OTJHS
Online Turkish Journal of Health Sciences

e-ISSN: 2459-1467

OTSBD
Online Türk Sağlık Bilimleri Dergisi

Online Turkish Journal of Health Sciences 2022;7(2):313-318 *Online Türk Sağlık Bilimleri Dergisi 2022;7(2):313-318*

Tip 2 Diabetes Mellitus Tanılı Hastalarda Ortostatik Hipotansiyon ile D Vitamini Eksikliği Arasındaki İlişki

The Relationship between Orthostatic Hypotension and Vitamin D Deficiency in Patients with Type 2 Diabetes Mellitus

[1]Ece YIĞIT, [1]Rıdvan SIVRITEPE, [2]Dilay KARABULUT, [3]Umut KARABULUT

[1] Department of Internal Medicine, Istanbul Medipol University Faculty of Medicine, Istanbul, Turkey
[2] Department of Cardiology, Bakırköy Dr.Sadi Konuk Training and Research Hospital, Istanbul, Turkey
[3] Department of Cardiology, Acıbadem International Hospital, Istanbul, Turkey

Ece Yiğit: http://orcid.org/0000-0002-8293-3554
Rıdvan Sivritepe: http://orcid.org/0000-0003-0547-1883
Dilay Karabulut: http://orcid.org/0000-0003-1896-0096
Umut Karabulut: http://orcid.org/0000-0002-3947-9173

ÖZ

Amaç: D vitamini eksikliği diyabetik hastalarda sık görülmekte ve çalışmalarda nöropatiye yol açabileceği gösterilmiştir. Bu çalışmada diyabetik hastalarda otonom nöropatinin bir bileşeni olan ortostatik hipotansiyon (OH) ile 25-hidroksivitamin D (25(OH)D) seviyesi arasındaki ilişkiyi belirlemeyi amaçladık.

Materyal ve Metot: Çalışmaya 50-65 yaş arası diyabetik toplam 118 hasta dahil edildi. Hastalar OH varlığına göre iki gruba ayrıldı. 25(OH)D ve diğer değişken parametreler bu iki grup arasında değerlendirildi.

Bulgular: Bu kesitsel çalışmaya 66 kadın ve 52 erkek olmak üzere toplam 118 hasta dahil edildi. Hastaların yaş ortalaması 56,2±3,2 yıl idi. 25(OH)D düzeyleri OH olan grupta anlamlı olarak daha düşük bulundu (p <0,026). 25 (OH)D düzeyi ile OH arasındaki ilişkiyi incelemek için yaş ve cinsiyete göre ayarlanmış regresyon analizi yapıldı. Tek değişkenli ve çok değişkenli analizlerde 25(OH)D'nin OH varlığını öngörmediği bulundu (p >0,05).

Sonuç: OH'li diyabetik hastalarda 25(OH)D düzeyleri anlamlı olarak daha düşüktür. Aralarında bağımsız bir ilişki gösterilemese de OH tedavisinde D vitamini eksikliğinin düzeltilmesinin faydalı olacağı düşünülebilir.

Anahtar Kelimeler: D vitamini eksikliği, ortostatik hipotansiyon, tip 2 diabetes mellitus

ABSTRACT

Objective: Vitamin D deficiency is common in diabetic patients, and studies showed that it could lead to neuropathy. Therefore, we aimed to determine relationship between 25-hydroxyvitamin D (25(OH)D) levels and orthostatic hypotension (OH) which is a component of autonomic neuropathy in diabetic patients.

Materials and Methods: A total of 118 patients with Type 2 diabetes mellitus and aged 50-65 years were included. Patients were divided into two groups as OH present and OH not present. 25(OH)D and other variable parameters were evaluated between these two groups.

Results: A total of 118 patients, 66 female and 52 male, were included in this cross-sectional study. The mean age of the patients was 56.2±3.2 years. 25(OH)D levels were found to be significantly lower in the group with OH (p<0.026). Age and sex-adjusted regression analysis were performed to examine the relationship between 25(OH)D level and OH. It was found that 25(OH)D didn't predict the presence of OH in the univariate and multivariate analyses (p >0.05).

