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Research Article……!!!

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A STUDY ON THE ROLE OF VARYING DOSES OF VITAMIN D IN STAGE ONE HYPERTENSION

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ABSTRACT

OBJECTIVES: To evaluate the efficacy of Vitamin D as an adjuvant to regular antihypertensive therapy with calcium channel blockers in doses of 400 IU /day, 800 IU/day and 1200 IU/day in Stage 1 Hypertension and tolerability of vitamin D.

METHODOLOGY: This open label, randomised, comparative, prospective, parallel group study, was conducted in stage 1 hypertensive patients, whose blood pressure not controlled with calcium channel blockers monotherapy for 3 months, at Madras Medical College & Rajiv Gandhi Government General Hospital ,Chennai , from September 2008 to February 2009.220 patients screened and 120 patients randomised to 4 groups (30 each), control group i. e, Group Dreceived calcium channel blockers, 3 study groups – Group A 400IU, Group B 800 IU and Group C 1200 IU of Vitamin D.8 weeks treatment period per patient.

RESULTS: The mean Systolic and Diastolic Blood Pressures showed statistically significant difference (p = 0.05) and (p =0.001) respectively within the study groups. On comparison with control, Group A showed statistically significant difference in Diastolic Pressure from 6 th week (0.001) while groups B and C showed statistically significant difference from 2nd week(P=0.01) and 4th week onwards (p = 0.01). in Systolic and Diastolic Blood pressure respectively. No adverse events in study period.

Conclusion: Thus Vitamin D therapy in dose of 800 IU and 1200 IU lowers Systolic and Diastolic Blood pressure in hypertensive patients along with calcium channel blocker and well tolerated.

1.0 INTRODUCTION

An elevated arterial blood pressure is probably the most important public health problem in both developing and developed countries. It is common , asymptomatic, readily detectable, treatable, and leads to lethal complications if left untreated.[1] Hypertension is directly responsible for 57% of all stroke deaths and 24% of all coronary artery disease deaths in India..[2] Anti-hypertensive drugs like ACE inhibitors, diuretics, beta blockers, calcium channel blockers and angiotensin receptor blockers are suitable for single drug therapy based on efficacy and tolerability. The drug of choice for the treatment of hypertension is ACE inhibitors. [3]. The Calcium channel blockers are the only group of drugs that do not interfere with RAS pathway.

Vitamin D is a fat soluble vitamin . Normal requirements for adults is 200 I.U [4]Several animal studies show an inverse relationship between vitamin D and Blood Pressure. Vitamin D deficient mice show increased renin synthesis , whereas injection of vitamin D reduces renin synthesis .Vitamin D acts as a potent endocrine suppressor of RAS system which has a major role in hypertension, by acting as an inhibitory ligand for renin gene expression and activity. [5,6.].Short term supplementation of vitamin D and calcium has reduced systolic BP in elderly women. [7]. Studies also suggest that, the inhibitory role of vitamin D in rennin gene expression .is calcium independent [8]Hence in this study , we added vitamin D in varying doses for a period of eight weeks in stage 1 Hypertension patients not controlled with standard single drug therapy with calcium channel blockers.

2.0 METHODOLOGY

2.1OBJECTIVE: To evaluate the efficacy of Vitamin D as an adjuvant to regular antihypertensive therapy with calcium channel blockers in varying doses of 400 IU /day, 800 IU/day and 1200 IU/day in Stage 1 Hypertension and the tolerability of vitamin D.

2.2. STUDY DESIGN

This was a open label,randomized , comparative, prospective, parallel group study done at Hypertension clinic, Department of Internal Medicine, Madras Medical College & Rajiv Gandhi Government General Hospital ,Chennai , between September 2008 to February 2009. Study period of 8 weeks per patient .Adult patients ,with stage 1 Hypertension whose blood pressure were not controlled with calcium channel blockers monotherapy for a period not less than 3 months were the study population. Out of total 120 patients, enrolled 30 were randomized to each group (1 control and 3 study groups).

