Is vitamin C an effective antihypertensive supplement? A review and analysis of the literature

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ABSTRACT
Objective: Hypertension is a common condition with high mortality from associated diseases. Epidemiological evidence suggests that a dietary deficiency of vitamin C may be a risk factor for hypertension. However the literature on vitamin C interventional trials appears divided on the efficacy of vitamin C utilization clinically.

Methods: A literature search and review of published trials using vitamin C in treating patients with hypertension was undertaken. Relevant references were located using MEDLINE (1966–2005) and the bibliographies of located articles.

Results: Thirteen trials making up 14 separate groups were identified and analyzed providing a pooled population of 284 hypertensive patients (52% female), with a weighted mean age of 58.8 ± 9.5 years. Median vitamin C dose and study intervention duration was 500mg/day and 6 weeks respectively. The weighted mean baseline and post treatment systolic blood pressures across all 14 groups were 149.6 ± 11.1 and 145.7 ± 11.0 mmHg respectively. This represented a systolic blood pressure decrease of 3.9 mmHg. Seven of the 14 groups ascertained statistically significant reductions (p < .05) in systolic blood pressures. However only 2 of the 14 groups found significant reductions in diastolic blood pressure. The weighted mean baseline and post treatment diastolic blood pressures across all 14 groups were 84.6 ± 4.4 and 82.5 ± 4.1 mmHg respectively. This represented a diastolic blood pressure decrease of 2.1 mmHg.

Conclusion: Vitamin C supplementation in hypertensive patients appears to possess modest effects on reducing systolic and diastolic blood pressure. (J Chiropr Med 2006;5:60–64)

Key Indexing Terms: Vitamin C; Ascorbic Acid; Blood Pressure; Hypertension

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.2–7 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.8–20 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.21 This study was undertaken in order to evaluate the current clinical evidence that vitamin C supplementation lowers both systolic and diastolic blood pressure in hypertensive individuals, and to also review the hypothesized mechanisms of action.

METHODS
A literature search using MEDLINE (January 1966 through October 2005) for published studies that examined the effects of vitamin C on blood pressure was performed using the terms [“Vitamin C” OR “Ascorbic Acid”] AND [“Blood Pressure” OR “Hypertension”]. Studies identified as experimental trials utilizing hypertensive subjects supplemented...
with vitamin C as a mono therapeutic were retrieved for analysis and additional publications were identified from the bibliographies of previously retrieved papers. Data was extracted from the published reports and the following items were entered into an Excel spreadsheet: study design; number of subjects; mean age or age range; vitamin C dose/day; duration of treatment; baseline and post treatment measures for systolic and diastolic blood pressure. Based on population size the weighted mean differences between baseline and post treatment measures for systolic and diastolic blood pressure were calculated and compared. Comparisons were not statistically analyzed because the standard deviation of weighted means does not reflect between-subject variances, but only between-study variances.

**RESULTS**

Thirteen trials\(^8\text{-}20\) making up 14 separate group populations were identified and analyzed providing a total pooled population of 284 hypertensive patients (52% female), with a weighted mean age of 58.8 ± 9.5 years and a weighted mean body mass index of 28.5 ± 1.9 Kg/m\(^2\). Median vitamin C dose and study intervention duration was 500mg/day and 6 weeks respectively (Table 1).

Seven of the 14 group populations ascertained significant differences (p < .05) between baseline and post treatment systolic blood pressure.\(^8\text{-}11,14,15,16,19\) The weighted mean baseline and post treatment systolic blood pressures across all 14 group populations were 149.6 ± 11.1 and 145.7 ± 11.0 mmHg respectively. This represented a systolic blood pressure decrease of 3.9 mmHg.

However, only 2 of the 14 groups found significant differences between baseline and post treatment diastolic blood pressure.\(^11,19\) The weighted mean baseline and post treatment diastolic blood pressures across all 14 group populations were 84.6 ± 4.4 and 82.5 ± 4.1 mmHg respectively. This represented a diastolic blood pressure decrease of 2.1 mmHg.

Of the 7 of 13 trials which recorded baseline and post treatment plasma vitamin C levels, all 7 showed significant increases in plasma vitamin C concentrations post treatment.\(^8\text{-}9,11,14,16,17,19\) The baseline plasma vitamin C levels ranged between 44 to 74 µmol, while the range in post treatment levels ranged between 78 to 122 µmol. The average change between baseline and post treatment levels was 40.7 µmol.

