Therapeutic Use of Fish Oil in Gynecology

A Seldom Used Option in Gynecological Practice

by Dr. Wolfgang Rothe
**Introduction**

The therapeutic effectiveness of fish oil was discovered in the Scandinavian countries, as it became clear that a fish rich diet reduced the frequency of cardiovascular disease. A bit later, it was noted that children whose mothers preferentially consumed marine products had a significantly higher birth weight. We now not only understand the mechanism of this effect, but also the significance of the possibilities for application of fish oil in gynecology.

After a correlation had been established between higher birth weight and a longer term of pregnancy as the basis for delayed date of birth, the opportunity was opened up of utilizing this therapeutically with patients who had a tendency to premature birth. It later turned out that n-3 fatty acids are not just essential for the intrauterine development of the fetus’s CNS; these dietary components must be supplied in adequate amounts during early infancy as well, in order to prevent developmental disorders.

Fish oil has also proven helpful in treating dysmenorrhoic disturbances [menstrual problems]. Last but not least, it has been confirmed that the lowering of triglycerides effected by n-3 fatty acids is of special importance to menopausal women. It turned out that, for women, an elevated triglyceride level is an independent risk factor (which has not been able to be demonstrated for men). Since, in addition, the mortality rate from heart attacks seems to be relatively high among women, this connection is especially significant.

**Prophylactic Use of Fish Oil for Premature Births**

Due to the strikingly high birth weight of children born in the Faeroe Islands, S.F. Olsen registered the course of pregnancies and births of all first time mothers there between 1982 and 1984, and compared them with those in the rest of Denmark. The number of deliveries that occurred after the estimated date of birth turned out to be twice as high in the Faeroe Islands as in the control group. Olsen surmised that the reason for this difference lay in the differing dietary habits, since the island dwellers consumed, on average, 50 percent more fish with unsaturated fatty acids as the comparison group in the rest of the country, or in the Netherlands or Canada. How much more polyunsaturated n-3 fatty acids were consumed in the diet was able to be accurately estimated by their presence in the phospholipids of the erythrocytes of the patients under investigation.

According to Olsen’s supposition, the high consumption of n-3 fatty acids lengthens the gestation period, because these fatty acids inhibit uterine prostaglandin production, which in turn plays a role in uterine contractions and the maturation of the cervix. Increased ingestion of n-3 fatty acids might also explain the higher infant mortality rate in the Faeroes. As has been learned from the use of prostaglandin synthesis inhibitors in obstetrics, Botallo’s duct closes up prematurely under this kind of treatment, leading to elevated pressures in the pulmonary vascular bed.

Because of the prolonged pregnancy as a consequence of an increased supply of n-3 fatty acids, the possibility opened up of helping women whose contractions started too soon or too late by altering their intake of n-3 fatty acids. This meant, first, that pregnant women should not - as was common in the Faeroes - eat a lot of fish. If this hypothesis should prove correct, however, this also means that, for women with a higher risk of premature birth, a properly dosed administration of fish oil could have a welcome therapeutic effect.

Based on these considerations, Olsen carried out a clinical study along these lines. In this study, 533 female patients in the 30th week of pregnancy were divided into three groups. The patients in one group (n = 266) received four fish oil capsules per day, corresponding to a daily supply of 2.7 g of n-3 fatty acids. Those in the second group (n=131) took the same number of capsules filled with olive oil; the third group received no preparation.

The duration of pregnancy was significantly higher in the fish oil group compared to the other groups. The difference was four days an average. Also, the average birth weight of the newborns was 107 g higher in the verum group. In the two control groups, there was no difference with regard to these variables. Among women who, before the study, had seldom consumed fish, the effect achieved by the fish oil supplement was especially pronounced.

It also proved possible to establish a dosage/effect relationship - based,
In fact, on compliance behavior. The effects were more pronounced among patients with good compliance than among those for whom the regularity of taking the capsules left something to be desired. The birth process itself was not influenced by this treatment.

