Original Article

Modulation of Blood Pressure in Hypertensive Patients by Vitamin C

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Background: Essential hypertension is characterized by endothelial dysfunction, arterial stiffness, and increased oxidative stress. We evaluated the effect of short-term treatment with the antioxidant vitamin C on blood pressure in essential hypertensive patients.
Patients and Methods: A total of 50 participants with essential hypertension were evaluated before and after the study. They received 250 mg vitamin C twice daily for one month. Blood pressure, weight and height were measured before and after intervention. Body mass index was calculated and dietary pattern was assessed by using food frequency questionnaire and 24 dietary recalls.
Results: We observed a significant decline in both systolic blood pressure (138.1±12.7 vs 134.2±11.5 mmHg, $p<0.005$) and diastolic blood pressure (87.2±10.1 vs 85±8.8 mmHg, $p<0.005$) of the participants after one month of vitamin C intake. These effects were independent of patient's BMI .
Conclusion: Our results indicates that daily intake of 500 mg supplementary vitamin C (250mg twice daily) may have beneficial effects on blood pressure and thus reducing the risk of complications.

Key words: Vitamin C, Hypertension, Supplementation

Introduction

The hypothesis that anti-oxidant vitamins may exert potential protective effects against cardiovascular disease has long been the focus of considerable research.[1,2] Several biologic mechanisms have been proposed to explain the association of vitamin C with cardiovascular disease, including an antioxidative effect on LDL, lowering of blood pressure (BP), serving as a marker of other preventive factors or healthy behaviors, and possibly other as yet unknown mechanisms.[3-5] Several observational epidemiologic studies[6-8] have raised the possibility that agents with antioxidant properties (including the dietary antioxidants ß-carotene, vitamin C, and vitamin E) might play a potential role in reducing the risk of cardiovascular disease through lowering BP.

Several cross-sectional epidemiologic studies suggested that vitamin C status was inversely associated with BP.[2,3,9-11] Although some,[9,10] but not all,[12,13] intervention trials have suggested the lowering effect on BP of vitamin C, the scientific evidence is scarce, especially in Asian populations.

Based on proposed biological mechanisms and previous reports on vitamin C and BP, we

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compared BP in hypertensive participants before and after prescribing 250 mg, twice daily, of vitamin C.

Materials and Methods

Between March 2002 and August 2002, a total of of 50 participants with essential hypertension presented to the Motahari Clinic in Shiraz from March to August 2002 were studied with regard to changes in BP prior to and after receiving 250 mg vitamin C twice daily for a period of one month. High blood pressure, also called hypertension was defined as sustained systolic pressure over 140 mm Hg and/or diastolic blood pressure over 90 mm Hg on at least three separate occasions ,or the use of anti hypertensive medications. Criteria for case inclusion were: a) absence of any systemic disease b) age within the range of 35 – 65 years, c) no use of dietary supplements.

At the start of the study, participants were given an oral and a written explanation of the treatment and its benefits, and asked to provide a signed informed written consent.

The study protocol and ethical aspects were approved by the ethics committee of the Research Council of the Shiraz University of Medical Sciences.

Tablets containing 250 mg of vitamin C were obtained from the Daroupaksh Company (Tehran, Iran) and were given at a dose of 250mg twice a day. Participants were asked not to take any vitamin or mineral supplements during the trial. Researcher supervised the ingestion of the supplements.

All subjects underwent 24 hour blood pressure holter monitorings in the first and in the last day of the study.

Demographic data and history of any concurrent medical illness , medication, and vitamin and mineral supplementations were collected by interviews. Anthropometry and food consumption history were collected twice, at baseline and after completion of the procedure. All subjects underwent 24 hour blood pressure holter monitorings in the first and in the last day of the study. Body weight was measured to the nearest 0.1 kg using a Seca 713 scale while subjects were minimally clothed. Height was determined using measuring tape in subjects with bare feet, and body mass index was calculated by dividing weight (kg) by squared height (m^2). The food consumption pattern was evaluated by a 24-h dietary recall questionnaire and food frequency questionnaire. This questionnaire asked about the average frequency of intake of over 100 meals. Macro and micronutrient components were calculated by using Food Processor Software modified by incorporating the conventional Iranian diet.

Statistical analyses

The normality of distributions was checked for all variables. Differences between groups during supplementation were tested using paired t-tests, and variables not normally distributed were compared using the Wilcoxon test. Spearman correlation coefficient was used to test for possible correlation. Data were expressed as mean and standard deviation (SD) unless otherwise noted, and statistical significance was considered as $P<0.05$.

All statistical analyses were computed using SPSS version 11 for Windows (SPSS Inc., Chicago, 2001).

Results

The number of individuals included in the study was 50. After the start of the study, 15 individuals had to be excluded due to non- adherence and poor compliance. Thus, the study was performed on 12 males (34.3%) and 23 females (65.7%). Information about participants before and after intervention are represented in Table 1.

