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Serum Vitamin D Level and Hypertensive Crises

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ABSTRACT

Introduction: Vitamin D deficiency is associated with hypertension; however, there is no study on the relationship between vitamin D deficiency and hypertensive crises. This study aimed to determine the relationship between serum vitamin D levels and hypertensive crises.
Material and Methods: This descriptive-analytical, cross-sectional study was conducted on 120 individuals in Shafa Hospital in 2016 within the age range of 40-80 years, selected through simple random sampling technique. The research population was divided into two groups of hypertensive crises (n=60) with blood pressure over 180/120 mm/Hg and hypertensive patients without history of hypertensive crises (n=60). For the purpose of the study, 5 ml peripheral venous blood samples were collected. The blood serum was isolated by a centrifugal device, and the serum vitamin D levels were analyzed by radioimmunoassay.
Results: The mean levels of vitamin D in hypertensive and non- hypertensive crises groups were 29.73 and 30.23 ng/ml, respectively. There was no significant difference between the two groups in terms of vitamin D levels (P>0.05). However, no statistically significant difference was observed between the two groups considering gender (P>0.05). Serum vitamin D levels showed a direct correlation with the duration of hypertension and age (P<0.05 and P<0.01, respectively).In addition, there was a significant correlation between serum vitamin D levels and the number of hypertensive crises over the past year. In this regard, the reduction of serum vitamin D levels was accompanied with the enhancement of the number of hypertensive crises (P<0.01).
Conclusion: There is evidence on the relationship between serum vitamin D levels and cardiovascular diseases, including hypertension. Nonetheless, in the present study, no significant relationship was observed between serum vitamin D level and hypertensive crises.

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Introduction

Hypertension defined as systolic and diastolic blood pressure above 140 and 90 mmHg, respectively, in patients currently taking antihypertensive medication or diagnosed with hypertension for a minimum of two times by a physician. It is one of the most common chronic medical conditions that affect 72 million people in the United States.

Systolic blood pressure above 180 mmHg or diastolic over 120 mmHg in hypertensive

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patients are known as hypertensive crises (1). Hypertensive crises, divided into hypertensive emergencies and urgencies, are differentiated by the presence or absence of end-organ damage, respectively. It is important to separate these two categories for the adoption of proper therapeutic procedures. In hypertensive emergencies, the blood pressure should be reduced rapidly, not necessarily to the normal level, while in hypertensive urgencies, it should be reduced within 24-48 h (2-3).

Annual mortality rate in untreated hypertension is 79% with a mean survival rate of 10.5 months. Prior to the emergence of antihypertensive drugs, about 7% of people with hypertension had hypertensive crises (4). Hypertensive crises are more prevalent in the elderly and non-Hispanic black population; however, men are affected two times more often than women. The most common cause of hypertensive crises is chronic hypertension with an acute exacerbation (5). The main and possible causes of hypertension can be genetic disorders in renal sodium excretion, as well as in sodium and calcium transmission in smooth muscle cells, changes in the angiotensin-encoding genes and other proteins in the renin-angiotensin system, and vasoconstriction due to hormonal-neurogenic causes. In addition, environmental factors have a significant impact on blood pressure (6).

Vitamin D deficiency is a common medical problem in the world, especially in populations living in temperate regions (7). Living conditions, such as low outdoor activities, environment, and air pollution, result in low contact with ultraviolet radiation. Lack of exposure to ultraviolet radiation, which is needed for vitamin D production, can cause vitamin D deficiency. Furthermore, factors, such as high-altitude, industrial cities, and dark skin, lead to the reduction of vitamin D production, which results in hypertension (8).

Vitamin D regulates calcium and bone homeostasis, and its receptor is present in many tissues, such as vascular endothelium and myocardial tissue. This indicates the biological role and function of vitamin D, which can suppress renin production by affecting the juxtaglomerular system (9).

Vitamin D can lead to the suppression of parathyroid hormone and pro-inflammatory cytokine production. In addition, there are a number of possible pathophysiological pathways that show the effects of vitamin D and vascular protection against hypertension (10). Moreover, observational studies suggest that a low level of vitamin D is associated with high blood pressure. They also revealed a high chance of developing hypertension is correlated with the increased risk of mortality and high levels of cardiovascular events in the future (11-13).

According to the third National Health and Nutritional Examination Survey, systolic blood pressure and pulse pressure have a reverse and significant relationship with vitamin D levels. It has also been proved that people with a sufficient level of vitamin D have low systolic blood pressure.

In another study, the prevalence of hypertension was demonstrated to have an association with a low level of vitamin D (14-17). According to the above mentioned results and due to the lack of study on the association between vitamin D deficiency and hypertensive crises, the present study aimed to assess the relationship between serum vitamin D levels and hypertensive crises.

