The efficacy of vitamin C supplementation on reducing total serum cholesterol in human subjects: a review and analysis of 51 experimental trials

McRae M P

CRD summary
The author concluded that vitamin C is effective in reducing total serum cholesterol levels, particularly in patients with very high total serum cholesterol levels who also have low plasma vitamin C levels. The data presented are not sufficient to support this assertion and, given the methodological limitations of the review, the author's conclusions should be interpreted with caution.

Authors' objectives
To evaluate the efficacy of vitamin C supplementation in reducing total serum cholesterol in patients with high serum cholesterol levels (greater than 240 mg/dL).

Searching
MEDLINE was searched from inception to December 2004; the search terms were reported. Further publications were identified from the bibliography of retrieved papers. The search was restricted to published studies.

Study selection
Studies of vitamin C supplementation were eligible for inclusion. The dosage of vitamin C administered in the included studies ranged from 300 to 5,000 mg/day. The duration of the intervention ranged from 2 to 48 weeks. Inclusion criteria for the participants were not defined. The mean age of participants in the included studies ranged from 20 to 81.8 years, the mean baseline total serum cholesterol ranged from 156.8 to 337 mg/dL, and the mean baseline plasma vitamin C levels ranged from 0.35 to 1.58 mg/dL. Studies that assessed total serum lipids were eligible for inclusion. The outcomes reported in the included studies were change in total serum cholesterol and change in plasma vitamin C levels. Inclusion criteria for the study design were not specified. Experimental studies of a variety of designs were included in the review.

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

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

Data extraction
For each study, baseline and post-treatment measures of total serum cholesterol and plasma vitamin C were extracted and entered into an Excel spreadsheet. A percentage change from baseline was then calculated for total serum cholesterol and plasma vitamin C in each study.

The author did not state how many reviewers performed the data extraction.

Methods of synthesis
Correlation coefficients were calculated for baseline total serum cholesterol versus percentage change in cholesterol, for baseline plasma vitamin C versus change in total serum cholesterol, and for change in cholesterol versus change in plasma vitamin C. The method used was not specified. The studies were stratified into four groups based upon mean baseline total serum cholesterol levels, with data from each category pooled across studies: normal (total serum cholesterol <199 mg/dL), borderline-high (total serum cholesterol 200 to 239 mg/dL), high (total serum cholesterol 240 to 280 mg/dL) and severe (total serum cholesterol >280 mg/dL). Within each of these groups, weighted mean differences (WMDs) from baseline for total serum cholesterol and plasma vitamin C levels were compared.
Results of the review
Fifty-one studies (n=1,666) were included for review. A variety of study designs were included, of which six were double-blind placebo-controlled parallel-design randomised controlled trials (RCTs; n=150).

The methodological quality of the included trials was not formally assessed, however the author stated that many of the included trials lacked randomisation and blinding, had small sample sizes and short treatment durations.

A higher baseline serum cholesterol level was associated with a greater decrease in total serum cholesterol (correlation coefficient = -0.585, p=0.000). Higher baseline vitamin C levels appeared to be associated with a greater decrease in total serum cholesterol (correlation coefficient 0.500, p=0.003), although this is unclear as the axes of the graph appear to have been mislabelled. There was no association between change in total serum cholesterol and change in plasma vitamin C levels.

When studies were compared according to the baseline total serum cholesterol levels, the group with the most severe baseline cholesterol demonstrated the greatest percentage reduction in total serum cholesterol levels (WMD 14.30 ±8.3) compared with the normal cholesterol (WMD 0.91 ±6.8) and borderline high cholesterol groups (WMD 3.90 ±5.78). The most severe cholesterol group also had the lowest baseline vitamin C levels (weighted baseline plasma vitamin C: 0.55 ±0.19 mg/dL versus 1.24 ±0.17 mg/dL in the normal cholesterol group).

Authors’ conclusions
The author appears to conclude that vitamin C is effective in reducing total serum cholesterol levels, particularly in patients with total serum cholesterol levels greater than 280 mg/dL who also have plasma vitamin C levels of less than 0.6 mg/dL.

CRD commentary
The review question was unclear. Broad inclusion criteria were stated for the intervention and outcomes. However, the inclusion criteria for participants and study design do not appear to have been determined a priori. The search was limited to published studies in one database, therefore relevant studies might have been missed and publication bias introduced. There was insufficient information to rule out the possibility of error and bias in the study selection and data extraction processes. The validity of the included studies was not formally assessed. However, the majority of the included studies were of less rigorous design and the author highlighted several methodological weaknesses that undermine the validity of the results. Data were extracted from the single arms of trials, thereby losing the randomisation and relevant comparisons. Furthermore, statistical heterogeneity was not assessed and the use of correlation does not permit inferences about causal relationships. A more appropriate analysis would have focused on the differences between the intervention and control groups in the controlled trials. Given the limitations in the literature search, apparent poor quality of many included studies, and failure to appropriately synthesise the results, the author’s conclusions should be interpreted with caution.

Implications of the review for practice and research
Practice: The author stated that daily supplementation of at least 400 mg of vitamin C for people with total serum cholesterol levels of greater than 240 mg/dL may possess substantial health benefits.

Research: The author stated that further randomised double-blind placebo-controlled trials are required in high to severe hypercholesterolaemic patients, particularly in those patients who also have low plasma vitamin C levels.

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**Record Status**
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.