ABSTRACTS

PREVENTING AND TREATING HEART DISEASE NATURALLY

An interesting review in the *British Medical Journal* of 3 January 2004[1] examines the role of omega 3 fatty acids in cardiovascular disease, looking for something other than the expensive interventions with statins and other drugs. As one correspondent in the Rapid Response section pointed out, the authors failed to mention physical activity as an important part of the primary and secondary prevention of cardiovascular disease, but the review is very useful nonetheless.

It is becoming increasingly clear that omega 3 fatty acids from fish and fish oils can protect against coronary heart disease. However, there are still several areas of uncertainty. The optimal intake of omega 3 fatty acids is not yet established, nor is their mechanism of action. Some studies are equivocal, and there are concerns about environmental pollution in fatty fish. The authors have set out to review the current evidence regarding fish oils and cardiovascular disease, their possible mechanism of action and the potential future research developments and strategies.

The association between omega 3 fatty acids and cardiovascular disease was established when the Danish investigators Dyerberg *et al.*[3] suggested that the low rate of coronary artery disease in Greenland Inuit people was due to the high content of omega 3 fatty acid in their diet, which consisted mainly of fish, seal and whale. Humans need to obtain omega 3 fatty acids from their diet as we lack the enzymes necessary to convert the omega 6 fatty acids found in vegetables to omega 3 oils. Alpha-linoleic acid (ALA) is found in certain vegetables, but eicosapentanoic acid (EPA) and docosahexanoic acid (DHA) are found in fish and fish oils. Their review is limited to the two marine-derived omega 3 fatty acids.

Most studies have found that the higher the amount of fish in the diet, the lower the risk of cardiovascular disease. There also appears to be a reduced risk of sudden death associated with consumption of fish and higher blood levels of omega 3 fatty acids.

The possible mechanisms of action of omega 3 fatty acids are:

- Antiarrhythmic — studies have not yet demonstrated a direct antiarrhythmic effect in humans and trials are currently underway using implantable defibrillators in patients.
- Antithrombotic — the effects of omega 3 fatty acids on platelet function and thrombosis are controversial. Large doses reduce platelet aggregation, but smaller amounts have more modest effects. Omega 3 fatty acids have inconsistent effects on fibrinolysis and little effect on blood coagulability.
- Atherosclerotic — atherosclerosis may be influenced by omega 3 fatty acids. Fish oils fed to animals inhibit the progression of atherosclerotic plaques. In humans supplementation with omega 3 fatty acids resulted in modest improvements in atherosclerosis. A recent study showed that patients waiting for carotid endarterectomy who were given fish oils had plaque which was more likely to have a thick fibrous cap and less inflammatory infiltrate, making it possibly less liable to rupture.
- Inflammatory — omega 3 fatty acids have recognised anti-inflammatory actions, which may contribute to their beneficial effects in cardiovascular disease, although the mechanism is far from clear.
- Endothelial — omega 3 fatty acids improve endothelial function in persons with established cardiovascular disease or established risk factors.
- Blood pressure lowering — fish oils can produce a modest reduction in blood pressure, possibly through their effects on endothelial function.
- Triglyceride lowering — omega 3 fatty acids reduce triglyceride concentrations in a dose-dependent manner. Their effect on cholesterol is small and of uncertain clinical importance.

The American Heart Association recommends that patients with known coronary heart disease should eat a variety of (oily) fish at least twice weekly and take 1 g EPA and DHA daily, preferably from oily fish, or from supplements in consultation with a doctor. Those with hypertriglyceridaemia should take 2 - 4 g EPA and DHA daily, provided as capsules by their doctor.

The authors point out that current consumption of marine-derived omega 3 fatty acids is low and that oily fish such as mackerel, herring, tuna, salmon, sardines and trout are rich sources of these oils. However, they also mention the concerns about declining fish stocks, which will be under even more pressure if the benefits of fish oils in cardiovascular disease are confirmed and suggest other possible sources of omega 3 fatty acids through supplementing animal feed, enriching available foods or biotechnology.

