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Mini-Review

Ameliorative impact of vitamin D on hypertension

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Abstract

Hypertension is a chronic disorder with serious risk factors for clinically important events including myocardial infarction, heart failure, stroke and death. It is estimated that, 1.56 billion adults will be living with high blood pressure in 2025 and one in three adults has hypertension in world. Vitamin D is a micronutrient with important implications for human health and has recognized functions in calcium and bone metabolism. Low 25-hydroxyvitamin D levels are related to higher prevalence of blood pressure and evidences from meta-analysis of cohort studies showed that vitamin D deficiency, predicts enhanced risk of all-cause mortality, cardiovascular disease, and hypertension. Several mechanisms proposed that vitamin D decreases blood pressure. However, more studies are necessary to find the influence of vitamin D on blood pressure in normal individuals and patients with chronic hypertension.

Keywords: Vitamin D, Hypertension, Myocardial infarction, Heart failure, Stroke, Renin–angiotensin system

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Introduction

Hypertension is a chronic disorder with serious risk factors for clinically important events including myocardial infarction, heart failure, stroke and death (1). It is estimated that, 1.56 billion adults will be living with high blood pressure in 2025 and one in three adults has hypertension in world (2). Vitamin D is a micronutrient with important implications for human health and has recognized functions in calcium and bone metabolism (3).

Recently, vitamin D deficiency has been related to illnesses in many organ systems including the cardiovascular system (4). It was shown that low levels of vitamin D have been associated with increased development of high blood pressure (3). The mechanism by that vitamin D may control blood pressure is not confidently recognized (5).

Population studies have shown positive and negative associations between blood pressure and plasma levels of 1,25-dihydroxy vitamin D (6). Results of randomized clinical trials on vitamin D supplementation and blood pressure have been inconsistent (4). These observations increase the possibility that vitamin D supplementation could decrease blood pressure in humans. However, other studies found contradictory results (7).

Materials and Methods

While, hypertension is a public health problem, the aim of this review article is to determine the effects of vitamin D on improvement of high bold pressure.

For this review, we used a diversity of sources by searching through PubMed/Medline, Scopus, EMBASE, EBSCO and directory of open access journals (DOAJ). The search was conducted, using combination of the following key words and or their equivalents; vitamin D, hypertension, myocardial infarction, heart failure, stroke and renin–angiotensin system.

Mechanisms of interaction of vitamin D in hypertension

Several possible mechanisms exist to reduce blood pressure by vitamin D one of them is renin–angiotensin system (RAS) (4). Animal studies showed that 1,25(OH)2D negatively regulates the expression of renin independently from PTH and levels of calcium, and renin expression and plasma angiotensin II production were enhanced is extremely raised in vitamin D receptor null mice (4).

Deficiency of vitamin D can activate the RAS (3). Some studies stated that reverse association between plasma 25(OH) vitamin D and plasma renin activity have been known in individual with normal and high blood pressure (4) and established that pharmacological improvement of vitamin D levels could blunt activity of RAS in essential hypertensive patients with deficiency of vitamin D (3,8).

Additionally one study stated that, the RAS had an important function in regulating blood volume, that can clarify the more great influence of vitamin D on diastolic blood pressure rather than systolic blood pressure (3).

Vitamin D deficiency also is related with inflammation and enhances vascular inflammatory reactions (9).

An important factor in the pathogenesis and progression of atherosclerosis and blood pressure, is inflammation of the vessel walls and various studies proposed that vitamin D suppresses pro-inflammatory cytokines and enhances anti-inflammatory cytokines (3).

Additionally, a randomized placebo-controlled trial assessed effect of vitamin D and nifedipine in the treatment of patients with grades I and II essential hypertension and stated that the high-sensitivity CRP (hs-CRP) levels signifi-

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Implication for health policy/practice/research/medical education

High blood pressure is one of the most vital causes of early death worldwide and the problem is developing. Low 25-hydroxyvitamin D levels are related to higher prevalence of blood pressure and evidences from meta-analysis of cohort studies showed that vitamin D deficiency, predicts enhanced risk of all-cause mortality, cardiovascular disease, and hypertension. Several mechanisms proposed that vitamin D decreases blood pressure. However, more studies are necessary to find the influence of vitamin D on blood pressure in normal individuals and patients with chronic hypertension.

cantly reduced in vitamin D supplementation group. It may be assumed that vitamin D decreases the inflammation and improves vascular tone (3).

The PTH receptor has been recognized in vascular endothelium and smooth muscle cells, which suggests that PTH may have regulatory influences on the vessel wall, directly (4). In one trial study, blood pressure enhanced during PTH infusion, and PTH was an important predictor of blood pressure in elderly patients with hypertension (10). It is recognized that PTH increases calcium levels in intracellular by reducing cellular calcium intake in the cardiomyocytes that cause an enhancing vascular tone (3). The reduction in PTH level, secondary to vitamin D supplementation results in diminishing vascular tone and moderating blood pressure (3).

Vitamin D is associated with level of blood pressure via its regulation of calcium absorption from the gut and its interaction with parathyroid hormone in the maintenance homeostasis of calcium (11).