2.3SELECTION CRITERIA

2.3.1INCLUSION CRITERIA

- Age : 40 -60 yrs.
- Sex : both genders.
- Patients with Stage 1 hypertension (140-159/90-99mmof Hg) whose BP is not controlled with calcium channel blocker monotherapy for a period of 3 months .
- Patients with normal serum calcium levels (9-11 mgs %) .
- Patients willing to give informed consent.

2.3.2 EXCLUSION CRITERIA

- Patients with Secondary Hypertension.
- Patients on other antihypertensives exceptCCB.
- Patients receiving any other vitamin D supplementation.
- Patients with serum calcium > 11 mg/dl.
- Patients with major systemic illness.

2.4 STUDY PROCEDURE

The study was started after approval and clearance from the institutional Ethics Committee (16328). Information sheet and informed consent form in regional language was provided to each patient, and those willing to participate in the study signed the required forms. Out of 220 patients screened,120 who fulfilled the inclusion and exclusion criteria were recruited and randomized to control orstudy group by lots,with30 patients in each group (1 control,3 study groups).

2.5 TREATMENT PLAN

Study periodwasfor8 weeks.30 patients in each group. The control group received standard therapy, while vitamin Dwas added to standard therapy, in doses of 400 ,800,1200 IU to the three study groups.

2.6 EVALUATION

The collected data were statistically analysed. The difference within the group before and after treatment was analysed by student paired test, and difference between study groups by ANOVA .

3.0 RESULTS:

TABLE 1 AGE DISTRIBUTION

STUDY GROUP	n	Mean	Std. Deviation	Oneway ANOVA F-test
Group A (400 IU)	30	51.77	6.044	F=0.98 P=0.41
Group B (800 IU)	30	50.93	6.045	
Group C (1200 IU)	29	50.83	6.524	
Group D (Control)	28	49.07	6.496	

TABLE 2 : SEXWISE DISTRIBUTION

Study group	Sex				Chi square test
	Male		Female		
	n	%	n	%	
A	9	25.0%	21	25.0%	$\chi 2=2.22$ P=0.53 Not significant
B	10	27.8%	20	23.8%	
C	11	30.6%	19	22.6%	
D	6	16.7%	24	28.6%	
Total	36	100.0%	84	100%	

TABLE 3: SYSTOLIC BLOOD PRESSURE

STUDY GROUPS	BASELINE		2WEEKS		4WEEKS		6WEEKS		8WEEKS		Repeated Measures of ANOVA
	Mean	SD	Mean	SD	Mean	SD	Mean	SD	Mean	SD	
Group A (400 IU)	153.67	4.49	152.60	5.59	151.07	6.27	150.33	6.37	149.67	6.24	Between groups P=0.01 Within group P=0.001
Group B (800 IU)	154.67	4.01	153.20	3.99	151.20	4.89	150.13	4.75	148.40	5.83	
Group C (1200 IU)	155.47	3.52	152.93	3.67	149.27	4.80	146.87	5.42	145.13	5.03	
Group D (Control)	155.00	2.15	154.33	3.20	153.87	2.67	153.93	3.50	153.00	5.82	
ANOVA**	P=0.64		P=0.05*		P=0.05*		P=0.05*		P=0.05*		
Control Vs A	P=0.67		P=0.29		P=0.15		P=0.67		P=0.29		
Control Vs B	P=0.19		P=0.05*		P=0.01*		P=0.01*		P=0.001*		
Control Vs C	P=0.14		P=0.05*		P=0.01*		P=0.01*		P=0.001*		

FIGURE.1.

