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Research Article

CLINICAL EFFICACY OF HIGH DOSE WATER-SOLUBLE VITAMINS SUPPLEMENTATION ON LIPID PROFILE IN PRE-HYPERTENSIVE SUBJECTS

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ABSTRACT

Objective: Hypertension (HTN) is one of the preventable cardiovascular diseases (CVD) but it causes significant morbidity and mortality. Recently, incidence of pre-hypertension is increasing and it has a greater chance of developing into HTN. Dyslipidemia is one of the main risk factors for the development of CVD among the pre-hypertensive subjects. Water soluble vitamins display potent antioxidant and anti-inflammatory effects and also elicits favorable effect on lipid profile in HTN. In this backdrop, the present study was carried out to evaluate the supplementation of water-soluble vitamins on lipid profile in pre-hypertensive patients.

Methods: This was a randomized, single blinded, and placebo-controlled study conducted on 60 pre-hypertensive subjects and was allocated into water soluble vitamins group (n=30) and received Becosules capsule for 4 months and placebo group (n=30) received starch capsule for 4 months. The blood was withdrawn at 2–4 months and the lipid profiles such as total cholesterol, triacylglycerol, HDL cholesterol (HDL-C), low-density lipoprotein (LDL)-C, and VLDL were measured. Then, the lipid profiles were compared with in the group and between the groups at 2–4 months using two-way repeated measures ANOVA.

Results: In this study, the triglycerides and VLDL level were significantly ($p<0.05$) decreased in water soluble vitamin groups as compared to the placebo groups. Meanwhile there was no significant alteration in the total cholesterol, HDL-C, and LDL-C level between the groups.

Conclusion: Thus, the study shows that water soluble vitamins displayed significant anti-dyslipidemia effect in pre-hypertension and might also confer protection in the future progression of HTN.

Keywords: Water soluble vitamins, Pre-hypertension, Dyslipidemia, Lipid profile.

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INTRODUCTION

Hypertension (HTN) orchestrates a major role in the development of cardiovascular diseases (CVD). HTN is one of the vital risk factor the global mortality and morbidity and it has marked association with various diseases such as dyslipidemia, cardiomyopathy, and acute myocardial infarction [1]. According to NICE guidelines 2019, HTN in adults is defined as a systolic/diastolic blood pressure (BP) of 140/90 or higher [2]. According to AHA 2017 guidelines, pre-hypertension is defined as systolic BP (SBP) of 120–129 mmHg and diastolic BP (DBP) of 80–89 mmHg [3]. Further, as per Joint National Committee (JNC), eighth guideline pre-hypertension was stated as SBP 120–139 mmHg and DBP 80–89 mmHg [4]. Based on the health survey-based nationwide BP data, the prevalence of HTN in India is reported to be 26.5% [5]. In a recent study conducted in India, the prevalence of pre-hypertension in young adults aged 20–39 years is reported to be 33.3% [6].

Pre-hypertension is an alarming sign for the future development of CVD. The strong heart study revealed that the pre-hypertension subjects showed higher levels of inflammatory markers, elevated triglycerides, and decreasing HDL cholesterol (HDL-C) which are the predisposing factors for the development of CVD [7]. In a study done by Lin *et al*. [8], the prevalence of dyslipidemia is higher in patients with pre-hypertension as compared to the healthy controls. Further, report shows that BMI, dyslipidemia, diabetes, and impaired glucose resistance displayed significant association with pre-hypertension [9]. Thus, early detection and treatment is essential required to combat the progression of pre-hypertension to HTN and various complications.

Vitamins generally are organic compounds which differ based on the chemical structures and it requires for the certain metabolic process within the cell. The vitamins are classified as fat soluble and water soluble such as folate, thiamine, riboflavin, niacin, pantothenic acid, biotin, Vitamin B6, and Vitamin B12 and Vitamin C, respectively. The previous studies shows that Vitamin B12 and Vitamin C deficiency are associated with dyslipidemia, HTN, and insulin resistance [10,11]. In this backdrop, the present study was carried out to evaluate the effect of water-soluble vitamins supplementation on lipid profile in pre-hypertension subjects.

