular basis with the majority of their aging patients. MGD is a chronic, diffuse abnormality of the Meibomian glands, characterized by terminal duct obstruction and/or qualitative/quantitative changes in the glandular secretion. The ocular surface is covered by the tear film that is a mixture of mucin, aqueous, and lipids produced by various structures. The lipid layer stabilizes the tear film and reduces the evaporation of tears. In MGD, blockage of the orifice and stasis of the oil within the gland resulting in decreased secretion and abnormal composition of the tear film lipid layer. These factors lead to increased tear evaporation, tear osmolarity and inflammation in the gland along with the adjacent ocular surface. The resultant scarring and hyperkeratosis further aggravates ductal stenosis leading to Meibomian gland dropout [13].

One of the principal treatments of dry eye disease is the supplementation of fatty acids, which are the natural components of fats and oils. Fatty acids can be further broken down into non-essential and essential. Essential fatty acids (EFAs) are beginning to play a big role in eye care because they cannot be produced by the body and therefore must be consumed in the diet. The two primary EFAs are known as linoleic acid (Omega-6) and alpha-linolenic acid (Omega-3). EFAs are incorporated into the lipid bilayer membrane in every cell in the body and perform critical functions including influencing the fluidity of the cell membranes, signaling pathways, and recycling the membrane itself. They also influence gene expression. EFAs are derived from polyunsaturated fats which have at least one double bond in the carbon chain [14]. Some types of Omega-3 fatty acids are alpha-linolenic acid (ALA), eicosapentaenoic acid (EPA), and docosahexaenoic acid (DHA) [12]. Excellent dietary sources of Omega-3 fatty acids include salmon, sardines, flaxseeds, and walnuts [15,16]. Types of Omega-6 fatty acids include linoleic acid (LA), gamma-linolenic acid (GLA), dihomo-gamma-linolenic acid (DGLA), and arachidonic acid (AA). Omega-6 fatty acids are found in these common oils: corn, peanut, safflower, rapeseed, and sunflower. Some other common sources of Omega-6 fatty acids include poultry, eggs, cereals, and whole grain breads.

EFAs are beneficial for some systemic diseases including cardiovascular disease, arthritis, and inflammatory diseases. One important safety concern to keep in mind is that excessively high doses of Omega-3 fatty acid supplements, such as fish oil, could cause bleeding problems due to their anti-coagulant properties [12]. A deficiency in Omega-3 fatty acid can result in the Meibomian glands producing less oil and a lower quality tear film that is more prone to evaporation [17]. Along with their systemic benefits, essential fatty acids can help reduce the inflammatory component of MGD [18]. One study shows that fatty acids are believed to be involved in the inflammatory cycle via two pathways: (1) by

blocking the gene expression of pro-inflammatory cytokines, tumor necrosis factor- α , interleukin-1 α , interleukin-1 β , proteoglycan degrading enzymes (aggrecanases), and cyclooxygenase-2 or (2) by producing anti-inflammatory factors (e.g., prostaglandin E3 and leukotriene B5). These factors may help to clear the meibomianitis, allowing a thinner, more uniform lipid layer to be secreted from the Meibomian glands. This in turn may retard the evaporation of the tear film and help restore the tear film [10]. Essential fatty acids like Omega-3 and Omega-6 need to be consumed together within a certain ratio to be effective with their anti-inflammatory effects [12]. These supplements need strict commitment from patients over a lengthy period of time to achieve their desired effects [19]. The ideal ratio of Omega-3 to Omega-6 is less than 1:4. However, in the United States the consumption of Omega-6 fatty acids is much higher than this, leading to a pro-inflammatory state [20]. The average American diet provides sufficient Omega-6 fatty acids, so supplementation is not needed.

