Original Article

Assessment of Safety and Efficacy of Vitamin C Along With Telmisartan in Mild to Moderate Hypertensive Patients in a Tertiary Care Hospital in Tamil Nadu.

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Abstract

Introduction: Hypertension is a worldwide health problem and one of the preventable cause of heart disease and stroke. Uncontrolled hypertension can result in a myocardial infarction, left ventricular hypertrophy, and ultimately heart failure. During oxidative stressful condition like hypertension, Vitamin C an important antioxidant, that is effective in trapping oxygen-derived free radicals and lowers the blood pressure.

Objectives: To assess the efficacy and safety of supplementing vitamin C to telmisartan as a treatment in mild to moderate hypertension patients to reduce blood pressure.

Materials And Methods: An open label, randomised, prospective study, participants were enrolled in one of two groups. A total of 110 participants were randomized into 2 groups in which group 1 has 55 participants who received Tab.Vitamin C 500mg OD along with Tab.Telmisartan 40 mg OD and the next 55 participants were into group 2 who received only Tab.Telmisartan 40 mg OD. The participants were followed for 16 weeks and they were asked to visit us at week 1, week 9, and week 16 during which their blood pressures were monitored and noted.

Results: In this study, the average baseline Systolic blood pressure (SBP) was 154.36 mm Hg in group - 1 (Tab.Vitamin C with Tab.Telmisartan) and 152.11 mm Hg was in group 2 (Tab.Telmisartan), and the Diastolic blood pressure (DBP) was approximately 94.36 mm Hg - group 1 and 93.67mm Hg - group 2. During the last visit i.e.,16th week, the average SBP decreased significantly in group 1 (132.98 mm Hg) than group 2 (144.33 mm Hg) and the DBP showed significant reduction in group 1(75.93mm Hg) than group 2 (85mm Hg).

Conclusion: Vitamin C when it is given as an add on therapy to telmisartan it shows significant reduction in blood pressure.

Key words – Vitamin C, Hypertension, Telmisartan, Systolic blood pressure, Diastolic blood pressure, Antioxidant.

INTRODUCTION

Hypertension a chronic condition which is a leading cause of premature death across the world [(1)]. In accordance with Imperial College of London and WHO's first complete global research hypertension trends, the number of persons aged 30-79 who have hypertension has raised to 1.28 billion from 650 million in the past 30 years [(2)]. By 2025, India wants to achieve a 25% relative decrease in the hypertension prevalence. Around 63% deaths in India are due to noncommunicable diseases in which 27% are because of cardiovascular disease [(2)].

Vitamin C, which is a water-soluble vitamin acts as powerful reducing agent which decreases the oxidation of low-density lipoproteins, protects many organs from oxidising agents, and lowers the risk of stroke. Vitamin C which is a powerful antioxidant effective in removing oxygen derived free radicals [(3)]. Through its action on prostacyclin, antiplatelet, and vasodilatory mechanisms, vitamin C aids in maintaining vascular integrity. Nitric oxide activity is increased by vitamin C in hypertensive patients, which enhances the endothelium dependent vasodilatation of arteries [(4)]. Therefore, the aim of our study is to prove that vitamin C on addition with telmisartan, helps in lowering blood pressure among hypertensive patients.

MATERIALS AND METHODS

A prospective, open label, randomized study was conducted from July 2021 to May 2022 at the general medicine outpatient clinic of a tertiary care hospital in Tamil Nadu. This study was documented in Clinical Trial Registry of India

(CTRI) database - CTRI/2021/09/036310. After receiving approval from the institutional ethical committee, the study was commenced. Before enrolment into the trial informed consent was obtained from each participant.

Participants fulfilling the following criteria were included in the study, both male & female who comes under the age ranging from 18 to 65 years were included. Patients taking only telmisartan for hypertension, who had mild (Systolic blood pressure 140-159 mm Hg & Diastolic blood pressure 90-99 mm Hg) to moderate hypertension (160-179 mm Hg Systolic blood pressure & 100-109 mm Hg Diastolic blood pressure) according to JNC 8 guidelines and had history of diabetes mellitus and the participants who were willing to provide written informed consent were included.

Participants who had the following exclusion criteria were excluded from the study, Age <18 year and >65 years were excluded. Those who had uncontrolled hypertension, previous history of myocardial infection, pregnancy/ Lactation, Chronic kidney disease, H/O psychiatric illness were also excluded from the study.

