Research Paper

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Effect of Vitamin D Supplementation in Hypertensive Patients with Vitamin D Defiency: A Comparative Study

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ABSTRACT

Study Design: to study the effect of Vitamin D3 supplementation on Blood pressure in Hypertensive subjects.
Background: Low 25-hydroxy-vitamin D (25(OH) D) levels are inversely related to blood pressure (BP) and have been associated with hypertension. We wanted to test the hypothesis that correction of Vitamin D3 deficiency by supplementation lowers BP in patients with hypertension.
Methods: We investigated the effect of 1000mg calcium and 1000IU Vitamin D3 per day in a prospective, cohort study in 146 hypertensive patients visiting in OPD of NHL Municipal Medical College, Ahmedabad, India
Results: A total of 108 patients (mean age 67 ± 3.6years) with a baseline vitamin D3 of 15 ± 3.2 ng/ml completed the study. Compared with Calcium Only group, a significant decrease in the Blood pressure was seen in-group treated with Vitamin D3 and Calcium. 36 subjects (65%) in the vitamin D3-calcium group compared with 27 (51%) subjects in the calcium group showed a decrease in SBP of 15 mm Hg or more (P =0.04).
Conclusions: Vitamin D3 supplementation, by a dose that effectively increased vitamin D levels, systolic BP decreased significantly as compared to the diastolic Blood pressure. A larger randomized controlled study is required to further substantiate the results.

Introduction

Cardiovascular diseases caused 2.3 million deaths in India in the year 1990; this was projected to double by the year 2020. Hypertension is directly responsible for 57% of all stroke deaths and 24% of all coronary heart disease deaths in India(1). The prevalence of hypertension in urban areas of India ranged from 2.6-5.2 per cent between 1960-1980 and it has increased to 20-33 per cent in last decade. The high prevalence of hypertension in the current study (32.2%), confirms this increasing trend (2).

Vitamin D is known to play an important role in calcium homeostasis. Several workers have reported that Vitamin D also has a role in blood pressure regulation and cardiovascular system (3). Laboratory studies indicate that 1,25-dihydroxyvitamin D suppresses renin expression and vascular smooth muscle cell proliferation; clinical studies demonstrate an inverse association between ultraviolet radiations, a surrogate marker for vitamin D synthesis, and blood pressure (4).

There are numerous reports available in literature with conflicting evidence of the effect of vitamin D on hypertension, Since both hypertension and vitamin D deficiency are highly prevalent worldwide, establishing an association among these two may potentially have wide public health implications but may also be the result of the high prevalence of both conditions rather than a causative link between them, which prompted us to take up this cohort study in the Indian Population to study the effect of Vitamin D supplementation in vitamin D deficient subjects with hypertension.

Material and methods

The study was conducted in NHL Municipal Medical College, Ahmedabad in the Department of Medicine from January 2012 to December 2012 after getting clearance from the ethics committee.

146 hypertensive subjects with vitamin D deficiency (<20ng/ml) were enrolled in the study after taking an informed consent.

The Inclusion criteria were 1) patients of either sex 2) patients with hypertension (SBP<170mm of Hg and Diastolic <110 mm of Hg) and vitamin D deficiency together 3) patients receiving same form of antihypertensive treatment during the course of treatment.

The exclusion criteria were 1) associated Diabetes Mellitus 2) any hepatic or renal disease. 3) Patients previously taken any form of vitamin supplementation, bisphosphonates, hormone replacement therapy 4) patients with hyperparathyroidism or hypercalcaemia. 5) Patients with history of smoking, alcoholism or Tabaco use 6) patients who required a change in the hypertension management protocol.

The subjects who met the inclusion and exclusion criteria were randomized in two groups for the study.

Group 1: patients who received anti-hypertensive treatment and calcium only.

Group 2: patients who received both Anti-hypertensive as well as Vitamin D supplementation with calcium.

The patients deficient in Vitamin D were given supplementation of 1000 IU Vitamin D3 and 1000 mg of calcium for 3 months in the morning with breakfast. The calcium group was given only 1000mg calcium.

The blood investigations were done in all subjects, which included routine Complete blood count, serum Creatinine, Serum Urea, S. Vitamin D_3. The blood for the followed up subjects was collected between 800 and 900 hours with minimum of 8 hours of fasting. Serum 25OHD3, and 1,25-(OH)2 D3 were measured by RIA, serum creatinine by the Jaffe´ method, Erythrocytes, leukocytes, and platelets were counted by an electronic counter; hemoglobin was determined by the cyanhemoglobin method.