Patients and physicians have turned to nutritional therapies in an attempt to alleviate symptoms of dry eye [21]. Pharmacologically, current treatments are mainly focusing on addressing inflammation and tear restoration [7]. Although these treatments are effective, lubricants only suppress negative symptoms temporarily and chronic use of topical steroids can cause severe ocular side effects such as cataracts and glaucoma [22]. It is reasonable to prescribe oral supplements, such as Omega-3, for patients not satisfied with topical medications alone [23]. However, there is no consensus on the dose, composition or length of treatment for polyunsaturated fatty acid (PUFA) supplements [20]. Some health organizations recommend a daily dose of ALA Omega-3 at 1.6 grams (g) a day for men and 1.1g per day for women. Also recommended is a diet of non-fried fatty fish two or more times a week, providing of at least 500 milligrams (mg) of EPA and DHA for healthy adults per day [24]. The research shows that essential fatty acid supplements are beneficial for dry eye; however, there is limited data available that shows if most optometrists have started to incorporate this knowledge in their management of dry eye [1]. In this study, our purpose was to investigate whether optometrists are recommending essential fatty acid supplements to their dry eye patients and if so, what dosage and which brands they are recommending. With many different brands of supplements on the market with varying contents of Omega-3, we found out which ones are being used most in a clinical setting in an attempt to establish a uniform protocol for prescribing.

Physicians will find many Omega-3 supplements on the market. Below is a list of supplements that are marketed specifically for dry eye. These supplements contain varying amounts of Omega-3. Many include other vitamins as well, but since they are unrelated to our research they are not listed.

Table: 1 Brands of Omega-3 supplements, cost, and composition of EPA and DHA

Supplement	Manufacturer	Dose (softgels)	Count	Cost	Cost/month	EPA (mg)	DHA (mg)	Total (mg)	Form
BioTears®	Biosyntrx®	2	120	\$37	\$19	21	24	45	TG
EZ Tears™	ZeaVision	2	60	\$36	\$36	590	440	1030	EE
Fortifeye® Super Ome-ga™	Fortifeye®	2	60	\$30	\$30	860	580	1440	TG
HydroEye®	ScienceBased Health®	4	120	\$39	\$39	100	70	170	TG
LipoTriad Dry Eye	LipoTriad LLC	2	60	\$23	\$23	504	378	882	TG
MaxiTears®	MedOp Health, Inc.	4	120	\$34	\$34	600	400	1000	TG
Omega-3 Dry Eye Formu-la™	Eye Love	3	90	\$30	\$30	500	400	900	TG
PRN Dry Eye Omega	PRN	4	240	\$100	\$50	1680	560	2240	rTG
retaine FLAX™	OCuSOFT®	4	120	\$38	\$38	*	*	1000	EE
retaine OM3™	OCuSOFT®	2	60	\$35	\$35	800	400	1200	EE
TheraTears Eye Nutrition	Akorn	3	90	\$12	\$12	450	300	750	TG
Ultra Dry Eye TG™	OcuSci™	3	60	\$95	\$143	1515	630	2145	TG
VisiVite® Dry Eye Re-lief®	Vitamin Science, Inc.	4	120	\$47	\$47	600	400	1000	TG
Ultimate Omega®	Nordic Na-turals®	2	180	\$60	\$20	650	450	1100	TG
Tears Again® Hydrate™	OCuSOFT®	4	120	\$68	\$68	*	*	1000	EE

EE- ethyl ester

TG- triglyceride

rTG- re-esterified triglyceride

*retaine FLAX™ and Tears Again® Hydrate™ achieve 1000 mg of Omega-3 supplementation through flaxseed oil which is ideal for patients who cannot tolerate fish-oil based supplements.

