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Association of 25 OH-Vitamin D and hs-CRPin adults with Essential Hypertension

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Abstract

Essential hypertensionis a typical example of complex, multifactorial trait and a well studied risk factor for cardiovascular disease. hs-CRP is well known marker of inflammation resulting in atherosclerosis and cardiovascular disease. Recent studies showed that 25-OH-vitamin-D has ananti-inflammatory role and decreased levels may increase the cardiovascular risk in subjects with essential hypertension. The study included 30 adults both male and female with essential hypertension (Systolic Blood Pressure ≥ 140 mm Hg and Diastolic Blood Pressure ≥ 90 mm Hg) as cases. 30 age and sex matched healthy individuals both male & female between the age group of 24-60 years attending General OPD, General Medicine Department, NMCH, were taken as controls. The inverse relationship of Vitamin D with hs-CRP levels leads to cardiovascular risk in subjects with essential hypertension.

Keywords: Essential hypertension, hs-CRP, Vitamin D and Inflammation.

Introduction

Essential hypertension is a systemic hypertension of unknown cause. It results from dysregulation of normal homeostatic control mechanisms of blood pressure in the absence of detectable known secondary causes over 95%. Vitamin D3 is synthesized in the skin from cholesterol under the action of ultraviolet B light.(1) Furthermore, Vit D can be ingested as cholecalciferol (vitamin D) or ergocalciferol (Vitamin D2). Vitamin D is subsequently converted to 25-Hydroxy Vitamin D (calciferol) in the liver or stored in adipose tissue. In the kidney, 25-OHVitamin D is converted to 1,25 dihydroxy Vitamin D (calcitriol), which is the biologically active form of Vitamin D.(2) Present research carried out over recent decades indicates that Vitamin D deficiency plays an important role in many causes incresed inflammation and hypertension.(3) High sensitive C-reactive protein (hs-CRP) is acute phase protein which is described as sensitive systemic marker of inflammation and tissue damage especially in Cardio Vascular disease (CVD).(4)

Vitamin D being a potent endocrine suppressor of renin biosynthesis as demonstrated in recent studies plays an important role in the regulation of the Renin Angiotensin System.(5)

Renin Angiotensin System is one of the several mechanisms that exist to reduce the blood pressure by Vitamin D.(6) Some studies stated an inverse relationship of plasma Vitamin D levels with plasma renin activity in individuals with normal and high blood pressure.(7) Another study stated that, vitamin D had a great influence on diastolic blood pressure than systolic blood pressure. Vitamin D also plays a very important role in inflammation, there by leading to progression of atherosclerosis and blood pressure.(8) Randomized placebo controlled trailsshowed that hs-CRP levels were significantly reduced in vitamin D supplementation group.(9,10)

However, supplementation with vitamin D for 1 year in one study could not result in decrease of blood pressure or an improvement in glucose tolerance.(11) There are receptors for vitamin D on beta cells of pancreas that produce insulin. The beta cells of pancreas also have hydroxylase enzyme that is important in conversion of 25-OH Vit D to 1,25 (OH) Vitamin D. Hence, we can say that glucose metabolism might be affected by vitamin D.(12)

Essential hypertension is a typical example of complex, multifactorial trait and a well studied risk factor for cardiovascular disease. hs-CRP is well known marker of inflammation resulting in atheroscleros is and cardiovascular disease.(13) Injection of vitamin D3 reduces rennin synthesis. It was shown in cell cultures that vitamin D3 directly suppressed renin gene transcription by a vitamin D receptor mechanism.(14)

Materials and Method

Thirty adults both male and female with essential hypertension (Systolic blood pressure ≥ 140mmHg and/ or Diastolic blood pressure ≥ 90mmHg) and 30 age and sex matched healthy controls both, male and female between the age group of 24 -60 years of age were recruited from the General Medicine department of NMCH, Nellore, A.P.25-OH-Vitamin D levels were assayed by High Performance Liquid Chromatography and hs-CRP was estimated by immunoturbidometric method.

