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SERUM VITAMIN D LEVELS IN DIFFERENT MORPHOLOGIC FORMS OF AGE RELATED CATARACT

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Abstract

Purpose. Vitamin D insufficiency and age related cataract (ARC) are public health problems. We evaluated serum vitamin D levels in ARC patients.

Method. A prospective hospital-based cross-sectional study was designed to measure the vitamin D status of patients with ARC. Patients have grouped either presence of any type of posterior subcapsular cataract (PSC) (group 1) or ARC without the PSC component (Group 2). After full ophthalmologic consideration, patients over 40 years of age with no history of ocular trauma, multivitamin supplement ingestion, chronic renal failure, thyroidectomy, parathyroidectomy, skin cancer, and cigarette smoking were included in the study.

Results. Totally, 79 subjects of which 26 (32.9%) subjects in group 1 and 53 (67.1%) subjects in group 2 were included in the study. Group 1 had mean vitamin D levels of 17.31±13.30 ng/mL. Vitamin D levels in Group 2 were 13.34±7.87 ng/mL. Group 1 did not show vitamin D insufficiency (P = 0.31; one-sample t-test). However, Group 2 showed a statistically significantly lower vitamin D level compared to the insufficiency level of 20ng/mL (P= 0.00; one-sample t-test).

Conclusion. Vitamin D may have an important function in lens metabolism. Vitamin D deficiency and cataract development need further extensive researches.

Key words: Age related cataract, posterior subcapsular cataract, Vitamin D, Vitamin D deficiency, Vitamin D receptor.

INTRODUCTION

Age related cataract (ARC) is a cause of treatable blindness due to the loss of lens transparency (1). The etiology of cataract formation is complex and unrevealed aspects still present (2). Cigarette smoking, low antioxidant capacity, metabolic disturbances, and vitamin deficiencies have all been postulated with some role in the formation of different types of cataract due to increased oxidative damage (3-8). Vitamin D has the antioxidant capacity and relieves oxidative stress (9, 10). Vitamin D exerts some inverse relation with some of the major ophthalmic diseases such as age related macular degeneration and glaucoma (11, 12). In addition, some external forces such as ultraviolet radiation (UVR) and infrared radiation may induce cataract formation (13).

A morphologic classification for ARC is Lens Opacities Classification System III (LOCS III) (14). Posterior subcapsular cataract (PSC) is a subtype of cataract which decreases vision possibly due to the degeneration of basal membrane complex near the posterior subcapsular region (15). Recently, Brown and Akaichi have studied retrospectively the potential role of vitamin D and PSC development with the hypothesis that PSC is resembling the hypocalcemic cataract (16). They find an association between low serum vitamin D levels and PSC formation (16). In contrast, a secondary analysis of the Korea National Health and Nutrition Examination Survey (KNHANES) about serum 25-hydroxyvitamin D and ARC revealed an inverse relationship between higher serum 25-hydroxyvitamin D and ARC in man (17).

There is a gap in prospective studies that address the relationship between serum vitamin D levels and ARC in the current medical literature. Because there is a relevant study showing an inverse relation between vitamin D and PSC development, here, we evaluated the serum 25-hydroxyvitamin D (here on vitamin D) levels of ARC patients according to their cataract morphology.

MATERIAL AND METHOD

General information

This hospital-based prospective study was conducted in Bagcilar Training and Research Hospital between October 2016-June 2017 and October 2017-January 2018. This research followed the tenets

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of the Declaration of Helsinki. Approval was obtained from the local ethics committee of Bagcilar Training and Research Hospital with the identification code of "GOKAEK/2016-483". Participants were informed of the study, and informed consent was obtained from them. The study was interrupted in the summer season to diminish the effect of the significant number of sunbathing days on natural vitamin D production. All patients underwent a complete ophthalmologic evaluation with the sequence of autorefractor keratometer measurement, best-corrected visual acuity measurement (BCVA), intraocular pressure (IOP) reading, non-mydriatic and mydriatic anterior segment evaluation with biomicroscopy, and a mydriatic posterior segment examination.

Characteristics of patients

Only the patients with the complaint of gradual visual decline and no identifiable cause of visual loss other than cataract were included in the study. Patients over 40 were included to rule out any presenile causative condition with potential metabolic interaction in vitamin D metabolism. Patients with a previous history of ocular trauma, multivitamin supplement ingestion, and cigarette smoking were not included in the study. In addition, patients were inquired for the history of thyroidectomy, parathyroidectomy, diabetes mellitus, skin cancer, chronic liver, and renal failure and a positive history was an exclusion criterion for our study. LOCS III is grading PSC from P1to P5. In our study patients at any grade of PSC groups as Group 1 and all other morphologic types of cataracts grouped as Group 2.