Conclusion: 25(OH)D levels are significantly lower in diabetic patients with OH. Although an independent relationship between them has not been demonstrated, it can be thought that correcting Vitamin D deficiency will be beneficial in the treatment of OH.

Keywords: Orthostatic hypotension, type 2 diabetes mellitus, vitamin D deficiency

Sorumlu Yazar / Corresponding Author:
Rıdvan SIVRITEPE
Department of Internal Medicine, Istanbul Medipol University Faculty of Medicine, Istanbul, Turkey. Bahcelievler Quarter, Adnan Menderes Boulevard No:31-33 Pendik Istanbul/ Turkey
Tel: +90 (545)260 59 57
E-mail: dr.ridvansivritepe@gmail.com

Yayın Bilgisi / Article Info:
Gönderi Tarihi/ Received: 10/01/2022
Kabul Tarihi/ Accepted: 16/04/2022
Online Yayın Tarihi/ Published: 01/06/2022

Atıf / Cited: Yiğit E and et al. The Relationship between Orthostatic Hypotension and Vitamin D Deficiency in Patients with Type 2 Diabetes Mellitus. *Online Türk Sağlık Bilimleri Dergisi* 2022;7(2):313-318. doi: 10.26453/otjhs.1056045

INTRODUCTION

Autonomic neuropathy is one of the most frequent complications of type 2 diabetes mellitus. Although it has a negative influence on the quality of life and survival, it may be unnoticed. The primary mechanism of neuropathy is oxidative stress and the formation of toxic glycosylation products, which leads to neuronal malfunction.[1] Orthostatic hypotension (OH) is a common symptom of diabetic neuropathy. OH, is a clinical syndrome of exaggerated transient orthostasis and is defined as a decrease of ≥20 mmHg in systolic blood pressure (SBP) and/or ≥10 mmHg in diastolic blood pressure (DBP) within 3 minutes of active standing. The most frequent symptoms are dizziness, blackout, presyncope, and syncope. Also, fractures, hemorrhages, and other catastrophic injuries can be caused by OH. Therefore, diagnosis, prevention, and treatment are critical in patients.[2]

Vitamin D deficiency, which is common in diabetics, has been shown to reduce insulin sensitivity, deteriorate beta cell activities, and promote systemic inflammation, contributing to the development of type 2 diabetes mellitus.[3] 25(OH)D is also a neuroactive hormone that controls the sympathetic and parasympathetic nervous systems. Recent studies concluded that Vitamin D deficiency might be associated with autonomic neuropathy.[4,5] Since treatment options for OH are limited, it may be crucial to establish the link between OH and 25(OH)D deficiency. 25(OH)D replacement therapy, a simple and affordable therapeutic option, might be a potential treatment option for OH.

It is known that OH is more frequently seen in older patients. Studies on the relationship between 25(OH) D and OH were similarly conducted with patients 65 years and older.[6-9] There are no similar studies in the lower age. Therefore, this study aimed to reveal the relationship between OH and 25(OH)D deficiency in pre-geriatric patients with diabetes.

MATERIALS AND METHODS

Ethical Status: Ethical approval was obtained by Istanbul Medipol University Clinical Research Ethics Committee (Date:21/01/2021, decision no:101), and it was carried out in accordance with the Helsinki Declaration principles. For the present study, all patients were informed about the purpose and procedure, and written informed consent was obtained.

For the power analysis, the study of Annweiler et al[8] was taken as reference. Considering the association between 25(OH)D concentration and change in diastolic blood pressure being $\beta = 0.07$, $P = 0.046$, the sample size per group was calculated as minimum 29, with a Type 1 error of 0.05 and the strength of the study being 80%. With a 20% loss, a total of 118 patients were incorporated in the study.

