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The role of vitamin D in ocular diseases – a literature review

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Keywords: vitamin D; vitamin D deficiency; dry eye syndrome; vitamin D supplementation.

ABSTRACT

Introduction: Vitamin D is a steroid hormone that can modulate immune and inflammatory responses. Recent investigations have shed light on its potential role in the pathogenesis of many diseases affecting the eyes.

Aim of the study: This paper aims to provide a comprehensive review of the existing findings on the relationship between vitamin D and ocular diseases. The intention is to present new perspectives that will contribute to a better understanding of the complicated nature of this aspect.

Material and methods: This review included relevant papers from PubMed database using specified keywords.

Analysis of the literature: The role of vitamin D in ocular and visual health has been observed in many studies. A deficiency of vitamin D may play a significant role in the development of many ocular diseases such as dry eye disease, myopia, diabetic retinopathy, keratoconus, and thyroid eye disease.

Conclusions: Adequate vitamin D levels are significant for maintaining ocular health. Recognition of the pivotal role of vitamin D in ocular diseases opens new possibilities for potential therapeutic interventions. Ongoing research is needed to further investigate that aspect. Supplementation of vitamin D may prevent or modulate many diseases affecting the eyes.

Introduction

Vitamin D is a steroid hormone that can modulate immune and inflammatory responses. Recent investigations have shed light on its potential role in the pathogenesis of many diseases affecting the eyes.

Vitamin D stands for a group of fat-soluble secosteroids that can be obtained with food or produced in the skin (1). Vitamin D3 and D2 are the most important ones in this group (2). During the first hydroxylation, vitamin D is converted to 25-hydroxyvitamin D (25(OH)D) in the liver (2). Second hydroxylation converts it to physiologically active 1,25-dihydroxyvitamin D (1,25(OH)2D) in the kidneys (1). Vitamin D influences many biological functions apart from regulating the homeostasis of calcium (3). A large number of studies investigate the role of vitamin D in ocular diseases due to its positive effect in modulating immune and inflammatory responses.

In the eyes, vitamin D receptor is expressed in the retinal pigment epithelium, ciliary body, lens, and epithelium of the cornea but also retinal photoreceptors, ganglion cell layer, and corneal endothelium (4). Vitamin D hydroxylases were found in endothelial, corneal epithelial, non-pigmented ciliary body epithelial, scleral fibroblasts, and adult retinal pigment epithelial cell lines which can convert 25D into the active 1,25D (5, 6). Vitamin D influences many functions of these epithelial cells such as barrier function, response to inflammation, and infections (7). It shows that many ocular cells can metabolize and activate vitamin D. Hypovitaminosis D can impair the wound healing process, gap junctions, and integrity of corneal epithelial and tight junctions (8). A deficiency of that vitamin can affect the ocular surface by interfering with inflammatory, apoptotic, and oxidative mechanisms (9).

Aim

This paper aims to provide a comprehensive review of the existing findings on the relationship between vitamin D and ocular diseases. The intention is to present new perspectives that will contribute to a better understanding of the complicated nature of this aspect.

Methodology

This review included relevant papers from PubMed database using specified keywords: “vitamin D”, “eye”, and “ocular diseases”. The search was performed from February 25th, 2024, through September 28th, 2024. Only articles in English were considered. Manuscripts unrelated to the subject were excluded.

Analysis of the literature

Changes in vision

Vitamin D has an influence on non-skeletal tissues with neurons (10). Its deficiency might lead to worse contrast sensitivity function (10) (11). Tear break-up time and tear secretion are correlated with serum vitamin D levels. These parameters were found to be shorter in patients with vitamin D deficiency (12). It was stated that vitamin D deficiency may lead to an increase of macular thickness in certain areas of retinal nerve fiber layers and in that mechanism negatively affect contrast sensitivity (11). Moreover, patients with age-related macular degeneration experienced functional losses when looking at objects of low contrast (13).

Dry eye syndrome

Dry eye syndrome (DES) is a chronic condition that results in reduced tear secretion from lacrimal glands, production of low-quality tears, or increased tear water evaporation (1). The most common symptoms include redness, dryness, blurred vision, itchiness, sensitivity to light, burning sensation, and feeling of the foreign body in the eye (14). Some previous studies doubted the association between vitamin D and the risk of DES. Since then, many studies proved that this relationship is important (15-17). It is advised that patients with low levels of vitamin D should be evaluated for dry eye symptoms (18). Tear film vitamin D levels are different from vitamin D levels in serum, so it is vital to assess the relationship between vitamin D levels and ocular surface diseases (7). In one study, low vitamin D levels were observed in postmenopausal women with DES (15). In another study, a significant difference in the mean values of the Schirmer I and Schirmer I test was seen in patients with DES in patients with vitamin D deficiency (16). Moreover, managing vitamin D deficiency in patients with DES will prevent the worsening of that disease and post-operative complications after refractive surgery (7).