Five of the 13 trials utilized randomized double-blind placebo controlled parallel designs,\(^11,13,16,17,19\) 2 utilized randomized single-blind placebo controlled parallel designs,\(^15,20\) 2 utilized randomized double-blind placebo crossover designs,\(^10,14\) 1 used a single blind placebo crossover design\(^9\) and 1 more used a randomized double-blind cross-over design using supplemental magnesium for the other arm of the trial.\(^12\) The remaining two studies were baseline comparisons.\(^8,18\)

### Table 1

**Summary of Trials Investigating the Effect of Vitamin C on Blood Pressure**

<table>
<thead>
<tr>
<th>Author and Year [Ref]</th>
<th>Sample Size</th>
<th>Mean Age</th>
<th>Dose Vitamin C/Day (mg)</th>
<th>Study Design*</th>
<th>Duration (weeks)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Osilesi et al. 1991 [9]</td>
<td>20</td>
<td>57.8</td>
<td>1000</td>
<td>CO</td>
<td>6</td>
</tr>
<tr>
<td>Lovat et al. 1993 [10]</td>
<td>24</td>
<td>72</td>
<td>400</td>
<td>CO</td>
<td>4</td>
</tr>
<tr>
<td>Gokce et al. 1999 [13]</td>
<td>21</td>
<td>56</td>
<td>500</td>
<td>RCT</td>
<td>4</td>
</tr>
<tr>
<td>Fotherby et al. 2000 [14]</td>
<td>17</td>
<td>72</td>
<td>500</td>
<td>CO</td>
<td>12</td>
</tr>
<tr>
<td>Rolla et al. 2000 [15]</td>
<td>8</td>
<td>49.9</td>
<td>1000</td>
<td>RCT</td>
<td>4</td>
</tr>
<tr>
<td>Duffy et al. 2001 [16]</td>
<td>19</td>
<td>48</td>
<td>500</td>
<td>RCT</td>
<td>4</td>
</tr>
<tr>
<td>Darko et al. 2002 [17]</td>
<td>18</td>
<td>55.5</td>
<td>1500</td>
<td>RCT</td>
<td>4</td>
</tr>
<tr>
<td>Hajjar et al. 2002 [18]</td>
<td>24</td>
<td>62</td>
<td>1000</td>
<td>BC</td>
<td>12</td>
</tr>
<tr>
<td>Mullan et al. 2002 [19]</td>
<td>15</td>
<td>61</td>
<td>500</td>
<td>RCT</td>
<td>4</td>
</tr>
<tr>
<td>Magen et al. 2004 [20]</td>
<td>17</td>
<td>52.6</td>
<td>500</td>
<td>RCT</td>
<td>8</td>
</tr>
</tbody>
</table>

* BC (Baseline Comparison); CO (Cross Over); RCT (Randomized Controlled Trial)
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. 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.

Regardless of the observed statistical significant findings within individual studies, the pooled effects of vitamin C supplementation on the reduction of both systolic and diastolic blood pressure is consistent with epidemiologic observations that there exists an inverse relationship between blood pressure and plasma vitamin C status. This finding supports that a modest change in mean population vitamin C intake has the potential to positively impact cardiovascular disease rates in the population.

In regard to mechanism of action, hypertension is associated with higher than normal lipoperoxidation and an imbalance in antioxidant status, suggesting that oxidative stress is an important driving factor in the pathogenesis of hypertension. Hypertension has been shown to be associated with impaired nitric oxide (NO) production. Vascular endothelium derived nitric oxide (eNOS) plays a critical role in the regulation of vascular tone and it appears that vitamin C can improve endothelium vasodilation by augmenting NO bioavailability. However, it has been reported that supraphysiological concentrations of vitamin C are required to prevent the superoxide radical destruction of NO. Vitamin C may also increase NO production by enhancing eNOS activity. This effect appears to be mediated through increasing the intracellular content of tetrahydrobiopterin. Tetrahydrobiopterin is as a cofactor for eNOS which requires vitamin C for stabilization as well as protection from oxidation (figure 1). These effects were