The present study is a cross-sectional study. A total of 118 patients (66: female, 52: male) with diabetes (at least five years) patients with poor glucose regulation (Hba1c>7%) and aged 50-65 years, who applied to the outpatient clinic between January and June 2021, were included in the study. Under 50 or over 65, type 1 diabetes mellitus, hypo-hyperthyroidism or hyperparathyroidism, use of drugs that may change serum 25(OH)D levels (such as vitamin D, bisphosphonates, corticosteroid, anticonvulsant, estrogen) or dietary supplements, and body mass index> 30 kg / m2 were not included. Also, patients with additional chronic disease that may cause neuropathy (malignancy, myopathy, stroke, cardiovascular disease, infection, etc.) and patients with tobacco and alcohol consumption were excluded from the study since these substances might cause neuropathy.

Biochemical blood tests of all patients were analyzed. Blood samples were taken from the patients, then they were analyzed in the same laboratory. Plasma glucose by the enzymatic test method, glycosylated hemoglobin by HPLC method were measured with Architect plus device. The serum sample taken to measure the 25(OH)D levels of the patients were centrifuged at 3500 rpm for 15 minutes and then measured by electrochemiluminescence method. 25(OH)D was measured using the IDS-iSYS, Immunodiagnostic Systems device with an intra and inter test coefficient of variation of 3.0% and 3.3%, respectively. The serum 25(OH)D detection limit was 2 ng / ml. According to their 25(OH)D levels patients were divided into 4 groups: Extreme deficiency (≤10 ng/ml), deficiency (between ≤20 and >10 ng/ml), inefficiency (between ≤30 and >20 ng/ml), sufficient (>30 ng/ml).[10]

Blood pressure was measured with an electronic device (Omron M2 Basic HEM-7121JE Arm Meter Digital Sphygmomanometer) in sitting position after a rest period of more than 5 minutes. Blood pressure and blood samples of the patients were taken between 08:00 and 10:00 hours on an empty stomach. OH is defined as a decrease of ≥20 mmHg in SBP and/or ≥10 mmHg in DBP within 3 minutes of ac-

tive standing.[2] Patients were divided into two groups as OH present and OH not present. 25(OH)D levels and other variables compared between the two groups.

Statistical Analysis: SPSS 22.0 program (Statistical Package for the Social Sciences 22.0, IBM, Armonk, NY, United States) was used in the analysis of variables. The suitability of the data to normal distribution was evaluated using the Shapiro-Wilk Francis test. The Mann-Whitney- U test was used to compare two independent groups according to quantitative data. Spearman's rho test was used to examine the correlations of variables. Pearson's chi-square and Fisher's Exact tests were used to comparing categorical variables. Variables with clinical relevance were added to the multivariate analysis. Quantitative variables are indicated as mean ± standard deviation in the tables. And median (minimum/maximum), while categorical variables are shown as n (%). Variables were examined at a 95% confidence interval (CI), and $p < 0.05$ was considered significant.

RESULTS

The mean age of the patients was 56.1±3.2 years, the mean HbA1c was 8.6±0.3%, the mean 25(OH)D level was 20.6±16.6 ng / ml, and the mean duration of diabetes was 7.9 years. While 33 of the patients (28%) met the OH criterion, 85 patients (72%) did not meet the criteria for OH. The demographic data, biochemical and clinical parameters, of the patients are shown in Table 1.

When we evaluate the OH status according to gender, while 30.3% of women had orthostatic hypotension, 25% of men had orthostatic hypotension. The difference in ratio between the groups was not statistically significant (Yates Continuity correction $p>0.05$) (Table 2).

Patients were divided into four groups according to their 25(OH)D levels and compared in terms of OH. No statistically significant difference was found between the presence of OH and 25(OH)D groups (Table 3).

Table 1. Demographic data, clinical and biochemical parameters of the patients.

