Dietary supplements for the prevention and treatment of coronary artery disease

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CRD summary
With the exception of support for the use of policosanol and garlic for hyperlipidaemia, the authors revealed an inconclusive evidence base. The complexity of this topic area, together with some methodological limitations of the review process, means that the extent to which the conclusions are reliable is unclear.

Authors’ objectives
To evaluate dietary supplements for the prevention and treatment of coronary artery disease.

Searching
MEDLINE, ProQuest and the Cochrane Library were searched from May 2004 to May 2006 for relevant studies published in the English language; the search terms were reported. The reference lists of relevant papers were screened for further studies.

Study selection
Study designs of evaluations included in the review
Double-blind, randomised placebo-controlled trials of more than 1 week’s duration were eligible for inclusion in the review.

Specific interventions included in the review
Studies of isolated dietary supplements were eligible for inclusion. Combination therapies, diet-based treatments (e.g. soy, fish oil, stanols and linoleic acid), niacin, and red yeast rice (Cholestin, Provo, UT) were excluded from the review. The included interventions were beta carotene, coenzyme Q10 (CoQ10), vitamin E, blackcurrant seed oil, calcium, garlic, hawthorn, magnesium, vitamin C, artichoke extract, chromium, gugul, magnesium-pyridoxal-phosphate-glutamate, policosanol and red clover. The duration of treatment ranged from 3 weeks to 12 years. A wide range of daily doses were reported in the paper.

Participants included in the review
There were no inclusion criteria for the participants. Details of the participants included in the review were not reported, although it was reported that the populations were variable.

Outcomes assessed in the review
Studies that assessed hypercholesterolaemia, hypertension, or the incidence of cardiac events were eligible for inclusion. Adverse events were also reported in the included studies.

How were decisions on the relevance of primary studies made?
It appears that the study selection process was carried out independently by two reviewers only in the event of uncertainty about inclusion. Any disagreements were resolved by consensus.

Assessment of study quality
The quality of the included studies was assessed using the Jadad scale, which considers the method of randomisation, blinding and drop-outs. Studies were scored up to a maximum of 5, which represented the highest quality. It appears that the validity assessment was carried out independently by two reviewers only in the event of uncertainty about quality scoring. Any disagreements were resolved by consensus.

Data extraction
The authors did not state how the data were extracted for the review, or how many reviewers performed the data extraction. Data were extracted on cardiovascular events (including deaths) expressed as percentages or relative risks; percentage changes in systolic and diastolic blood-pressures (BP); and in low- and high-density lipoprotein levels (LDL and HDL, respectively), and total cholesterol. The p-values were reported. Authors were contacted for additional
information where necessary.

**Methods of synthesis**

How were the studies combined?
The trials were grouped by outcome and intervention and combined in a narrative.

How were differences between studies investigated?
Differences between the trials were explored in the tables and text.

**Results of the review**

Ninety-two trials (approximately 129,000 participants) focusing on 15 dietary supplements were included in the review.

Overall, 5 trials achieved a quality of score of 5. The scores ranged from 2 to 5.

**Cardiac outcomes.**

All 3 trials of beta-carotene (n=85,091) reported no effect on cardiovascular outcomes; beta-carotene was associated with an increased risk of lung cancer in one of the included trials. Both trials of CoQ10 (n=217) found a statistically significant decrease in total cardiac events (p<0.02). One of 5 trials of vitamin E reported a significant decrease in major coronary events (n=1,035; p=0.005); the other four reported no effect on cardiovascular events. The highest quality scores (4) were in trials of vitamin E.

**Hypertension.**

Four of the 12 trials of calcium supplementation reported statistically significant reductions in either systolic or diastolic BP, or both (n=218; p<0.05); the other studies reported no change. Both trials of CoQ10 reported significant decreases in BP (n=142; p<0.05), as did both trials of garlic (n=107; p<0.05). Four of the 10 trials of magnesium supplementation reported some reductions in BP (n=144; p<0.05). The most frequent side-effect of magnesium was reported to be loose stools. Three trials of vitamin C supplementation (n=94) reported mixed results. One small trial (n=70) evaluating vitamin E reported reductions in systolic and diastolic BP (p<0.05). Small trials of blackcurrant seed and hawthorn reported no change in BP. The highest quality score (5) was in a trial of CoQ10.

**Hyperlipidaemia.**

Sample sizes in these studies ranged from 19 to 589. The highest quality scores (5) were found in trials of gugul and policosanol. Two trials of gugul (n=146) reported mixed results. Most of the 22 trials of policosanol reported a significant reduction in LDL (p<0.05). Ten trials reported increases in HDL (p<0.05); the other eight reported no effect. Three trials of magnesium-pyridoxal-phosphate-glutamate (n=255) reported mixed results. Seven of the 18 trials of garlic reported positive effects, mostly reductions in total cholesterol and LDL, with little effect on HDL (n=555; p<0.05). The only trial of artichoke extract (n=143), both trials of chromium (n=104) and the only trial of vitamin E (n=60) reported positive effects (p<0.05). Two trials of red clover (n=119) reported no effects. The reported side-effects in all trials with positive effects on this condition were found to be mild, infrequent, or similar to placebo.

**Authors' conclusions**

The evidence for dietary supplements is largely inconclusive. The most support was for the use of policosanol and garlic, both for hyperlipidaemia.

**CRD commentary**

The review addressed a complex topic area which was supported by some detailed inclusion criteria in all aspects, except for participants. The omission of the latter, and the absence of participant details in the included studies, means that it would be difficult to comment on the generalisability of the findings. The search strategy seemed lacking in potential sources of complementary therapies, and the restriction to articles published in English means that relevant studies might have been missed and biases introduced. An appropriate validity assessment tool was used, and the
relative quality of the studies was highlighted in the discussion of the findings. Adequate details of the interventions were provided, which revealed substantial heterogeneity amongst the included studies. The potential for biases in the review process cannot be ruled out, as the studies appear to have been selected and appraised independently only in the event of uncertainty. The authors’ conclusions reflect the evidence presented but, given some of the methodological limitations mentioned, the extent to which they are reliable is unclear.

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

Practice: The authors did not state any implications for practice.

Research: The authors stated that more research is needed to establish and standardise the active ingredients in herbal supplements, and also to assess the efficacy and safety of these interventions.

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