The total sample size is 110, calculated using the formula $n = \frac{Z2\sigma2}{S.E2}$. Totally 178 participants were screened for the eligibility and exclusion criteria in which 110 participants were enrolled into the study and randomized in the ratio of 1:1. Randomization was performed using sealed envelope, in which group 1 received Tab.Vitamin C 500mg OD along with Tab.Telmisartan 40 mg OD and in group 2 participants received only Tab.Telmisartan 40 mg OD. The participants came for 4 visits. During the initial visit (week 0) participants, basal demographic characteristics and their baseline systolic and diastolic blood pressure were noted and the medication was started on the same day. Participants were asked to come for next visit 2(week 1) to know their compliance. At visit 3, at the end of 9th week their systolic and diastolic blood pressure were noted. At visit 4, at the end of week 16 their blood pressures were noted. During each visit the participants were asked to return their empty drug strips and were followed up periodically through telephone for compliance.

Safety and the tolerability of the drugs were assessed based on monitoring the occurrence of side effects.

STATISTICAL ANALYSIS

The analysis has been carried out using SPSS v.28.0 and all the data has been entered into the Microsoft Excel sheet. Descriptive statistics such as frequency, percentages, mean & standard error and inferential statistics such as unpaired t test & paired T test was analyzed and presented.

RESULTS

178 participants was screened out of which 110 participants were eligible and given informed consent, were enrolled in the study. Among the remaining participants, 68 were excluded as 28 refused to participate and 40 were not meeting the inclusion criteria. The outlook of the participants in two groups were schematically illustrated, (Figure 1).

The demographic characteristics and baseline details of the study population were shown in Table 1.

Figure 1 : Schematic diagram of enrolment

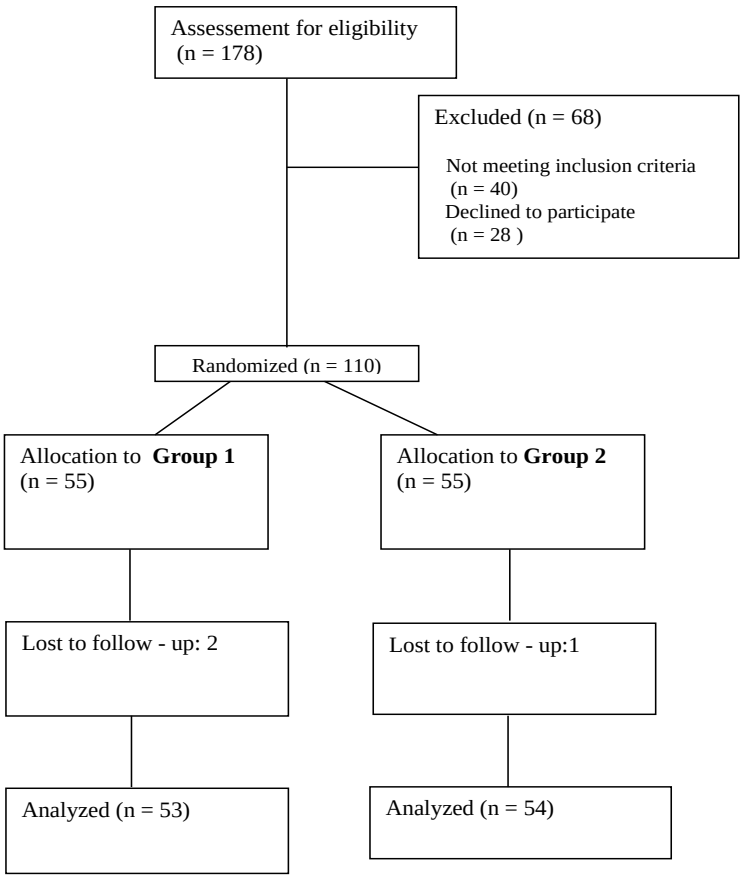

Table 1 Demographic characteristics and baseline features

PARAMETERS	GROUP - 1	GROUP - 2	P VALUE
Age - years	52±8	50±8	>0.05
Male sex	42 (76%)	33 (60%)	>0.05
Female sex	13 (23%)	22 (40%)	>0.05
BMI, kg/m2	25.05 ±3.19	25.76 ±4.06	>0.05
Total cholesterol	230.31±20.22	220.33±19.33	>0.05
Alcohol	12	9	<0.05
Smoking	17	12	>0.05

The systolic blood pressure of participants was measured during 4 visits (week 0, week1, week 9, week 16). In comparison to the baseline SBP (154.36 mm Hg) in group - 1 and (152.36 mm Hg) group 2, there is a significant reduction of SBP - group 1 during the 3rd visit as (143.42 mm Hg) compared to group 2 (147.35 mm Hg) and in the 4th visit (week 16) SBP there is significant reduction in group 1 (132.98 mm Hg) compared to group 2 (132.98 mm Hg) (Table 2).

