

Original research article

A comparative prospective research looked at the efficacy and tolerability of vitamin C as an add-on treatment to a typical antihypertensive regimen.

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Abstract

Aim: The aim of the present study to evaluate the efficacy and tolerability of vitamin C as add on therapy to standard antihypertensive regimen.

Methods: A comparative prospective study was conducted in the Department of Pharmacology, Anugrah Narayan Magadh Medical College and Hospital, Gaya, Bihar, India for 1 year. The study was undertaken in mild to moderate hypertensive patients to find out the efficacy and tolerability of vitamin C as an add-on therapy to the standard anti-hypertensive regimen in the reduction of blood pressure and C-reactive protein levels. Total 160 patients with systolic blood pressure in the 140-179 mm Hg range and diastolic blood pressure in the 90- 109 mm Hg range with C-reactive protein levels in the 10-12 mg/dl range were recruited for the study out of 720 patients screened.

Results: Out of 720 patients screened, 160 patients were included in this study. They were randomized into four groups, group 1, group 2, group 3 and group 4, each consisting of 40 patients. In group 1, mean age was 44.22 ± 6.88 , group II 44.97 ± 9.87 , group III 47.01 ± 7.23 whereas in group 4 45.14 ± 6.81 . On comparison we found non-significant difference with P value. At baseline there was non-significant difference among all the four group with p value 0.25, whereas at all the visit at 1, 3 and 6 month there was significant difference among the four group with p value <0.01 , <0.001 and <0.001 . At baseline there was no significant difference among different groups in diastolic BP, whereas there was significant difference among all four groups at all 3 visit i.e 1, 3 and 6 months with p value <0.001 .

Conclusion: Vitamin C at the dose of 500 mg OD as an add on therapy to enalapril 5 mg BD causes significant reduction of both systolic and diastolic blood pressure, vitamin C 500 mg OD supplementation to the standard anti-hypertensive drugs may produce better reduction of blood pressure, vitamin C 500 mg may be recommended as an adjuvant to regular anti-hypertensive regimen to reduce cardiovascular and cerebrovascular risks associated with hypertension.

Keywords: Vitamin C, supplement, blood pressure

Introduction

Hypertension affects at least one-quarter of the adult population in the United States and is an important determinant of the incidence of coronary heart disease and stroke.¹ Epidemiological evidence suggests that a deficiency of vitamin C may lead to hypertension, and a negative association between plasma vitamin C status and blood pressure has been reported.²⁻⁴ However this association only suggests, but does not prove, that the intake of extra vitamin C lowers blood pressure. Clinical trials performed to assess the effect of vitamin C supplementation on blood pressure in hypertensive individuals have met with mixed results.⁵⁻⁷ In 1997 Ness et al. concluded that there were too few clinical trials, and those reported at that time were generally too small and too varied to provide confirmatory evidence for a casual relationship.⁸

Vitamin C (L-ascorbic acid) is a water-soluble vitamin with a variety of biologically important functions. Humans and few other mammals do not possess the capacity of vitamin C biosynthesis from glucose due to the lack of the enzyme L-gulonolactone oxidase, essential for this metabolic pathway.⁹ Most vitamin C biological functions are associated with the presence of a lactone ring with electron rich 2-en-2,3-diol-1-one moiety in its molecule. Under physiological pH conditions, vitamin C exists predominantly as the ascorbate anion, arising from the completely dissociated 3-hydroxyl group.¹⁰ Although ascorbic acid serves both as a reducing agent and antioxidant, it is best known for its capacity to act as an antioxidant able to undergo two consecutive one-electron oxidation reactions and deprotonation of both hydroxyl groups at positions 2 and 3, resulting in the formation of dehydroascorbic acid (DHA), which is unstable in neutral pH.^{10,11} In the above mentioned process, intermediate radical species are formed, such as relatively stable ascorbyl radical.^{11,12} Although dehydroascorbic acid and ascorbate free radicals can be easily reduced by both NADH- and NADPH-dependent mechanisms, the main pathway of ascorbate recycling is enzymatic, mediated largely by glutaredoxin and thioredoxin reductase.¹³

C-reactive protein (CRP) is an acute phase reactant produced in the liver, and is produced by the stimulation of interleukin-6. It has been widely used for the evaluation of various inflammatory states.^{14,15} Recently, the role of inflammations on the patho-physiology of cardiovascular diseases has been emphasized, and CRP, which is the indicator for inflammatory reactions, has been reported to be related to the incidence of stable or unstable angina pectoris and prognosis, and to be a prognostic factor for limb vascular disease, stroke, and myocardial infarction, which are later found even after compensating for the different risk factors in middle-aged men and women who are seemingly healthy.¹⁶ This prospective comparative study is therefore undertaken to evaluate the effectiveness of vitamin C in blood pressure as an addition to therapy in the regular antihypertensive regimen.