Vitamin D supplementation might play an important role in relieving symptoms. One study suggested that the use of topical vitamin D drops might be effective in alleviating symptoms of dry eye in patients with meibomian gland dysfunction (19). It has been observed, that patients with dry eye post-LASIK operation might have better visual acuity and alleviation of

dry eye symptoms after oral vitamin D supplementation (17). Oral supplementation of vitamin D might have a positive effect on dry eye treatment. Studies revealed that it improves ocular surface homeostasis parameters, leads to better tear stability, and improves tear osmolarity in patients who have vitamin D deficiency (18, 20). What is more, vitamin D supplementation enhances the efficacy of topical artificial tears in patients with dry eye syndrome and may be helpful in treating patients with DED refractory to topical treatment (21).

Age-related macular degeneration

Age-related macular degeneration (AMD) is associated with the accumulation of extracellular deposits and degeneration of photoreceptors and nearby tissues (22). Angiogenesis, chronic inflammation, and oxidative stress play major roles in its pathogenesis (23). Studies suggest that vitamin D may be a factor that modulates the course of AMD (24). Patients suffering from AMD had lower vitamin D levels in comparison to healthy patients (25). Moreover, one study suggests that patients with vitamin D deficiency are at a bigger risk of neovascular AMD (26) , and that supports its role in the regulation of angiogenesis (27). Patients with a dry form of AMD also have low levels or deficiency of vitamin D (13). Perceiving objects of low contrast may remain a difficulty for patients with AMD (13). It was stated that high 25OHD concentrations may be protective and that 25OHD concentrations below 50nmol/L are linked with late AMD (28). One very important aspect is the role of nutrition. A diet with vitamin D may prevent or stop progression to advanced neovascular AMD (29).

Diabetic retinopathy

Diabetic retinopathy (DR) is a microangiopathy which is caused by chronic diabetes mellitus (30). Hypovitaminosis of vitamin D is mentioned as one of the risk factors of DR (31). Vitamin D plays a role in the development of that disease because it reduces blood sugar, hypertension, and atherosclerosis (32). This vitamin can inhibit neovascularization (3). According to most studies, there is an increased risk of DR in patients with vitamin D deficiency (31). Vitamin D deficiency may lead to a three times bigger risk of diabetic retinopathy in patients with type 2 diabetes so it is advised for patients to monitor their eyes regularly (33). Another study stated that the tear break-up time, Schirmer test, corneal staining score, and values of the tear meniscus height and area were much lower in children with diabetes mellitus 1 and coexisting vitamin D deficiency in comparison to tear measurements

in healthy children (34). Vitamin D supplementation has a neuroprotective effect and leads to thinning and reduction of mean retinal nerve fiber layer thickness in early-stage DR subjects (35). Vitamin D deficiency is associated with sight-threatening DR and should be managed to reduce the risk of blindness (36). More studies are needed to assess the direct relationship between vitamin D levels and DR. Further research should focus on the influence of dietary intake of vitamin D on DR (37).

Keratoconus

Keratoconus is a bilateral and progressive disease of the cornea. It leads to thinning and steeping of the cornea which leads to astigmatism and decreased visual acuity (38). Although it is considered a non-inflammatory disease, many inflammatory mediators are elevated (39). Due to abilities of vitamin D to influence inflammatory processes, it has a positive effect on extracellular matrix remodeling (7). Study shows that patients with keratoconus have lower serum vitamin D levels in comparison to age- and sex-matched healthy patients (40, 41). Etiology might be caused by a lower antioxidative activity (42). Vitamin D receptors are present in the lens, corneal epithelium and endothelium, retinal photoreceptors, and retinal pigment epithelium (43). Patients with KC had decreased expression of vitamin D receptor (VDR) in epithelium over the ectatic zones of the cornea (44). Vitamin D helped to induce VDR in epithelial cells under oxidative stress (44). Studies suggest that there is an association between thyroid disorders with co-existing low vitamin D levels and the development of keratoconus (45). Vitamin D administration might play an important role in alternative treatment for keratoconus because it affects systemic and ocular biomarkers in keratoconus (46). Future studies should focus on the benefits of vitamin D supplementation in that ocular disease.