Regular follow up was done in Out patient department for all patients was followed up by one physician and the blood pressure recordings were done by the same physician in all subjects. Blood pressure was measured after at least 5 min of rest in a quiet room using a mercury sphygmomanometer with an appropriate cuff. Systolic and diastolic blood pressures were taken at Korotkov sounds I and V.

Results:

At the end of the 3 months follow-up there were total of 28 cases, which were lost to follow up; (group 1: n=16;group 2:n=12). There were 8 patients who were non-compliant with the medication (group 1: n=4; group 2:n=6) and therefore, excluded from the study.

At the end of the study, 108 patients were analyzed. Group 1(HT and Calcium) n= 53 and group II (HT + Vit.D + calcium) n= 55.

The base line parameters of the two groups are stated in table 1:

parameters	Group I (n=53)	Group 2 (n=55)
Age	67.7 +- 3.2 years	68.4 +- 3.8 years
Range	59- 82 years	60 – 81 years
weight	64.7 +- 9.2kgs	64.1 +- 7.8 kgs.
Height	170 +- 6.7cms	169 +- 7.2 cms.

Table 1 : baseline clinical parameters of all subjects.

Both treatment groups were comparable concerning age, height, weight, physical activity and concomitant diseases (Table 1). There were no changes in the Anti-hypertensive medications in both groups during the study. All patient were managed on Angiotensin receptor blockers. In addition, there were no group differences with regard to dietary calcium, vitamin D, and salt intake (data not shown) as all patients stuck to the basic dietary patterns.

	GROUP I		GROUP II	
Parameters	Pre	At 3 months Follow-up	pre	At 3 months Follow-up
Systolic BP	152.1+- 14.2	144.9+- 19.6	154.0 +-16.7	141 +- 17.0
Diastolic BP	92.2 +- 6.2	85.8 +- 10.6	94.8 +- 6.8	84+- 9.7
Vitamin D_3	14.5 +- 3.2	19+- 4.1	13.7+- 3.7	36+- 4.8
S. Calcium	9.0 +- 2.0	9.6+- 2.3	9.3+- 2.7	9.8 +- 2.9
S. Phosphorous	3.6+-1.8	3.7+- 2.2	3.5+- 1.6	3.7 +- 1.8

Table 2: Initial and final Blood pressures and vitamin D3 levels.

Compared with baseline, significant increases in serum-ionized calcium, were found in both treatment groups. Compared with group I (calcium group), a significant increase in serum Vitamin D3 (P = 0.01) was observed in the vitamin D3-calcium group.

The changes in blood pressure and Vitamin D3 are documented in Table 2. Compared with baseline, significant decreases were found in systolic blood pressure (SBP) and diastolic blood pressure (DBP) in both treatment groups.

Compared with calcium, treatment with vitamin D3 and calcium led to a significant reduction in SBP (P=0.02). The reduction in DBP was more pronounced in the vitamin D3-calcium group, but this difference did not reach the level of statistical significance (P= 0.10).

36 subjects (65%) in the vitamin D3-calcium group compared with 27 (51%) subjects in the calcium group showed a decrease in SBP of 15 mm Hg or more (P =0.04).

Discussion:

Vitamin D is a collection of fat-soluble steroids with two dominant forms: vitamin D2 (Ergocalciferol) and vitamin D3 (Cholecalciferol). Vitamin D3 is naturally present in a small number of foods and is derived endogenously in the skin through exposure to sunlight. Vitamin D3 can also be obtained by dietary and pharmacologic supplementation. Exogenous- acquired vitamin D (dietary or supplements) is inactive and requires two hydroxylation reactions for activation: the first occurs in the liver in the form of 25 hydroxy vitamin D (25-OHD), which undergoes further hydroxylation in the kidney and is converted to 1,25 hydroxy vitamin D (1,25 OHD). 25-OHD has a long half-life and is the major form of vitamin D circulating in the blood and its measurements are useful clinically. Vitamin D deficiency is defined by the current International Osteoporosis Guidelines as vitamin D insufficiency if 25-OHD levels are < 50 nmol / L and as vitamin D deficiency if 25-OHD levels are < 25 nmol / L (5).

Studies have shown that low Vitamin D levels are associated with a higher risk of having hypertension and coronary artery disease. (6,7). Observational studies report an association between low vitamin D status and cardiovascular disease. Potential mechanisms include a vitamin D effect on the endothelium,vascular smooth muscle, and/or cardiomyocytes,all of which possess the vitamin D receptor(8).