Parameter	Mean ± Sd	Median	Minimum	Maximum
Age (years) n: 118	56.12±3.2	58	50	65
BMI (kg / m2)	26.2±0.6	25.41	24.9	29.1
Systolic Blood Pressure (mmHg)	123.4±13.5	125	100	160
Diastolic Blood Pressure (mmHg)	71.45±8.9	70	55	110
Vitamin D (ng / ml)	20.68±16.67	14	3	152
HBA1C (%)	8.66±0.32	8.875	7.8	9.2
Diabetes Duration (years)	7.9±6.1	7	2	21

Sd: Standard Deviation; BMI: Body mass index; HBA1C: Hemoglobin A1c.

Table 2. Evaluation the orthostatic hypotension status according to gender.

	Female n (%)	Male n (%)	Toplam n (%)
Orthostatic Hypotension Absent	46 (69.7)	39 (75)	85 (72)
Orthostatic Hypotension Present	20 (30.3)	13 (25)	33 (28)

Table 3. Percentage distribution of patients according to vitamin D levels and the presence of orthostatic hypotension.

	Orthostatic Hypotension Absent n (%)	Orthostatic Hypotension Present n (%)	All patients n (%)	p
Severe Vitamin D Deficiency	18 (22.1)	13 (39.4)	31 (26.3)	0.058
Vitamin D Deficiency	32 (37.6)	11 (33.3)	43 (36.4)	0.664
Vitamin D Inefficiency	15 (17.6)	5 (15.2)	20 (16.9)	0.756
Vitamin D Sufficiency	20 (23.5)	4 (12.1)	24 (20.3)	0.169
Total	85 (100)	33 (100)	118 (100)	

Ki-Kare p:0,197.

When the 25(OH)D levels are examined by gender, only 10 female and 14 male patients had sufficient 25(OH)D levels. Although severe vitamin D deficiency was more common in female patients, this was not statistically significant. Also, there was no statistically significant difference in 25(OH)D groups by gender (Yates Continuity correction $p>0.05$) (Table 4).

When the 25(OH)D level was compared in the group with and without OH, while the median 25(OH)D level was 17 ng/ml in the group with OH, it was 13 ng/ml in the group without OH. This difference between groups was statistically significant ($p <0.026$) (Table 5).

DISCUSSION AND CONCLUSION

This study found that 25(OH)D levels are significantly lower in patients with OH. However, 25(OH) D is not an independent predictor of OH.

The prevalence of diabetic autonomic neuropathy ranges between 25% and 75% in diabetic patients.[5,11] Several studies showed that autonomic neuropathy could be found in newly diagnosed diabetics and even prediabetics, but the risk increases with the duration of diabetes.[12,13] Diabetes-related neuropathy is caused by the complex interactions of glycemic control, disease duration, blood pressure, and aging-related neuronal loss.[14] Hyperglycemia induces oxidative injury to the tiny arteries that supply these peripheral neurons by increasing mitochondrial synthesis of free oxygen radicals.[1]

The risk of all-cause neuropathy rises with age. The studies on OH in the literature has frequently been conducted on older patients >65 years of age.[15-17] The age range was restricted, and patients <65 were included in our study. Our study may be novel in examining the relationship between OH and 25(OH) D in the younger age group.

25(OH)D deficiency is widespread in our country. 25(OH)D inefficiency was 66% and deficiency 24% in a large-scale study with the Turkish population.[18] In another study conducted in our country on 294 diabetic patients, vitamin D deficiency was found in 47.9% of patients and vitamin D insufficiency was found in 32.9% of patients.[19] Only 20.3% of the patients had sufficient 25(OH)D levels in our study, which indicates that 25(OH)D deficiency is still prevalent in our society and should be closely monitored and treated. Gender differences in the prevalence of 25(OH)D are controversial.[20,21] The mean 25(OH)D level of female patients was significantly lower than males' patients in our study.

