Health effects of omega-3 fatty acids

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During the last eight years, scientific research has been conducted to explore the beneficial role of fish and fish oils in human nutrition. Much of this research has focused on the omega-3 fatty acids, which are a unique component of fish and fish oils.

This article will review the role of omega-3 fatty acids in human nutrition as well as the recent research and theories exploring the positive health effects of omega-3 fatty acids. These include reducing the risk factors for atherosclerosis and providing protection against immunological reactions. Also, the essentiality and dietary levels of omega-3 fatty acids needed to produce protective effects will be addressed.

Omega-3 fatty acids

The recent interest in fish oils began to blossom after two Dutch scientists, Dyerberg and Bang, proposed that the relative lack of atherosclerotic diseases among Greenland Eskimos was the result of their high intake of fish oils. These oils contain an unusual class of polyunsaturated fatty acids known as the omega-3 fatty acids. The name reflects their chemical structure in which the first double bond is located three carbons from the terminal (omega) end of the molecule.

These can be contrasted with the omega-6 fatty acids which have their first double bond on the sixth carbon from the omega end. The omega-6 fatty acids are the class of polyunsaturated fatty acids which are found in most vegetable oils (ie, linoleic acid).

The two most common omega-3 fatty acids in fish oils are eicosapentaenoic acid (EPA) and docosahexaenoic acid (DHA). The former fatty acid contains 20 carbons with five double bonds, whereas the latter contains 22 carbons with six double bonds.

The other member of this family of omega-3 fatty acids is linolenic acid (18 carbons; three double bonds). It is not found in fish oils but in soya- bean oil and green, leafy vegetables and is the major fatty acid in linseed oil.

Linolenic acid can be converted into both EPA and DHA in the human body but the conversion is quite slow, especially when large amounts of linoleic acid are also present. Linolenic acid and linoleic acid (which is converted to the omega-6 fatty acid arachidonic acid) compete for the same enzyme systems in the body. Omega-6 and omega-3 fatty acids are not interconvertible in the body's metabolic pathways, thus, a dietary source of each may be necessary.

These fatty acids are used to synthesise prostaglandins, important local, chemical mediators that control many physiological and biochemical functions. A variety of different types of prostaglandins are produced in the body, depending on the substrate available (EPA or arachidonic acid), and recent research indicates that diet can influence this process. Thus, a significant increase in dietary omega-3 fatty acids can alter the synthesis of certain prostaglandins which appear to have an impact on a number of human diseases, such as atherosclerosis.

Atherosclerotic disease

Dyerberg and Bang reported that Eskimos eating a marine-based diet had low plasma cholesterol and triglyceride (TG)
The low incidence of vascular disease among Eskimos is probably due to fish oil intake. Fish oil contains omega-3 fatty acids.

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levels, somewhat prolonged bleeding times and very little heart disease or stroke. This led investigators at the Oregon Health Sciences University to begin controlled studies on the effects of fish oils on risk factors associated with atherosclerosis.

In one study, seven volunteers with normal blood lipid levels were fed diets in which all the fat was derived from salmon or vegetable oil (100-120 g/day). Plasma cholesterol levels were lowered by 11% by both of these diets, whereas triglyceride levels fell only on the fish oil diet (33%). Subsequent studies using 20 hypertriglyceridaemic patients resulted in decreases in plasma TG levels (up to 79%) with about 25% of the calories as salmon oil (100 g/day). Lower intake of omega-3 rich oils (20 - 40 g/day) were also shown to prolong bleeding times. However, in no studies has undesirable bleeding been reported because the prolonged bleeding time is still within the normal range.

These platelet effects are probably the result of alterations in prostaglandin synthesis in the presence of omega-3 fatty acids. There are two major prostaglandin-like compounds that influence platelet reactivity – thromboxane A2 and prostacyclin. The former causes platelets to aggregate; the latter is a potent antiaggregator. The balance between these two influences how readily platelets will stick together. EPA and DHA inhibit the formation of thromboxane A2 more so than they inhibit prostacyclin activity. Thus, the omega-3 fatty acids tend to be antiaggregatory.

**Platelet function**

Omega-3 fatty acids have also been shown to reduce the inevitable damage which follows the interruption of blood flow to a tissue (ischaemia). When a vessel in the heart is blocked, the result is a heart attack; in the brain, a stroke results. In animal studies, fish oil-rich diets reduced tissue destruction when a vessel was tied off and blood flow stopped. For example, in dogs with blocked coronary arteries, 25% of the left ventricle was damaged in the control dogs, whereas only 3% of the muscle was damaged in the animals fed omega-3 fatty acids.

One potential mechanism to explain these effects on blood flow (as well as the reduced incidence of clinical atherosclerosis in fish-eating populations) is a decrease in blood viscosity. Omega-3 fatty acids, when incorporated into a cell membrane, make that membrane more fluid, more deformable. Studies have shown that dietary fish oils can produce a 15% reduction in whole blood viscosity. The presence of omega-3 fatty acids in the blood cells apparently enables them to squeeze through constricted capillaries more easily and keep the tissues supplied with oxygen.

**Ischaemic damage**

The increased bleeding times and decreased platelet adhesiveness seen in Eskimos has also been reproduced by feeding fish oils in controlled clinical trials. In another study from Oregon, bleeding times increased from 6.75 to 10 minutes in subjects taking 40% of their calories as salmon oil (100 g/day). Lower intake of omega-3 rich oils (20 - 40 g/day) were also shown to prolong bleeding times. However, in no studies has undesirable bleeding been reported because the prolonged bleeding time is still within the normal range.

**Ischaemic damage**
Omega-3 fatty acids alter the synthesis of some prostaglandins which appear to have impact on atherosclerosis.