A total of 13 randomized trials have reported results for change in blood pressure comparing cholecalciferol or ergocalciferol with placebo. Only 2 trials were specifically designed to examine effects on blood pressure, such that use of antihypertensive medications was not permitted, and blood pressure was the primary end point (9). There are various studies, which showed that there is no association between vitamin D and blood pressure.

An optimal vitamin D status may influence cardiovascular health by changing the lipid profile in a favorable direction and decreasing the incidence of the metabolic syndrome (9,10).

Various dosage regimens have been used to treat vitamin D defiency. The dosage that we used in our study was comparable to that used by Pfiefer et al. they has used. They received 1000 mg calcium plus 1000 IU vitamin D3 or 1000 mg calcium/day. In a meta-analysis by Pittas AG et al. the found that No significant overall effect of vitamin D supplementation on blood pressure was found. However, when only trials that used higher doses of vitamin D (1000 IU per day) were included, a significant lowering of diastolic blood pressure was noted **(**P 0.04) (13).

In our study we found that there was a significant decrease in the Systolic Blood pressure in the Vitamin D supplemented group. Pfiefer et al concluded in their study that a short-term supplementation with vitamin D3 and calcium is more effective in reducing SBP than calcium alone. Inadequate vitamin D3 and calcium intake could play a contributory role in the pathogenesis and progression of hypertension and cardiovascular disease in elderly women. (11,12)

Conclusion

The majority of observational data suggest that lower levels of vitamin D may be associated with a higher blood pressure and a higher risk of developing hypertension, although conflicting studies exist. Experimental data suggest that vitamin D and its metabolites are integrally related to blood pressure and the RAS. Athough our short term supplementation regimen supports the role of Vitamin D3 Supplementation in hypertension, additional evidence is required before recommending widespread vitamin D supplementation to treat blood pressure or prevent hypertension.

REFERENCE

1. Gupta R. Trends in hypertension epidemiology in India. J Hum Hypertens. 2004 Feb;18(2):73-8. | 2. Gupta R, al-Odat NA, Gupta VP. Hypertension epidemiology in India: meta-analysis of 50 year prevalence rates and blood pressure trends. J Hum Hypertens. 1996 Jul;10(7):465-72. | 3. Goel RK, Lal H. Role of Vitamin D Supplementation in Hypertension. Ind J Clin Biochem (Jan-Mar 2011) 26(1): 88–90. | 4. Forman JP, Giovannucci E, Holmes MD, et al.: Plasma 25-hydroxyvitamin D levels and risk of incident hypertension. Hypertension 2007,49:1063–1069. | 5. Cohen DL, Townsend RR. Should we be recommending vitamin d supplementation for hypertension and cardiovascular disease prevention? J Clin. Hypertension (Greenwich). 2012 Nov;14(11):816-8. | 6. Kendrick J, Targher G, Smits G, Chonchol M. 25-Hydroxyvitamin D deficiency is independently associated with cardiovascular disease in the Third National Health and Nutrition Examination Survey. Atherosclerosis. 2009 Jul;205(1):255-60. | 7. Martins D, Wolf M, Pan D, Zadshir A, Tareen N, Thadhani R, Felsenfeld A, Levine B, Mehrotra R, Norris K. Prevalence of cardiovascular risk factors and the serum levels of 25-hydroxyvitamin D in the United States: data from the Third National Health and Nutrition Examination Survey. Arch Intern Med. 2007 Jun 11;167(11):1159-65. | 8. Binkley N, Ramamurthy R, Krueger D. Low vitamin D status: definition, prevalence, consequences, and correction. Endocrinol Metab Clin North Am. 2010 Jun;39(2):287-301. | 9. Vaidya A, Forman JP. Vitamin D and hypertension: current evidence and future directions. Hypertension. 2010 Nov;56(5):774-9. | 10. Skaaby T, Husemoen LL, Pisinger C, Jørgensen T, Thuesen BH, Fenger M, Linneberg A. Vitamin D status and changes in cardiovascular risk factors: a prospective study of a general population. Cardiology. 2012;123(1):62-70. | 11. Pfeifer M, Begerow B, Minne HW, Nachtigall D, Hansen C. Effects of a short-term vitamin D(3) and calcium supplementation on blood pressure and parathyroid hormone levels in elderly women. J Clin Endocrinol Metab. 2001 Apr;86(4):1633-7. | 12. 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 Nov;25(11):1215-22. | 13. Pittas AG, Chung M, Trikalinos T, Mitri J, Brendel M, Patel K, Lichtenstein AH, Lau J, Balk EM. Systematic review: Vitamin D and cardiometabolic outcomes. Ann Intern Med. 2010 Mar 2;152(5):307-14. |