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Research Article

To Study the Effect of Oral Vitamin D Supplementation in Dry Eye Patients in a Tertiary Eye Care Center

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ABSTRACT

Purpose: To establish possible association between serum vitamin D deficiency and dry eye disease and determine beneficiary effect of vitamin D supplementation in dry eye patients.

Materials and methods: A randomized controlled clinical study was conducted in a hospital-based tertiary eye care center including 497 outpatients between age group 18-58 years. Patients were screened randomly for dry eye. Tear film Break-Up Time (TBUT), Schirmer's test and Ocular Surface Disease Index (OSDI) were used to diagnose dry eye.

Results: Forty patients were diagnosed with dry eye. After vitamin D supplementation in dry eye patients, TBUT and schirmer's score was found to be significantly higher at 2 weeks ($p<0.001$) and at 6 weeks of treatment ($p<0.001$). Also, OSDI score was significantly lowered at 6 weeks of treatment ($p<0.001$).

Conclusion: Supplementation of oral vitamin D improved tear secretion and reduced tear instability as indicated by development of Schirmer's score and tear breakup time. Also, higher OSDI scores and lower TBUT value and schirmer's scores in vitamin D deficient patients indicates positive correlation between serum vitamin D level and dry eye disease.

Keywords: Dry eye; Vitamin D; Tear film break-up time; Schirmer's test; Ocular surface disease index scores; Lacrimal functional unit

INTRODUCTION

Dryness of eyes is a multifactorial disease of the eye caused due to abnormalities in the tear film as well as ocular surface, which results in instability of tear film, with possible damage to the ocular surface. A condition when the film is unable to provide required amount of moisture to the eyes is known as dry eye. Dry eye is characterized by redness, discomfort, stinging, itching, pain and tiredness in the eyes which may lead to vision blurring and light sensitivity. Dry eye is more common in women and elderly population [1].

Lacrimal glands, ocular surface (cornea and conjunctiva), eyelids, meibomian glands, and associated nerves form the Lacrimal Functional Unit (LFU). Dysfunction of any of the LFU component leads to dryness in eye which could be because of the changes in the volume, distribution, composition, and tear clearance. Aqueous deficient dry eye is caused when less tear is formed by lacrimal gland while evaporative dry eye is caused due

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to inflammation of eyelid and Meibomian Gland Dysfunction (MGD) [2].

Treatment for dryness in eye includes the use of lubricants, drugs having anti-inflammatory effects, occlusion of puncta and autologous serum. Lubricating drops help relieve the discomfort in aqueous deficiency, but the inflammatory symptoms are not reduced. A relation between serum vitamin D level and dry eye disease has been studied previously. Though studies have established association between serum vitamin D deficiency and dry eye disease but the effect of supplementing vitamin D in dry eye patients lacks evidence. The objective of our study is to find whether supplementing vitamin D in dry eye patients is having any beneficiary effects or not which can lead to opening of a new horizon in management of dry eye disease [3].

MATERIALS AND METHODS

We have conducted a randomized controlled study from June 2018 to May 2019, involving 497 patients between age group of 18-58 years visiting tertiary eye care center presenting with various ophthalmic complaints which may or may not involve dry eye symptoms. Patients were screened randomly for dry eye. The methodology includes patient's history taking, general examination, systemic examination, visual acuity and refractive error evaluation, facial symmetry and extraocular motility and thorough slit lamp examination. Dry eye was established in patients by taking specific tests as Tear Film Break-Up Time (TBUT); schirmer's tear secretion test and Ocular Surface Disease Index (OSDI). Forty patients had dry eye [4].

Sample size for the present study was calculated statistically and was found to be 20 in both groups (group A and group B). All the screened cases were randomly allocated into 2 groups based on random allocation sequence. The study was approved by the institutional review board and ethics committee and complied with the tenets of the declaration of Helsinki. In both the groups an informed consent was taken by the patient and guardian mentioning the pros and cons of the procedure and study. The patient and their guardians were given full opportunity to discuss about the study and had full right to quit anytime from the study when desired. The data was recorded on a well-structured proforma. Care was taken to minimize the risk for missing and erroneous data. Unwilling patients or guardians, patients with corneal pathologies like corneal ulcers, degenerations, dystrophies, patients with history of previous intraocular surgery, prolonged contact lens users, patients with other ocular disorder like conjunctivitis, scleritis, episcleritis, uveitis were excluded from the study [5].

