Relationship between hypertension and vitamin D

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Abstract

Vitamin D plays a vital role in many processes in human body. Previous reports have suggested that Vitamin D deficiency is a significant component of the progression of hypertension. Here we discuss the possible mechanisms by which this might occur and the importance of being aware of the relationship between the two.

Keywords: Vitamin D, hypertension, vessel, inflammation

Introduction

With the rapid development of society, the incidence of hypertension among Chinese people has become more prevalent. Hypertension is closely related to many factors, including genetic and environmental factors such as, age, gender, blood lipids, life style and dietary habits (1, 2). Interestingly, the incidence of hypertension in patients that are deficient in Vitamin D is higher than in normal subjects (3−5).

Calcium supplementation is effective in patients with hypertension. In animal models of hypertension, blood pressure is reduced after calcium supplement (6). However, other experiments showed that increasing dietary calcium can only reduce systolic blood pressure, and has no effect on diastolic blood pressure (7). The concentration of calcium probably effects on the contraction of vascular smooth muscle. Vitamin D can increase the absorption of calcium, so this may be how vitamin D is related to hypertension (8, 9). Thus, it is important to understand the role of vitamin D in hypertension.

Vitamin D plays an important role in many processes in our body. Research suggests that vitamin D deficiency is closely related to cardiovascular disease, as it can increase the incidence of cardiovascular disease (CVD) and hypertension (10, 11). A randomized clinical trial was established to assess the role of vitamin D-deficiency in CVD, and we found that if vitamin D is deficient, the level of both systolic and diastolic blood pressure were increased (11, 12). However, it is unclear whether vitamin D supplementation can reduce blood pressure. More research should be done to investigate whether vitamin D can be used as a new therapeutic target for hypertension in the future.

Vitamin D is negatively correlated with blood pressure (12). The Women's Health randomly assigned 36, 282 postmenopausal women to receive either 1000 mg of calcium plus 400 IU of vitamin D3 daily or placebo (13). The result was that calcium plus vitamin D3 supplementation does not reduce blood pressure and the incidence of hypertension (14). However, a recent study shows that Vitamin D supplementation is effective in reducing blood pressure in patients with hypertension if taken with antihypertensive drugs. Martains et al. find that the incidence of hypertension increased when vitamin D is deficient, especially among the obese or elder population (15−18). Scragg et al. suggest that the level of vitamin D is negatively correlated with blood pressure (16). A reduction systolic pressure is seen with the supplement of vitamin D. Future trials of vitamin D supplementation are needed to confirm the specific mechanistic role on blood pressure as there is not enough evidence to determine whether vitamin D can reduce blood pressure in patients with hypertension.

The possible mechanisms of hypertension in vitamin D deficient patients

Activation of sympathetic nervous system

With the activation of the sympathetic nervous system, the number of the sympathetic transmitters released increase dramatically, especially catecholamines such as epinephrine and norepinephrine. These mainly activate the rennin-angiotensin-aldosterone system, increasing shrinkage factors, and causing the contraction of vessels and the promotion of blood volume (19).

The augmented activity of the renin-angiotensin-aldosterone system (RAAS)

Vitamin D can suppress the activity of the renin-angiotensin-aldosterone system but once the level of vitamin D is decreased, the renin-angiotensin-aldosterone system (RAAS) can be activated.
activated (20–22). A number of randomized double-blind trials have shown that low 25-hydroxyvitamin D (25(OH) D) levels are closely associated with an increased risk of hypertension (23–26).

Obese patients with hyperlipidemia have a lower level of vitamin D than normal people and both obesity and vitamin D deficiency are linked to the activity of the renin-angiotensin-aldosterone system (RAAS)(19, 27). Supplementation of Vitamin D along with weight loss can likely reduce the activity of RAAS; however, studies evaluating the effect of vitamin D supplementation on vascular RAAS activity in obesity are needed in the future (28).