Table 1

<table>
<thead>
<tr>
<th>Systolic Blood Pressure</th>
<th>Diastolic Blood Pressure</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>BEFORE</strong></td>
<td><strong>AFTER</strong></td>
</tr>
<tr>
<td>143.9</td>
<td>136.3</td>
</tr>
<tr>
<td>139</td>
<td>128.8</td>
</tr>
<tr>
<td>173</td>
<td>168</td>
</tr>
<tr>
<td>173.2</td>
<td>162.9</td>
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<tr>
<td>139</td>
<td>143</td>
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<tr>
<td>149</td>
<td>155</td>
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<tr>
<td>145</td>
<td>142</td>
</tr>
<tr>
<td>149</td>
<td>145.3</td>
</tr>
<tr>
<td>150.6</td>
<td>141.2</td>
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<tr>
<td>155</td>
<td>142</td>
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<tr>
<td>141</td>
<td>141</td>
</tr>
<tr>
<td>144</td>
<td>140</td>
</tr>
<tr>
<td>142.1</td>
<td>132.3</td>
</tr>
<tr>
<td>150.6</td>
<td>150.6</td>
</tr>
</tbody>
</table>
evident as an increase in the half-life of tetrahydro- 
bipterin inside the endothelial cell has been ob-
served.\textsuperscript{35}

If the antihypertensive effects of vitamin C are due 
to its antioxidant properties, then antioxidants other 
than vitamin C should also show antihypertensive 
properties. However, the results of 3 randomized 
trials to test the effects of vitamin E on hypertension 
have proven disappointing.\textsuperscript{36,37,38} One explanation 
for the negative results may be in part due to the 
use of vitamin E as a sole antioxidant. When vita-
min E reacts with a free radical, it subsequently 
becomes a free radical, which itself may participate 
in pro-oxidative events leading to LDL oxidation 
and subsequent NO inactivation. However under 
normal dietary conditions vitamin C regenerates vi-
tamin E and therefore reduces the pro-oxidant load. 
Only one clinical trial has investigated a combined 
antioxidant trial using vitamin C and E on hyper-
tension. This trial found a significant reduction in 
systolic blood pressure (168.7 to 159.7mmHg) but a 
non-significant decrease in diastolic blood pressure 
(89.3 to 85.5 mmHg).\textsuperscript{39}

A major limitation of this study is the pooling 
together of clinical trials which include a considerable 
amount of heterogeneity in design and population 
characteristics. Average subject age varied between 
43 and 73 years and it is known that vitamin C 
concentration in serum decreases with aging, while 
a concomitant increase in blood pressure occurs.\textsuperscript{40} 
Differences in age and dietary characteristics may 
result in unevenly matched baseline plasma vitamin 
C concentrations. In the 7 studies which observed 
plasma vitamin C concentrations, the range varied 
between 44 to 74 µmol. This may confound both 
the starting baseline blood pressures as well as the 
absorbability of vitamin C supplementation which is 
dependent upon pre-absorption plasma concentra-
tions. Also, not having evenly matched baseline 
blood pressures could confound the results as popu-
lations with higher baseline blood pressures could 
possible exhibit more of a hypotensive effect with 
vitamin C supplementation.

Confounders also included differences between 
studies with vitamin C supplementation dose 
(ranged between 400 to 2000mg/day) and study 
duration (ranged between 4 to 12 weeks). Finally, 
subject characteristics such as populations with and 
without type 2 diabetes could result in differences in 
how the individual populations respond to vitamin 
C supplementation. Diabetic patients have greater 
levels of oxidative stress than other groups of pa-
tients at risk of cardiovascular disease\textsuperscript{41} and there-
fore may respond more favorably to vitamin C 
supplementation. Previous studies using type 2 dia-
betics has revealed diminished tissue levels and im-
paired vitamin C recycling mechanisms.\textsuperscript{42} However, 
when comparing the 4 group populations\textsuperscript{12,17,19} 
comprised of diabetic subjects against the remaining 
10 group populations, there was no observable dif-
ference between changes in systolic or diastolic 
blood pressure after vitamin C supplementation be-
tween these two groups.

**CONCLUSIONS**

This analysis and review has shown that supple-
mentation with at least 500mg/day of oral vitamin C 
for 6 weeks can lower both systolic and diastolic 
blood pressure, which is known to result in a reduc-
tion in the incidence of cardiovascular disease and 
death due to cardiovascular complications. Al-
though the reduction in systolic and diastolic blood 
pressure was modest with vitamin C supplementation, 
yet any decrease will be beneficial especially in 
light of the low cost and absence of toxicity within 
ranges of 500 to 1000mg/day.\textsuperscript{43}

**REFERENCES**

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2. Yoshioka M, Matsushita T, Chuman Y. Inverse association of serum 
ascorbic acid level and blood pressure or rate of hypertension in male 