METHODS

This was a randomized, single-blinded, and placebo-controlled study conducted on pre-hypertension subjects attending the urban health center. All the subjects were recruited from an urban health center after obtaining the institutional ethical clearance. Patients with pre-hypertension were defined based on JNC 8 guidelines. A written informed consent was obtained from all the patients before the initiation of the study.

Inclusion criteria

Patient between the age group 24–45 years and BMI <30 kg/m^2 were included in the study.

Exclusion criteria

Patients having previous history of diabetes, kidney disease, metabolic disorders, and CVD were excluded from the study. Further, patients with infection and subjects on hypolipidemic drugs and any other medication were excluded from the study. Smokers, alcoholics were also excluded from the study.

BP was measured using manual sphygmomanometer. The patients were allowed in sitting position with legs uncrossed and allowed to rest for 5 min. Then, the BP was recorded on both arms and the higher value

was taken into consideration. Three BP measurements were taken with a gap of 5 min and the average of three values was taken for the study.

Study design

In this study, 60 pre-hypertensive were recruited based on the inclusion and exclusion criteria. The patients were allocated into two groups with 30 patients in each group as follows,

Water soluble vitamin group (n=30): Pre-hypertensive patients supplemented with water soluble vitamins capsules (Becosules capsules, B-complex forte with Vitamin C, Pfizer India, Limited) for 4 months. The composition of Becosules capsules was displayed in Table 1.

Placebo group (n=30): Pre-hypertensive patients received placebo starch (500 mg) in the form of 250 mg capsule twice a day for 4 months.

Study procedure

Before the initiation of the study, the blood was collected after overnight fasting and stored for analysis. Then, Group A instructed to take the Becosules capsules twice a day and in group B, the patients were instructed to take the placebo (starch capsules) twice a day. Further, again the blood samples were collected at the end of 2nd month and 4th month respectively, respectively and stored for further analysis.

Evaluation of lipid profiles

The stored blood was subjected to centrifugation and serum was separated. Then, the lipid parameters such as total cholesterol, triacylglycerol, HDL were analyzed using commercially available kits suitable for automated analyser AU 400.

Data analysis

Data were expressed as mean±SD. Unpaired student t-test was used to analyze the demographic variables between the groups. Further, comparison of lipid profile at baseline, 2, and 4 months between the groups was done using two-way repeated measures ANOVA followed by Bonferroni's multi comparison *post hoc* test. $p<0.05$ was found to be statistically significant. The data analysis was done using SPSS v 24.

RESULTS

The demographic characteristics of the study participants are shown in Table 2.

As shown in Table 3, there was no marked alteration in the cholesterol level among the patients in water soluble vitamin group and when compared at 2 (200.9±26.3 vs. 208.3±22.9 mg/dl; $p>0.05$) and 4 months (199.9±24.2 vs. 205.9±26.2 mg/dl; $p>0.05$). Further, within both the group there was no significant change in the cholesterol when compared between baseline, 2, and 4 months respectively.

In this study, the triacylglycerol level was significantly lower in water soluble vitamin group as compared to placebo group at 2 (113.3±22.3 vs. 133.1±28.9 mg/dl; $p<0.001$) and 4 (114±19.6 vs. 131.7±11.7 mg/dl; $p<0.05$) months, respectively. However, within both the group, there was no significant change in the triacylglycerol when compared between baseline, 2, and 4 months, respectively (Table 3).

There was no marked alteration in the HDL level among the prehypertensive subjects in water soluble vitamin group and placebo, and when compared at 2 (37.2±3.7 vs. 36.6±4.9 mg/dl; $p>0.05$) and 4 months (37.1±3.4 vs. 37.2±3.7 mg/dl; $p>0.05$). Further, within both the group, there was no significant change in the HDL-C when compared between baseline, 2, and 4 months, respectively (Table 3).