Statistical analysis

Assuming mean and standard deviation of pre and post-test of two important parameters namely TBUT and OSDI from prior published study the sample size was calculated assuming the probability of type I error alpha as 0.05 and power (1-ß) as 0.80. The sample size obtained was 19 and 17 respectively. Therefore the sample size was considered as. Further assuming 10% loss to follow up during study the required sample size for the present study will be 21 (20) in each group. All the screened cases will be randomly allocated into two groups based on random allocation sequence.

Paired t test was used to evaluate the mean, standard deviation, and p value for different variables. Results are being represented as mean standard deviation. Results corresponding to the value of $p<0.05$ were considered as significant [6].

RESULTS

A total of 40 patients were included in the study (Table 1). Of these 20 patients were given oral vitamin D (group A, treatment group) and 20 patients were kept on conventional treatment and not given oral vitamin D (group B, control group). The mean age of the patients was 34.50 ± 13.50 years. There were 18 men and 22 women. Mean serum 25(OH) D level was 20.70 ± 5.91 ng/mL. The effect of vitamin D supplementation on DED patients in group A was assessed (Table 2 and Figure 1). TBUT RE and LE was found to be 3.35 ± 0.93 s and 3.45 ± 0.88 s at pre-treatment, increased to 5.10 ± 1.44 s and 5.01 ± 1.35 s after 2 weeks and to 7.45 ± 0.98 s and 7.15 ± 1.27 s after 6 weeks respectively before returning to the pre-treatment levels after 10 weeks ($p<0.001$, 0.001 and 0.001, respectively, paired t-test).

Tear secretion by Schirmer's test in RE and LE was found to be 3.70 mm ± 0.80 mm and 3.75 mm ± 0.78 mm at pre-treatment, 5.55 ± 0.82 mm and 5.80 ± 0.77 mm after 2 weeks, 7.64 mm ± 0.81 mm and 7.85 ± 0.74 mm after 6 weeks, and 8.30 mm ± 0.73 mm and 8.81 mm ± 0.77 mm respectively after 10 weeks ($p<0.001$, 0.001 and 0.001, respectively, paired t-test). OSDI score was 35.2 ± 2.14 at pre-treatment, 23.85 ± 1.66 after 6 weeks ($p<0.001$) [7].

A comparison between the vitamin D treated and untreated group was performed by using t test two tailed paired depicted in Table 3. The average p value obtained for TBUT in vitamin D untreated and treated group was 0.1663 (not significant) at pre-treatment, 0.0385 (significant) at 2 weeks, 0.0017 (significant) at 6 weeks, and 0.0035 (significant) at 10 weeks. Similarly the average p value obtained for schirmer's score in vitamin D untreated and treated group was 0.3090 (not significant) at pre-treatment, 0.0000 (significant) at 2 weeks, 0.0000 (significant) at 6 weeks, and 0.0011 (significant) at 10 weeks. Figure 2 clearly showed that vitamin D supplementation increases TBUT and schirmer's scores in vitamin D supplemented group than the vitamin D non-supplemented group.

In-group B, oral vitamin D supplementation was not given, hence no significant changes were observed in the parameters for improvement of dry eye (Table 2). However, conventional treatment was given to all the 40 dry eye patients with insignificant changes in the TBUT, schirmer's tear secretion test and OSDI score in patients of group B [8].

Table 1: Demographic data of subjects.

	Total subjects
N	**40**
Age (mean ± SD)	34.5 ± 13.5 years
Gender (male: female)	18:22
Serum 25 (OH)D level	20.7 ± 5.9 ng/ml

Table 2: The effect of vitamin D supplementation on dry eye disorder in treatment and control group.