Table: 2 Common names of essential fatty acids

Fatty Acid	Abbreviation	Lipid name
Omega-3 fatty acids		
Alpha-linolenic acid	ALA	18:3 ω-3
Eicosapentaenoic acid	EPA	20:5 ω-3
Docosahexaenoic acid	DHA	22:6 ω-3
Omega-6 fatty acids		
Linoleic acid	LA	18:2 ω-6
Gamma-linolenic acid	GLA	18:3 ω-6
Dihomo-gamma-linolenic acid	DGLA	20:3 ω-6
Arachidonic acid	AA	20:4 ω-6

Methods

After receiving approval from the Northeastern State University Institutional Review Board we surveyed Oklahoma optometrists who are active members of the Oklahoma Association of Optometric Physicians (OAOP) to see if they are recommending essential fatty acid supplements and if so, what they are recommending. We invited them to fill out a short ten question anonymous online survey. Our survey was also extended to include Facebook groups: Corporate Optometry and ODs on Facebook. Our questions included:

- 1) Do you treat dry eye patients in your practice?
 - a) Yes
 - b) No (Discontinue survey if answered ‘No’)

- 2) What percentage of your patients do you treat for dry eye?
 - a) 0-25%
 - b) 26-50%
 - c) 51-75%
 - d) 76-100%
- 3) Which of the following do you recommend in the treatment of your dry eye patients?
 - a) Omega-3 supplements
 - b) Increase dietary fish intake
 - c) Both omega-3 supplements and increase dietary fish intake
 - d) I don’t recommend any of the above (Discontinue survey if answered ‘D’)

- 4) How often do you recommend an omega-3 supplement to your dry eye patients?
- Always
 - Most of the time
 - Sometimes

(5) When you recommend an omega-3 supplement, how often do you recommend each of the following omega-3 dry eye supplements? (Please check all that apply)

Supplement	Always	Sometimes	Never
VisiVite® Dry Eye Relief®			
BioTears®			
EZ Tears™			
Fortifeye® Super Omega™			
HydroEye®			
LipoTriad® Dry Eye			
MaxiTears®			
Omego-3 Dry Eye Formula™			
retaine FLAX™			
retaine OM3™			
Tears Again® HYDRATE™			
TheraTears® Eye Nutrition			
Ultra Dry Eye TG™			

- 6) Do you recommend any brands not listed above?
- Yes
 - No (If no skip next question)
- 7) Other brand(s) of omega-3 supplement(s) you recommend _____

- 8) How many total milligrams/day of omega-3s do you recommend to your dry eye patients?
- Less than 1000 mg
 - 1000-1500 mg
 - 1501-2000 mg
 - 2001-2500 mg
 - 2501-3000 mg
 - No specific recommendation

- 9) Do you sell dry eye supplements in your practice/ workplace?
- Yes
 - No

- 10) How familiar are you with the different forms of omega-3 fatty acids? (triglyceride, re-esterified triglyceride, ethyl ester, free fatty acid, and phospholipid)
- Very familiar
 - Somewhat familiar
 - Not familiar at all

Once all the surveys were completed and returned to us, we analyzed the results to see how much essential fatty acid supplements are being recommended to dry eye patients, as well as which brand is being recommended most. We then compared these results to

recommended guideline dosages of Omega-3 and -6 for dry eye syndrome.

Results

We surveyed private practice and corporate optometrists nationwide for a two-month pe-riod starting from March 20, 2017 and ending on May 20, 2017. Ninety-five optometrists responded. As shown in (Fig. 1), 36.84% of optometrists stated that between 0-25% of their patient population have dry eye, while the largest margin of eye care physicians at 43.16% stated that their dry eye patients number between 26-50% of their practice. 14.74% and 5.26% of optometrists revealed that their dry eye patients number between 51-57% and 76-100% of their practices, respectively. When polled about recommenda-tions, 60% responded that they recommend Omega-3 supplements, while 1.05% said they recommend increasing dietary fish intake alone and 37.89% said they tell patients to in-crease dietary fish intake and take Omega-3 supplements (Fig. 2). Using eye-related Omega-3 supplement brands in our survey, we compiled the results into a bar graph in (Fig. 3) that shows the number of optometrist recommending each supplement.