The notion that autonomic neuropathy is a common complication of diabetes, and 25(OH)D deficiency is frequently associated with diabetes; we hypothesized that there might be a link between OH and 25(OH)D deficiency. Two central mechanisms explain 25(OH) D's potential effect on blood pressure control and intravascular volume. 25(OH)D regulates the renin-angiotensin-aldosterone system. The 25(OH)D receptor can also be found in cardiomyocytes and vascular endothelial cells.[22,23] Its deficiency has been linked to endothelial dysfunction, which may have an impact on the vasopressor response. There is also evidence that 25(OH)D supplementation promotes vascular regeneration. The possible reasons why the relationship between 25(OH)D and OH could not be revealed in our study can be classified as; different reasons, and the number of affecting factors for the occurrence of OH, the relatively younger patients

Table 4. Evaluation vitamin D levels the according to gender.

	Female n (%)	Male n (%)	All patients n (%)	p
Severe Vitamin D Deficiency	22 (33.3)	9 (17.3)	31 (26.3)	0.051
Vitamin D Deficiency	26 (39.4)	17 (32.7)	43 (36.4)	0.455
Vitamin D Inefficiency	8 (12.1)	12 (23.1)	20 (16.9)	0.115
Vitamin D Sufficiency	10 (15.2)	14 (26.9)	24 (20.3)	0.119
Total	66 (100)	52 (100)	118 (100)	

Table 5. Comparison of vitamin D levels of patients with and without orthostatic hypotension.

Orthostatic Hypotension	Vitamin D levels		
	Mean $\pm$ Standard Deviation	Median (Minimum - Maximum)	p Value
Orthostatic Hypotension Absent	22.3$\pm$17.9	17 (3.9-122)	0.026*
Orthostatic Hypotension Present	16.5$\pm$12.4	13 (3-55.93)	
All patients	20.7$\pm$16.6	16.7 (3-122)	

*: Mann Whitney U Test..

age, the small sample size of the study and the regression analysis with all three groups with low 25 (OH)D levels (extreme deficiency, deficiency, and inefficiency).

OH, is more common in the elderly. This is because adaptive mechanisms such as increased heart rate and vascular resistance cannot be activated and are insufficient to compensate for the blood pressure drop caused by standing upright. In a large-scale meta-analysis, it was revealed that the frequency of OH was significantly higher in those with 25(OH)D deficiency. Moreover, it was shown that this relationship continued after confounding factors affecting OH were adjusted.[24] However, it has been observed that this relationship becomes significant when 25(OH)D levels fall below a certain level. Therefore, a study with only the patients with extreme 25(OH)D deficiency may be significant in terms of OH.

OH, might be symptomatic or asymptomatic. Although it can happen at any time, it is more common in the morning.[25] Therefore, we evaluated the presence of OH in the morning hours. Treatment is both non-pharmacological and pharmacological. Non-pharmacological treatments are patient education and correct posture change, activity, exercise, diet recommendations, salt balancing, adequate water intake, and the use of compression stockings. Pharmacological therapy based on intravascular volume expansion with vasopressor drugs such as fludrocortisone and midodrine is used when non-pharmacological approaches fail.[26-28] OH was more common in both the deficient and non-deficient groups in our study. This could be because the entire group studied in our study was diabetic, and 25 (OH)D deficiency affects diabetic patients who already have a proclivity for neuropathy. The present study had some limitations. Firstly, the study was a cross-sectional study. Therefore, we could not establish a causal relationship between OH and 25(OH)D deficiency. Secondly, the patients' vitamin D levels, and blood pressure measurements were evaluated at a single time point. Thirdly, our study was a single center study, so our results may not be representative of all patients with diabetes mellitus. Despite these limitations, our study is important and valuable in raising awareness of OH and 25(OH)D deficiency in diabetic patients.

In conclusion; 25(OH)D levels are significantly lower in diabetic patients with OH. 25(OH)D deficiency may play an etiological role in the development of OH. OH, is common not only in the elderly population but also in younger patient populations with risk factors and should not be overlooked. Although an independent relationship between them has not been demonstrated, it can be thought that correcting 25(OH)D deficiency will be beneficial in the treatment of OH. However, larger, prospective studies are needed.

