ORIGINAL ARTICLE

Serum Vitamin D Levels In Central Serous Chorioretinopathy

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ABSTRACT

Purpose: To determine the effect of vitamin D in the pathophysiology of central serous chorioretinopathy.

Material-Methods: The study included 30 patients diagnosed with central serous chorioretinopathy (CSCR) with optic coherence tomography (OCT) and fundus fluorescein angiography (FFA) (group 1) and an age and gender-matched healthy control group (group 2). The vitamin D levels of both groups were examined.

Results: There was no significant difference between the groups in respect of age or gender ($p>0.05$, $p>0.05$, respectively). Vitamin D levels were determined as 20.16 ±7.03 ng/ml in group 1 and 28.56±6.59 ng/ml in group 2. The mean vitamin D level of group 1 was determined to be statistically significantly lower than that of group 2 ($p<0.05$).

Conclusions: The low vitamin D levels determined in the cases with central serous chorioretinopathy could play a role in the pathophysiology of the disease. There is a need for further studies to determine the effect of vitamin D on the disease process and the changes that could occur with vitamin replacement therapy.

Key Words: Vitamin D, Central serous chorioretinopathy, Pathophysiology.

INTRODUCTION:

Central serous chorioretinopathy (CSCR) is the 4th most common non-surgical retinopathy,[1] characterised by serous retinal detachment and/or RPE detachment, and is a disease which is generally limited to the macula, with leakage from the RPE to the retinal cavity. It usually affects young males with no systemic disease. It was first defined by Von Graffe in 1866,[2] and since that time there have been changes in opinions about the pathophysiology with the development of imaging methods. Von Graffe disease was first defined as recurrent central retinitis, then in 1922 it was renamed capillorospastic central retinitis by Horniker as vasospasm was thought to be the underlying mechanism. With the later identification of fluoroscein angiography findings, the disease was defined as RPE detachment which developed associated with leakage orginating from the choroid. Due to the developments in imaging technology, the disease is now known to be RPE-mediated neurosensorial retinal detachment associated with hyperpermeability that develops in the choroid, and therefore, the name of central serous chorioretinopathy is now preferred.

Vitamin D is a group of fat-soluble prohormones that can be synthesised endogenously in the appropriate conditions. Vitamin D plays an important role in bone formation and mineral hemostasis, and is found in the body in two forms; Vitamin D3 (cholecalciferol) and vitamin D2 (ergocalciferol). Deficiency of vitamin D is seen widely throughout the world. Various epidemiological studies have reported that up to 40% of the adult population are at risk of vitamin D deficiency.[3] The effects of vitamin D have been examined in many ophthalmological diseases, such as ocular inflammation, ocular angogenesis, glaucoma, diabetic ophthalmological diseases and optic neuritis.[4,5] There are also studies that have shown that vitamin D has an effect on inflammation, fibrosis, angiogenesis, oxidative stress and retinal circulation.[6] However, to the best of our knowledge, there has been no previous study in literature that has shown the effects of vitamin D on CSCR.

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The aim of this study was to be able to explain the possible effect of vitamin D in the pathophysiology of CSCR in the light of current data in literature.

MATERIALS AND METHODS

Approval for the study was granted by the Ethics Committee for Non-Interventional Research of Firat University (decision no: 10561). All procedures were in accordance with the principles of the Helsinki Declaration. Informed consent was obtained from all the participants.

The study included 30 patients who presented at the Eye Diseases Polyclinic of Elazig Health Sciences University Medical Faculty Hospital because of reduced vision and were diagnosed with acute central serous chorioretinopathy (CSCR) with optic coherence tomography (OCT) (figure 1) and fundus fluorescein angiography (FFA) (figure 2) (group 1) and an age and gender-matched healthy control group (group 2). Blood samples of 5cc were taken from all participants. After centrifugation of the samples at 4000 rpm for 5 mins, the serum 25 (OH) vitamin D levels of both groups were examined with the electrochemiluminescence

