Is vitamin C an effective antihypertensive supplement: a review and analysis of the literature

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CRD summary
The author concluded that vitamin C supplementation has a modest effect on reducing systolic and diastolic blood-pressure in patients with hypertension. Given the limitations of the literature search, the uncertain quality of the included studies and the failure to appropriately synthesise the results, the author’s conclusions should be interpreted with caution.

Authors’ objectives
To evaluate the evidence that vitamin C supplementation lowers systolic and diastolic blood-pressure (BP) in patients with hypertension.

Searching
MEDLINE was searched from January 1966 to October 2005; the search terms were reported. The bibliographies of retrieved papers were also checked.

Study selection
Experimental studies of vitamin C supplementation administered as a monotherapy in patients with hypertension were eligible for inclusion. The included studies were of vitamin C in doses ranging from 400 to 2,000 mg/day (median 500). The duration of administration in the included studies ranged from 4 to 12 weeks (median 6). In the majority of comparative trials vitamin C was compared with placebo; in one trial magnesium supplementation was used as a control. In the included studies, 52% of the participants were female and the mean age ranged from 43 to 73 years. Four studies were of patients with diabetes. Eligible studies had to measure systolic and diastolic BP; plasma vitamin C level was a secondary outcome in some studies. A variety of study designs were included in the review.

The author did not state how the studies were selected for the review, or how many reviewers performed the study selection.

Assessment of study quality
The author did not state that he assessed validity.

Data extraction
Changes in systolic and diastolic BP and plasma vitamin C levels from baseline were extracted. The author did not state how the data were extracted for the review, or how many reviewers performed the data extraction.

Methods of synthesis
The weighted mean baseline and post-treatment systolic BP and diastolic BP were calculated on the basis of population size. The difference between baseline and post-treatment means was calculated to give a measure of the reduction in BP. For plasma vitamin C levels, the difference between baseline and post-treatment levels was calculated for each study and the mean of these differences was reported. Individual study results were reported and some differences between the studies were discussed in a narrative synthesis, with accompanying data tables presented. A subgroup analysis comparing diabetic and non-diabetic study populations was also reported.

Results of the review
Thirteen trials of 14 separate study populations were included (n=284). There were 5 double-blind randomised controlled trials (RCTs; n=95), 2 single-blind RCTs (n=25), 3 double-blind crossover trials (n=97), 1 single-blind crossover trial (n=20) and 2 baseline comparison studies (n=47).

The weighted mean baseline and post-treatment systolic BPs were 149.6 (± 11.1) mmHg and 145.7 (± 11.0) mmHg.
respectively, representing a decrease of 3.9 mmHg. Seven of the 14 study populations showed a significant difference between baseline and post-treatment systolic BP (p-value ranged from p<0.001 to p<0.05).

The weighted mean baseline and post-treatment diastolic BP were 84.6 (± 4.4) mmHg and 82.5 (± 4.1) mmHg, respectively, representing a decrease of 2.1 mmHg. Only 2 studies found a significant reduction in diastolic BP between baseline and post-treatment (p=0.003, p=0.03).

Plasma vitamin C levels significantly increased in all 7 studies that measured it. The average change across all trials was 40.7 μmol.

A subgroup analysis comparing the 4 diabetic populations with the other 10 group populations found no significant differences between these groups on any of the outcome measures.

**Authors' conclusions**

Vitamin C supplementation of patients with hypertension has a modest effect in reducing systolic and diastolic BP.

**CRD commentary**

This review addressed a clear question, although inclusion criteria for the participants and study design were broad. Only one database was searched. Unpublished data does not appear to have been sought and it is unclear whether language restrictions were applied, therefore relevant studies might have been missed and publication and language bias introduced. There was insufficient information about the study selection and data extraction processes to rule out the possibility of error and bias. A validity assessment was not performed and there was insufficient study details for the reader to judge the internal or external validity of the included studies. The data were pooled to give mean baseline and post-treatment BP values and statistical heterogeneity was not assessed. The author, however, reported that clinical heterogeneity between the studies was a major limitation of the review, but data from the single arms of the trials were still pooled, which loses the benefits of randomisation and relevant comparisons. A more appropriate analysis would have focused on comparisons between the intervention and control groups in the comparative trials. Given the limitations of the literature search, the uncertain quality of the included studies and the failure to appropriately synthesise the results, the author’s conclusions should be interpreted with caution, especially given that the value reported is obtained by pooling data from one arm of controlled trials.

**Implications of the review for practice and research**

Practice: The author stated that supplementation with at least 500 mg/day of oral vitamin C for 6 weeks can lower systolic and diastolic BP. However, the review made no attempt to establish a relationship between response to treatment and dosage or duration of treatment.

Research: The author did not state any recommendations for further research.

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This is a critical abstract of a systematic review that meets the criteria for inclusion on DARE. Each critical abstract contains a brief summary of the review methods, results and conclusions followed by a detailed critical assessment on the reliability of the review and the conclusions drawn.