Mean age of the subjects was 51±0.3 years (range: 37-65 years) and mean height was 161.25± 9.21cm. As shown in Table 1, body mass index (BMI) was higher than normal, thus indicating a population of overweight males and females. The lack of a significant difference in BMI in both baseline and after completion of vitamin C supplementation indicated no change in weight of the participants during study.

Twenty-one subjects (60%) reported a familial history of hypertension and 3 (8.6%) were cigarette smokers. Twenty-nine participants (82.95%) used anti-hypertensive drugs to control their blood pressure; twenty-six used beta-blockers and three a combination of two or more drugs. We observed a significant decline in both systolic blood pressure (138.1±12.7 vs 134.2±11.5 mmHg, P<0.005) and diastolic blood pressure (87.2±10.1 vs 85±8.8 mmHg, P<0.005) of the participants after one month of vitamin C intake.

After one month of vitamin C intake, decline in diastolic blood pressure was correlated with the baseline diastolic blood pressure (r=-0.461, P=0.005); similarly decline in systolic blood pressure was correlated to the baseline systolic blood pressure (r=-0.34, p=0.043).

The analysis of 24-h dietary recall and food frequency questionnaire showed no significant difference between dietary intake in participants before and after study.

Discussion

This syudy shows that BP in hypertensive subjects is reduced following daily administration of 500 mg vitamin C supplement which is consistent with the results of previous studies. This effect was associated with a significant decline in both systolic and diastolic blood pressures which may persist for prolonged period.[15]

Previous studies have reported that vitamin C level is lower in hypertensive patient, compared to the general population.[16,17] Mayer Davis et al. reported that vitamin C level was unrelated to cardiovascular risk factors in long term[18] while Khaw et al. reported a significant association between plasma vitamin C levels and long term sequels of hypertension.[19] The results of more recent studies which have more rigorous and robust designs are generally in favor of a long-term effect of vitamin C supplementation and cardiovascular risk factors.[20,21]

Table 1. Characteristics of study participants at baseline and after one month supplementation (n = 35)

	Before study	After study
Weight (kg)	70.50 ± 12.50	70.00 ± 12.00
BMI (kg/m^2)	27.69 ± 4.35	27.21 ± 4.32
Systolic blood pressure (mmHg)	138.05 ± 12.73	134.17 ± 11.55
Diastolic blood pressure(mmHg)	87.20 ± 10.08	85.14 ± 8.77

Several mechanisms have been proposed for the blood pressure-reducing effect of vitamin C. As an antioxidant, it can interfere with production of free oxygen radicals and peroxides and also stimulate the synthesis of prostaglandins such as prostacyclin, which have a vasodilatory effect.[22] Also, vitamin C induces release of norepinephrine from adrenal glands, which reduces the plasma level of sodium.[22] Vitamin C is more than an antioxidant and its effects on neurotransmitters may contribute to its anti-hypertensive activity.[23]

Other studies suggest that this effect is possibly caused by restoring vasodilatory activity of nitric oxide[24] or by improving angiotensin II-induced endothelium-dependent vasodilation.[25] Both of these theories are consistent with the suggested pathophysiology of hypertension, which states that increased production of vascular reactive oxygen species, particularly the production of superoxide anions, contributes to the functional abnormalities in hypertension[26] and increasing vascular superoxide production by angiotensin-II.[27,28] In addition to enhancement of nitric oxide synthase activity, vitamin C also augments guanylate cyclase sensitivity to nitric oxide.[29] Finally, vitamin C may reduce insulin resistance which in turn causes endothelium-dependent, nitric oxide–mediated vasodilation.[30,31] Apart from its direct effect on hypertension, vitamin C attenuates hypertension-related conditions such as endothelial damage or arterial stiffness.[21,32] Increasing evidence suggests that arterial stiffness may be an important additional and independent risk factor for cardiovascular disease.[33] This indicates that vitamin C can play a similar role in non-systemic forms of high blood pressure. Indeed, vitamin C is shown to improve intrahepatic endothelial dysfunction in portal hypertension.[34] However, this is not always the case for example, although oxidative stress has been implicated in the pathogenesis of pre-eclampsia and vitamin C has been supposed to be the first antioxidant defense mechanism which is impaired in pre-eclampsia, no relationship was observed between dietary intake of vitamin C and the occurrence or outcome of pre-eclampsia.[35] Although high dose vitamin C has also been shown to have anti-hypertensive effects,[23] in most of the studies, the dosage of vitamin C supplementation was no more than 500 mg per day. As a water-soluble vitamin, ascorbic acid is safe at conventional doses and in regard to its other beneficial effects as well as its potential in reducing blood pressure, long-term vitamin C supplementation may be a cost-effective adjunctive therapy for patients with high blood pressure.

In summary, although, our study showed that vitamin C supplementation reduced blood pressure in hypertensive patients, because of the small sample size of this study, further studies employing larger population are warranted to confirm the results of present investigation.

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