Treatment group A (n=20)							
	Pre-treatment (n=20)	**After vitamin D supplementation**					
		2 weeks (n=20)		**6 weeks (n=19)**		**10 weeks (n=18)**	
	Mean ± SD	**Mean ± SD**	**p-value**	**Mean ± SD**	**p-value**	**Mean ± SD**	**p-value**
TBUT (sec) RE	3.35 ± 0.93	5.10 ± 1.44	<0.001*	7.45 ± 0.98	<0.001*	4.10 ± 1.44	<0.066
TBUT (sec) LE	3.45 ± 0.88	5.01 ± 1.35	<0.001*	7.15 ± 1.27	<0.001*	4.05 ± 1.35	<0.081
Schirmer's tear secretion test (mm) RE	3.70 ± 0.80	5.55 ± 0.82	<0.001*	7.64 ± 0.81	<0.001*	5.30 ± 0.73	<0.045*
Schirmer's tear secretion test (mm) LE	3.75 ± 0.78	5.80 ± 0.77	<0.001*	7.85 ± 0.74	<0.001*	4.81 ± 0.77	<0.060
OSDI score	35.2 ± 2.14			23.85 ± 1.66	<0.001*		
Control group B (n=20)							
	Pre-treatment (n=20)	**2 weeks (n=20)**		**6 weeks (n=18)**		**10 weeks (n= 6)**	
	Mean ± SD	**Mean ± SD**	**p-value**	**Mean ± SD**	**p-value**	**Mean ± SD**	**p-value**
TBUT (sec)RE	4.25 ± 0.97	4.41 ± 0.91	0.37	4.52 ± 0.90	0.12	4.2 ± 0.97	0.056
TBUT (sec) LE	4.73 ± 0.99	5.01 ± 1.00	0.48	5.10 ± 1.01	0.23	6.00 ± 1.01	0.015
Schirmer's tear secretion test (mm) RE	3.50 ± 0.77	3.50 ± 0.77	0.5	3.51 ± 0.90	0.52	3.67 ± 0.77	0.671
Schirmer's tear secretion test (mm) LE	4.05 ± 0.78	4.05 ± 0.79	0.21	4.10 ± 0.73	0.61	5.04 ± 0.77	0.081
OSDI score	34.08 ± 1.62			32.80 ± 0.81	0.06		

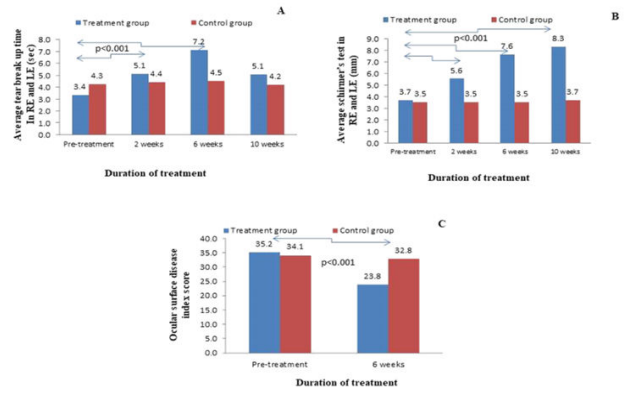

Figure 1: Association of vitamin D supplementation on dry eye disorder in control group (without oral vitamin D supplementation) and treatment group (Oral vitamin D supplementation). (A) Average break up time in right eye and left eye in treatment group showed significant increment at 2 weeks and 6 weeks in comparison to control group showing improvement in dryness before returning to pre-treatment level after 8 weeks. (B) Average schirmer's test in right eye and left eye in treatment group showed significant increment at 2 weeks, 6 weeks in comparison to control group showing improvement in dryness before returning to pre-treatment level after 8 weeks. (C) Ocular surface disease index score significantly decreased after 6 weeks in treatment group in comparison to control group showing improvement in dryness.

Table 3: Comparison of TBUT and Schirmer's score between the vitamin D treated and untreated group.

TBUT					
		Pre-treatment (sec) (n=20, mean ± SD)	**2 weeks (sec) (n=20, mean ± SD)**	**6 weeks (sec) (n=18, mean ± SD)**	**10 weeks (sec) (n=16, mean ± SD)**
Vitamin D untreated group	RE	4.25 ± 0.97	4.41 ± 0.91	4.52 ± 0.90	4.2 ± 0.97
	LE	4.73 ± 0.99	5.01 ± 1.00	5.10 ± 1.01	6.00 ± 1.01
Vitamin D treated group	RE	3.35 ± 0.93	5.10 ± 1.44	7.45 ± 0.98	4.10 ± 1.44
	LE	3.45 ± 0.88	5.01 ± 1.35	7.15 ± 1.27	4.05 ± 1.35
p value	RE	0.1444	0.0338	0.0005	0.002
	LE	0.1882	0.0432	0.003	0.005
Schirmer's score					
		Pre-treatment (mm) (n=20, mean ± SD)	**2 weeks (mm) (n=20, mean ± SD)**	**6 weeks (mm) (n=18, mean ± SD)**	**10 weeks (mm) (n=16, mean ± SD)**
Vitamin D untreated group	RE	3.50 ± 0.77	3.50 ± 0.77	3.51 ± 0.90	3.67 ± 0.77
	LE	4.05 ± 0.78	4.05 ± 0.79	4.10 ± 0.73	5.04 ± 0.77
Vitamin D treated group	RE	3.70 ± 0.80	5.55 ± 0.82	7.64 ± 0.81	5.30 ± 0.73
	LE	3.75 ± 0.78	5.80 ± 0.77	7.85 ± 0.74	4.81 ± 0.77
p value	RE	0.481	0	0	0.0015
	LE	0.1371	0	0	0.0008