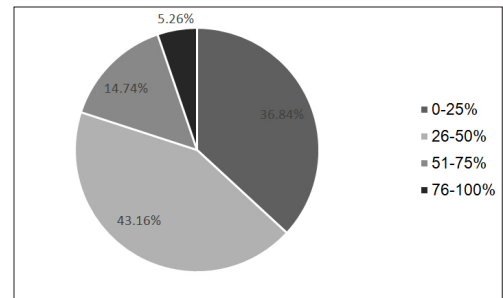


Figure 1: Percentage of dry eye patients treated in the practice.

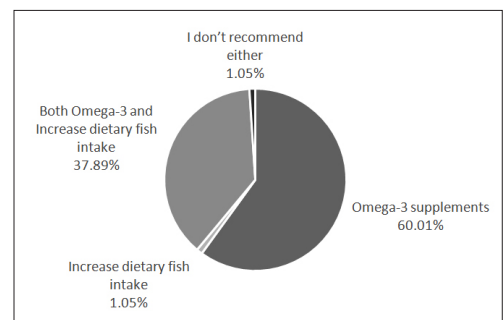


Figure 2: Percentage of optometrists recommending Omega-3 supplements or increasing dietary fish intake.

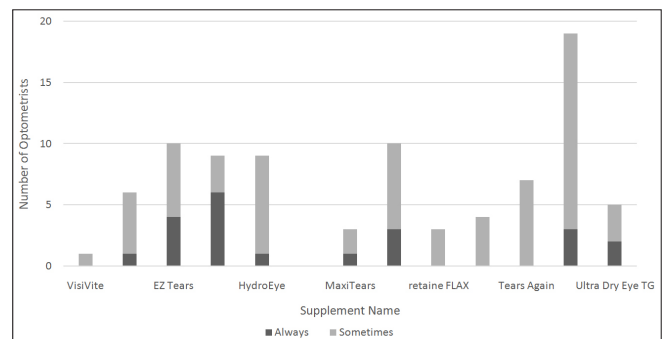


Figure 3: Number of optometrists recommending specific brands of Omega-3.

Of the brands offered, many optometrists picked the option to comment on specific brands not mentioned in the survey. An astounding number of optometrists stated they recommend Nordic Naturals to their patients (32 out of the 59 respondents that chose to leave comments regarding question number 7). The second most common response was Physician Recommended Nutraceuticals (PRN) Dry Eye Omega (18 out of the 59 respondents). Other brands listed within the comments section included Blink Omega-3 Gel, Webber Naturals Liquid Omega-3, Scope Omega Eye, and Cormega Omega-3 Orange Squeeze. (Figure 4) presents the daily dosage of Omega-3 in milligrams that surveyed optometrists recommend to their dry eye patients. 50% of eye care physicians responded that they do sell Omega 3 supplements out of their office and 50% responded that they do not. When asked about how familiar optometrists are with the different forms of Omega-3 fatty acids (triglyceride, ethyl ester, re-esterified triglyceride, free fatty acid and phospholipid), 30.85% stated they are very familiar, while 54.26% stated they are somewhat familiar and 14.89% stated they are not familiar at all with the different types.

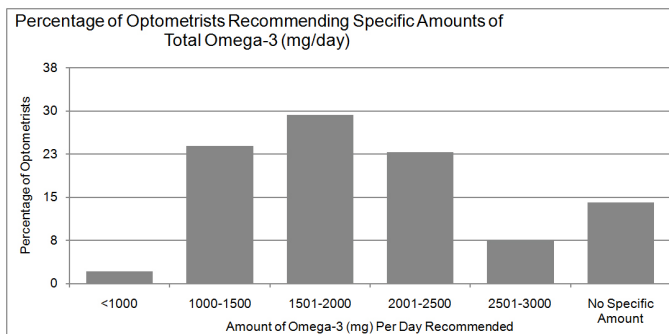


Figure 4: Percentage of optometrists recommending specific amounts of total Omega-3 in milli-grams per day.