Increased activity of the RAAS system leads to an increase in rennin, which activates a series of physiological and pathological processes that lead to a rise in blood pressure. Aldosterone reserves sodium and ejects potassium, but with an increase of aldosterone, sodium water retention occurs. Blood pressure elevates with the increase in blood volume. Angiotensin enzyme inhibitors (ACEI) and angiotensin 2 enzyme inhibitors (ARB) can reduce the formation of the angiotensin enzyme, block the angiotensin receptor, and reduce the level of catecholamines, thereby lowering blood pressure(22, 29). These two kinds of drugs can also reduce the incidence of kidney disease by reducing proteinuria. Blood pressure can also be lowered by adding a low-dose beta-blocker to thiazide diuretics or calcium channel blockers(29).

The level of calcium and hypertension

Calcium level directly affects blood pressure and Vitamin D is closely related to calcium levels. High level of vitamin D can directly reduce the secretion of the renin, probably through the influence of blood calcium levels, and lower blood pressure. The occurrence of cardiovascular diseases such as hypertension and coronary heart disease (CHD) can be reduced when the level of Vitamin D is over 30 ng/ml(30). This is the level at which calcium metabolism is regulated normally. The absorption of calcium increases with the level of vitamin D and the level of calcium directly determines the function of endothelial cells.

Vitamin D level is negatively correlated to blood pressure in white patients, but is not in black patients. The lack of vitamin D leads to an imbalance of the cardiovascular system, accelerates the formation of atherosclerosis, left ventricular hypertrophy, and ultimately heart failure(5).

In patients with vitamin D deficiency, the balance of calcium inside and outside the cells is disordered, the contraction of vascular smooth muscle cells is strengthened and total peripheral resistance is increased. In addition, the change of blood calcium may also promote the hardening of arteries. These factors are all likely to be related to the increased occurrence of hypertension. Similarly, the secretion of insulin is closely related to calcium so the deficiency of vitamin D can also increase the risk for diabetes. Clinical evidence indicts that thiazide diuretics can be used to regulate the sodium chloride conversion channel and reduce the excretion of calcium(31).

Endothelial cell injury and the inflammation factors

Several factors affect the function of endothelial cells, including exercise, dietary factors, vitamin D levels and age. Vitamin D can reduce endothelial cell vascular inflammation, decrease speed of the progress of atherosclerosis, reduce the incidence of cardiovascular disease and lower the incidence of hypertension. Vitamin D, can inhibit the release of inflammatory factors, regulate the immune response, stimulate the secretion of insulin and reduce the risk of high blood pressure in patients with insulin resistance(32, 33).

Vitamin D plays anti-inflammatory role by inhibiting the effect of polysaccharides on adenosine RNA polymerase(27, 33, 34). High doses of vitamin D and insulin can significantly reduce the expression of myocardial inflammatory factors, including TLR4, NF-KBp65, and MCP-1. Inflammation is closely related to hypertension and is important to its progression. The main inflammatory factors implicated in hypertension are CRP, IL-6, and TNF-α. They cause injury to endothelial cells, leading to a change in the balance of secretion in vascular endothelial cells. There is an increase of the vasoconstrictor factors (endothelin and angiotensin) and a decrease of vasodilatory factors (bradykinin, prostaglandin I2 (PGI2), and NO)(35), increasing blood pressure. The vasoconstrictor factors mainly including PGI2 which has a strong impact on diastolic blood vessels and decreases platelet aggregation. The relaxation of arteries can be attributed to an increased production of nitric oxide, an important vessel-relaxing signal molecule. The increase in peripheral resistance elevates blood pressure.

Insulin resistance

Evidence shows that vitamin D deficiency may be related to insulin resistance. Insulin resistance is a key factors in hypertension (32, 33).

Insulin increases the uptake and utilization of myocardial glucose. However, insulin resistance and hyperinsulinemia can disturb the uptake and utilization of glucose, cause retention of water and sodium, proliferation of vascular smooth muscle cells, and increase the risk of cardiovascular events. Insulin resistance is inversely proportional to systolic and diastolic blood pressure. Islet B cells are destroyed by a variety of mechanisms, leading to insulin resistance when vitamin D is deficient, and causing hypertension(33).

Studies in vitro have shown that vitamin D can promote the expression of insulin receptor, which further increases the response of islet cells to glucose transport.