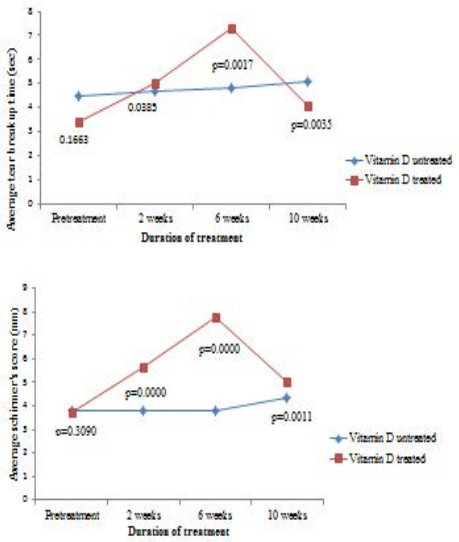

Figure 2: Comparison of p value obtained for TBUT and schirmer's score between the vitamin D treated and vitamin D untreated group at different time interval.

DISCUSSION

Dry eye is a disease of ocular surface with multifactorial etiology with characteristic loss of tear film stability, in which hyperosmolarity of tear film, inflamed and damaged ocular surface, and neurological disturbances play a role in etiology [9].

To the body, vitamin D (particularly, D_3) is a crucial nutrient. Vitamin D affects many parts of our body, if a number is to be given to it, it would be somewhere near 2000 individual parts, thus it is one of the highest researched drugs throughout the world. Virtually every cell of our body contains a receptor for vitamin D. Vitamin D deficiency is associated in dry eye has been proposed in several literatures.

In our study 47.5% of the participants were vitamin D insufficient and 52.5% of the participants were vitamin D deficient. Both the vitamin D insufficient and deficient groups had dry eyes as per schirmer's test and tear breakup time test. We established a negative correlation between serum 25 (OH) levels and OSDI scores. Our findings goes well with the study performed by P. Yildrim et al. and A. Tovey et al. in which they established a link between vitamin D deficiency and dysfunctions in tear and dryness and negative correlation between vitamin D levels and OSDI scores [10].

Our result clearly shows that vitamin D deficiency decreases the TBUT and schirmer's test values and may be associated with severity of dry-eye symptoms. Also, we noted supplementation of oral vitamin D improved tear secretion and reduced tear instability as indicated by development of schirmer's score and tear breakup time. This observation is well defended by the study performed by Kurtul et al. in which he investigated the effect of vitamin D deficiency on Tear Break-Up Time (TBUT) and schirmer's test scores and assess their relationship in non-Sjogren's dry-eye patients [11].

Our study findings indicate a significant improvement in schirmer's score, tear breakup time and OSDI score in-group patients who were administered vitamin D orally while there was an insignificant improvement in group B patients who didn't receive oral vitamin D. The possible explanation for insignificant improvements in group B patients was their treatment with conventional drugs. The obtained p value for the average TBUT and average schirmer's score in the vitamin D treated group is significant than the vitamin D untreated group (Figure 2). Hence, we can say that a protective role is played by vitamin D in the development of dry eye, which could be due to the enhancement of the tear film parameters and reduction of ocular surface inflammation. Supplementation of vitamin D may be useful in dry eye symptoms, including ocular discomfort, soreness, redness, ocular fatigue, sensitivity to light and blurred sight. Vitamin D supplementation also improved severity of dry eye disease and subjective symptoms including OSDI score [12].

CONCLUSION

In summary, vitamin D supplementation promoted tear secretion with improved symptoms of dry eye syndrome. Hence we can conclude that vitamin D supplementation is a beneficial and effective treatment in dry eye patients.

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