Laboratory method

Blood samples were obtained from fasting patients during routine preoperative cataract surgery evaluation with standard venipuncture. Samples were taken in gel-free flat tubes for C reactive protein (CRP) and vitamin D analysis whereas erythrocyte sedimentation rate (ESR) tubes with 3.8% sodium citrate were used for ESR measurement. Samples for analysis of vitamin D waited for 30 minutes to coagulate and then centrifuged at 1500 g for 15 minutes. After that serum samples were separated and stored in Eppendorf tubes at -80°C until the working day. The assay method of vitamin D was competitor enzyme immunoassay. All biochemical parameters were studied in Roche Diagnostic Cobas 8000 machine which is a reliable device for analysis of vitamin D (18).

Statistical method

BCVA measurements converted to logMar for statistical purposes. A statistical software program namely Statistical Package for Social Sciences (SPSS) version 16 was used for statistical analysis. The power analysis was conducted with the 3.1 version G*Power software program. Kolmogorov-Smirnov test was the preferred method for determining normality. Data were expressed as mean±standard deviation. Vitamin D levels were compared with one sample Student test. The cutoff level for vitamin D was 20 ng/mL in both groups because this level is described as vitamin D insufficiency by the Institute of Medicine (19). A $p<0.05$ was considered statistically significant for the analysis of measured data.

RESULTS

Alltogether, 79 subjects of which 26 (32.9%) subjects in group 1 and 53 (67.1%) subjects in group 2 were included in the study. Of the patients in group 1, 14 (53.8%) were male and 12 (46.2%) were female. 27(50.9%) male and 26(49.1%) female patients constituted group 2. A post hoc power analysis was done for both groups. The power of the study (1-β) was found 0.98 at the α=0.05 level when the effect size is selected to 0.8 for group 1. The estimated 1-β value at the α=0.05 level was 0.99 with the effect size of 0.8 for group 2. Table 1 presents the preliminary and demographic data of each group.

Patients in Group 1 had mean vitamin D levels of 17.31±13.30 ng/mL. vitamin D levels in Group 2 patients were 13.34±7.87 ng/mL. When the level of

Table 1. Preliminary data of patients

	Group 1				Group 2			
	n	Minimum	Maximum	Mean±SD	n	Minimum	Maximum	Mean±SD
Right eye IOP* (mmHg)	26	10	23	16.4±3.8	53	11	28	17.1±3.9
Left eye IOP* (mmHg)	26	10	28	16.5±4.5	53	10	28	17.6±4.1
BCVA* of Eye with cataract	26	1.30	0.22	0.88±0.43	53	1.30	0.22	0.82±0.39
CRP* (mg/L)	26	0.81	17.90	4.7±4.6	50	0.67	45.10	5.5±8.1
ESR* (mm/hr)	24	2.00	43.00	16.9±13.7	51	1.00	64.00	17.6±15.6

* Group1: Patients with any type of posterior subcapsular cataract (PSC); Group 2: Patient with any type of cataract without PSC; IOP: Intraocular pressure; BCVA: Best corrected visual acuity; CRP: C reactive protein; ESR: Erythrocyte sedimentation rate.

vitamin D insufficiency was accepted as 20 ng/mL, the mean serum vitamin D levels of the patients were not significantly different in Group 1 (P = 0.31; one-sample t-test) and statistically significantly lower in Group 2 patients (P = 0.00; one-sample t-test).

There was no significant relationship between sex and vitamin D levels in both Groups (P = 0.14 for Group 1 and P = 0.56 for Group 2, chi-square). In Group 1, patients' ages ranged between 56 and 83 years (69.8±6.5 years). In Group 2, patients' ages ranged between 49 and 92 years (69.4±9.2 years). There was, however, a significant negative correlation between vitamin D levels and patient ages in patients in Group 2 (P = 0.035, r = -0.29). There was no significant correlation between patient age and vitamin D levels in Group 1 (P = 0.9, r = 0.16).The correlation analysis of the patients' ages and vitamin D levels are shown in Table 2.

DISCUSSION

Low levels of vitamin A, vitamin C, and vitamin E can predispose cataract formation (6-8). Hypocalcemic states can induce cataract formation, and in some retrospective reports, low levels of vitamin D were associated with ARC formation (16, 20). Here, we prospectively investigated serum vitamin D levels in cataract patients and found significantly low serum levels in patients without PSC (P =0.00) but no difference in patients with any type of PSC (P =0.31).

Calcium is an important constituent of both serum and aqueous humor and hypocalcemia is a known predisposing factor for cataract formation (20). The human lens fibers possess an extracellular calcium-sensing receptor (CaR) which becomes activated due to small alterations extracellular calcium levels (21). The CaR has some protective functions against cell death due to experimental high glucose-induced energy metabolism disorder (22). Vitamin D alters calcium metabolism with some complex relation to parathyroid hormone (PTH) (11, 23, 24). If serum vitamin D concentrations are higher than the 31 ng/mL level, serum PTH levels stay steady at normal levels of 36 pg/mL (24). However, the decreased serum vitamin D concentrations below 31ng/mL increase PTH levels abruptly. Considering the calcium metabolism of CaR, PTH, and vitamin D and the multifaceted associations in cellular levels, vitamin D levels below normal levels may contribute to the degeneration of lens fibrils.(25) In our study, we found the decreased serum vitamin D levels in ARC patients without PSC component and normal levels of vitamin D in any type of PSC patients.

