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Is Vitamin D Important for Elderly Patients in Intensive Care?

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ABSTRACT

Objective: According to the World Health Organization's old age classification, 65-74 years is considered as young-old, 75-84 years as middle-old, and over 85 years as old-old. Effects of vitamin D on cardiac, renal, and endocrine diseases are closely associated with morbidity/mortality in intensive care units. This study evaluated the difference in vitamin D levels of intensive care patients below and above 75 years, and the associations between vitamin D levels and age as well as mortality/organ failure in both groups.

Methods: This study was designed as a retrospective, non-interventional, non-drug, observational clinical trial. Age, gender, vitamin D, and acute physiology and chronic health evaluation II (APACHE II) and sequential organ failure assessment scores on admission to the intensive care unit were recorded.

Results: Of all patients, 60 were female and 31 were male. The mean age was 77.7±13.8 years. There were 29 patients aged below 75 years and 62 patients above. The mean vitamin D level was 13.7510 ng/mL-1. The mean APACHE II score of patients of or above 75 years was significantly higher than that of patients below 75 years (p=0.024). There was a significant negative correlation between age and vitamin D in patients of or above 75 years (p=0.042).

Risk factors associated with vitamin D deficiency include age, gender, lifestyle, ethnic origin, diet, medical history, drugs, and acute critical illness. With aging, the concentration of 7-dehydrocholesterol in the skin decreases, as well as the vitamin D3-forming capacity of the skin. In this study lower vitamin D levels were detected with increasing age in intensive care unit patients.

Conclusion: No significant relationship was detected between age and vitamin D levels in patients below 75 years whereas a significant decrease in vitamin D level with increasing age was detected in patients of or above 75 years (p=0,042).

Keywords: Vitamin D, intensive care unit, elderly patient

INTRODUCTION

The definition made by the World Health Organization (WHO) as regards chronological age considers old age to be "65 years and older." According to the WHO's old age classification, 65-74 years is considered as young-old, 75-84 as middle-old, and over 85 years is as old-old (1).

The effects of vitamin D on cardiac, renal, and endocrine diseases are closely related to morbidity and mortality in intensive care units (2,3). Of 513 patients aged from 18 to 69 years, admitted in hospitals in Turkey, 51.8% had vitamin D insufficiency and 20.7% had vitamin D deficiency (4). The risk of vitamin D deficiency is higher in elderly people. Because they prefer to spend more

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time at home, they take less vitamin D, are more obese, and have weaker kidney functions (5).

This study evaluated the difference in vitamin D levels of intensive care patients below and above 75 years, and the associations between vitamin D levels and age as well as mortality/organ failure in both groups.

METHODS

This study was a retrospective, non-interventional, non-drug, observational clinical trial [Ethics Committee approval was received from the Giresun University Clinical Research Ethics Committee (approval number: 29/09/2017-11)]. Age, gender, vitamin D, and acute physiology and chronic health evaluation II (APACHE II) and sequential organ failure assessment (SOFA) scores of patients at anesthesiology, neurology, internal medicine, and coronary intensive care units were recorded. The patients were divided into 2 groups: below 75 years and of or above 75 years.

Statistical Analysis

SPSS 22.0 was used for statistical analyses and t-test was used to compare groups. Pearson's correlation analysis was used to evaluate intragroup correlations and p<0.05 was accepted as statistically significant.

RESULTS

Sixty patients were female and 31 were male. The mean age was 77.7±13.8 years. Twenty-nine patients were below 75 years, while 62 patients were at or above this age. The mean vitamin D level was 13.7510 ng/mL-1. The mean APACHE II score was 28.41 and the mean SOFA score was 7.78. The mean vitamin D level and APACHE II and SOFA scores are demonstrated in Table 1.

No significant difference could be found between the 2 groups in vitamin D levels (p=0.713). The mean APACHE II score of patients of or above 75 years was significantly higher than that of patients below 75 years (p=0.024). No significant difference could be detected between the two groups in mean SOFA scores (p=0.508). A comparison of the levels of vitamin D and the APACHE II and SOFA scores among the groups is shown in Table 2.

