Dry Eye Assessment in Patients With Vitamin D Deficiency

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Objectives: The aim of this study was to evaluate tear film function in patients with vitamin D deficiency.

Methods: In a single center, 60 eyes of 30 patients with vitamin D deficiency (group 1), and 60 eyes of 30 healthy individuals (group 2) were evaluated using the Ocular Surface Disease Index (OSDI) questionnaire, Schirmer I test, tear break-up time (TBUT), scoring of ocular surface fluorescein staining using a modified Oxford scale, and tear osmolarity.

Results: Tear osmolarity values, OSDI, and Oxford scale scores were significantly higher in group 1 (309±9 mOsm/L, 35.78±21.44 and 1.3±0.9, respectively) compared with group 2 (295±10 mOsm/L, 18.69±17.21 and 0.4±0.8, respectively) ($P<0.001$ for all). Schirmer I test and TBUT results in group 1 (8.5±3.7 mm and 8.7±0.6 sec, respectively) were significantly lower compared with group 2 (16.6±2.4 and 18.1±0.5, respectively) ($P<0.001$ for all).

Conclusions: This study demonstrates that vitamin D deficiency is associated with tear hyperosmolarity and tear film dysfunction. Patients with vitamin D deficiency may be prone to dry eye.

Key Words: Dry eye—Vitamin D deficiency—Schirmer test—Tear osmolarity.

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Vitamin D refers to a group of fat-soluble secosteroids responsible for enhancing intestinal absorption of calcium, iron, magnesium, phosphate, and zinc. It is not strictly a vitamin, and may be considered a hormone as its synthesis and activity occur in different locations. Although commonly known for its role in calcium homeostasis, vitamin D also plays important roles in immune regulation, proliferation, differentiation, apoptosis, and angiogenesis. Vitamin D deficiency and genetic variations may cause a wide range of ocular pathologies, such as myopia, age-related macular degeneration, diabetic retinopathy, uveitis, and dry eye.[1,2]

Vitamin D deficiency may also cause dry eye, as studies have reported dry eye syndrome (DES) to be a localized autoimmune disease, and researchers recently hypothesized that vitamin D plays a role in the disorder because of its antiinflammatory properties.[3] Dry eye, described by increased osmolarity of the tear film and inflammation of the ocular surface, causes ocular discomfort, visual disturbance, and tear film instability with potential damage to the ocular surface.[4] Hyperosmolarity provides proinflammatory stress to the ocular surface.[5]

In this study, we aimed to investigate tear film function in patients with vitamin D deficiency.

MATERIALS AND METHODS

A total of 60 eyes of 30 patients with vitamin D deficiency (group 1) and 60 eyes of 30 healthy individuals without signs or symptoms of dry eye disease or other ocular pathologies (group 2) were included in this single-center, cross-sectional observational study. The mean data of two eyes for each patient were assessed.

All participants were examined by an internal medicine specialist (O.O.) for routine check-up, and then referred to ophthalmology department. Subjects were excluded if they presented with primary Sjögren syndrome or other systemic rheumatic disease history, vitamin B12 deficiency, a history of smoking, current or recent drug use that could affect the lacrimal functional unit, active ocular infection or allergy, ocular surface scarring, previous eye surgery, or current contact lens use. The ophthalmologist (S.K.E.) who examined the subjects was blind to their vitamin D levels. Vitamin D deficiency was defined as a 25 (OH) D serum level less than 20 ng/mL. The serum vitamin D levels of the participants were assessed by enzyme-linked immunosorbent assay.

The study was reviewed and approved by the Istanbul Medipol University Ethics Committee, and written informed consent was obtained from each patient before enrollment. The study was conducted in accordance with the tenets of the Declaration of Helsinki.

Initially, patients completed the International Ocular Surface Disease Index (OSDI) survey. All subjects underwent a full ophthalmological examination in the same order, including visual acuity assessment, standardized slit-lamp examination, and fundus examination. The dry eye examinations were performed in a specific order: the tear osmolarity measurement, tear break-up time, corneal fluorescein staining scoring using the Oxford Schema, and anesthetized Schirmer test. The testing for all subjects was performed in the same room at the same stable conditions (humidity, temperature, etc). The interval between each of the measurements/tests on the ocular surface was at least 5 min.