Materials and Methods

This descriptive-analytical, cross-sectional study was conducted on 120 all hypertensive patients in Shafa Hospital, Kerman, Iran in 2016 within the age range of 40-80 years, referring to the Cardiac Emergency Department. The study population was selected through simple random sampling technique. The participants were assigned into two groups of hypertensive crises (n=60) and non-hypertensive crises (n=60). The hypertensive crises group consisted of the patients with a blood pressure of over 180/120 mm/Hg who were admitted to the emergency department. On the other hand, the non-hypertensive crises group contained patients with hypertension regardless of any history of hypertensive crises in the past one year admitted for other etiologies.

Hypertensive crises was defined as the frequency of admission due to hypertensive crises over the past year. The two groups were matched in terms of age and gender. Age range of 40-80 years and non- smoking were considered as the inclusion criteria. On the other hand, the exclusion criteria were: 1) age of < 40 or > 80 years, 2) smoking, 3) secondary hypertension, 4) history of renal disease, 5) consumption of vitamin D over a past year, and 6) acute illness, 7) recent history of acute or chronic hepatitis or renal disease, hypercortisolism, and malabsorption, 8) breastfeeding and pregnancy, 9) alcohol consumption, and 10) administration of drugs affecting the level of 25-hydroxy vitamin D.

All patients were informed about the research process, and the written consents were also obtained from them. Demographic forms were filled out for each subject, containing information, such as age, gender, duration of hypertension, and number of hypertensive crises over the past year. The blood pressure of the patients was measured using the Riester Germany mercury barometric instrument twice with a 15-minute interval.

In the next stage, 5 cc blood samples were collected from the peripheral venous, and the serum was separated by UNIVERSAL centrifugal device at 4000 rpm for 5 min. Moreover, the serum level of vitamin D was determined by radioimmunoassay. The measurement of vitamin D level was accomplished by using the Monobind kit manufactured in the USA. A biochemical study was performed for all patients in a single laboratory with a standard method, and common quality control techniques were used to ensure the accuracy of the tests throughout the duration of the laboratory tests. The sensitivity of the kit was 0.67 ng/ml for the measurement of serum vitamin D level.

The data were analyzed in SPSS software (version 18). The quantitative data were described using the central and dispersion indicators. Mann-Whitney U and Pearson correlation test was also utilized to analyze the data.

Results

Based on the data, the hypertensive and non-hypertensive crises groups entailed 39 and 40 females, respectively. The mean ages of the hypertensive and non-hypertensive crises groups were 64.47±11.28 and 64.45±10.01 years, respectively (Table1).Moreover, the mean serum vitamin D levels in the hypertensive and non-hypertensive crises groups were obtained as 29.73±23.14 and 30.23±32.98 ng/ml, respectively (Table2).

Given the non-normal distribution of serum vitamin D levels in the two groups (P<0.0001), Mann-Whitney U test was used to compare this variable levels between the research groups. The results showed no significant difference between the two groups in terms of serum vitamin D levels (P=0.169).Furthermore, there was no correlation between serum vitamin D level and gender in any of the groups (Table2).

Serum vitamin D levels was also directly associated with the duration of hypertension and patients' age (Table3). In patients with hypertensive crises, there was an indirect correlation between serum vitamin D levels and the number of hypertensive crises during the past year (P=0.005, r=-0.356). In this regard, with a decrease in serum vitamin D level, the number of hypertensive crises increased and all the correlation found in our study were weak.

Table 1. Patients' characteristics according to the hypertensive crises

Variable	With crises	Without crises
Sex		
Female (%)	39 (65)	40 (66.67)
Male (%)	21 (35)	20(33.3)
Age (Mean±SD*)	11.28±64.47	10.01±64.45
Number of years with hypertension (Mean±SD*)	5.70±7.82	6.08±9.12
Number of crises in year (Mean±SD*)	0.80±1.12	-

* Standard Deviation

Table 2. Serum vitamin D levels in patients with and without hypertension crises

Variable		Mean of vitamin D level	SD*	Median	Min	Max	Statistic	P.value
With crises	Total	29.73	23.15	20.85	8.10	83.90	391.00	0.774
	Female	30.49	23.57	22.70	8.10	83.90		
	Male	28.31	22.85	19.90	9.20	81.80		
Without crises	Total	30.23	32.98	14.90	8.10	126.0	368.00	0.612
	Female	33.39	35.17	15.15	8.10	125.40		
	Male	23.94	27.87	12.50	8.10	126.0		

* Standard Deviation

Table 3. Correlation between age, years with hypertension and vitamin D levels according to Pearson correlation test

	Age	Number of years with hypertension	Serum vitamin D level
Age	-	r = 0.383 P<0.0001	r = 0.259 P=0.004
Number of years with hypertentin	r = 0.368 (P<0.001)	-	r = 0.211 P=0.02
Serum vitamin D level	r = 0.265 (P=0.003)	r = 0.165 (P=0.072)	-

Discussion

Vitamin D plays a leading extracellular role in the function of various tissues. Different studies have shown vitamin D inhibitory effects on renin-angiotensin system, coronary calcification, proliferation of smooth muscle cells, and myocardial hypertrophy. In addition, in recent years, several studies have examined the relationship between serum vitamin D levels and cardiovascular events.