Vitamin D and hypertension in blacks

Blacks have significantly greater rates of hypertension rather than whites, and circulating levels of 25-hydroxyvitamin D in Blacks is lower. Therefore, the more prevalence of vitamin D deficiency among blacks may clarify an important ratio of the racial difference in blood pressure. In the largest randomized, double blind, placebo-controlled trial that assessed the influences of cholecalciferol supplementation among black individuals (12).

This study showed that, supplementation with cholecalciferol during three months reduced systolic blood pressure significantly, though no effect was observed on diastolic blood pressure. Furthermore, a more enhance in plasma 25(OH)D level in response to supplementation was related with a greater reduction in systolic blood pressure significantly (12).

Vitamin D and calcium and hypertension

For the reason that vitamin D is essential for calcium absorption and homeostasis, thus the metabolism of these two elements are closely related (13).

The key role of calcium and vitamin D deficiency in the pathogenesis of osteoporosis is mostly established. Decreased intracellular calcium may increase lipolysis and reduce lipogenesis, and cause of raise insulin-stimulated signal transduction, and suppress vascular smooth muscle tone. Additionally, further evidences imply that calcium intake may have influences in a type of unrelated disorders such as arterial hypertension (14,15).

In a recent study, short-term supplementation with calcium and vitamin D3 is more efficient in lowering systolic blood pressure rather than calcium. This impact is probably to be due to the return of parathyroid gland function to its basal level by vitamin D supplementation (14).

Between 1995 and 2000, 36 282 women were randomized into the CaD trial and time of follow-up was 7.0 years: 18 176 were assigned to the calcium + vitamin D supplementation (1000 mg plus 400 IU daily), and 18 106 to placebo. Calcium + vitamin D3 supplementation did not decrease blood pressure during years of follow-up and no benefit was shown overall. Though the dose of both supplements was moderate, specifically the vitamin D, the lack of benefit in individuals with low intake of calcium and vitamin D or low levels of vitamin D are the reasons for a different result (16).

Vitamin D and hypertension in patients with type 2 diabetes mellitus

One study showed that vitamin D supplementation (cholecalciferol; 50 000 units during 12 weeks) had positive effect on the level of blood pressure in type 2 diabetic patients. Therefore, oral vitamin D may improve hypertension in these patients (17).

Many human clinical studies examined the potential relative between levels of vitamin D metabolites with control of glycemic and the incidence of diabetes. In different small supplementation studies, interventions to increase 25-hydroxy vitamin D has been established to lower blood pressure in individuals at risk of cardiovascular disease. There is additionally several evidences that vitamin D supplementation enhances insulin release of pancreas and improves, insulin resistance and impaired glucose tolerance in patients with type 2 diabetes (17).

Vitamin D and hypertension in overweight individuals

In one study, supplementation with 20 000 or 40 000 IU vitamin D per week during 1 year, that caused a considerable enhance in the serum 25(OH)D levels, did not result in improvement in glucose tolerance, decrease in blood pressure or an improved lipid profile. This was the case similarly when individuals with low serum 25(OH) D values were assessed independently (18).

There are some mechanisms that glucose metabolism affected by vitamin D. Therefore, the insulin that produced by beta-cells have receptors for the active form of vitamin D [1,25-dihydroxyvitamin D (1,25(OH)2D)], and they even have the hydroxylase enzyme essential for changing 25(OH) D to1,25 (OH)2D (18). Additionally vitamin D may increase the expression of the insulin receptor in peripheral tissues and thus enhance glucose transport. According to this finding, it is possible the presence of a reverse association between fasting serum glucose and25 (OH)D, which explain the reason that subjects whom are overweight or obese, had elevated serum insulin levels and insulin resistant (18).

Vitamin D level in patients with hypertension

Some studies served the effects of vitamin D supplementation on the level of blood pressure in hypertensive patients, could not show the effect of vitamin D on decreasing of high blood pressure (4,6,7,19,20).

Several reasons are possible for the no influence of vitamin D seen in these studies, such as the dose of vitamin D was inadequate to produce the needed biological effect or one more possibility is that those with various genetic backgrounds may respond differently (19).

In one study, cholecalciferol significantly decreased PTH and enhanced Ca++ proposing that at least a part of the blood pressure reducing is the influence of cholecalciferol and may be PTH-mediated. While there was a highly invers significant association between changes in 25(OH)D and PTH, only a weak positive association was seen between changes in PTH and systolic 24 hours blood pressure monitoring (4).

Conclusion

High blood pressure is one of the most vital causes of early death worldwide and the problem is developing. Low 25-hydroxyvitamin D levels are related to higher prevalence of blood pressure and evidences from meta-analysis of cohort studies showed that vitamin D deficiency, predicts enhanced risk of all-cause mortality, cardiovascular disease, and hypertension. Several mechanisms proposed that vitamin D decreases blood pressure. However, more studies are necessary to find the influence of vitamin D on blood pressure in normal individuals and patients with chronic hypertension.