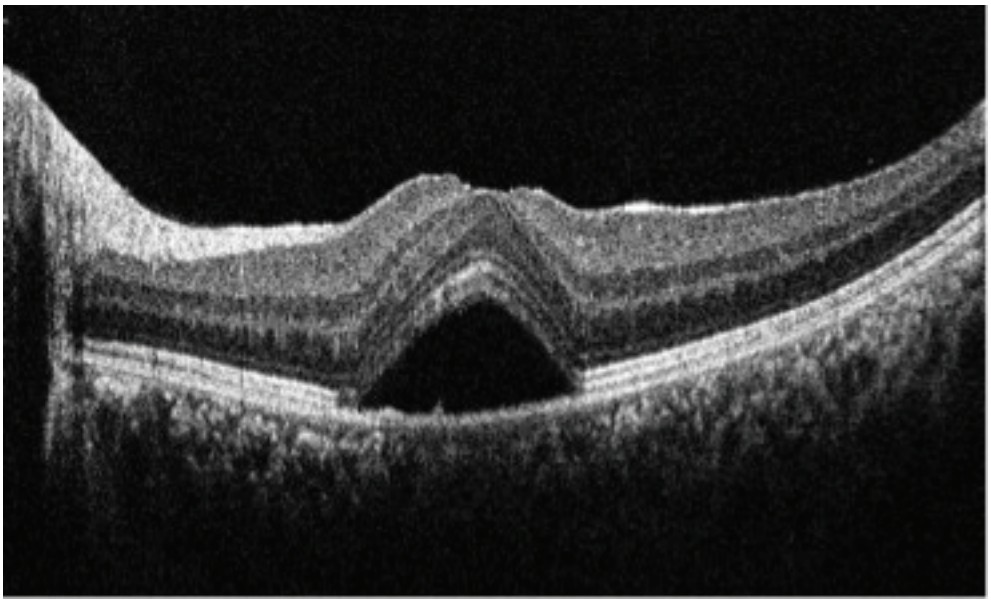

Figure 1. *OCT image in a CSCR patient.*

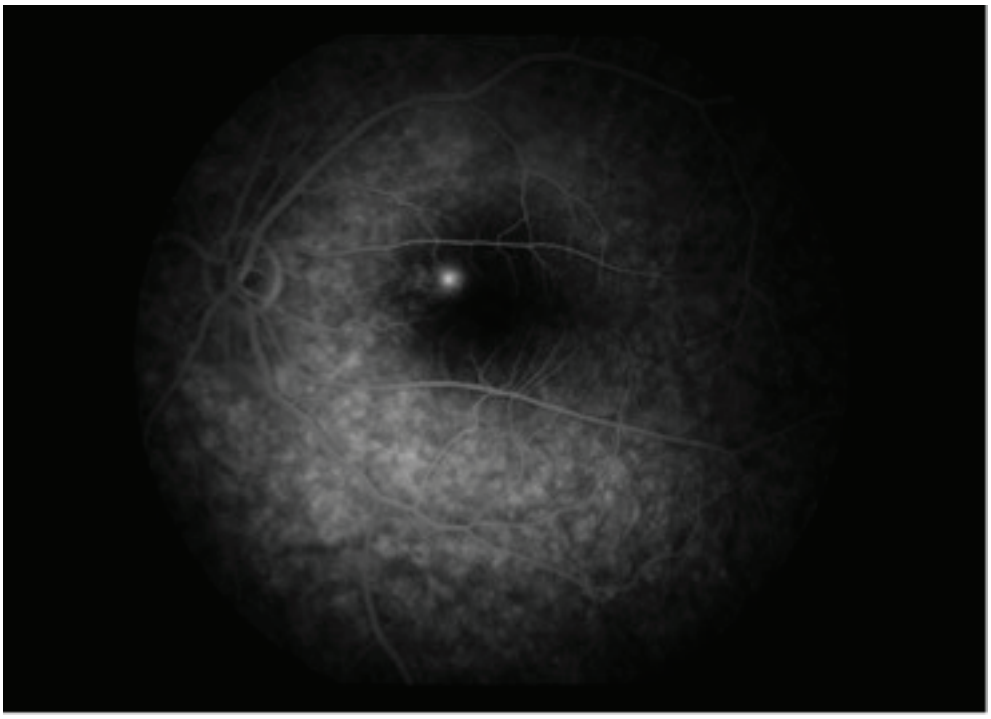

Figure 2. *Fundus fluorescein angiography image in a CSCR patient.*

method on a Trinity Biotech Premier device (HB9210, 2018, Republic of Ireland).