Ethics Committee Approval: Ethical approval was obtained by Istanbul Medipol University Clinical Research Ethics Committee (Date:21/01/2021, decision no:101), and it was carried out in accordance with the Helsinki Declaration principles.

Conflict of Interest: No conflict of interest was declared by the authors.

Author Contributions: Concept – EY; Supervision – EY, RS; Materials – EY; Data Collection and / or Processing – EY, RS, DK, UK; Analysis and / or Interpretation – EY, RS, DK, UK; Writer – EY, RS.

Peer-review: Externally peer-reviewed.

REFERENCES

1. Spallone V. Update on the Impact, Diagnosis and Management of Cardiovascular Autonomic Neuropathy in Diabetes: What Is Defined, What Is New, and What Is Unmet. Diabetes Metab J. 2019;43(1):3-30. doi:10.4093/dmj.2018.0259
2. Joseph A, Wanono R, Flamant M, Vidal-Petiot E. Orthostatic hypotension: A review. Nephrol Ther. 2017;13(Suppl 1):S55-S67. doi:10.1016/j.nephro.2017.01.003
3. Issa CM. Vitamin D and Type 2 Diabetes Mellitus. Adv Exp Med Biol. 2017;996:193-205. doi:10.1007/978-3-319-56017-5_16
4. Wadhwania R. Is Vitamin D Deficiency Implicated in Autonomic Dysfunction? J Pediatr Neurosci. 2017;12(2):119-123. doi:10.4103/jpn.JPN_1_17
5. Hansen CS, Fleischer J, Vistisen D, Ridderstråle M, Jensen JS, Jørgensen ME. High and low vitamin D level is associated with cardiovascular autonomic neuropathy in people with Type 1 and Type 2 diabetes. Diabet Med. 2017;34(3):364-371. doi:10.1111/dme.13269
6. Tran J, Hillebrand SL, Meskers CGM, Iseli RK, Maier AB. Prevalence of initial orthostatic hypotension in older adults: a systematic review and meta-analysis. Age Ageing. 2021;50(5):1520-1528. doi:10.1093/ageing/afab090
7. Gilani A, Ramsay SE, Welsh P, et al. Vitamin D deficiency is associated with orthostatic hypotension in older men: a cross-sectional

analysis from the British Regional Heart Study. Age Ageing. 2021;50(1):198-204. doi:10.1093/ageing/afaa146

