Association of Vitamin D deficiency with Dry Eye syndrome

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ABSTRACT

Objective *To find out the association of dry eye syndrome with vitamin D deficiency.*

Study design *Cross sectional study.*

Place & Duration of study *Department of Ophthalmology, Ziauddin Hospital Karachi, from September 2020 to May 2021.*

Methodology *Patients of dry eye with vitamin D deficiency were included in this study. They were evaluated for dry eye symptoms. These patients were provided treatment and followed up in outpatient department at 8th and 12th weeks. The outcome was analyzed in terms of serum vitamin D level, Ocular Surface Diseases Index (OSDI) score, tear breakup time (TBUT), Schrimer's 1 test to check the basic and reflex tearing, and Fluorescein Staining Score (FSS).*

Results *Seventy-four patients with vitamin D deficiency and dry eye were included in this study. The mean age of patients was 29.3±8.4 year. The mean serum 25(OH)D level before treatment was 12.48±4.53 ng/mL, which at the 12th week of treatment improved to 36.54±8.34 ng/mL (0.016). The mean pretreatment TBUT was 5.07±1.52 seconds and improved to 11.36±3.14 seconds (0.0006). This was statistically significant.*

Conclusion *Vitamin D deficiency is a significant risk factor for dry eye syndrome. Immunomodulatory effect of vitamin D is helpful in reducing the ocular inflammation and improving the tear film stability.*

Key words *Vitamin D deficiency, Dry eye syndrome, Vitamin D supplements.*

INTRODUCTION:

Vitamin D is essential for regulation of calcium and phosphate levels as it keeps the musculoskeletal system healthy.[1] However, vitamin D is important for optimal function of many organs and tissues throughout the body.[2] Vitamin D deficiency is a major health issue globally with almost one billion people having relatively low levels of this vitamin in their blood. More than 70% of South Asians are vitamin D deficient.[3] This is due to their darker skin tone which makes it harder for them to make vitamin D. Due to the cultural and religious values, most south Asian women dress with full coverage that affects metabolism of vitamin D.[4] The 25 hydroxy (OH) D levels in serum are measured in order to check vitamin D levels in the body. A >30ng/mL is considered normal, while a value between 21-29ng/mL represents an insufficiency and <20ng/mL means vitamin D deficiency. Vitamin D deficiency can result in poor intestinal absorption of calcium leading to mobilization of calcium from bones in order to maintain circulatory levels. This then increases the risk of osteomalacia and bone fracture in adults and rickets in children. Due to its role as a potent stimulator of bone resorption, vitamin D is also very important for bone remodeling.[5]

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Vitamin D deficiency may also cause ocular manifestations such refractive error, uveitis and dry eye syndrome. Dry eye is a multifactorial disease occurring mostly in old age. However, in recent studies it has been shown that dry eye syndrome is common in younger population as well.[6] Ocular inflammation and increased tear osmolality are major problems in patients with dry eye syndrome. Dry eye results in ocular discomfort, visual acuity disturbances and tear film instability which damages the corneal epithelium.[7] Vitamin D has anti-inflammatory properties which help in preventing the dry eye by producing cathelicidin that helps in enhancing the corneal epithelium barrier function. It also increases the lipid component of tear film by producing surfactants.[8] The purpose of this study was to determine the association between dry eye and vitamin D deficiency, both of which are common in the younger population.

METHODOLOGY:

A cross sectional study was conducted in the Department of Ophthalmology, Ziauddin Hospital Karachi, from September 2020 to May 2021. Patients between 18 years to 40 years of age with vitamin D deficiency (serum levels <20ng/ml or < 50nmol/L) along with dry eye were included. Patients with auto-immune diseases, on vitamin supplements, previous intraocular surgeries, contact lens users and with any systemic or ocular diseases and risk factors for dry eye, were excluded.

The study was approved by the ethical committee. Written consent was taken from all the patients. Patients were asked to fill out a survey form for Ocular Surface Diseases Index (OSDI). The overall OSDI score of 0-12 points represents a normal ocular surface, 13-22 mild, 23-32 moderate and 33-100 points represents a severe disease. Complete ocular examinations were performed, which included visual acuity assessment, Slit lamp examination and fundus examination.

The dry eye examinations included tear breakup time, Schirmer's 1 test to check the basic and reflex tears, and fluorescein staining score (FSS). For the tear film breakup time, 2% fluorescein drops were instilled into the patient's eye and examined on a slit lamp. The time taken for the first dry spot to appear on the cornea after blinking once was noted. Time >10 seconds was considered normal, 5-10 seconds was considered as marginal and <5 seconds represented a severe case of dry eye.

In the Schrimer's 1 test a >15mm wetting of strip was considered normal, 11-15mm mild dry eye, 5-10mm moderate dry eye while a <5mm wetting severe dry eye. In order to evaluate the fluorescein Oxford staining score, a 2% fluorescein dye was instilled in the eye and staining was represented by punctate dots on a series of panels, which ranges from 0-5.

The patients with vitamin D deficiency were treated with oral supplements (50 000 IU). It was advised to continue for eight weeks after which levels were re-checked. If more than 30ng/mL value was reported then patients were put on maintenance dose of 1500-2000 IU per day. They were then re-assessed after 12th week of the treatment and all parameters of dry eye were performed.

Demographic data, including age and sex were collected in a pre-designed form and variables also included serum vitamin D levels, TBUT, Schirmer's 1 test, fluorescein staining score and Ocular Surface Diseases Index. The collected data was entered into SPSS version 23. Quantitative variables, such as age, are presented in the form of mean ± standard deviation and qualitative variables as frequency and percentages. The pre and post treatment results were compared using independent paired t tests. A p value < 0.05 was considered significant.