Parathyroid hormone (PTH)

Previous research has shown parathyroid hormone (PTH) level is associated with blood pressure. Vitamin D is always low in patients with hyperparathyroidism (27). PTH is negatively correlated with blood vessels, and the lack of vitamin D may cause PTH levels rise, and thus blood pressure rises. Increased PTH levels can interfere with calcium metabo-
Vitamin D supplementation

D deficiency can also accelerate vascular remodeling(39). Some studies show that vitamin D deficiency may affect renin secretion. Hypertension is increased by increasing the level of inner cell cyclic adenosine monophosphate (cAMP), reducing the intracellular calcium concentration, and renin gene expression(36). Both systolic and diastolic blood pressure levels of the patients in hypertension are associated with vitamin D deficiency and hyperparathyroidism. The high level of PTH causes an increase in renin. The main stimulus of PTH is a low calcium ion concentration; however, some studies have suggested that relationship between calcium ion concentration and PTH level with high blood pressure is not significant and that middle and lower levels of serum vitamin D is an independent risk factor for hypertension(36).

Conversely, some studies shows that the rise of PTH may cause a temporary increase in blood pressure, but for over a long period of time, the rise in PTH will lead to lower blood pressure. Low levels of PTH may reflect a rise in norepinephrine which would lead to a rise in blood pressure.

Possible effects of vitamin D on the heart and blood vessels

Vitamin D receptors are widely distributed, so the cardiovascular system may be regulated indirectly by vitamin D. Studies suggest possible mechanisms by which vitamin D deficiency may affect the heart and blood vessels. 1,25-dihydroxyvitamin D is the active form of vitamin D. It can directly or indirectly regulate renin gene transcription while reducing the expression of angiotensin and angiotensin receptors, inhibit the hypertrophy of myocardial cells by decreasing the level of calcium and cAMP; it can also inhibit the calcification of vessels and decrease the proliferation and differentiation of smooth muscle cells by lowering the amount of IGF-1, TGF-α, MCP-1 and PTH.

Vitamin D can be used as an endogenous renin inhibitor, and vitamin D supplements may increase the activity of carbon monoxide, inhibit the production of inflammatory cells, thus protecting the vascular endothelium and improving blood vessel compliance, keeping the balance of blood pressure(35, 37).The lack of vitamin D will directly affect vascular endothelium, reducing blood vessel compliance and increasing blood pressure(38).

On one hand, Vitamin D can decrease the contraction of cardiac muscle by lowering the amount of calcium and inhibiting the hypertrophy of myocardial cells by decreasing the level of CAMP. On the other hand, it can also affect blood vessels by inhibiting the calcification of the vascular tissue leading to anticoagulation and decreasing the proliferation and the differentiation of smooth muscle cells. Vitamin D deficiency can also accelerate vascular remodeling(39).

Vitamin D supplementation

In order to reduce the risk of hypertension and its complications, it is necessary to supplement the amount of vitamin D in patients vitamin D deficiency. Many studies show that participants with high levels of 25-hydroxyvitamin D (25(OH)D) have reduced blood pressure and are at a lower risk of developing hypertension (30). Diabetic patients who were treated with large doses of vitamin D have improved endothelial cell function. In addition, vitamin D supplements can reduce insulin resistance thus lowering blood pressure (7, 40).

Sufficient vitamin D reduces the occurrence of high blood pressure and increases the tissue sensitivity to angiotensin II (Ang II). However, too much vitamin D increases the risk of high blood pressure, and may cause myocardial hypertrophy.

Conclusions

Vitamin D level is considered a significant factor in the development of hypertension. The effect of vitamin D on blood pressure is apparent. However, further research is needed to explore the association of vitamin D with hypertension and to determine whether vitamin D supplementation is beneficial or detrimental in the prevention and/or treatment of hypertension.

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Conflict of interest

All authors declare that there is no conflict of interest.

References

5. The loss of sustained Ca(2+) signaling underlies lipid, causing the a higher incidence cardiovascular disease. Vitamin D deficiency is related to the high level of immunoreactive parathyroid hormone (iPTH), possibly contributing to the occurrence and development of hypertension(27).


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