Intragroup comparisons showed a significant positive correlation between age and APACHE II score in the group below 75 years (p=0.012). There was a significant positive correlation between the APACHE II and the SOFA scores (p=0.000). There was no significant relationship between age and vitamin D levels (p=0.136), and no significant correlation was detected between vitamin D level and APACHE II and SOFA scores (p=0.923, p=0.488). Comparison of vitamin D level and APACHE II and SOFA scores in the group below 75 years is shown in Table 3.

Intragroup comparisons showed a significant negative relationship between age and vitamin D levels in patients of or above 75 years (p=0.042). No significant correlation was detected between age and APACHE II and SOFA scores (p=0.266 and p=0.687, respectively). There was no significant correlation between APACHE II and SOFA scores (p=0.187). No significant correlation was detected between vitamin D level and APACHE II and SOFA scores (p=0.154 and p=0.088, respectively). The comparison of vitamin D levels and APACHE II and SOFA scores in the group of or above 75 years is shown in Table 4. The correlation between age and vitamin D levels in patients of or above 75 years is shown in Figure 1.

DISCUSSION

Vitamin D affects many cells in addition to its effects on calcium and phosphorus metabolism and the skeletal system. Also, it is a hormone that has effects on many systems and diseases like immunomodulation and prevention of autoimmune diseases, some chronic diseases, and cancer development (6,7). Because of the immunomodulating effect of vitamin D and its relation to chronic diseases and age, the idea that it is also important in the course of critical patients is strengthened (8).

Table 1. Mean vitamin D levels and APACHE II and SOFA scores

	n	Minimum	Maximum	Mean	SD
Vitamin D ng/mL	91	3.00	52.76	13.7510	9.45736
APACHE II score	91	8	38	28.41	6.119
SOFA score	91	2	11	6.78	2.235

SD: Standard deviation, APACHE: acute physiology and chronic health evaluation, SOFA: sequential organ failure assessment

Table 2. Comparison of vitamin D levels and APACHE II and SOFA scores between groups

	Age <75 (n=29)	Age >=75 (n=62)	p
	Mean ± SD	Mean ± SD	
Vitamin D ng/mL	14.288±11.888	13.500±8.179	0.713
APACHE II score	25.966±7.490	29.548±5.033	0.024
SOFA score	6.552±2.369	6.887±2.181	0.508

SD: Standard deviation, APACHE: acute physiology and chronic health evaluation, SOFA: sequential organ failure assessment

Table 3. Comparisons of vitamin D levels and APACHE II and SOFA scores in the group below 75 years

		Vitamin D ng/mL	APACHE II score	SOFA score
Age	r	-0.284	0.458	0.186
	p	0.136	0.012	0.334
	n	29	29	29
Vitamin D ng/mL	r	-	0.019	0.134
	p	-	0.923	0.488
	n	-	29	29

SD: Standard deviation, APACHE: acute physiology and chronic health evaluation, SOFA: sequential organ failure assessment

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Vitamin D can be synthesized endogenously or taken in the diet. It consists of two forms: cholecalciferol (Vitamin D3) and ergocalciferol (Vitamin D2). The majority of vitamin D in the body is Vitamin D3. Vitamin D2 is produced in plants and yeast (9). Endogenous vitamin D precursor 7-dehydrocholesterol, found in the epidermis, forms previtamin D3 after activation by ultraviolet B (10). With aging, the concentration of 7-dehydrocholesterol in the skin decreases as well as the vitamin D3-forming capacity of the skin (8).

Risk factors associated with vitamin D serum 25-hydroxyvitamin D [25(OH)D] deficiency include age, gender, lifestyle, ethnic origin, diet, medical history, drugs, and acute critical illness (11). Vitamin D levels below 20 ng/mL-1 are considered as a deficiency, between 20-30 ng/mL-1 as insufficiency, between 40-50 ng/mL-1 as optimal, and above 150 ng/mL-1 as toxic. The optimal serum vitamin D concentration is 30 ng/mL-1 (12,13).

Vitamin D deficiency may further deteriorate the aging of skeletal muscles. However, current evidence for the reversal of age-related muscular dysfunction with vitamin D supplementation is controversial, and rather than targeting too high vitamin D levels in elderly people, the safest option is to target conservative vitamin D levels sufficient for normal calcium homeostasis (14). Vitamin D deficiency should be treated per the severity of deficiency. In high-risk adults, serum 25(OH)D concentrations should be measured 3-4 months after the initiation of treatment and should be followed up for target levels (15).