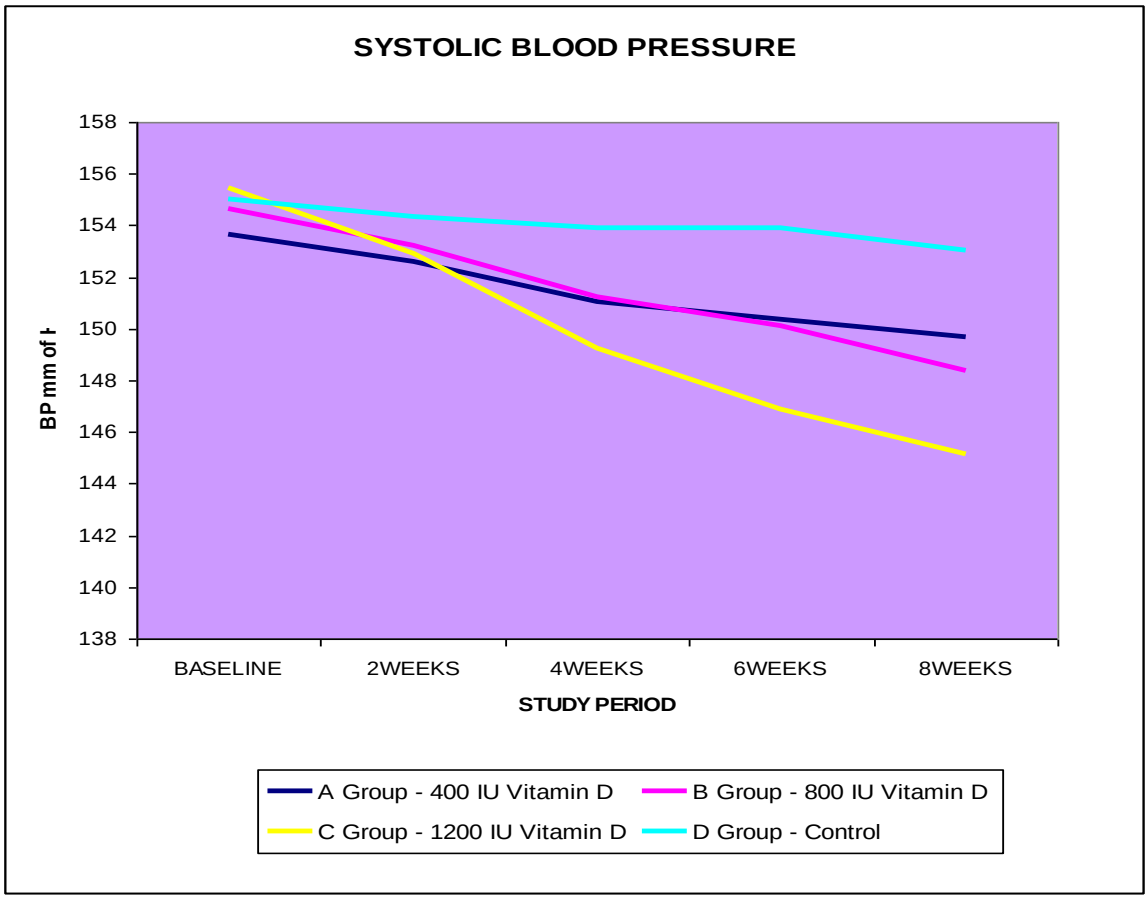


TABLE: 4 .DIASTOLIC BLOOD PRESSURE

STUDY GROUPS	BASELINE		2WEEKS		4WEEKS		6WEEKS		8WEEKS		Repeated Measures of ANOVA
	Mean	SD	Mean	SD	Mean	SD	Mean	SD	Mean	SD	
Group A (400 IU)	94.93	3.27	93.53	3.51	92.20	3.94	91.00	4.42	90.33	4.30	Between groups P=0.001 Within group P=0.001
Group B (800 IU)	94.73	3.50	93.47	3.15	91.87	3.56	90.07	4.02	88.60	4.43	
Group C(1200IU)	94.27	3.39	91.93	3.26	89.87	3.44	87.60	3.69	86.27	3.47	
Group D (Control)	93.53	3.09	93.60	3.04	93.80	2.89	94.33	3.20	95.60	3.62	
ANOVA**	P=0.37		P=0.05*		P=0.001*		P=0.001*		P=0.001*		
Control Vs A	P=0.09		P=0.94		P=0..95		P=0..001*		P=0.001*		
Control Vs B	P=0.16		P=0.87		P=0.02*		P=0.001*		P=0.001*		
Control Vs C	P=0.38		P=0.05*		P=0.001*		P=0.001*		P=0.001*		

FIGURE.2.