Myopia

Myopia is a refractive error, which is caused by an increase in the axial length of the eyeball (47). There has been a suggestion that vitamin D might have an association with myopia. Epidemiologic studies stated that time spent outdoors protects from myopia development (48, 49). It was explained that long sun exposure linked with vitamin D production, may cause a protective effect on myopia (23). However, studies conducted that there is no correlation between vitamin D levels and myopia in children (50, 51). Low vitamin D levels were not

associated with the risk of that disease in children (52). It was also proved that there is no association between low neonatal vitamin D levels and increased risk of myopia (53). Moreover, there are no seasonal changes caused by vitamin D levels (53). Vitamin D status might be only a marker of outdoor exposure, which is known to be a protective factor for myopia (54).

Thyroid eye disease

Thyroid eye disease (TED) is an autoimmune disease in which autoantibodies are directed against antigens in the thyroid gland which cross-react with orbital antigens (55). Vitamin D deficiency was suggested in many autoimmune diseases and studies decided to examine if that relationship plays a role in TED (56). A study showed that a deficiency of vitamin D is linked with the development of TED (57). Another study found a 20% prevalence of vitamin D deficiency in patients with TED (55). It would be crucial to early assess the level of vitamin D and implement supplementation in patients with Graves' disease (57).

Non – infectious uveitis

As previously said vitamin D plays a crucial role in the development of many autoimmune diseases. A recent study indicates a potential role of hypovitaminosis D in the pathophysiology of non-infectious uveitis and scleritis (58). However, more studies are needed to strongly confirm that finding due to low potential bias in included studies. Another study indicates that for every 1 nanogram/ml increase in vitamin D level, the patient has 5% lower odds of developing uveitis (59). What is more, there is a difference between active and inactive uveitis. Patients with active disease have significantly lower levels of vitamin D in comparison to patients with inactive disease and population-based controls (60).

Taking all this knowledge into consideration, vitamin D seems to play an important role in many ocular diseases due to its immunomodulatory abilities. The principal findings of the review are presented in Table 1.

Table 1.

Ocular diseases and the principal findings of the review

Ocular disease	**Key findings**
Changes in vision	• Vitamin D deficiency might lead to worse contrast sensitivity function (10) (11). • Tear break-up time and tear secretion are shorter in patients with vitamin D deficiency (12).
Dry eye syndrome	• Use of topical vitamin D drops might be effective in alleviating symptoms of dry eye in patients with meibomian gland dysfunction (19). • Managing vitamin D deficiency in patients with DES will prevent the worsening of that disease and post-operative complications after refractive surgery (7). • Studies revealed that oral vitamin D supplementation improves ocular surface homeostasis parameters, leads to better tear stability, and improves tear osmolarity in patients with deficiency (18, 20).
Age-related macular degeneration	• Patients with vitamin D deficiency are at bigger risk of neovascular AMD (26). • A diet with vitamin D may prevent or stop progression to advanced neovascular AMD (29).
Diabetic retinopathy	• Vitamin D deficiency may lead to a three times bigger risk of diabetic retinopathy in patients with type 2 diabetes so it is advised monitor eyes regularly (33). • Tear break-up time, Schirmer test, corneal staining score, and values of the tear meniscus height and area are much lower in children with diabetes mellitus 1 and coexisting vitamin D deficiency in comparison to tear measurements in healthy children (34).

Keratoconus	• Study shows that patients with keratoconus have lower serum vitamin D levels (40, 41). • Vitamin D helps to induce VDR in epithelial cells under oxidative stress (44).
Myopia	• Long sun exposure linked with vitamin D production, may cause a protective effect on myopia (23). • Studies conducted that there is no correlation between vitamin D levels and myopia in children (50, 51).
Thyroid eye disease	• One study showed that a deficiency of vitamin D is linked with the development of TED (57). • It would be crucial to early assess the level of vitamin D and implement supplementation in patients with Graves' disease (57).
Non-infectious uveitis	• Another study indicates that for every 1 nanogram/ml increase of vitamin D level, patient has 5% lower odds of developing uveitis (59). • Patients with active disease have significantly lower levels of vitamin D in comparison to patients with inactive disease and population-based controls (60).

Conclusion

The literature review points to the association between vitamin D levels and the development of ocular diseases. It seems that adequate vitamin D levels are significant for maintaining ocular health. More studies are needed to investigate in depth the underlying mechanisms and efficacy of vitamin D supplementation in ocular diseases.

Disclosure:

Author's contribution:

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