Authors' contribution

SBR prepared the primary draft. HN edited the manuscript.

Conflicts of interest

The authors declared no competing interests.

Ethical considerations

Ethical issues (including plagiarism, data fabrication, double publication) have been completely observed by the authors.

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References

1. Golzarand M, Shab-Bidar S, Koochakpoor G, Speakman J, Djafarian K. Effect of vitamin D3 supplementation on blood pressure in adults: an updated meta-analysis. Nutr Metab Cardiovasc Dis. 2016; In press.
2. World Health Organization, regional office for south-east Asia. Hypertension fact sheet. Geneva: WHO; 2011.
3. Chen WR, Liu ZY, Shi Y, Wang H, Sha Y, Dai Chen Y. Vitamin D and nifedipine in the treatment of Chinese patients with grades I–II essential hypertension: a randomized placebo-controlled trial. Atherosclerosis. 2014;235:102-9.
4. Larsen T, Mose FH, Bech JN, Hansen AB, Pedersen EB. Effect of cholecalciferol supplementation during winter months in patients with hypertension: a randomized, placebo-controlled trial. Am J Hypertens. 2012;25:1215-22.
5. Judd SE, Raiser SN, Kumari M, Tangpricha V. 1, 25-Dihydroxyvitamin D 3 reduces systolic blood pressure in hypertensive adults: a pilot feasibility study. J Steroid Biochem Mol Biol. 2010;121:445-7.
6. Jespersen B, Randløv A, Abrahamsen J, Fogh-Andersen N, Olsen NV, Kanstrup IL. Acute cardiovascular effect of 1, 25-dihydroxycholecalciferol in essential hypertension. Am J Hypertens. 1998;11:659-66.
7. Arora P, Song Y, Dusek J, Plotnikoff G, Sabatine M, Cheng S, et al. Vitamin D therapy in individuals with prehypertension or hypertension. Circulation. 2015;131:254-62.
8. Carrara D, Bernini M, Bacca A, Rugani I, Duranti E, Virdis A, et al. Cholecalciferol administration blunts the systemic renin–angiotensin system in essential hypertensives with hypovitaminosis D. J Renin Angiotensin Aldosterone Syst. 2014;15:82-7.
9. Chen WR, Qian YA, Dai Chen Y, Shi Y, Wang H, Zhu P, et al. The effects of low vitamin D on coronary artery disease. Heart Lung Circ. 2014;23:314-9.
10. St John A, Dick I, Hoad K, Retallack R, Welborn T, Prince R. Relationship between calcitrophic hormones and blood pressure in elderly subjects. Eur J Endocrinol. 1994;130:446-50.
11. Vimaleswaran KS, Cavadino A, Berry DJ, Jorde R, Dieffenbach AK, Lu C, et al. Association of vitamin D status with arterial blood pressure and hypertension risk: a mendelian randomisation study. Lancet Diabetes Endocrinol. 2014;2:719-29.
12. Forman JP, Scott JB, Ng K, Drake BF, Suarez EG, Hayden DL, et al. Effect of vitamin D supplementation on blood pressure in blacks. Hypertension. 2013;61:779-85.
13. Wang L, Manson JE, Buring JE, Lee I-M, Sesso HD. Dietary intake of dairy products, calcium, and vitamin D and the risk of hypertension in middle-aged and older women. Hypertension. 2008;51:1073-9.
14. Pfeifer M, Begerow B, Minne HW, Nachtigall D, Hansen C. Effects of a short-term vitamin D3 and calcium supplementation on blood pressure and parathyroid hormone levels in elderly women 1. J Clin Endocrinol Metab. 2001;86:1633-7.
15. Bohr DF. Vascular smooth muscle: dual effect of calcium. Science. 1963;139:597-9.
16. Margolis KL, Ray RM, Van Horn L, Manson JE, Allison MA, Black HR, et al. Effect of calcium and vitamin d supplementation on blood pressure. The Women's Health Initiative Randomized Trial. Hypertension. 2008;52:847-55.
17. Nasri H, Behradmanesh S, Ahmadi A, Rafieian-Kopaei M. Impact of oral vitamin D (cholecalciferol) replacement therapy on blood pressure in type 2 diabetes patients; a randomized, double-blind, placebo controlled clinical trial. J Nephropathol. 2014;3:29-33.
18. Jorde R, Sneve M, Torjesen P, Figenschau Y. No improvement in cardiovascular risk factors in overweight and obese subjects after supplementation with vitamin D3 for 1 year. J Intern Med. 2010;267:462-72.
19. Witham MD, Ireland S, Houston JG, Gandy SJ, Waugh S, MacDonald TM, et al. Vitamin D therapy to reduce blood pressure and left ventricular hypertrophy in resistant hypertension randomized, controlled trial. Hypertension. 2014;63:706-12.
20. Witham MD, Price RJ, Struthers AD, Donnan PT, Messow C-M, Ford I, et al. Cholecalciferol treatment to reduce blood pressure in older patients with isolated systolic hypertension: the VitDISH randomized controlled trial. JAMA Intern Med. 2013;173:1672-9.