Materials and methods

A comparative prospective study was conducted in the Department of Pharmacology, Anugrah Narayan Magadh Medical College and Hospital, Gaya, Bihar, India for 1 year, after taking the approval of the protocol review committee and institutional ethics committee.

Methodology

The study was undertaken in mild to moderate hypertensive patients to find out the efficacy and tolerability of vitamin C as an add-on therapy to the standard anti-hypertensive regimen in the reduction of blood pressure and C-reactive protein levels. Total 160 patients in the age group of 18- 60 years, patients with mild to moderate hypertension and patients with body mass index (BMI) of 18-25 included in this study. Patients with any other active infection, patients with any history of surgery in the recent past 3 months, patients with history of malignancies and patients with evidence of gastrointestinal tract, renal, endocrine, cardiovascular abnormalities and any other major systemic illness and pregnant and lactating women were excluded from this study .

Baseline visit

Detailed medical history, blood pressure monitoring, estimation of C-reactive protein levels, physical and systemic evaluation and baseline demographic characteristics were reported for patients who gave written informed consent to participate in the study. For the haematological and serum biochemical tests, blood was drawn. We screened 580 patients.

Grouping

Group 1: Enalapril 5 mg BD

Group 2: Enalapril 5 mg BD +vitamin C 100 mg OD

Group 3: Enalapril 5 mg BD +vitamin C 250 mg OD

Group 4: Enalapril 5 mg BD + vitamin C 500 mg OD

Total 160 patients with systolic blood pressure in the 140-179 mm Hg range and diastolic blood pressure in the 90- 109 mm Hg range with C-reactive protein levels in the 10-12 mg/dl range were recruited for the study out of 720 patients screened.

1) patient were given medication for two weeks 2) instructed to come fortnightly to collect the medication 3)patients were instructed to bring the empty foils at the end of 2 weeks to check the patients compliance 4) patient's blood pressure was recorded 5) detailed medical history and clinical examination was done 6) blood samples were collected for the estimation of C-reactive protein levels and routine hematological and biochemical parameters 7) patients were advised to report to the investigator as soon as possible in case of occurrence of any adverse effects 8)patients were instructed to report to the investigator in case of occurrence of any other illness and intake of other medications for the same. This study was undertaken to find out the efficacy and tolerability of vitamin C as an add-on therapy to the standard anti-hypertensive regimen.

Results

Out of 720 patients screened, 160 patients who fulfilled the inclusion and exclusion criteria were recruited for the study. They were randomized into four groups, group 1, group 2, group 3 and group 4, each consisting of 40 patients.

Table 1: Distribution of study subjects as per age

Groups	N	Mean	Std. deviation	ANOVA F-test
Group 1	40	44.22	6.88	F=0.42P=0.81 Not Significant
Group 2	40	44.97	9.87	
Group 3	40	47.01	7.23	
Group 4	40	45.14	6.81	
Total	160	45.66	7.33	

Table 1 shows distribution of study subjects as per age. In group 1, mean age was 44.22 ± 6.88 , group II 44.97 ± 9.87 , group III 47.01 ± 7.23 whereas in group 4 45.14 ± 6.81 . On comparison we found non-significant difference with P value.

Table 2: Comparison of SBP among all four group at different visit

Parameter	Groups								Test of significance
	Group 1		Group 2		Group 3		Group 4		
	Mean	SD	Mean	SD	Mean	SD	Mean	SD	
Baseline SBP	157.02	5.87	154.93	6.91	156.05	6.56	154.15	6.77	F=1.33P=0.25 (NS)
1-month SBP	153.11	5.75	148.11	5.97	147.11	6.23	144.04	7.12	F=10.54 P<0.01 (S)
3-month SBP	149.07	5.33	144.02	6.97	143.02	7.55	132.04	4.12	F=42.32, P=0.001 (S)
6-month SBP	137.13	6.98	127.11	15.71	120.13	20.12	119.33	3.23	F=11.13, P=0.001 (S)

Table 3: Comparison of DBP among all four group at different visit

Group

Parameter	Group 1		Group 2		Group 3		Group 4		Significance
	Mean	SD	Mean	SD	Mean	SD	Mean	SD	
Baseline DBP	90.77	3.97	89.54	3.75	90.11	2.98	90.88	4.12	F=0.89, P=0.39(NS)
1-month DBP	88.12	4.63	87.36	3.55	85.32	3.67	84.75	3.75	F=5.13P=0.01(S)
3-month DBP	84.69	4.01	54.19	3.02	83.77	2.79	79.36	2.45	F=21.82 P<0.01(S)
6-month DBP	81.22	4.63	80.54	3.12	78.98	3.74	75.71	2.23	F=22.01P=0.001(S)

Table 2 shows comparison of SBP among all four group at different visit. At baseline there was non-significant difference among all the four group with p value 0.25, whereas at all the visit at 1, 3 and 6 month there was significant difference among the four group with p value <0.01, <0.001 and <0.001.

