Clinical review
Science, medicine, and the future
Omega 3 fatty acids and cardiovascular disease
Fishing for a natural treatment

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FROM ABSTRACT

Omega 3 fatty acids from fish and fish oils can protect against coronary heart disease.

This article reviews the evidence regarding fish oils and coronary disease and outlines the mechanisms through which fish oils might confer cardiac benefits.

SUMMARY POINTS

Coronary heart disease is the most common cause of death in the United Kingdom.

Omega 3 fatty acids from fish and fish oils can protect against coronary heart disease.

There is evidence to support the use of fish or fish oil supplements after myocardial infarction.

THESE AUTHORS ALSO NOTE:

"Omega 3 fatty acids from fish and fish oils can protect against coronary heart disease."

"In this era of multiple pharmacological treatments for cardiovascular disease many believe that simple dietary interventions or nutritional supplements may be a more natural and acceptable method of providing benefits."

The optimal intake of omega 3 fatty acids is not firmly established.

There are concerns about increasing environmental contamination of certain fish.

These authors searched PubMed for articles by using the key words "fish," "fish oils," "omega 3 fatty acids," and "cardiovascular disease."

Omega 3 fatty acids and omega 6 fatty acids are essential polyunsaturated fatty acids.

"The Western diet is abundant in omega 6 fatty acids, mainly from vegetable oils rich in linoleic acid."

Humans lack the enzymes to convert omega 6 fatty acids to omega 3 fatty acids, and therefore omega 3 fatty acids must be obtained from separate dietary sources.

"While alpha-linolenic acid (ALA) is available from certain plants, eicosapentanoic acid (EPA) and docosahexanoic acid (DHA) are derived from fish and fish oils. "

The omega 3 fatty acids have their first double bond at the third carbon molecule from the methyl (CH3) end of the fatty acid, whereas the omega 6 fatty acids have their first double bond at the sixth carbon molecule.

The omega 6 linoleic acid is mainly converted into arachidonic acid.

The omega 3 alpha-linolenic is elongated and desaturated into eicosapentanoic acid and then docosahexanoic acid.

Studies show an inverse association between fish consumption and the risk of coronary heart disease.

The consumption of fish and higher blood concentrations of omega 3 fatty acids are associated with a reduced risk of sudden cardiac death.

A systematic review of 11 prospective cohort studies concluded that fish intake notably reduced mortality due to coronary heart disease in populations at increased risk.

A study of 11,324 patients after myocardial infarction taking a daily capsule of about 850 mg omega 3 fatty acid, and 300 mg vitamin E. The relative risk of cardiovascular death was also reduced, by 30%, and of sudden death by 45%. These benefits were apparent within just four months of randomisation.

Possible mechanisms of action of omega 3 fatty acids:

Antiarrhythmic
Antithrombotic
Antiatherosclerotic
Anti-inflammatory
Improves endothelial function
Lowers blood pressure
Lowers triglyceride concentrations

ARRHYTHMIAS

"The benefits of fish oils were originally thought to be due to their antithrombotic effects, but recent evidence has indicated that the predominant effect may be antiarrhythmic."

Eicosapentanoic acid or docosahexanoic acid can prevent or terminate pharmacologically induced arrhythmias in cultured cardiomyocytes.

THROMBOSIS

Activation of platelets and their deposition at sites of unstable plaque rupture promotes thrombus formation.

Omega 3 fatty acids have an antithrombotic effect.

ATHEROSCLEROSIS

"Omega 3 fatty acids may also influence the atherosclerotic process."

"These effects may be due to a reduction in lipids, inflammation, production of growth factor, or suppression of smooth muscle cell proliferation."

Fish oils may be important in establishing plaque stability.

INFLAMMATION

"Inflammation has a central role in the development and progression of coronary artery disease." **[IMPORTANT]**

"Omega 3 fatty acids have recognised anti-inflammatory actions that may contribute to their beneficial cardiac effects." **[IMPORTANT]**

"Omega 6 fatty acids can be converted into arachidonic acid and then metabolised into the omega 6 eicosanoids. These cellular mediators enhance platelet aggregation and are generally pro-inflammatory."

"Consumption of omega 3 fatty acids increases eicosapentanoic acid in the cell membrane. This competes with arachidonic acid for enzymatic conversion into its own metabolites, the omega 3 derived eicosanoids."

Omega 3 derived eicosanoids oppose or antagonise the pro-inflammatory actions of the omega 6 eicosanoids. **[IMPORTANT]**

"Arachidonic acid and eicosapentanoic acid compete for the cyclo-oxygenase and lipoxygenase enzymes for conversion into eicosanoids. Those derived from arachidonic acid are pro-inflammatory and pro-aggregatory, whereas those derived

from omega 3 fatty acids are anti-inflammatory and inhibit platelet aggregation."

ENDOTHELIAL FUNCTION

"Abnormal endothelial function is found in individuals with cardiovascular risk factors or established coronary heart disease."

"Omega 3 fatty acids have direct effects on endothelial vasomotor function."

Higher concentrations and supplementation with omega 3s are associated with vasodilator responses.

BLOOD PRESSURE

"Fish oils can produce modest reductions in blood pressure, possibly through their effects on endothelial function discussed above."

"Concerns about the depletion of fish stocks will become more pressing if the benefits of fish oils are confirmed beyond the population after myocardial infarction, as this may result in an unsustainable increase in demand."