In this study, the VLDL level was significantly lower in water soluble vitamin group as compared to placebo group at 2 (22.7±3.9 vs. 26.6±5.7 mg/dl; $p<0.05$) and 4 (22.7±3.9 vs. 26.1±7.1 mg/dl; $p<0.05$) months, respectively. However, within both the group, there was no significant change in the VLDL level when compared between baseline, 2, and 4 months, respectively (Table 3).

Table 1: The composition of becosules capsules

Vitamins	Composition of becosules
Vitamin B1	10 mg
Vitamin B6	3 mg
Vitamin B12	15 µg
Folic acid	1.5 mg
Riboflavin	10 mg
Niacin	100 mg
Biotin	100 µg
Panthothenic acid	50 mg
Vitamin C	150 mg

Table 2: Demographics characteristic of water soluble vitamins and placebo group

Variables	Group A (n=30)	Group B (n=30)	p-value
Age (years)	38.2±7.7	37.5±8.3	0.76 (NS)
Male/Female	20/10	19/11	-
Weight (kg)	65.2±10.2	61.6±8.7	0.35 (NS)
BMI (kg/m^2)	25.2±5.8	23.8±7.2	0.42 (NS)

Values are expressed as mean±SD, NS: Not significant

Meanwhile, there was no marked alteration in the low-density lipoprotein (LDL) level among the prehypertensive subjects in water soluble vitamin group and placebo group, when compared at 2 (141±24.4 vs. 145.8±18.5 mg/dl; $p>0.05$) and 4 months (140.0±22.3 vs. 142.6±25.0 mg/dl; $p>0.05$). Further, within both the group, there was no significant change in the cholesterol when compared between baseline, 2, and 4 months, respectively (Table 3).

DISCUSSION

HTN still continues as a global problem and also imposes significant health burden among the patients. HTN or pre-hypertension alone or in association with other comorbid conditions such as obesity and diabetes elevates the CVD risk such as ischemic heart disease and stroke [12]. Pre-hypertension is an intermediate stage between HTN and normal BP and it is associated with sub-clinical atherosclerosis and organ damage [13]. The previous meta-analysis showed that pre-hypertension markedly increased the risk of CVD, coronary heart disease, and stroke mortality [14]. In addition, it has been reported that even a mild increase in BP inside the normal range might lead to end organ damage [15].

Dyslipidemia orchestrate is an important role in the pathogenesis of HTN as a result of endothelial dysfunction and an increased LDL-C level blocks the endothelium-mediated vasodilator response to acetylcholine and in this oxidized LDL provokes the development of atherosclerosis, but native LDL does not have a significant role in these process [16]. Further, reports also highlight that metabolic disturbances such as impaired glucose tolerance, dyslipidemia, and central obesity can trigger sympathetic activation and further augments pre-hypertension state [17].

Hypercholestremia causes cholesterol deposits in the arterial wall and leads to dysregulation of endothelial function as a result of increased generation of free radicals. This free radical inhibits the release of nitric oxide, which is an endothelial relaxing factor. Hence, elevated cholesterol and triglycerides level for a chronic period leads to increased endothelial permeability and causes accumulation of lipoproteins. Further these lipoproteins are oxidized as a result of increased free radical level [18].

Till date, there has been no proper treatment guideline for pre-hypertension. The most preferred treatment approaches in pre-hypertension are life style modifications and dietary interventions; however, the outcome was not found to be satisfactory. Mounting studies

Table 3: Comparison of lipid profiles between Water soluble vitamins group and placebo group

Lipid profiles	Water soluble vitamins group (n=30)			Placebo group (n=30)		
	Basal	2 Month	4 Month	Basal	2 Month	4 Month
Cholesterol (mg/dL)	200.7±28.8	200.9±26.3	199.9±24.2	191.4±26.8	208.3±22.9α	205.9±26.2
TG (mg/dL)	117.6±12.9	113.3±22.[a]**	114±19.6[b]*	119.5±25.3	133.1±28.9	131.7±11.7
HDL-C (mg/dL)	36.1±5.6	37.2±3.7	37.1±3.4	34.2±0.2.8	36.6±4.9	37.2±3.7
VLDL-C (mg/dL)	23.1±2.1	22.6±4.4[a]*	22.7±3.9[b]*	24.7±5.7	26.6±5.7	26.1±7.1
LDL-C (mg/dL)	136.5±25.3	141±24.4	140.0±22.3	132.4±25.1	145.8±18.5	142.6±25.0