Table 3 shows comparison of DBP among all four group at different visit. At baseline there was no significant difference among different groups in diastolic BP, whereas there was significant difference among all four groups at all 3 visit i.e 1, 3 and 6 months with p value <0.001.

Discussion

Vitamin C supplementation in hypertensive patients appears to possess modest effects on reducing both systolic and diastolic blood pressure. It has been previously estimated that a sustained 2 mmHg reduction of diastolic blood pressure is associated with 14% less stroke and 8% less coronary heart disease.¹⁷ From a public health standpoint this is important because the average weighted mean change in diastolic blood pressure observed in this analysis was 2.1 mmHg. But it should be clarified that the change in diastolic blood pressure observed within 12 of the 14 individual study groups was not large enough to be statistically significant, and hence may be nothing more than random fluctuations in blood pressure over time.

In our study 720 patients screened, 160 patients who fulfilled the inclusion and exclusion criteria were recruited for the study. They were randomized into four groups, group I, group II, group III and group IV, each group consisting of 40 patients. Group I received Enalapril 5 mg BD, group II received Enalapril 5 mg BD with vitamin C 100 mg OD, group III received enalapril 5 mg BD with vitamin C 250 mg OD and Group D Efficacy variables were assessed at baseline, at the end of the 1st month, at the end of the 3rd month, and at the end of the 6th month of the study, such as systolic blood pressure, diastolic blood pressure and C reactive protein levels. Other haematological studies such as full hemogram, blood sugar, blood urea, serum creatinine, measures of liver function such as SGOT, SGPT, serum alkaline phosphatase, total bilirubin, total protein, albumin were performed at baseline, at the end of the first month, at baseline, at the end of the first month received enalapril 5 mg BD with vitamin C 500 mg OD for a period of 6 months causes statistical significant reduction of systolic blood pressure of 12.5% at the end of 1st month, reduction of 20% at the end of 3rd month and 25% at the end of 6th month of the study.

At the end of the 1st month, 7.5 percent at the end of the 3rd month and 12.5 percent at the end of the 6th month of the study, 2.5 percent reduction in systolic blood pressure produced by Enalapril 5 mg BD. One analysis, comparing vitamin C supplementation of 500 mg/day for 1 month, showed a substantial decrease in systolic BP of 9.9 mm Hg.¹⁸ Another research found that once daily, vitamin C 500 mg created a 9 percent drop in blood pressure after 4 weeks of study.¹⁹⁻²¹ In this study, when a dose of 500 mg was given, with enalapril 5 mg BD causes

statistical significant reduction of diastolic blood pressure of 12.5% at the end of 3rd month and 15% at the end of 6th month of the study. Enalapril 5 mg BD alone group produces reduction of diastolic blood pressure of 7.5% at the end of 3rd month and 10% at the end of 6th month of the study. In our study, it has been found even though group III showed significant reduction of C reactive protein levels, only patients in group IV (vitamin C 500 mg) showed reduction of C reactive protein to the desirable level (<1mg/dl).

In our study, it was observed that when administered with enalapril 5 mg BD, vitamin C at a dosage of 500 mg once daily induces a decrease in C reactive protein levels to 50 percent at the end of the 1st month, 87.5 percent at the end of the 3rd month and 97.5 percent at the end of the 6th month, compared to enalapril 5 mg OD alone, in which the decrease in C reactive protein level was 0.25 percent at the end of the 6th month. One study showed that ingestion of vitamin C 250 mg/day and 500 mg/day showed significant reduction of C reactive protein levels at the end of 2 months.

Hence, it has been found even though vitamin C 100 mg and 250 mg group showed reduction of systolic and diastolic blood pressure, only patients in group 3 (vitamin C 500 mg) showed reduction of C reactive protein to desirable levels. Other hematological and biochemical parameters were measured at the baseline, at the end of 1st month, at the end of 3rd month and the end of 6th month and found to have no statistical difference among the study groups.

Conclusion

Vitamin C at the dose of 500 mg OD as an add on therapy to enalapril 5 mg BD causes significant reduction of both systolic and diastolic blood pressure, vitamin C 500mg OD supplementation to the standard anti-hypertensive drugs may produce better reduction of blood pressure, vitamin C 500 mg may be recommended as an adjuvant to regular anti-hypertensive regimen to reduce cardiovascular and cerebrovascular risks associated with hypertension.

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