RESULTS:

A total of 80 patients with dry eye were included however six were lost to follow up and excluded from analysis. Of the remaining 74 patients 56 (75.7%) were females and 18 (24.3%). The female to male ratio was 3:1. The mean age of patients was 29.3±8.4 year. The minimum age was 20.9 years while the maximum was 37.7 years. The mean serum 25 (OH) D level before treatment was 12.48±4.53 ng/mL. The mean pre-treatment Ocular Surface Disease Index was 31.55±10.29. The number of patients with a mild condition of dry eye were 13 (17.57%), 29 (39.19%) had a moderate dry eye symptoms and 33 (44.59%) with severe dry eye. The mean pre-treatment TBUT was 5.07±1.52 seconds. Forty (54.1%) patients had a marginal TBUT, while 34 (45.9%) had a severe dry eye. The pre-treatment mean value for Schrimer's 1 test was 6.32±2.69mm. Nine (12.16%) patients had a mild dry eye, 35 (47.3%) moderate while 30 (40.54%) had a severe condition. Fluorescein staining score showed that 29 (39.19%) patients had a mild condition while 45 (60.81%) patients had a moderate condition.

The mean serum vitamin D level was 33.24±8.11 ng/mL. Of the total, 28 (37.8%) patients had a vitamin D insufficiency with levels between 21-29ng/mL

Table I: The Effect of Vitamin D Supplementation on Dry Eye

Test	Pre-treatment Mean ±SD	8th week follow up Mean ±SD	p Value	12th week follow up Mean ±SD	p Value
Serum 25 (OH) D	12.48 ± 4.53	33.24 ± 8.11	0.00001*	36.54 ± 8.34	0.016*
OSDI	31.55 ± 10.29	21.55 ± 9.55	0.00001*	18.47 ± 7.65	0.033*
TBUT	5.07 ± 1.52	8.28 ± 2.32	0.0001*	11.36 ± 3.14	0.0006*
Schrimer's 1 test	6.32 ± 2.69	11.69 ± 3.77	0.00001*	13.54 ± 4.32	0.03*

while 46 (62.2%) had normal level. The patients with insufficient levels were given the 50 000 IU dose of vitamin D for further four weeks. The patients whose levels became normal were put on a maintenance dose of 1500 IU for next four weeks. After treatment at eighth week follow up the mean OSDI was 21.55±9.55. The OSDI score was normal for 26 (35.14%) patients, mild for 19 (25.68%) patients; moderate for 23 (31.08%) patients while 6 (8.10%) were in severe category. The mean TBUT after 8 weeks of treatment was 8.28±2.32 seconds. The TBUT was normal in 18 (24.32%) patients, marginal in 51 (68.91%) and severe in 5 (6.75%) patients. The mean Schrimer's test was 11.69±3.77 mm. The Schrimer's 1 test results showed that 13 (17.57%) patients were normal, 32 (43.24%) had a mild dry eye, 26 (35.14%) moderate condition and 3 (4.05%) had a severe condition. Fluorescein staining scores showed that 23 (31.08%) patients were normal, 47 (63.51%) were mild, and 4 (5.41%) were moderate. The details of outcome after the 12th week is given in table I.

The mean serum vitamin D levels were 36.54±8.34 ng/mL. The result showed that 68 (91.9%) patients had normal levels while the remaining 6 (8.10%) had a borderline insufficiency. All patients were kept on a maintenance dose of 1500 IU. The mean OSDI score became 18.47±7.65. The OSDI was normal for 56 (75.67%) patients and mild in 18 (24.32%). The mean TBUT was 11.36±3.14 seconds. The TBUT was normal for 65 (87.84%) patients while the remaining 9 (12.16%) were in the marginal range. The mean of Schrimer's 1 test was 13.54±4.32 mm. The results showed that 28 (37.84%) patients were normal while 46 (62.16%) had mild dry eye. Fluorescein staining scores showed that 62 (83.78%) were normal while 12 (16.21%) patients had mild dry eye. Overall 66.6% of the patients having vitamin D deficiency were found to have dry eye. Almost 98% of the patients were successfully treated for both dry eye and vitamin D deficiency.

DISCUSSION:

Dry eye is a multifactorial disease caused by insufficient production or impaired stability of the tear film. Understanding etiology and treatment of dry eye has always been a challenge.[9-11] Recently, researchers have gotten intrigued by Vitamin D deficiency's association with dry eye syndrome. This resulted in hypothesizing that vitamin D improves the symptoms and signs of dry eye by decreasing inflammatory cytokines and increasing antioxidant cytokines in tears. Studies showed that vitamin D supplements significantly improve symptoms of dry eye.[12-14]

Galor et al study found that improvement in dry eye syndrome was associated with higher vitamin D levels.[15] A similar study conducted by Chih-Huang Yang et al also reported that vitamin D supplements improved various symptoms of dry eye such as tear quality.[16] Bae SH et al studied a total of 105 patients having dry eyes and treated them using vitamin D supplements. Comparison of ocular tests conducted before and after treatment showed that there was a significant improvement in their condition.[17] Our study shows similar results as all parameters like OSDI and TBUT improved significantly from their baseline levels. Patients with dry eye should be evaluated for vitamin D deficiency as it is fairly easy to treat through supplements. This study has provided an evidence based data regarding vitamin D deficiency that was associated with dry eye and improvement noted after treating the vitamin deficiency.

CONCLUSION:

Vitamin D supplementation improves tear secretion and tear film stability and reduces inflammation of eyelid margin. Vitamin D supplements hence improve the symptoms of dry eye by enhancing tear film parameters.

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