Tear osmolarity measurements were evaluated using a TearLab osmometer (TearLab Corp., San Diego, CA). Tears were collected from the inferior lateral tear meniscus. Three consecutive measurements were obtained, and their mean was used for statistical

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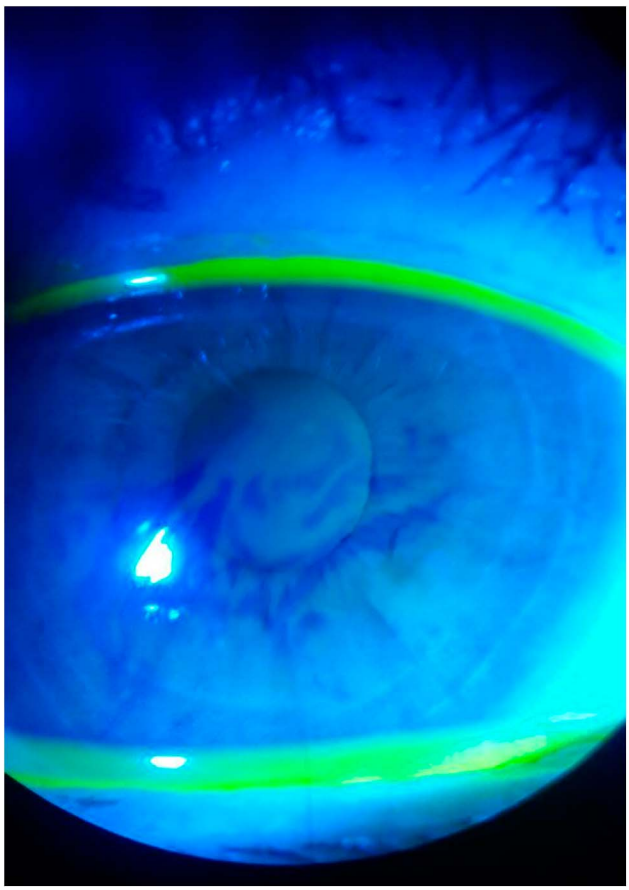

FIG. 1. Tear break-up time showing breaks in the fluorescein after 8 sec on an eye of a patient with vitamin D deficiency. full color online

analysis. For corneal fluorescein staining, after moistened fluorescein strips were introduced to the conjunctival sac, the entire cornea was examined by slit-lamp evaluation with a yellow barrier filter and cobalt blue illumination. The staining was graded using the Oxford Scheme 6-point scale (from 0 through 5).[6]

TABLE 1. *The Comparisons of the Mean Tear Film Parameters and OSDI Scores Between Two Groups*

Parameter	Group 1	Group 2	P^a
Tear osmolarity, mOsm/L			<0.001
Mean±SD	309±9	295±10	
Range	282–330	270–318	
Schirmer test, mm			<0.001
Mean±SD	8.5±3.7	16.6±2.4	
Range	2–21	11–30	
Oxford scores			<0.001
Mean±SD	1.3±0.9	0.4±0.8	
Range	0–4	0–3	
TBUT, sec			<0.001
Mean±SD	8.7±0.6	18.1±0.5	
Range	3–18	13–24	
OSDI			<0.001
Mean±SD	35.78±21.44	18.69±17.21	
Range	8–77	3–83	

[a]Independent samples *t* test.

OSDI, Ocular Surface Disease Index; SD, standard deviation; TBUT, tear break-up time.