Discussion

There is no clear standard on what dosage, ratio of Omega-3 to Omega-6, and length of treatment that should be used for dry eye [20]. National cardiovascular health organizations have recommended at least 1,000 mg/day of EPA and DHA [24]. From our survey, of the top 3 optometrist recommended brands of oral fatty acid supplements (Nordic Naturals, PRN Dry Eye Omega, TheraTears Eye Nutrition) only PRN Dry Eye Omega provides 1,000 mg/day of EPA and has the highest amount of DHA at 560 mg/day. It is in the re-esterified triglyceride form, Nordic Naturals is in the triglyceride form, and TheraTears Eye Nutrition is in the triglyceride form. As an important safety precaution, almost all commercial fish oils employ a process of adding alcohol to detoxify these compounds. However, this addition of alcohol induces a chemical change in the natural triglycerides found in fish oil and converts the triglyceride to an ethyl ester compound. Our bodies have difficulty processing and absorbing the ethyl ester compound, which is not found in nature. Re-esterification is a process that removes the artificially induced alcohol in chemically modified ethyl ester fish oil to create a more natural form of Omega-3 fatty acid that is not only better tolerated with less gastrointestinal side effects but also better absorbed than Omega-3 fatty acids in the ethyl ester form. The great majority of commercially available Omega-3 fatty acids are in the ethyl ester form, whereas a limited number of Omega-3 fish oils are converted back to the more bioavailable triglyceride form [25]. The re-esterified triglyceride form has the highest bioavailability of EPA and DHA followed by the natural fish oil triglyceride form and

the lowest bioavailability is from the ethyl ester form [26]. Another factor that affects bioavailability is taking supplements with a meal that contains a sufficient amount of fat [27].

Conclusion

After comparing optometrist's recommendations to those outlined by research studies, we found the majority of optometrists who responded to our survey are recommending between 1500-2000 milligrams of Omega-3 per day to aid in the treatment of dry eye. While many health professionals think that at least 1,000 mg/day of EPA and DHA should be consumed to aid in improving systemic health, we have found that there are no research articles offering concrete standards on the amount of Omega-3 fatty acids recommended to help dry eye specifically. Many research articles focus on the long-term effects of Omega-3 consumption that improve cardiovascular health, cancer prevention, arthritis and cognitive function. It is therefore reasonable to conclude that the amount recommended to better systemic health also stands to help ocular health as well. We intend for our paper to help clarify supplementation guidelines for eye care physicians (more specifically the 54.26% that stated they are somewhat familiar and the 14.89% that stated they are not familiar at all with the different types of Omega-3). We endeavor to create a more solid understanding of what supplements are available to help with dry eye and the different forms of fatty acids we can choose from to help our patients.

Limitations to our study include the difficulty of comparing Omega-3 supplements due to the wide variability in composition and dosage. Further studies could ask the specific amount of EPA and DHA recommended by optometrists and include survey questions consisting of oral Omega-3 supplement recommendations that are not specifically recommended for dry eye. Another limitation to our study was that our guidelines were specific to mostly fish-oil based products. Further studies could investigate plant-based sources of Omega-3s from algal oil, which typically provides 100-300mg DHA and some EPA as well. Supplements derived from algal oil usually contain Omega-3 in the triglyceride form and studies have shown that the bioavailability of DHA from algal oil is equivalent to that from cooked salmon [28]. Another potential study could investigate how many dry eye patients that optometrists are treating with Omega-3 supplements that concurrently take blood thinners, such as Warfarin (Coumadin®). Fish oil can have anti-platelet effects at high doses, although it appears to be less potent than aspirin [29]. Fish oil might prolong clotting times, as indicated by an elevated international normalized ratio (INR), when it is taken with warfarin [30]. While there is an overwhelming amount of research done on the topic of dry eye, much is still to be learned about the implementation of Omega-3 supplements to improve dry eye signs and symptoms.

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