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Original research article

Impact of oral vitamin D supplementation on the ocular surface in people with dry eye and/or low serum vitamin D

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ABSTRACT

Purpose: To determine the possible association between serum vitamin D levels and dry eye symptoms, and the impact of an oral vitamin D supplement.**Methods:** Three linked studies were performed. (i) 29 older adult participants, (ii) 29 dry eyed participants, and (iii) 2-month vitamin D supplementation for 32 dry eyed/low serum vitamin D levelled participants. All participants were assessed by the Ocular Surface Diseases Index (OSDI) to determine dry eye symptoms, and the phenol red thread test (PRT) and/or Schirmer's tear test, tear meniscus height, non-invasive tear break up time, grading ocular surface redness and fluorescein staining of the cornea to detect the tear quality and ocular surface conditions. Blood samples were collected for serum vitamin D analysis and interleukin-6 (IL-6) levels.**Results:** Among older adult participants, vitamin D levels were negatively correlated with dry eye symptoms, the severity of dry eye, and associated with tired eye symptom. Vitamin D levels of people with dry eye diagnosis were not correlated with OSDI scores and IL-6 levels; while IL-6 levels showed correlation with tear production. In supplement study, vitamin D levels increased by 29 nmol/l, while dry eye symptoms and grading of corneal staining appeared significant reductions. No significant changes in IL-6 levels.**Conclusions:** Low vitamin D levels (< 50 nmol/l) were associated with dry eye symptoms in older individuals but not those diagnosed with dry eye. Vitamin D supplement increased the vitamin D levels, and improved dry eye symptoms, the tear quality and ocular surface conditions.

1. Introduction

Dry eye disease is a common, chronic and severe ocular condition, affecting ~30% of the adult Caucasian population [1] and ~60% of the adult Asian population [2]. The observed higher prevalence of dry eye amongst the latter group might be due to ethnic variations and/or environmental conditions. The disease produces ocular discomfort (for example, foreign body sensation, irritation) and visual disturbance (blurred vision); ultimately it causes ocular surface inflammation and corneal and conjunctival abnormalities [3]. Current treatments (e.g. ocular lubricants) for this chronic condition are not very effective [4,5].

25-hydroxyvitamin D [25(OH)D], known as vitamin D, has long been regarded as one of the indispensable daily nutrients. There are two main forms of vitamin D: ergocalciferol (vitamin D₂) and cholecalciferol (vitamin D₃). Ergocalciferol can be acquired via specific food intake or

irradiation of plants, whereas cholecalciferol is mainly synthesised in the skin after exposure to ultraviolet light [6]. There is debate about the relationship between vitamin D and inflammation. While some studies have suggested elevated vitamin D levels reduced inflammation [7–9], others have hypothesized that vitamin D reduction results from inflammation [10–12]. The metabolites of vitamin D and the analogues have been demonstrated to have anti-inflammatory properties in animals [13–15].

Studies have found that older people tend to have lower vitamin D levels, and therefore they have been suggested to be prescribed higher supplementary doses [16]. Although dry eye can occur at any age [17], it is a condition that shows increased prevalence with advancing age [18] [19]. For example in one study the prevalence of dry eye in women younger than 50 years was < 6% but this increased to 10% in those aged greater than 75 years [19]. The prevalence of dry eye tends to be

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Table 1
Recent studies in the association between dry eye and vitamin D.

| Author(s) | Year | Number of participants | Design | Serum vitamin D levels | Outcome measures |
|----------------------|------|---|--|---|---|
| Bang et al. [21] | 2009 | 41 with primary Sjögren's syndrome (SS) (39 female and 2 male) | Two year follow-up examination of vitamin D levels | 28 ng/ml in normal controls, 21 ± 7 ng/ml in patients at the initial examination 20 ± 10 ng/ml at the two years follow-up | The mechanisms for the reduced levels of serum vitamin D levels in primary SS was unknown and could be a combination of many reasons Lower dry eye syndrome symptoms were significantly associated with higher vitamin D levels ($p = 0.01$) Lower scores in Schirmer's test and TBUT, and higher OSDI scores were detected in vitamin D deficient participants ($p < 0.05$) TBUT and Schirmer-1 test lower in vitamin D deficient group ($p = 0.01$ and 0.007) |
| Galor et al. [22] | 2014 | 247 male | Compared vitamin D levels in people with different severity of dry eye | Unavailable | |
| Yildirim et al. [23] | 2016 | 98 female (48 in control group and 50 in study group) | Cross-sectional comparison between people with and without vitamin D deficiency | Definition of vitamin D deficiency (< 20 ng/ml) | |
| Kurtul et al. [24] | 2015 | 34 (14 in control group and 20 in study group) | Cross-sectional comparison between people with and without vitamin D deficiency | 11.50 ± 1.8 ng/ml in study group 32.8 ± 8.72 ng/ml in control group | |
| Jee et al. [25] | 2016 | 16396 participants aged > 19 years (1579 in dry eye group and 14717 in non-dry eye group) | Investigation of the effect of vitamin D levels on ocular diseases, including dry eye syndrome | 16.9 ng/ml in dry eye group 17.4 ng/ml in non-dry eye group | An association between serum vitamin D levels and dry eye syndrome was not observed ($p < 0.05$) |

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