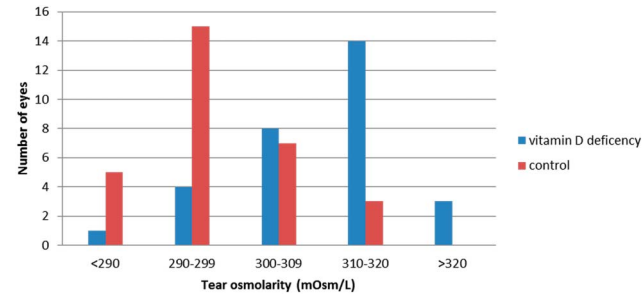

FIG. 2. Comparison of tear osmolarity values between groups. full color online

Tear break-up time (TBUT) was assessed after instillation of 2% fluorescein staining under a cobalt blue filter. The time interval between the last complete blink and the appearance of the first dry spot was recorded (Fig. 1). The mean of three consecutive measurements was obtained. The Schirmer I test was performed with topical anesthesia using a standardized filter strip (Bio-Tech Vision Care, Ahmedabad, India). The amount of wetting was measured after 5 min.

The normality of the distribution of each of the parameters was checked using the Kolmogorov–Smirnov normality test. The tear osmolarity, Schirmer I test with anesthesia, TBUT values, and Oxford and OSDI scores between groups were compared using independent student t test. A *P*-value less than 0.05 was considered statistically significant.

RESULTS

The mean subject age was 33.9±0.9 years (range: 25–42 years) in group 1 (14 women, 16 men) and 33.8±0.9 years (range: 25–43 years) in group 2 (15 women, 15 men). There were no significant differences between the groups with respect to age or sex (P=0.941 and P=0.796, respectively). Summary statistics are shown in the Table 1. The mean tear osmolarity was significantly higher in group 1 compared with group 2 (P<0.001) (Fig. 1).

The Schirmer I test values and TBUT measurements for group 1 were significantly lower compared with those for group 2 (P<0.001) (Figs. 2 and 3).

The mean superficial punctate staining, as measured by the Oxford scale, differed significantly between group 1 and group 2 (P=0.001) (Fig. 4). The mean Ocular Surface Disease Index scores were significantly higher in group 1 compared with group 2 (P<0.001) (Fig. 5).

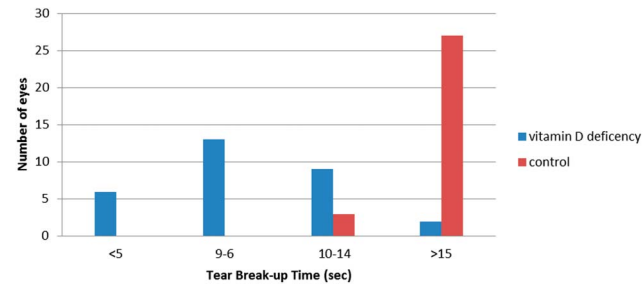

FIG. 3. Comparison of Schirmer test values between groups. full color online

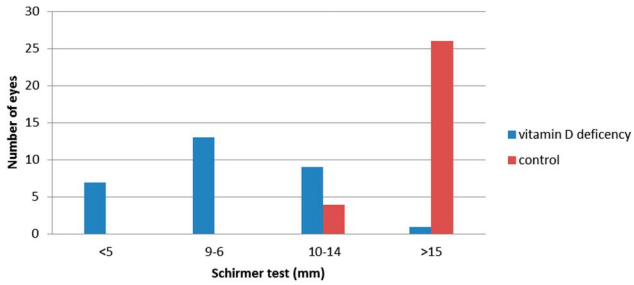

FIG. 4. Comparison of tear break-up time values between groups. full color online

DISCUSSION

Vitamin D, a fat-soluble vitamin produced in the skin after exposure to ultraviolet light, and which occurs naturally in a small number of foods, has found to be important in metabolism. It is well known that vitamin D regulates serum calcium and phosphate levels and thereby has an important role in maintaining bone health. Current studies also have shown the relationship between vitamin D and autoimmune diseases such as type I diabetes mellitus, multiple sclerosis, rheumatoid arthritis, systemic lupus erythematosus, and inflammatory bowel diseases.[7,8]