8. Annweiler C, Schott AM, Rolland Y, Beauchet O. Vitamin D deficiency is associated with orthostatic hypotension in oldest-old women. J Intern Med. 2014;276(3):285-295. doi:10.1111/joim.12201
9. Zuin M, Brombo G, Capatti E, Romagnoli T, Zuliani G. Orthostatic hypotension and vitamin D deficiency in older adults: systematic review and meta-analysis. Aging Clin Exp Res. 2021. doi:10.1007/s40520-021-01994-w
10. Holick MF. The Vitamin D deficiency pandemic: Approaches for diagnosis, treatment and prevention. Rev Endocr Metab Disord. 2017;18(2):153-165. doi:10.1007/s11154-017-9424-1
11. Zakin E, Abrams R, Simpson DM. Diabetic Neuropathy. Semin Neurol. 2019;39(5):560-569. doi:10.1055/s-0039-1688978
12. Vinik AI, Erbas T, Casellini CM. Diabetic cardiac autonomic neuropathy, inflammation and cardiovascular disease. J Diabetes Investig. 2013;4(1):4-18. doi:10.1111/jdi.12042
13. Bakkar NZ, Dwaib HS, Fares S, Eid AH, Al-Dhaheri Y, El-Yazbi AF. Cardiac Autonomic Neuropathy: A Progressive Consequence of Chronic Low-Grade Inflammation in Type 2 Diabetes and Related Metabolic Disorders. Int J Mol Sci. 2020;21(23):9005. doi: 10.3390/ijms21239005
14. Agashe S, Petak S. Cardiac Autonomic Neuropathy in Diabetes Mellitus. Methodist Debakey Cardiovasc J. 2018;14(4):251-256. doi:10.14797/mdcj-14-4-251
15. Hartog L, Kleefstra N, Luigies R, de Rooij S, Bilo H, van Hateren K. The clinical relevance of orthostatic hypotension in elderly patients. Geriatr Gerontol Int. 2017;17(11):1881-1885. doi:10.1111/ggi.12983
16. Bo M, Brunetti E. Orthostatic hypotension among elderly patients in Italian internal medicine wards: an observational study: comment. Intern Emerg Med. 2020;15(7):1355-1356. doi:10.1007/s11739-020-02327-x
17. Iseli R, Nguyen VTV, Sharmin S, Reijnierse EM, Lim WK, Maier AB. Orthostatic hypotension and cognition in older adults: A systematic review and meta-analysis. Exp Gerontol. 2019;120:40-49. doi:10.1016/j.exger.2019.02.017
18. Cigerli O, Parildar H, Unal AD, Tarcin O, Erdal R, Guvener Demirag N. Vitamin D deficiency is a problem for adult out-patients? A university hospital sample in Istanbul, Turkey. Public Health Nutr. 2013;16(7):1306-13. doi:10.1017/S1368980012003588
19. Kaya T, Akçay EÜ, Ertürk Z, Ergenç H, Tamer A. The relationship between vitamin D deficiency and erythrocyte sedimentation rate in patients with diabetes. Turk J Med Sci. 2018;48(2):424-429. doi:10.3906/sag-1712-28
20. Yan X, Zhang N, Cheng S, Wang Z, Qin Y. Gender Differences in Vitamin D Status in China. Med Sci Monit. 2019;25:7094-7099. doi:10.12659/MSM.916326
21. Vallejo MS, Blümel JE, Arteaga E, et al. Gender differences in the prevalence of Vitamin D deficiency in a southern Latin American country: a pilot study. Climacteric. 2020;23(4):410-416. doi:10.1080/13697137.2020.1752171
22. Lin L, Zhang L, Li C, Gai Z, Li Y. Vitamin D and Vitamin D Receptor: New Insights in the Treatment of Hypertension. Curr Protein Pept Sci. 2019;20(10):984-995. doi:10.2174/1389203720666190807130504
23. Gouni-Berthold I, Berthold HK. Vitamin D and Vascular Disease. Curr Vasc Pharmacol. 2021;19(3):250-268. doi:10.2174/1570161118666200317151955
24. Ometto F, Stubbs B, Annweiler C, et al. Hypovitaminosis D and orthostatic hypotension: a systematic review and meta-analysis. J Hypertens. 2016;34(6):1036-43. doi:10.1097/HJH.0000000000000907
25. Magkas N, Tsioufis C, Thomopoulos C, et al. Orthostatic hypotension: From pathophysiology to clinical applications and therapeutic considerations. J Clin Hypertens. 2019;21(5):546-554. doi:10.1111/jch.13521
26. Palma JA, Kaufmann H. Management of Orthostatic Hypotension. Continuum (Minneap Minn). 2020;26(1):154-177. doi:10.1212/CON.0000000000000816
27. Gibbons CH, Schmidt P, Biaggioni I, et al. The recommendations of a consensus panel for the screening, diagnosis, and treatment of neurogenic orthostatic hypotension and associated supine hypertension. J Neurol. 2017;264(8):1567-1582. doi:10.1007/s00415-016-8375-x
28. Chisholm P, Anpalahan M. Orthostatic hypotension: pathophysiology, assessment, treatment and the paradox of supine hypertension. Intern Med J. 2017;47(4):370-379. doi:10.1111/imj.13171