Table 4. Comparisons of vitamin D level and APACHE II and SOFA scores in the group of or above 75 years

		Vitamin D ng/mL	APACHE II score	SOFA Score
Age	r	-0.259	0.143	0.052
	p	**0.042**	0.266	0.687
	n	62	62	62
Vitamin D ng/mL	r	-	-0.183	0.219
	p	-	0.154	0.088
	n	-	62	62

SD: Standard deviation, APACHE: acute physiology and chronic health evaluation, SOFA: sequential organ failure assessment

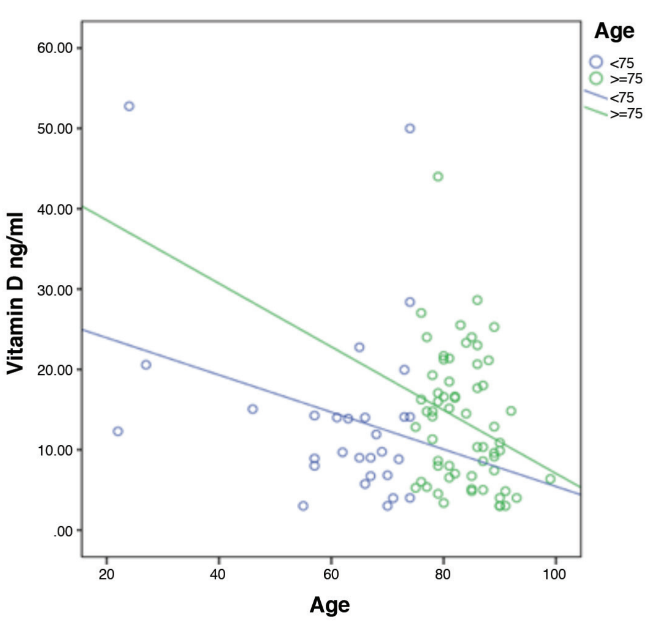

Figure 1. Correlation between age and vitamin D level in patients of or above 75 years

Patients in the intensive care unit are generally immobile and have multiple comorbidities. Their nutrition is impaired, exposure to sunlight is decreased, and they are at high risk for vitamin D deficiency (16).

In a study by Botros et al. (17) on Egyptian women, vitamin D deficiency was detected in 72.6% of breastfeeding women, 54% of pregnant women, 72% of childbearing age women, 39.5% of old age women, and 77.2% of geriatric age women. Vitamin D levels of women whose exposure to sunlight was poor, normal, or good were 14.1 ngmL-1, 14 ngmL-1, and 37 ngmL-1, respectively. In our study, 87.9% of patients were over 65 years. Of these patients, 96.9% had vitamin D levels below 20 ngmL-1, and the mean vitamin D level was 9.95 ngmL-1. A study in the United States also examined changes in vitamin D deficiency over the years and reported that serum 25(OH)D levels decreased by about 20% between 1988 and 2004, and the cause of this decrease was reported to be reduced exposure to sunlight (18).

Vitamin D deficiency is a predisposing factor for diabetes, left ventricular hypertrophy, congestive heart failure, hypertension, and chronic vascular inflammation (8,19,20). Some studies have shown that there is an increased association between vitamin D deficiency and pulmonary diseases, cardiovascular diseases, and cancer (21,22). It has also been shown that vitamin D supplementation reduces the incidence and mortality rate of these diseases (23-25).

The association between vitamin D deficiency and mortality in intensive care patients has been shown in different studies with controversial results. In a study conducted in intensive care patients, 25(OH)D and 1,25-dihydroxyvitamin D levels were found to be lower in patients who died (16,26). Another study reported that patients with 25(OH)D >60 nmol/L-1 had a mortality rate three times higher than patients with lower 25(OH)D levels (16,27). These studies performed with few patients resulted in conflicting outcomes and do not give definite results, raising the question "Is vitamin D important in intensive care patients?"