Based on the fact that DES is now widely accepted as a localized autoimmune disease, researchers recently hypothesized that vitamin D plays a role in dry eyes because of its antiinflammatory properties. The pathophysiology of DES involves osmotic, mechanical, and inflammatory insults to the tear film, epithelium, and subepithelial nerve plexus. As indicated in the Dry Eye Workshop (DEWS) report, osmolarity is considered to be one of the most objective assessments for dry eye disease and is thought to be the central mechanism in the pathogenesis of ocular surface damage.[3] Tear hyperosmolarity stimulates death of the epithelial surface cells and a cascade of inflammatory events, which lead to loss of mucin-producing goblet cells. This exacerbates the tear film instability and contributes to the circle of events that negatively affects ocular surface.[9]

Yildirim et al.[10] demonstrated that patients with vitamin D deficiency developed dry eye and impaired tear function. They reported lower scores in Schirmer test and TBUT, and higher in OSDI scores in patients with vitamin D deficiency than in controls.[11] Another study by Kurtul et al.[12] reported that vitamin D deficiency decreases the TBUT and Schirmer test values and may be associated with dry eye symptoms in non-Sjögren syndrome. They found TBUT scores and Schirmer-1 results of the study group were significantly lower than the control group. These results were similar with our findings. Additionally, we investigated tear osmolarity in patients with vitamin D deficiency. In our study, patients with vitamin D deficiency showed significantly higher tear osmolarity levels, lower Schirmer I scores, and lower TBUT values compared with controls.

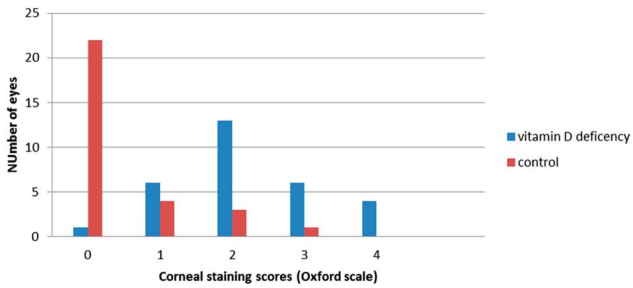

FIG. 5. Comparison of Oxford scores between groups. full color online

Yin et al.[13] demonstrated that 25(OH)D3 and its active metabolite 1,25(OH)2D3, both enhance corneal epithelial barrier function. Lin et al.[14] demonstrated that oral vitamin D supplementation affects vitamin D metabolite concentrations in the anterior segment of the eye. Reins et al.,[11] furthers our understanding of vitamin D's protective function, showing that vitamin D is able to diminish inflammation even after removal of the stimulus. Bang et al.[15] have shown that vitamin D metabolism may be involved in the pathogenesis of primary Sjögren's syndrome.

Recently, there is much interest in understanding how diet, hormones, and habits influence ocular surface health and tear production. Many studies have found a beneficial effect of omega-3 on ocular health.[16,17] Galor et al.[18] found no effect of Mediterranean diet on DES but found that higher vitamin D levels had a small, but favorable effect on DES symptoms. There may be a possible protective effect of vitamin D supplementation on tear film; however, recently no data have proved this hypothesis. Further studies including replacement of vitamin D may help us to understand the relationship between vitamin D and dry eye.

Limitations in this study include the low number of subjects and the lack of screening of inflammatory markers such as IL-6, TNF-alpha, and MMP-9. Another important limitation is the lack of a control group consisting of patients with dry eye without vitamin D deficiency. Comparing tear film parameters between dry eye patients with or without vitamin D deficiency could be more helpful to clarify the pathogenesis of dry eye disease. Nevertheless, this study has shown increased tear osmolarity and abnormal tear film in patients with vitamin D deficiency.

In conclusion, vitamin D is a multifunctional hormone, which plays an important role in ocular health.[19] There was no pathognomonic sign that we can distinguish dry eye with vitamin D deficiency only by a slitlamp. Patients with vitamin D deficiency should be further evaluated if they have syndromes causing dry eye and also dry eye patients be tested for vitamin D deficiency. Future research is needed with more patients to clear the role of vitamin D in dry eye pathogenesis.

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