Heart, Lung and Circulation (2015) **24,** 736–739
1443-9506/04/$36.00
http://dx.doi.org/10.1016/j.hlc.2015.05.007

EDITORIAL

Supplements and Cardiovascular Health

Rosemary A Stanton, OAM PhD, APD. AN *

School of Medical Sciences, University of New South Wales, Sydney, NSW, Australia

Received 18 May 2015; accepted 23 May 2015; online published-ahead-of-print 9 June 2015

Keywords Supplements • Omega 3 fatty acids • Antioxidants • Choline • L-carnitine • Red yeast rice

Seven years ago, the Heart Foundation recommended supplements of long-chain omega-3 polyunsaturated fatty acids for primary and secondary prevention of cardiovascular disease [1]. Their recent review of the evidence from randomised controlled trials revises this position and favours foods as the ideal sources of omega 3 fatty acids. For eicosapentaenoic acid (EPA) and docosahexaenoic acid (DHA), the recommendation is to eat fish; for alpha linolenic acid (ALA), choose walnuts, linseeds (also known as flaxseeds), and canola or soybean oils [2].

Omega 3 supplements are popular, with projected growth in sales estimated to reach a market value of $US 34.7 billion by 2016 [3]. Internet sites recommend (and market) omega 3 supplements not just for heart health, but also for building muscle and helping with fat loss, reducing the risk of various cancers, diabetes, asthma and arthritis, and as treatment for age-related cognitive decline, Alzheimer's disease, depression and attention-deficit hyperactivity disorder. Long chain omega 3 fatty acids, DHA and EPA, remain a valid treatment for hypertriglyceridaemia [2] and rheumatoid arthritis [4], may have modest but positive benefits in patients with heart failure and do not appear to have any adverse effects [2]. However, these supplements are expensive, and the Heart Foundation's advice to choose foods as sources of omega 3 fatty acids could save money for individuals and also increase the healthfulness of the total diet.

Many other supplements claiming benefits for cardiovascular disease are sold in supermarkets, pharmacies, health food stores and online sites and promoted on internet sites by sellers, some medical doctors, naturopaths, sportspeople, fitness coaches and authors of popular books and blogs. The offerings include a range of antioxidant vitamins and pills containing antioxidants extracted from plants, coenzyme Q10, choline, L-carnitine, garlic and red yeast rice. Is the popularity of many of these supplements matched by evidence of their efficacy?

Antioxidants

The Heart Foundation examined the evidence for antioxidant supplements in 2010 [5] and did not recommend vitamins E and C, carotenoids and other antioxidants, or combinations of any of these for the prevention or treatment of cardiovascular disease. The Foundation also noted concern over whether high doses (>800 IU/day) of vitamin E supplements might increase the risk of cardiovascular disease. As with the current omega 3 review [2], their recommendations favoured foods including fruit, vegetables, green or black tea and cocoa made from raw cocoa powder (but not chocolate, coffee or red wine) as ideal sources of antioxidants [5].

Meta-analyses have consistently found that antioxidant supplements do not offer protection against mortality. Indeed, Cochrane reviews have shown that beta carotene, vitamin E and higher doses of vitamin A may be associated with increased mortality [6]. Looking specifically at prevention of cardiovascular disease, a recent meta-analysis of 50 randomised control trials involving 156,663 people in intervention groups and 137,815 in control groups also reported no evidence to support the use of vitamin and antioxidant supplements [7].

Lack of evidence hasn't dinted the popularity of vitamin and antioxidant supplements with the public or those supplying supplements. Indeed, in response to yet another negative report, a chief executive in the vitamin industry notes that, ''The thing to do with these reports is just ride them out . . . We see no impact on our business'' [8].

To the public, oxidation is seen as 'bad', generating free radicals that attack cell membranes and the lining of arteries.

*2866 Moss Vale Road, Barrengarry 2577. Tel.: +61 2 4465 1711 Email: rosemary.stanton@westnet.com.au

Antioxidants neutralise free radicals and are therefore seen as 'good'. Once that idea is established, it may be extrapolated to the idea that the more consumed, the better. It is ironic that consumption of antioxidant foods such as vegetables continues to fall while supplement sales rise.

Co-enzyme Q10 (CoQ10)

Also known as ubiquinone, or as its reduced form, ubiquinol, CoQ10 is a powerful antioxidant produced within the body. Among its many roles, CoQ10 is essential for the synthesis of ATP in mitochondria, acts as an antioxidant in lipoproteins and is especially important in organs with high energy requirements such as the heart, liver and brain. Supplements of CoQ10 are popular with sportspeople (especially ubiquinol which sells at about three times the price of ubiquinone) but are also promoted to prevent or treat cardiovascular disease.