Exclusion Criteria: Patients with diabetes mellitus, secondary hypertension, known case of liver, renal and cardiac disorders were excluded from the study. Institutional ethical committee of Narayana medical college has approved the study. The total serum hs-CRP levels were expressed as mean ±SD. Standard unpaired student's 't' test was used for comparison of hs-CRP

levels between essential hypertensive patients and normotensive control subjects.

Results

In subjects with essential hypertension 25-OH-VitD levels (18.77± 3.63)ng/ml were significantly low when compared to control subjects and hs-CRP levels (5.33 ± 1.66) mg/L were significantly increased when compared to control subjects. Our study also showed a significant negative correlation between 25-OH VitD and hs-CRP levels (r = -0.28).

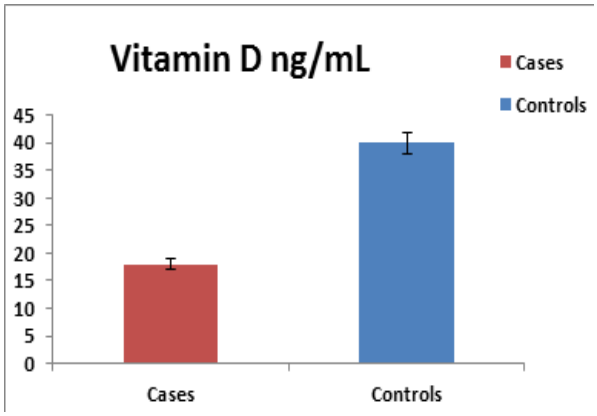

Fig. 1: Vitamin D in cases and controls

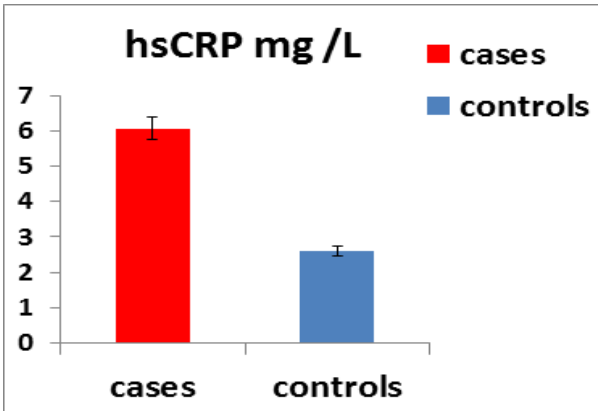

Fig. 2: hs-CRP values in cases and controls

The Mean±SD value for hs-CRP in controls and cases were 1.84 ± 0.62 mg/L and 5.33 ± 1.66 mg /L respectively. This was statistically significant (p<0.001).

The Mean±SD value forVitamin D in controls and cases were 40.18 ± 5.68 ng/ml and 18.77 ± 3.63 ng /ml respectively.

Recent studies have suggested an association between vitamin D deficiency and cardiovascular risk. Subjects was shown that vitamin D plasma levels below the recommended 75 nmol/L (30 ng/ml) have higher systolic and diastolic blood pressure levels.

Table 1: Biochemical parameters in cases and controls

Biochemical parameters	Mean ± SDcases	Mean ± SDControls	p value
25-OH Vit D	18.77± 3.63	40.18±5.68	p<0.0001
hs-CRP	5.33 ± 1.66	1.84 ± 0.62	p<0.0001

P value and statistical significance:

The two-tailed P value is <0.0001 (By conventional criteria, this difference is considered to be extremely statistically significant).