Table 2: Systolic blood pressure of 1st ,2nd ,3rd visit.
(*SBP – systolic blood pressure)

PARAMETERS	GROUP				TEST OF SIGNIFICANCE P - Value
	GROUP - 1		GROUP - 2		
	MEAN mm Hg	SD	MEAN mm Hg	SD	
SBP BASELINE	154.36	9.96	152.11	8.27	>0.05
SBP 9TH WEEK	143.42	10.17	147.35	8.07	<0.05
SBP 16TH WEEK	132.98	9.99	144.33	8.24	<0.05

The diastolic blood pressure of participants was measured during 4 visits (week 0, week1, week 9, week 16). In comparison to the baseline DBP in group - 1(94.36 mm Hg) and group 2(93.67 mm Hg) there is a significant reduction in DBP in group 1(84.36 mm Hg) compared to group 2 (89.71 mm Hg) during the 3rd visit (week 9).At visit 4 there is significant reduction in DBP in group 1(75.93 mm Hg) compared to group 2(85 mm Hg) which is during the 16th week (Table 3).
Few participants had side effects like headache and nausea due to various other reason (climatic condition, dehydration) (Table 4).

Table 3 –Diastolic blood pressure of 1st ,2nd ,3 visit
DBP* – Diastolic blood pressure

PARAMETERS	GROUP				TEST OF SIGNIFICANCE P - Value
	GROUP - 1		GROUP - 2		
	MEAN mm Hg	SD	MEAN mm Hg	SD	
DBP BASELINE	94.36	3.36	93.67	3.416	>0.05
DBP 9TH WEEK	84.36	4.30	89.71	3.40	<0.05
DBP 16TH WEEK	75.93	5.13	85.00	4.48	<0.05

Table 4 : Adverse events reported in both the groups during the trial.

ADVERSE EVENTS	GROUP - 1	GROUP - 2
HEADACHE	1	3
NAUSEA	3	4

DISCUSSION

In both developing and developed countries, hypertension is one of the primary cause of morbidity and mortality [5]. Untreated hypertension increases the chance of developing countless number of cardiovascular diseases, including atherosclerosis, coronary artery disease, and cerebrovascular hazards like stroke [6].

Hypertension is an oxidative stressful condition, wherein nitric oxide, an effective endogenous vasodilator, will gradually deteriorate [7]. Vitamin C, an antioxidant, has tetrahydrobiopterin, a cofactor of endothelial nitric oxide synthase, that stimulates the nitric oxide production in our vascular system which causes lowering of blood pressure during an oxidative stress [8].

In this study we had found that there is a significant lowering of blood pressure in group 1 (vitamin C + Telmisartan) by the end of 16th week compared to group 2. The reduction in blood pressure is visible from 9th week, though we cannot comment regarding the antihypertensive action of vitamin C alone [9].
According to Taddei et al review [8], The effect of inhibitor of nitric oxide synthase NG-monomethyl-L-arginine reversed by vitamin C, which improve the patients in hypertension by endothelial-dependent vasodilation [10]. By Lena Al-khudairy et al Currently, the major theory claims that vitamin C raises intracellular concentrations of the tetrahydrobiopterin a co factor, which is an endothelial nitric oxide synthase, that facilitates the generation of nitric oxide, which works as a potent vasodilator [11]. According to Ammar et al, there is research that states vitamin C increases biological activity of nitric oxide[12]. Further, in short-range human trials, vitamin C supplement enhanced endothelial function of the coronary and brachial arteries [13]. All of the studies that were stated above imply that vitamin C had a positive influence on reducing blood pressure in people with essential hypertension.
For proper physiological processes, the body needs vitamin C. Tyrosine, tryptophan, folic acid, glycine, lysine, catecholamine, proline and carnitine are all synthesised and processed. By facilitating the bile acid synthesis from cholesterol, it lowers serum cholesterol levels. As an antioxidant, it protects the body from the damaging effects of free radicals, toxins and environmental pollutants. [3].
Vitamin C rarely produce side effects like nausea, vomiting, headache. The National Academy of Sciences has defined a tolerable maximum limit for vitamin C supplementation at 2000 mg/day, which is relatively high and poses minimal hazardous issues According to experts, the safest dose of vitamin C is 500 mg/day [14,15]. In our study very few number of patients had side effects like nausea, headache which may be due to other conditions (climatic conditions, dehydration) also.
The limitation of our study is, being done for a shorter period of time with small number of people. There is no long-term assessment. In the future, this study can be extended by giving vitamin C for more than 1 year for best results.

CONCLUSION

From our study we concluded that vitamin c as add on therapy at a dose of 500 mg causes significant reduction in both systolic and diastolic blood pressure. Hence, vitamin C can be recommended as a add - on therapy to antihypertensives in improving the clinical outcome and preventing the long-term complication associated with hypertension.

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CONFLICT OF INTEREST

There is no conflict of interest.

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