Statistical Analysis:

Data obtained in the study were analysed statistically using the Statistical Package for the Social Sciences (SPSS) version 17.0 software (SPSS Inc., Chicago, IL, USA). To examine the significance of differences between the age and vitamin D levels of the groups, the Independent t-test and the Mann Whitney U-test were used respectively. A value of $p<0.05$ was accepted as statistically significant.

RESULTS

The patient group comprised 24 (80%) males and 6 (20%) females, and the control group comprised 24 (80%) males and 6 (20%) females. The mean age was 38.16±8.86 years in group 1 and 34.63±9.11 years in group 2. There was no significant difference between the groups in respect of age or gender ($p>0.05$, $p>0.05$, respectively). Vitamin D levels were determined as 20.16 ±7.03 ng/ml in group 1 and 28.56 ±6.59 ng/ml in group 2. The mean vitamin D level of group 1 was determined to be statistically significantly lower than that of group 2 ($p<0.05$), (Table 1).

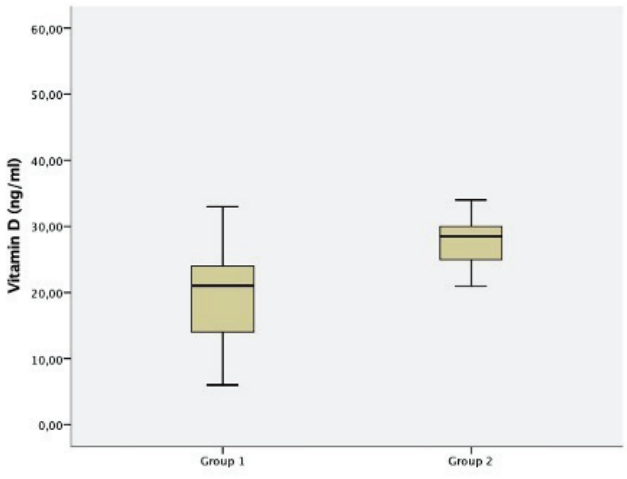

Table 1. *The serum vitamin D levels in groups.*

DISCUSSION

The role of vitamin D has been examined in many ocular diseases such as dry eye, glaucoma, uveitis, ocular angiogenesis, age-related macular degeneration, diabetic retinopathy and optic neuritis. The most significant property of vitamin D in these diseases has been shown to be the anti-inflammatory effect.[7] The aim of this study was to investigate the relationship between vitamin D and CSCR, which to the best of our knowledge, has not been previously examined in literature.

The pathophysiology of CSCR is not fully known, although it is thought that there may be a genetic predisposition, cardiovascular diseases and hypertension, endocrine changes such as in sympathetic-parasympathetic activity and reactivity, corticosteroid use, pregnancy and Cushing syndrome, the use of antipsychotic drugs, psychopathological reasons such as type A personality and psychological stress, gastrointestinal diseases such as H. pylori and gastro-oesophageal reflux, drugs such as pseudoephedrine and oxymethazoline and sleep disorders. Many researchers believe that as a result of the abnormal permeability occurring in the inner choroid with the effect of stasis, ischaemia and inflammation alone or together, there is an elevation in the retinal pigment epithelium.[8]

The change in choroidal circulation constitutes the main mechanism in CSCR.[9] Tewari et al. reported that because of the changes in permeability and choroid circulation, autonomic dysfunction led to the disease.[10] Lobular ischaemia in the choroid, venous congestion and choroidal hyperpermeability are observed with indocyanine green staining on the inner choroid in the mid-phase on angiography.[11,12] The primary role of the choroid in the pathogenesis of the disease has been supported by the observation of increased choroid thickness in both eyes of patients on EDI-OCT.[13]

In CSCR patients there is increased choroid thickening and permeability. Vitamin D deficiency has been shown to lead to disrupted retinal microvascular circulation independently of cardiovascular diseases. In a study by Mutlu et al., there was determined to be endothelial activation in microvascular circulation by inhibiting the inflammation processes through the specific signal pathways of vitamin D receptors in the retinal vessel endothelial cells and this led to changes in the vascular structure and organisation.[14] In the changes occuring in the endothelial cells, there is an effect on the antioxidant processes, and this can emerge when there is vitamin D deficiency. It is thought that the impaired circulation thought to occur in the choroid vessels in CSCR could lead to the disease with similar mechanisms.