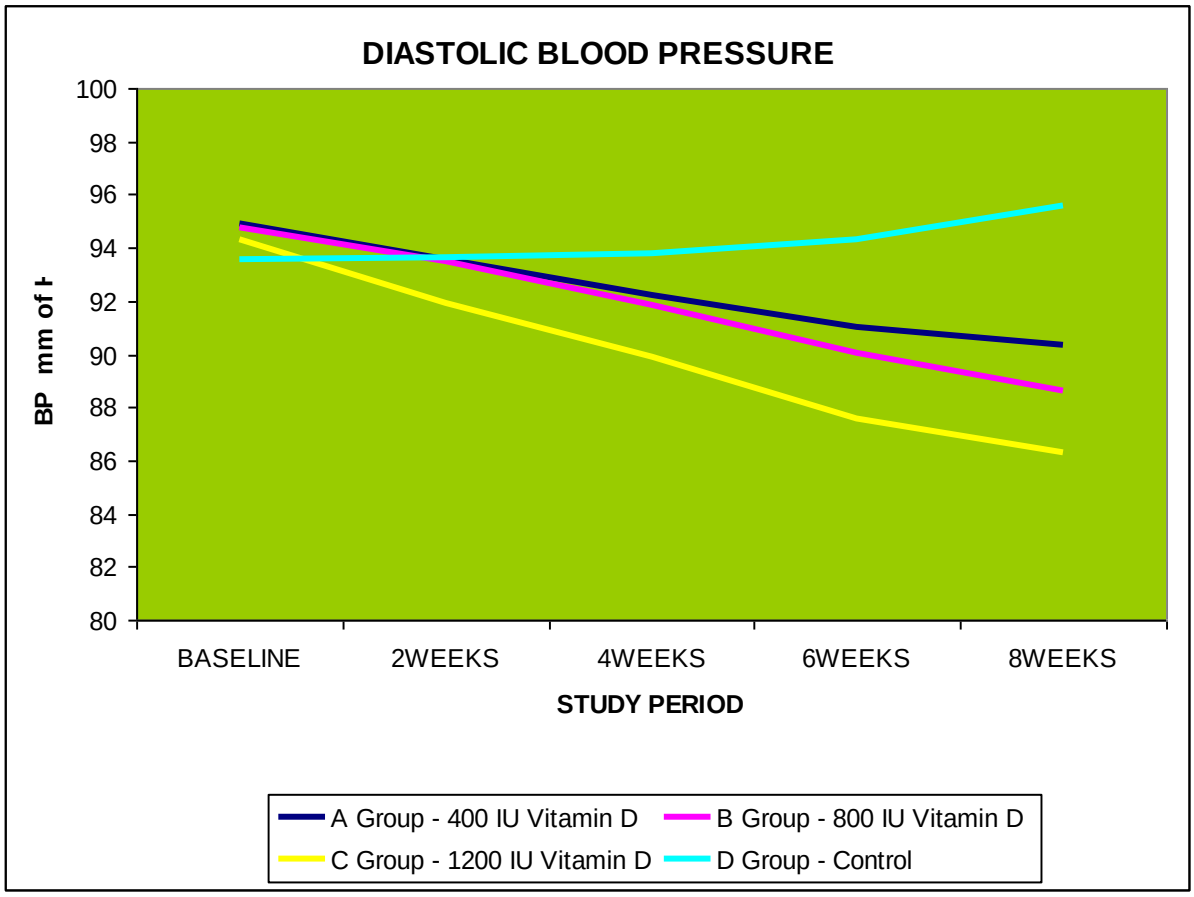
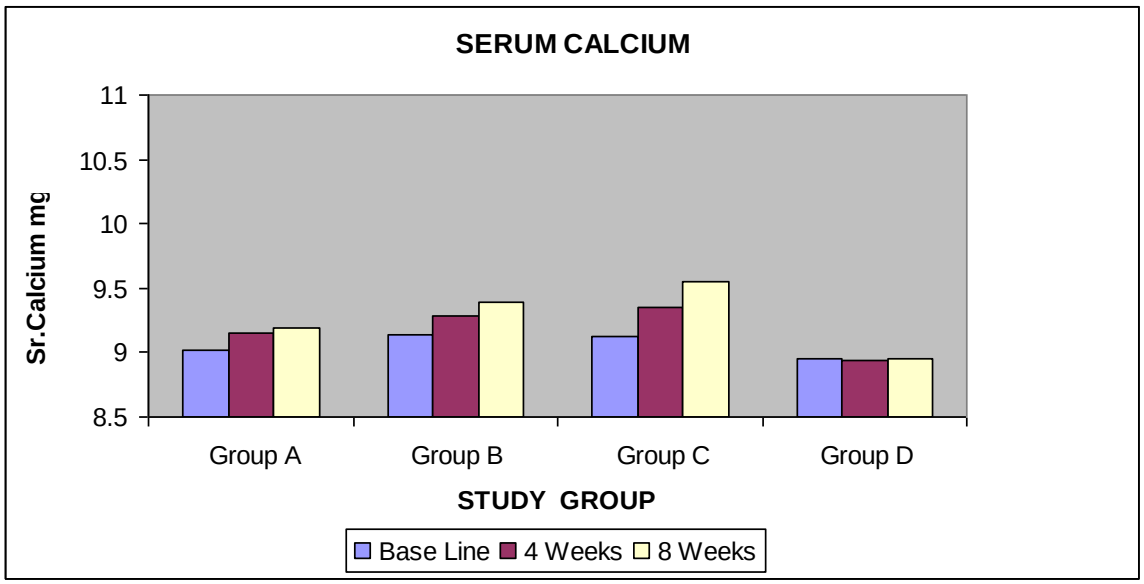