"Alternative strategies to increase omega 3 intake include supplementing animal feed with fish oil to augment the omega 3 content of eggs, meat, and milk."

Modern biotechnology could genetically modify certain plants species to produce plants and plant oils rich in eicosapentanoic and docosahexanoic acid. **[WOW]**

TRIGLYCERIDE LOWERING

"Omega 3 fatty acids reduce triglyceride concentrations in a dose dependent manner, with intakes of about 4 g per day lowering serum triglycerides by 25-30%."

"Omega 3 fatty acids from fish or fish oil supplements should be considered in the secondary prevention regimen of patients after myocardial infarction."

"Patients should consume about 1 g/day of eicosapentanoic acid and docosahexanoic acid, preferably by increasing their intake of oily fish to at least two servings per week."

Approved pharmaceutical grade fish oil capsules should be prescribed, rather than encouraging over the counter supplements. **[IMPORTANT]**

"Recent guidelines from the American Heart Association have gone further, supporting the use of fish oil supplements for patients with 'documented' coronary heart disease."

Side effects of fish oil supplementation include "fishy aftertaste are uncommon, and gastrointestinal upset is infrequent at moderate intakes."

"A recent study showed that mercury in fish might attenuate their cardioprotective effects. These contaminants accumulate in larger, predatory fish.

RECOMMENDATIONS

1) Patients without documented coronary heart disease:
Eat a variety of (preferably oily) fish at least twice weekly. Include oils and foods rich in alpha-linolenic acid (plant derived omega-3 fatty acids).

2) Patients with documented coronary heart disease:
Consume 1 g of eicosapentanoic and docosahexanoic acid daily, preferably from oily fish. Supplements could be considered in consultation with a doctor.

3) Patients with hypertriglyceridaemia:
Take 2-4 g of eicosapentanoic acid and docosahexanoic acid daily, provided as capsules under a doctor's care.

Current consumption of marine derived omega 3 fatty acids is low, at 100-200 mg/day.

An expert US panel of nutrition scientists has recommended an intake of 650 mg/day whereas the British Nutrition Foundation's recommendation is 1.2 g/day.

Secondary prevention trials after myocardial infarction indicate that consumption of 0.5-1.8 g/day of eicosapentanoic and docosahexanoic acid from fish or fish oil supplements may be beneficial.

Oily fish such as mackerel, herring, tuna, salmon, sardines and trout are rich sources of eicosapentanoic and docosahexanoic acid, and two to three servings per week should provide approximately 1 g/day omega 3 fatty acids.

Lean fish such as cod or haddock have smaller amounts, and fried fish (for example, from fast food establishments or frozen products) contains minimal amounts of omega 3 fatty acids.

KEY POINTS FROM DAN MURPHY

1) Coronary heart disease is the most common cause of death in the United Kingdom.

2) Omega 3 fatty acids from fish and fish oils can protect against coronary heart disease.

3) There is evidence to support the use of fish or fish oil supplements after myocardial infarction. One should take about 1.8 g / day of EPA plus DHA.

4) There are concerns about increasing environmental contamination of certain fish.

5) The Western diet is very high in omega 6 fatty acids and void in omega 3s.

6) Omega 6 fatty acids are converted into arachidonic acid and then metabolised into the pro-inflammatory omega 6 eicosanoids (Prostaglandin E2).

7) Inflammation has a central role in the development and progression of coronary artery disease.

8) Omega 3 fatty acids are anti-inflammatory.

9) Modern biotechnology could genetically modify certain plants species to produce plants and plant oils rich in eicosapentanoic and docosahexanoic acid.

10) 4 g per day of omega-3s lowers serum triglycerides by 25-30%.

11) Omega 3 fatty acids from fish oil supplements should be used in the secondary prevention regimen of patients after myocardial infarction.

12) Healthy people should take about 1.2 g of EPA/DHA omega-3 per day.

13) Consumed fish oil should be pharmaceutical grade fish and not over the counter supplements.

14) Because mercury in fish might attenuate their cardioprotective effects, fish oil supplements should be mercury free.

THIS ARTICLE GENERATED THE FOLLOWING EDITORIAL, in part:
Omega 3 fatty acids and cardiovascular disease
Algae can be source of "fish" oil

British Medical Journal;328:406 (14 February, 2004)

Barber, M. D

Concern about depletion of fish stocks will not be addressed by supplementing animal feed with fish oil, because this requires the harvesting of wild fish to provide the fish oil.

"Fish farming does not provide a solution as farmed fish contains fewer omega 3 fatty acids, this being dependent on what they are fed."

"The original source of the long chain omega 3 fatty acids found in fish is, however, the chloroplasts of marine algae and phytoplankton at the bottom of the food chain."

In the marine environment polyunsaturated fatty acids provide the degree of desaturation needed to keep cell membranes fluid in cold water.

Rather than genetically modifying terrestrial plants to produce eicosapentaenoic and docosahexanoic acid, marine algae can be cultured industrially to provide the "fish" oil while leaving the fish alone."
[Wen ZY, Chen F. Heterotrophic production of eicosapentaenoic acid by microalgae. *Biotechnol Adv* 2003:21: 273-94].

"If cod liver oil is used as a source of fish oil it is important to remember that this contains a comparatively high concentration of vitamin A, producing a risk of toxicity."
[Grubb BP. Hypervitaminosis A following long-term use of high-dose fish oil supplements. *Chest* 1990;97: 1260].