In a study conducted by Yarjanli et al, serum vitamin D levels was reported to be associated with cardiovascular events (18). Wang et al. studied the effect of serum vitamin D levels on cardiovascular events in Harvard University and reported an effect level of below 15 ng/ml. This increased risk was more pronounced in patients with hypertension. In a study performed on patients with hypertension, 15.3% of the subjects had hypertensive crises during the follow-up and 84% of the cases had symptoms associated with high blood pressure.

Moreover, factors, such as female gender, obesity, coronary artery disease, and no medication use, were revealed to have association with hypertensive crises (19). The results of several randomized controlled trials investigating menopausal women in Europe over a 7-year follow-up revealed that the combination of calcium and vitamin D would not reduce blood pressure or the risk of developing blood pressure. However, few studies have shown the relationship between vitamin D and high blood pressure in menopausal women in Asia (20-22).

In one study, vitamin D deficiency in menopausal women has been noted. The results of the mentioned study demonstrated that systolic and diastolic blood pressure in women with serum vitamin D levels below 15 ng/ml was higher than those with serum vitamin D levels above 15 ng/ml. It was also found that women with lower education levels and obesity had a higher risk of hypertension (23). In addition, hypertensive crises as hypertension was common in elderly people and was twice more prevalent in men than in women (5).

The results of the present study were not consistent with the mentioned findings. In the present study, there was no relationship between serum vitamin D levels and hypertensive crises. Moreover, no relationship was observed between gender and serum vitamin D levels in both groups with and without hypertensive crises. vitamin D deficiency is associated with living conditions, such as high altitude, low outdoor activity, air pollution, industrialization of cities, and dark skin, which results in lower vitamin D production and high blood pressure (8).

Based on the third National Health and Nutritional Examination Survey, systolic blood pressure and pulse pressure have an indirect relationship with vitamin D levels. It has also been shown that people with a sufficient level of vitamin D have lower systolic blood pressure. In another study, hypertension was reported to be associated with low levels of vitamin D (14-17).

In a study conducted on elderly people with vitamin D deficiency, systolic blood pressure was 9% lower in patients using vitamin D and calcium supplementation in comparison to that in the patients just consuming calcium (24). In another study, a direct correlation was observed between vitamin D deficiency and the incidence of hypertension regardless of age, physical activity, body mass index, race, and menopausal status (11).

In a broad study, there was no relationship between the intake of oral vitamin D and the incidence of hypertension (25). However, in the current study, a significant correlation was obtained between age and serum vitamin D level in both groups. Therefore, it can be concluded that the level of vitamin D increased with aging. In a recent clinical study,it was found that vitamin D supplements would not reduce blood pressure in patients with prehypertension and stage I hypertension (26).

In a study performed in Korea, it was shown that patients with hypertension had low serum vitamin D levels. In the mentioned study,serum vitamin D levels showed an indirect relationship with abdominal obesity, hypertriglycemia, and high blood pressure (27). The results of a meta-analysis showed a small but significant decrease in diastolic blood pressure among the people taking vitamin D supplementation; however, this reduction was not observed in systolic blood pressure.

Systolic blood pressure showed a higher reductionin people taking the inactive form of vitamin D than in those consuming the active form. However, in people with normal baseline blood pressure, the consumption of vitamin D did not reduce blood pressure (28).

In a review article, it reviews whether serum vitamin D concentration plays an important role in causing hypertension or not. Because of the opposing consequences of different reviews on the role of vitamin D in preventing hypertension development or its treatment, it appears that vitamin D levels in the body modulate the blood pressure indirectly and it suggested that physicians should keep a check on the vitamin D levels of their patients in order to curb the ever-increasing incidence of hypertension(29).

In another review article, to date, the results of RCTs and meta-analysis of them do not support the use of vitamin D or its analogues as an individual patient treatment for hypertension or as a population-level intervention to lower BP. Those discrepancies might be due to heterogeneity of patient baseline characteristics, differences in sample size and follow-up periods, and different vitamin D doses. However, many experimental and epidemiologic studies showed possible roles of vitamin D in controlling BP in various ways (30).

Conclusion

As the findings of the present study indicated, vitamin D was associated with the level of blood pressure and incidence of cardiovascular disease. So far, no studies have examined the relationship between serum vitamin D levels and hypertensive crises. However, our results revealed no relationship between serum vitamin D levels and hypertensive crises. The findings of the current study could provide a good starting point for further research. Other researchers are recommended to take effective steps to improve the health of public in the future.

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None.

Conflict of Interest

The authors declare no conflict of interest.

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