EPA and DHA - their importance in the treatment and prevention of cardiovascular and neurodegenerative diseases

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First references to cardio-protective properties of fish oil in Greenland Eskimos are dated in 1976 (1). Until then, it was rather difficult to explain why a population that tends to have overweight and obesity problems and is characterized by a diet with a relatively high amount of unsaturated fats and low intake of vegetables and fruits has the lowest coronary heart disease mortality rate.
Since then, fish oil as a nutritional supplement has been subject to an extensive research, including large-scale randomized controlled clinical studies, and in several European countries, it can be used today also on a prescription basis for the indication of adjuvant treatment to other standard therapies in patients after myocardial infarction. The most important component of fish oil responsible for its cardio-protective properties are the so-called omega-3 polyunsaturated fatty acids (n-3 PUFAs), which fall into a group of fats with at least one double bond located at the third carbon from the methyl end.

They include:

- 18:3 α-linolenic acid (of vegetable origin)
- 20:5 eicosapentaenoic acid
- 22:5 docosapentaenoic acid
- 22:6 docosahexaenoic acid

Human body is not able to synthesize α-linolenic acid and its insufficiency during the growth period is associated with developmental disorders and neurological diseases. It is a precursor for the synthesis of eicosapentaenoic acid (EPA) and docosahexaenoic acid (DHA), which are particularly abundant in so-called fat (greasy) fishes, such as mackerel, tuna and salmon. Main sources of α-linolenic acid include flaxseed oil (flax seeds), walnuts, canola oil, and in lower amounts also hazelnuts and almonds, but not peanuts. Flaxseed oil contains α-linolenic acid in particularly high quantities (almost one quarter of its total mass), but its resorption rate from the digestive tract is significantly lower (it varies individually between 0.3-20%). EPA is a precursor of n-3 eicosanoids, which have several important cardio-protective properties. The most important are antiarrhythmic properties, along with anti-inflammatory and antithrombotic effects (2,3,4). In randomized controlled clinical studies (dosage 1g daily), administration of highly purified fish oil led to a significant decrease in both cardiovascular and overall mortality rate, in particular by decreasing the incidence of sudden heart death (5,6,7). In higher concentrations (approx. 2-4g of purified fish oil daily), n-3 PUFAs also reduce the level of triacylglycerols. At such higher doses, an undesirable mild increase in LDL cholesterol is sometimes observed, which should be compensated by concomitant administration of statins as secondary ischemic heart disease prevention and in diabetic patients. The combination of n-3 PUFAs with statins also leads to a more significant reduction of cardiovascular diseases in comparison with statin monotherapy (8).

A growing body of evidence in favour of n-3 PUFAs in the form of fish oil (or capsules with highly purified n-3 PUFAs) is also reflected in the most recent Guidelines of American Heart Association (AHA), which recommend patients with documented coronary heart disease to use 1g EPA+DHA daily (9). Individuals with hypertriacylglycerolemia can use 2-4g DHA+EPA daily (9).

The importance of n-3 PUFA supplementation in Slovakia is even higher when considering a relatively high amount of omega-6 polyunsaturated fatty acids (n-6 PUFAs) in Slovak population's diet. However, it is known that the omega-6/omega-3 fatty acids ratio is important in terms of several diseases, pathogenesis of which includes inflammation (subclinical vascular inflammation in particular), for example atherosclerosis, hypertension, diabetes, bronchial asthma, etc.

An optimal ratio is 1-1.5:1, though a ratio of 4:1 is still associated with a decrease in inflammatory activity (10). Contrariwise, populations with a high n-6/n-3 ratio in their diet (Indian subcontinent in particular) have an extremely high incidence of cardiovascular diseases (ischemic heart disease) in spite of the lack of some typical risk factors of atherosclerosis (11,12). Considering that alimentary products in Slovakia contain relatively high amounts of n-6 PUFAs (mainly products on the basis of so-called hardened fats - margarines; often misleading commercials say that n-3 PUFAs have been added, although the ratio of n-6/n-3 PUFAs is still higher than 100:1!!!), probably the best way to adjust the n-6/n-3 PUFAs ratio is to increase the intake of n-3 PUFAs, which is extremely low in Slovakia (low consumption of fish).

The resulting effect is probably also determined by the EPA/DHA ratio in fish oil capsules (moreover, high content of EPA is also associated with better neuroprotection and an improvement of cognitive functions). EPA deficiency was also confirmed in various mental disorders, such as depressions, schizophrenia, etc. Better cardioprotection is achieved by shifting the EPA/DHA ratio towards the increase of DHA. Two unique products are available in Slovakia that contain EPA and DHA in two different ratios 500:140mg (ZenixX Balance) and 155:520mg (ZenixX Vital), which may be used in various diagnoses (neuro- or cardioprotection). Both products comply with the requirements for highly purified fish oil.

Some important facts should be considered before trying to adjust the intake of n-3 PUFAs mainly by eating fish. The content of n-3 PUFAs varies from fish to fish. Moreover, it must be said that the content of EPA and DHA may be decreased during the preparation of fish for the consumption (for instance, canned tuna only contains approximately one tenth of their initial content in fresh tuna). Preparation of fish using hardened fats is absolutely unsuitable, because the absorption of n-6 and n-3 PUFAs is competitive and n-6 PUFAs are absorbed in much higher quantities (10). It is also known that different individuals from the same fish species may contain completely different amounts of n-3 PUFAs, depending on whether they live freely or are cultured (fishes of carp family from fish cultures contain practically no n-3 PUFAs!). Another problem of an increased consumption of fish is a potential presence of some polluting substances. These mainly include compounds of methylmercury, polychlorinated biphenyls and some other organic substances (13). This is why the FDA (Food and Drug Administration - the highest regulatory office for the control of drugs and food in the USA) does not recommend certain subpopulations, in particular pregnant women and children, to eat fish with the highest risk of potential pollution (such as shark, swordfish, big mackerels). Instead, fishes with lower probability of

contamination (tuna, salmon, catfish, codfish) are more suitable. It is also important to know the locality of origin, particularly for fishes from local rivers and lakes (9). Potential exposure to pollutants contained in fish can be partly reduced by removing their skin, which contains the highest concentration of polluting substances.

Conclusion

Rich evidence from basic research, experimental and epidemiological studies, and recently also from randomized controlled clinical studies shows that n-3 PUFAs play an important role in the prevention and treatment of cardiovascular diseases. Moreover, the results from clinical studies disproved concerns about their potential side effects.

Fish oil in the form of capsules with highly purified n-3 PUFAs, particularly in combination with statins, seems to bring further improvement not only to the prognosis of patients after myocardial infarction, heart failure or dysrhythmias, but also in the prevention of atherosclerosis. The effect of n-3 PUFAs in the prevention of sudden heart death in patients after myocardial infarction is undeniable. Currently running large-scale clinical studies will probably bring about a potential expansion of their indications.

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