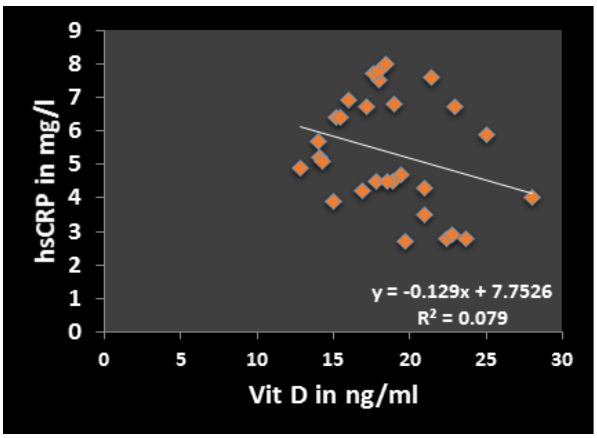

Fig.3: Scatter diagram showing the correlation between Vt. D and hsCRP

The diagram shows a negative correlation between Vit D and hs-CRP with a correlation co-efficient of r = -0.28.

Discussion

hs-CRP is a sensitive marker of inflammation. The prevalence of essential hypertension might be reduced by vitamin D. In our Present study the hs-CRP levels were statistically elevated in cases as compared to controls.Vitamin D levels were decreased statistically in comparison to controls. Our study was in accordance with the study conducted by S. Zangana et al who showed that higher hs-CRP levels significantly correlated with higher grades of hypertension and inversely correlated to Vitamin D.[15] Adham, I. Ahamed, Showed that Vitamin D deficiency was associated with elevated CRP in patients with Coronary artery disease.[16] Z. Atollah et al., demonstrated that Vitamin D supplementation for 9 wks in pregnant women led to significant reduction in SBP & DBP compared with placebo.[17] The finding in agrement with studies performed in India.[18] hs-CRP levels were higher in vitamin D deficient hypertensive patients, as hs-CRP is a marker for atherosclerosis and so it could be useful predictive marker for CVD in Vitamin D deficient essential hypertensive patients.

K.M. van de Luijtgaar denetal in their study showed a strong association between low vitamin D status and

arterial disease, that was irrespective of the type of vascular disease, that is, either occlusive or aneurysmatic disease.[19] Songcang Chen, et al in their study critically analyzed clinical findings on the effect of vitamin D on blood pressure, combined with progress in molecular mechanisms and found that vitamin D exerted a clinically significant antihypertensive effect in vitamin D deficient EH patients.[20]

Vitaminc D up-regulates the expression of mitogen-activated protein kinase phosphatase-5 (MKP5) there by promotes downstream antiinflammatory effects including a reduction in the level of expression of pro-inflammatory cytokines. Reck-Peterson SL et al.[21] Recent research also indicates that vitamin D interferes with the activation and signaling of nuclear factor-k (NFkB), a transcription factor that regulates the expression of numerous genes involved in inflammatory and immune response and cellular proliferation. Friedman DS,[22] NFkB is thought to play a key role in the process leading from inflamation to carcinogenesis.

High blood pressure is one of the most important causes of early death. Low 25-hydroxy vitamin D levels are related to higher prevalence of blood pressure and evidences from meta-analysis of cohort studies showed that vitamin D deficiency, predicts increased risk of hypertension and cardiovascular disease. Though several mechanisms had been proposed to state that vitamin D reduces blood pressure, Further studies are required to vlidate this hypothesis.

Conclusion

Previous studies reported that hypertension is in part an inflammatory, therefore elevated levels of CRP were observed in hypertensive individuals, which hypothesized that CRP may induce a decrease in endothelium dependent relaxation. Thus it is a potential risk factor for hypertension, reverse causation might also be implicated, where by high blood pressure may induce inflammation and raise CRP levels.

In our study we conclude that 25 OH-Vitamin D levels are significantly decreased and hs-CRP levels are increased in subjects with essential hypertension. Our study also showed a negative correlation between 25-OH Vitamin D and hs-CRP levels which leads to cardiovascular risk in subjects with essential hypertension. Further studies are needed to benicficial effects of Vitamin D supplementation on large group of population with essential hypertension.

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