TABLE 5 : SERUM CALCIUM

STUDY GROUPS	BASELINE		4EWEEKS		8WEEKS		Repeated Measures of ANOVA
	Mean	SD	Mean	SD	Mean	SD	
Group A (400 IU)	9.02	.77	9.15	.75	9.19	.76	Between groups P=0.001*
Group B (800 IU)	9.14	.81	9.28	.81	9.39	.80	
Group C (1200 IU)	9.12	.36	9.35	.38	9.55	.39	
Group D (Control)	8.95	.55	8.94	.51	8.95	.51	Within group P=0.001
ANOVA**	P=0.64		P=0.05*		P=0.001*		
Control Vs A	P=0.67		P=0.29		P=0.15		
Control Vs B	P=0.19		P=0.05*		P=0.001*		
Control Vs C	P=0.14		P=0.01*		P=0.001*		

FIGURE: 3



4.0 DISCUSSION

Vitamin D or calciotrophic hormones show inverse relationship in the resistance of peripheral vessels. Several animal studies show an inverse relationship between vitamin D and BP. Vitamin D mediated repression of renin gene expression is a receptor (VDR) dependent mechanism[8]. Reports from studies in cell cultures with $1,25(OH)_2D3$ also support the observations in animal studies, suggesting that vitamin D analogs may potentially be developed into new class of antihypertensive agents.[9]

In our study Vitamin D with amlodipine 5mg , producedreduction in Systolic blood pressure in the dose of 800 IU/day and 1200 IU/day at the end of 2 nd week(P value of 0.05). But in dose of 400 IU , did not produce significant reduction of systolic BP on comparison with the control group. There was a reduction in Diastolic blood pressure with 400 IU/day from 6th week onwards, (P value 0.001) , while with 800 IU/day and 1200 IU/day reduction was from 4th week onwards (P value 0.001).A statistically significant rise in serum calcium level within the physiologic reference range was observed .

No adverse events were reported during the study in any of the study groups.

5.0. CONCLUSION

From our study, we conclude that in stage 1 hypertension :

- Vitamin D in doses of 800 IU/day and 1200 IU/day is an effective adjuvant to Calcium Channel Blockers in reducing Blood Pressure.
- Vitamin D is well tolerated for 8 weeks.

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