Values are expressed as mean±SD. [a]water soluble vitamins 2 months versus placebo 2 months, [b]water soluble vitamins 4 months versus placebo 4, *p<0.05, **p<0.001, LDL: Low-density lipoprotein

have reported significant association between water soluble vitamins supplementation in the mitigation CVD and insulin resistance [19,20]. Our results are in line with the study by Liu *et al*. [20] where 12 weeks supplementation of Vitamin B complex significantly reduced the triglycerides and total cholesterol levels and also improved the HDL-C levels in patients with stable coronary artery disease. In another study, folic acid supplementation for 8 weeks among the post-menopausal diabetic subjects significantly reduced the LDL-C level and LDL-C [22]. The dyslipidemia inhibitory mechanism of folic acid is mediated by its anti-inflammatory effect and inhibition of oxidative stress and lipid peroxidation [23,24]. Likewise, in a study done by Sezgin and Becel [24]. Vitamin B12 supplementation significantly reduced the total cholesterol and triglycerides level when compared between baseline and post-treatment. A meta-analysis reveals that Vitamin C supplementation 500 mg/day for 4 weeks significantly reduced the serum LDL-C and triglyceride levels, as well as a non-significant elevation of HDL-C [26]. Vitamin C mediates its anti-hypertensive effect by improving the level of nitric oxide and prostaglandins and thus maintains the endothelial function and also serves as an angiotensin receptor blocker [27]. Further, the other actions of Vitamin C in the reduction of BP are upregulation of erythrocyte Na+/K+ ATPases, enhancing Na+ excretion (diuretic like action), decrease in cytosolic Ca^{2+} levels, and also reduce the vascular constriction mediated by regulation of sympathetic nervous system reduction (Ca channel blocker) and thus suppress the vascular constriction through regulating SNS and thus positively regulate BP [28]. In addition, hypolipidemic mechanism of Vitamin C is attributed by its LDL oxidation inhibition property and also by reducing the monocytes adhesion to the endothelium and thus mediates a pivotal role in CVS risk reduction [29]. Further, a recent meta-analysis based on eight RCTs reveals that niacin supplementation to Type 2 diabetic patients significantly reduced the total cholesterol (p=0.001), triglyceride (p<0.001), LDL-C (p<0.001), and also improved the level of HDL-C (p<0.001) [30]. The dyslipidemia inhibitory mechanism rendered by niacin is primarily due to the inhibition of the hepatic diacylglycerol acyltransferase and thus minifies the triacyl glycerol synthesis. Further, niacin also reduces the free fatty acids mobilization from adipose tissue, which leads to the reduced triglyceride synthesis in liver and also VLDL triglyceride content thereby reducing the TAG synthesis. Niacin also decreases the mobilization of free fatty acids from adipose tissue and the resultant decrease in triglyceride levels reduces hepatic synthesis and triglyceride content of VLDL. In addition, niacin enhances the capacity and efficiency of HDL-C transport [31].

Further, in the present study, prevention of pre-hypertension might be due to the antioxidant effect of water soluble vitamins. In our earlier study, we have reported that water soluble vitamins supplementation to pre-hypertension patients for 4 months significantly reduced the malondialdehyde and protein carbonyl content and thus reduced the oxidative stress burden [32].

The main limitations of the study were small sample size, less follow-up duration, and mainly the vitamin levels were not analyzed among the patients. The effect of physical activity and diet were not assessed.

CONCLUSION

The present study shows that in pre-hypertensive patients, there was significant alteration in the lipid profiles. Meanwhile, treatment with water soluble vitamin supplementation effectively restored the level of triglycerides and VLDL mediated by anti-inflammatory and oxidative stress inhibitory mechanism. Hence, regular monitoring of lipid levels is essential among the pre-hypertensive patients to mitigate the future risk of atherosclerosis.

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CONFLICTS OF INTEREST

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