**Hypertension**

In addition to its hypolipidaemic effects, fish oils have also been reported to lower blood pressure. Singer, et al, from Germany found that two weeks of a diet rich in canned mackerel (250 g/day) lowered blood pressure from 128/80 to 113/73 mm Hg in 15 normal volunteers. Further research is needed in order to confirm that omega-3 fatty acids can significantly affect blood pressure.

The fish oils appear to be a dietary component that can lower lipid levels, reduce platelet stickiness, increase blood fluidity, prevent ischaemic damage and possibly lower blood pressure. They clearly have antiatherogenic potential.

**Immune function**

A seemingly unrelated effect of diets rich in omega-3 fatty acids is that they can help protect the body when its immune system begins to attack its own tissues, such as in rheumatoid arthritis and lupus erythematosus. Researchers at Harvard have shown in two different animal models of autoimmune diseases that omega-3 fatty acids helped prevent kidney destruction and prolong life. In one study, 98% of the mice fed the control diet (beef tallow) had died of severe renal disease by 19 months of age, whereas only 16% of the fish oil-treated group were thus affected. They also found that if mice were started on the fish oil diet as late as four to five months of age (instead of at weaning), they, too, were protected.

In many respects, migraine headaches appear to be immunological reactions. In this regard, it is interesting to note the results of a recent preliminary trial using omega-3 fatty acids to treat refractory migraines. Six chronic migraine sufferers were given 20 g of fish oil each day in a double-blind, placebo-controlled study. Significant headache relief was found with fish oil in five of the six patients.

The possible mechanisms to explain this apparent protection against kidney disease and migraine headaches may lie in the ability of omega-3 fatty acids to change the balance of prostaglandins and leukotrienes (powerful mediators of inflammation and immune response).

**Are omega-3 fatty acids essential nutrients?**

The essentiality for humans of omega-3 fatty acids has long been disputed. Because linolenic acid could cure only some of the symptoms of essential fatty acid deficiency, it was not regarded as a human dietary essential. However, as analytical techniques have become more refined, large amounts of DHA have been detected in the brain, retina and sperm, suggesting that omega-3 fatty acids may be essential components of the diet.

Recently, Neuringer, et al, have shown that young rhesus monkeys whose mothers were fed diets deficient in omega-3 fatty acids during pregnancy had significantly reduced visual acuity. This was the first indication that physiological deficits result from an omega-3 fatty acid deficiency in primates. Whether behavioural problems due to omega-3 fatty acid deficiency during brain growth also develop in these monkeys is the object of continuing research.

Do human infants also need omega-3 fatty acids? Although the answer to that question is not yet known, it is known that human milk contains linolenic acid, EPA and DHA and that dietary fish elevates the concentration of omega-3 fatty acids in mothers' milk. Since brain cells contain large amounts of DHA and cell growth continues until about six months postpartum, it is...
Trials seem to show the influence of omega-3 rich fish oils on platelets, cholesterol, ischaemic damage and possibly on many other disease processes.

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possible that the development of brain tissue could be facilitated by increasing the intake of omega-3 fatty acid. Indeed, the need for omega-3 fatty acids in infant formulas should be carefully evaluated.

Effective dietary levels

Omega-3 fatty acids appear to have a variety of effects upon the human body. To what extent can these be influenced by diet alone? Does one need to take some millilitres of fish oil daily or can increasing the frequency of fish intake provide these effects?

In a dose-response study in eleven hypertriglyceridaemic patients, fish oil fed at 40, 25 and 15 ml/day over three six-week periods produced a significant fall in plasma cholesterol and a 50% decrease in TG levels. Fifteen millilitres/day was nearly as effective as the 40 ml dose. Ten millilitres/day of fish oil daily significantly lowered plasma TG levels over 25% (from 2,01 to 1,46 mmol/l) in men with peripheral artery disease. An equivalent amount of omega-3 fatty acids is found in about 250 to 750 grams of high-fat fish, like salmon, mackerel or trout, and in about one to one and a half kilos of the low-fat white fishes like cod or flounder.

In addition to the Eskimos, fish consumption is high in many Japanese villages. Kobayaski, et al., reported that fish intake averaged 250 g/day (2,5 g EPA) in a fishing village compared to 90 g/day (0,9g EPA) in a farming community. Platelet studies showed reduced platelet aggregation in the fishing villagers. In addition, blood viscosity was lower among the fishermen. Thus, this study implies that beneficial effects (such as reduced platelet aggregation) can be obtained by large daily intakes of high-fat fish.

A recent report from the Netherlands indicated that the 20-year mortality rate from coronary heart disease was reduced by 50% in those men consuming at least 30 g of low-fat fish per day (less than 0,3 g of omega-3 fatty acids). This relationship persisted even after controlling for the other major risk factors for heart disease. Since the daily consumption of 30 g of high-fat fish (providing about 1 g of omega-3 fatty acids) over a short period of time has been shown to produce only very mild effects in 118 normal men, there may be a time/dose-related effect.

Summary

Dietary fish oils rich in omega-3 fatty acids appear to affect several metabolic systems. Atherosclerosis may be retarded by the effects of these fatty acids on plasma lipid levels, platelet function, blood flow and hypertension. The immune system may be desensitised and migraine headaches managed. Well-controlled clinical trials using lower quantities of omega-3 fatty acids are needed in the areas of atherosclerosis, immunology and prostaglandin metabolism. Omega-3 fatty acids may even be shown to be essential nutrients as further studies examine the many and varied effects of these unusual dietary fatty acids.

References for this article are obtainable from the Editor, Box 375, Claremont 7735.