It is also thought that the changes occurring in the choroid in CSCR could be the result of inflammation, ischaemia and stasis. The exudation and increased thickness occurring in the choroid seen on high-resolution OCT slices has been determined to originate from protein accumulated

here. Gil de Venecia first reported that this accumulation was fibrin.[15] Originating from the choroid, fibrin emerges in the subretinal area and causes separation here in the retina pigment epithelium. As fibrin is a protein which can be formed as a result of inflammatory processes, its determination in CSCR pathophysiology is an important finding in respect of the role of inflammation.

Oxidation, inflammation and angiogenesis lead to dysfunction in ocular tissue and cell loss. vitamin D inhibits the production of pro-inflammatory cytokines such as IL-2, IL-12, IFN-gamma and TNF-a. İt has also been determined that it increases the production of anti-inflammatory cytokines such as IL-4, IL-10 and TGF-B.[16] In a rabbit model experimental study, vitamin D2 and vitamin D3 metabolites were determined in the aqueous humor and the vitreous and the amount of these metabolites was found to be correlated with the ratio of the vitamin taken in the diet.[17] When the inflammatory effects of vitamin D are taken into consideration, and especially the changes in the anterior chamber and the vitreous related to the amount of dietary intake, the potential inflammation in CSCR pathophysiology can be considered to be due to vitamin D deficiency.

Vitamin D has been determined to have an effect on cell proliferation and differentiation in tissue, apoptosis, angiogenesis and gene regulation. In lymphocytes exposed to vitamin D, there has been reported to be reduced apoptosis and cell proliferation.[18] Several studies have determined that vitamin D deficiency is related to increased oxidative stress and decreased antioxidant response. It has been shown to protect cultured human endothelial cells and retinal cone cells from oxidative damage and to have an effective role against antioxidant damage by activating the protective antioxidant Nrf2-KEAP-1 pathway in diabetic rats.[19]

In the absence of antioxidant enzymes such as manganese superoxide dismutase, it has been shown that there could be RPE dysfunction, choroid damage and photoreceptor loss.[20] Previous studies have shown that vitamin D deficiency reduced antioxidant capacity and increased oxidative stress. Pourgassem et al., found a positive correlation between vitamin D and total plasma antioxidant concentration.[21] In another study by Almeida et al., a relationship was determined between chronic hepatitis and vitamin D deficiency and low plasma antioxidant capacity.[22] A reduction in inflammation and amyloid beta levels in the retina of rats treated with vitamin D has also been reported.[23] In line with the above-mentioned findings, it can be considered that the changes occurring in CSCR could develop with the same antioxidant mechanisms as in vitamin D deficiency.

A correlation between vitamin D deficency and retinal ganglion cell loss has been previously determined[24]. It is thought that this loss could be related to the degeneration caused by vitamin D directly on the retinal structures, the neurodegeneration which develops, including in the generalised central nervous system, and finally with the impairments in the antioxidant mechanisms which can occur in vitamin D deficiency. The changes in the retinal structures in the pathophysiology of CSCR could originate from similar mechanisms.

There were some limitations to this study. First is that to confirm the study hypothesis, a larger number of patients could have been included. However, despite the low number of patients, ststistically signifcant results were obtained. Second, is the consideration that vitamin D levels exhibit differences between different populations. The low vitamin D levels obtained in this study were based on the serum levels of the Turkish population. To confirm these results, it would useful to conduct further studies of different races and populations. A third limitation is that the vitamin D measurements were examined in the serum and there was no measurement of levels in the vitreous or tissue. Finally, determination of whether or not the findings of patients recover with vitamin D replacement is important in respect of understanding the effect of vitamin D.

In conclusion, the results of this study suggest that inflammation in the choroid, impairments in the antioxidant mechanism and vascular changes that occur in vitamin D deficiency could have a signifcant role in the pathophysiology of CSCR disease. It can be considered that the low vitamin D levels determined in the CSCR patients in this study could play a role in the development of CSCR through these mechanisms.

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