1. Din JN, *et al. BMJ* 2004; **328:** 30-35.
2. Dyerberg J, *et al. Am J Clin Nutr* 1975; **28:** 958-966.

THE BENEFITS OF INTENSIVE INSULIN THERAPY IN TYPE 1 DIABETES

The ability of intensive insulin therapy to prevent microvascular complications in type 1 diabetes is now well established. What is not known is whether these benefits persist when insulin therapy becomes less intensive and begins to approximate that of conventional treatment.

In a randomised controlled trial,[1] 1 441 patients with type 1 diabetes were randomly assigned to receive either intensive insulin therapy to achieve normal glycosylated haemoglobin (HbA_{1c}) levels or conventional therapy (1 or 2 daily injections) without specific goals for glycaemic control. Patients had to have currently normal renal function and no advanced diabetic complications. After completion of the trial, the cohort who had been receiving intensive therapy were encouraged to continue it, and those on the conventional arm were encouraged to switch to intensive treatment. The patients were assessed for renal outcomes over 7 - 8 years.

After completion of the initial randomised controlled trial, those in the intensive therapy arm had significantly lower HbA_{1c} levels and a lower incidence of microalbuminaemia than those who received conventional treatment, although glomerular filtration and creatinine clearance were identical in both groups. As the study progressed the difference in HbA_{1c} levels between the 2 groups narrowed, but remained statistically significant. However, the interesting point is that patients in the intensive treatment group had significantly lower incidences of microalbuminaemia, clinical albuminuria, hypertension and improved creatinine levels.

This study suggests that the benefits of strict glycaemic control on renal function are long-lasting. Similar results have been found with diabetic retinopathy. However, the authors point out that high motivation is needed for intensive therapy and that the patient population in this study is probably not representative of all type 1 diabetics. However, the benefits of strict glycaemic control are becoming so apparent that clinical practice should reflect this, with patients being encouraged to use intensive therapy wherever possible.

1. Writing team for the Diabetes Control and Complications Trial/Epidemiology of Diabetes Interventions and Complications Research Group. *JAMA* 2003; **290:** 2159-2167.

PREVENTING ACUTE ADVERSE REACTIONS TO SNAKE ANTIVENOM

Having found a large puff adder in my garden last winter, I thought this study from Sri Lanka, published in the first edition of the *Medical Journal of Australia* in 2004,[1] seemed possibly relevant. I have often heard people say that they, or members of their family, are allergic to snake antivenom, assuming that they should not have it. However, it is generally accepted that it is better to give the antivenom and deal with the allergy simultaneously.

The aim of the study was to investigate the efficacy of continuous infusion of hydrocortisone with or without chlorpheniramine bolus against early adverse reactions to polyspecific antivenom. Fifty-two patients who had been bitten by venomous snakes were randomised to receive either an infusion of hydrocortisone (group A), hydrocortisone with chlorpheniramine bolus (group B) or placebo (group C) during the administration of antivenom.

The intervention was hydrocortisone 1 000 mg in 300 ml of normal saline infusion, started 5 minutes before and continued for 30 minutes after the antivenom. Chlorpheniramine as a 10 mg intravenous bolus dose was given 5 minutes after starting the antivenom. The main outcome measure was the occurrence and severity of adverse reactions to antivenom.

The researchers found that adverse reactions were seen in 80% of group A, 52% of group B and 81% of group C. Reactions were mild to moderate, except in 2 patients. There was a significant reduction in adverse reactions in group B compared with placebo, but not a significant difference between group A and the placebo group.

The conclusion was that prophylaxis with a parallel hydrocortisone infusion alone is ineffective in reducing the occurrence of acute adverse reaction to antivenom serum, and that combining it with chlorpheniramine seems effective.

1. Gawarammana IB, *et al. Med J Aust* 2004; **180:** 20-23.

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