Ultraviolet (UV) irradiation especially UV-A (320-400 nm) and oxidative stress are known to be major causatives for cataract formation (26, 27). UV-B (280-320 nm) is mainly responsible for the initial steps of endogenous synthesis of vitamin D from 7-dehydrocholesterol (28). Both of the UV-A and UV-B are mainly absorbed from direct sunlight. Oxidative stress induces the formation of some reactive species such as singlet oxygen, hydroxyl radical, and hydrogen peroxide ending up degeneration of lens proteins mainly due to denaturation of amino acid tryptophan (29, 30). The relative effect of sunlight on eye metabolism which is a counter-response with promotion oxidative stress and vitamin D production results in a dilemma to be solved. Jee *et al.* argue that the preventive effect of sunlight with vitamin D production through skin exposure may surpass the cataract predisposing effect of sunlight on the lens when they show the decreased amount of cataract in male patients (17). They also notify that women may use more frequently sunlight protective measures and men remain under sunlight more than women (17). However, we did not find a significant difference between sex and vitamin D levels in both of our studied groups (P =0.14 for group 1 and P =0.56 for group 2; chi-square test).

Until now, one of the studies on vitamin D levels and cataract development reported a negative relationship between PSC development and low serum vitamin D levels, in addition, Jee *et al.* reported less ARC in male patients with high vitamin D (16, 17). In their retrospective study, Brown and Akaichi used results from two different devices for the measurement of vitamin D and performed a logistic regression analysis of the systemic states of the patients' stories (16). Although this methodology is appropriate, we did not include patients with a known history of smoking, steroid use,

Table 2. The Mean age of each group of patients and the correlation with the Vitamin D levels

	Age (years±SD)	Vitamin D levels (ng/mL)	** P_2	** r
Group 1	69.85±6.52	17.31±13.30	0.9	0.16
Group 2	69.47±9.26	13.34±7.87	0.035	-0.29
* P_1	0.075	0.009		

*P1 indicates the statistical significance level of the age and Vitamin D levels of group 1 and group 2 compared to the independent sample t test ** P2 and r represent statistical significance (P2) and correlation coefficient (r) in the Pearson correlation test of groups according to age and Vitamin D levels.

diabetes mellitus, chronic renal failure, and skin disease in our prospective study because of the high number of interactions in the logistic regression test and we used a single device to study vitamin D levels. However, in our study, serum vitamin D levels in patients with PSC were not significantly lower than 20 ng/mL and that was not supporting the results of Brown and Akaichi. The KNHANES is a long-lasting health survey of Korea giving important insights about medical knowledge, one of which is the vitamin D status of participants (31). Jee *et al.* studied the association of vitamin D level and ARC and found no significant correlation in women; in contrast, they display a negative correlation between ARC and the high dose of vitamin D in males (17). However, as they notice in their study the seasonal variations were not controlled in the survey. To reduce the seasonal effect on vitamin D levels, samples were taken only out of summer in our study. Our research that we try to control the seasonal effect on vitamin D supports the conclusions of Jee *et al*.

Vitamin D is available in various concentrations in different tissues of the human body and exhibits various effects (32). Vitamin D binds to the vitamin D receptor (VDR) necessary for its action, and then acts on the nucleus, leading to protein synthesis (33). In addition, VDR gene polymorphism may alter the action of vitamin D and relate with the pathologic process some of the important chronic diseases thus resulting in a need for a high concentration of vitamin D (34). There is a benefit here that we have to mention some of the important limitations of our work. Firstly, there is no study on the effective concentration of vitamin D associated with serum level in the human eye. Second, due to strict inclusion criteria and the time limitation associated with seasonality of vitamin D levels the sample size of our study was small and unequal between groups for generalization of our results. For this reason, we think that it would be useful to investigate the effective dose of vitamin D and VDR gene polymorphism in the human lens and the systemic level of vitamin D with further research.

Conflict of interest

The authors declare that they have no conflict of interest.

Authors' contributions

KA drafted the manuscript. AK, HEK, and FGS critically revised manuscript. KA performed statistical analysis. KA and OZ supervised all measurements. All authors read and approved the final manuscript.

Ethics approval and consent to participate

This research followed the tenets of the Declaration of Helsinki. Approval was obtained from the local ethics committee of Bagcilar Training and Research Hospital with identification code of "GOKAEK/2016-483" and all patients gave their written informed consent.

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