The prevalence of vitamin D deficiency exceeds 70% in intensive care patients. Lower levels of vitamin D in the intensive care unit are associated with higher infection rates, prolonged hospitalization, increased health costs, and increased mortality rates. There is an increased tissue demand for vitamin D in critical diseases (28). In a study by Arnson et al. (29) with 130 patients, vitamin D deficiency was detected in 82% of critically ill patients, and the mean vitamin D level was measured as 14.04±6.9 ngmL-1 (29). In our study, the mean vitamin D levels of all patients was 13.75±9.4

ngmL-1, similar to vitamin D levels in this study. Most guidelines point to a cut-off value of 20 ngmL-1 for vitamin D deficiency, but the threshold value for intensive care patients has not yet been determined (13,30). Per literature, there is no clear cut-off value to define vitamin D deficiency, for the replacement or the dose/route of replacement in intensive care patients (13,30). Some authors suggest that organ failure, sepsis, and fluid deficiency and its treatment may change the level of vitamin D (31). However, in our study, there was no significant relationship between vitamin D levels and SOFA score, an indicator of organ failure, in both groups.

Vitamin D deficiency is among the risk factors that prolong the duration of hospital stay (32). A study conducted on patients admitted to an intensive care unit, with measured vitamin D levels, evaluated the duration of hospital stay, the risk of readmission to the intensive care unit, and mortality in 90 days. In this study, serum vitamin D level was positively correlated with a prolonged hospital stay, readmission to intensive care, and mortality within 90 days (28).

To promote the use of APACHE II in Turkey, it is provided online by the Ministry of Health. In this context, mortality can be calculated by this system after writing patient information and physiological values (33). Age was included in the APACHE II score as a factor affecting mortality independent of disease severity as it shows a decline in physiological reserves. The APACHE II score is the sum of 3 subscales: acute physiology score, age, and chronic health evaluation, with the highest value being 71. Mortality is 25% if the total APACHE II score is 25 and increases to 80% if the score is 35 points or higher (34,35). In our study, the mean APACHE II score of patients of or above 75 years was significantly higher than that of patients below 75 years.

In a retrospective study of patients treated in the intensive care unit with a diagnosis of sepsis and/or septic shock between 2006 and 2011, the vitamin D levels of patients when they are admitted to intensive care were compared with mortality rates within 30 days. In this study, vitamin D deficiency was found in 65 (54%) of 121 patients and the mortality rate was significantly higher in these patients (36). In another retrospective study, the mortality rates were evaluated in 3,509 patients whose vitamin D levels were measured and who had noncardiac surgery. High vitamin D levels were found to significantly decrease mortality rates. Also, vitamin D concentration was associated with mortality at the hospital, serious infection, and serious cardiovascular events (37). In contrast to these studies, there was no significant relationship between vitamin D levels and APACHE II scores, which indicate mortality, in both groups in our study.

There was a significant negative correlation between age and vitamin D in patients of or above 75 years in our study. In these patients, vitamin D levels decreased with increasing age. Inadequate vitamin D in the elderly adversely affects general health, speeds up the aging process, limits movement, and causes osteoporosis and brittleness in bones (38).

Vitamin D deficiency is associated with decreased muscle functions, impaired performance, and increased weakness. Supplementation of vitamin D, especially in the elderly, helps strengthen muscles (39). About one million people worldwide are thought to have vitamin D deficiency or insufficiency (19). In a study investigating the relationship between vitamin D status and the metabolic syndrome in the elderly, a negative correlation was found between vitamin D concentrations and the prevalence of the metabolic syndrome. Since vitamin D deficiency is widespread worldwide and the risk increases with age, the benefits of improving vitamin D levels in the elderly may be huge (40).

Study Limitations

The limitation of this study was the relatively small sample size.

CONCLUSION

We detected that vitamin D levels significantly decreased with age in patients of or over 75 years as per the literature. However, contrary to some studies linking low vitamin D levels with high mortality and organ failure especially in intensive care patients, there was no significant relationship between vitamin D levels and mortality/organ failure in our study. This result may be due to a limited number of patients. However, given that no clear consensus exists on critical vitamin D levels that require replacement in intensive care patients despite many studies that associate vitamin D levels and mortality/organ failure, we think that more comprehensive clinical studies with larger patient samples are warranted on this topic.

Ethics Committee Approval: This study was a retrospective, non-interventional, non-drug, observational clinical trial (Ethics Committee approval was received from the Giresun University Clinical Research Ethics Committee (approval number: 29/09/2017-11).

Informed Consent: Retrospective study.

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