A recent Cochrane review (2014) found few studies of CoQ10 supplementation and primary prevention of cardiovascular disease [9]. Six small studies with 20-52 subjects were identified. One study had incomplete outcome data, another had high risk of bias for selective reporting and all were unclear for selection bias. The studies look at the effect of supplements adding 100-200 mg of CoQ10 a day. One trial with 51 subjects found no effect on blood pressure, total cholesterol, HDL cholesterol or triglycerides. Another small trial of 20 people reported a reduction in systolic blood pressure but with large confidence intervals. The remaining four trials gave CoQ10 with statin therapy. In three, the CoQ10 had no effect while the fourth found an increase in total and LDL cholesterol, with no change in HDL cholesterol or triglycerides. As expected, the authors noted that longer trials with more subjects are needed to determine effects on cardiovascular events.

Some evidence favours supplements of CoQ10 taken before cardiopulmonary bypass surgery, although the first systematic review on this topic concluded that better quality randomised controlled trials are needed to clarify the role of this supplement [10]. There are also suggestions that impaired CoQ10 synthesis might be responsible for muscular side-effects caused by statins. However, a recent meta-analysis found no significant benefit from CoQ10 supplements in improving statin-induced myopathy [11] and a new randomised controlled trial confirms that while CoQ10 levels are reduced during statin therapy, no significant difference in the reduction in CoQ10 levels occurred between patients with or without myopathy [12]. The authors suggest that measuring CoQ10 levels in serum may not be a useful marker to predict statin-induced myopathy.

Some inconsistencies also exist with measurements of plasma levels of CoQ10 in individuals of different ages with varying levels of physical activity. Among young people, more physical activity may correlate with lower CoQ10 levels in plasma, but in older people, higher levels of physical activity are related to higher plasma levels of CoQ10 [13]. More physical activity in older people may thus negate any need for supplements of CoQ10.

Those seeking to increase CoQ10 via 'superfoods' may also be disappointed. The best food sources include organ meats, fish, and soy and olive oils [14], but note that these foods provide only a fraction of the amount produced within the body, or provided by supplements. Until further research into CoQ10 is published, convincing evidence that this is a worthy supplement remains elusive. Like omega 3 fatty acids, and unlike some antioxidant vitamins, there is no suggestion that CoQ10 supplements are harmful. But nor is there evidence that CoQ10 supplements deserve tags such as ''the miracle antioxidant'' or the ''essential spark in the production of energy''.

Choline

Once thought to be part of the B vitamin complex, choline has an essential role in membrane structure and the metabolism of lipids. A deficiency has been associated with non-alcoholic fatty liver disease. Choline is widely distributed in foods, especially liver, egg yolk, meat and fish and is also found in processed foods which include added lecithin (phosphatidylcholine) such as commercially produced mayonnaise, ice cream, chocolate and baked goods. Choline is also promoted to the public as a supplement for prevention of heart disease, although some are questioning the wisdom of high doses. The discussion involves gut microbes which convert choline to trimethylamine, which is further metabolised in the liver to trimethylamine-N-oxide (TMAO). TMAO is thought to promote atherosclerosis by increasing the transformation of macrophages into foam cells and increasing cholesterol deposits in arterial lesions [15]. In a large clinical cohort study, a high dietary source of choline (two large egg yolks) significantly increased plasma levels of TMAO and after adjustment for relevant risk factors, this was a significant predictor of the risk of major adverse cardiovascular events in those with high or low overall risk [16]. Choline supplements may be unwise.

L-Carnitine

Found in high quantities in red meat and also made in the liver and kidneys from lysine and methionine, L-carnitine is promoted to the public for prevention of heart disease. Recent studies from the same group investigating the effects of choline suggest that gut microbes may also metabolise L-carnitine to TMAO [17] and that this reaction may be at least partly responsible for the higher levels of atherosclerosis observed with high consumption of red meat [18]. Vegetarians given deuterium-labelled L-carnitine also show greater increases in TMAO compared with subjects who normally consume meat [18]. The mechanism for the atherogenic effects of TMAO appears to act through changes in cholesterol and sterol metabolism [18]. These early investigations need confirmation but suggest caution in the use or promotion of choline or L-carnitine supplements in those at risk of cardiovascular disease.