As was originally suspected, the triggering of the birth process, which is effected by prostaglandins, seems to be decisively delayed by the modification of the prostaglandin profile by fish oil. In the authors’ view, fish oil supplementation in the third trimester is an effective, cost-effective and comfortable treatment method for preventing premature births.

**n-3 Fatty Acids are Essential for Early Childhood Development**

Another important result of recent lipid research is the realization that n-3 fatty acids, especially DHA, are essential for the development of the fetal and newborn CNS. Therefore, even women who are not susceptible to premature birth should not do entirely without a supply of n-3 fatty acids. To be sure, relatively small amounts suffice for this purpose: 1-2 g fish oil per day. For normally proceeding pregnancies, a high dosage is not advisable because of the aforementioned pharmacological effects.

While Omega-6 fatty acids are normally present in sufficient amounts in the diet, this is not the case for n-3 fatty acids. The British Nutrition Foundation therefore recommends ingesting 0.5 percent of the total food energy in the form of long chain n-3 fatty acids. Since eicosapentaenoic acid and arachidonic acid compete as enzyme substrates, the Omega-6 and n-3 fatty acid ratio is important; it should be approximately 5:1. An adequate supply of n-3 fatty acids should be seen to especially during pregnancy, since the fetus cannot synthesize sufficient amounts of docosahexanoic acid. Women planning a pregnancy should therefore take care to ensure a basic supply of n-3 fatty acids before conception and in the first months of pregnancy.

Between the 20th and 40th week of pregnancy, the brain undergoes an especially rapid development phase, increasing in weight from 75 to 400 grams. For this growth spurt of the CNS, the fetus needs large amounts of long chain polyunsaturated fatty acids such as arachidonic acid and docosahexanoic acid for the synthesis of structural lipids, which must be provided by the mother’s body via the placenta. Moreover, the enrichment of infant’s milk with these essential long chain fatty acids has been officially recommended since 1991 for premature births.

In premature babies, who usually cannot synthesize these fatty acids endogenously in sufficient amounts, the concentration of arachidonic and docosahexanoic acids in the plasma and brain tissue declines rapidly, if they are not breast fed and fed commercial baby formula instead. This can then lead to functional impairment, particularly of psychomotor and visual development. However, adding fish oil or docosahexanoic acid to these milk mixtures can normalize the fatty acid status and effect mental development.

This was the result of a recent intervention study. In this study, 43 premature babies were divided into two roughly equal groups. One group received the regular “normal” diet, while the other half, for up to two months after being discharged from the hospital, was fed a diet enriched with n-3 fatty acids. At age one, the children of this group exhibited a higher learning capacity. The visual acuity of the children receiving an n-3 fatty acid enriched diet was better, and correlated with the docosahexanoic acid level.

The results also showed that, even for normal term births, the addition of longchain polyunsaturated n-3 fatty acids to the diet is necessary. Thus, children who were not breast fed had lower concentrations of arachidonic and docosahexanoic acids. Moreover, there was also a correlation between the dietary fatty acid profile and visual acuity.

**Prophylaxis of Dysmenorrhea with n-3 Fatty Acids**

Meanwhile, yet another area of application for fish oil in gynecology is beginning to emerge: the treatment of dysmenorrhea. Ovulation inhibitors are often used to treat this disorder, which usually appears on the first day of menstruation, afflicts roughly one woman in ten, and is accompanied by dysmenorrhoic pains and abdominal cramps, since dysmenorrhea only appears during ovulation cycles. There is also talk of a psychological component, as a consequence of which the disease...
Fatty acids have a stronger vasodilatory, but a weaker constrictive effect than those from Omega-6 precursors.

These initially purely theoretical assumptions seem to be confirmed by clinical studies: on a fish diet, patients with severe therapy resistant dysmenorrhea not only experienced an improvement of their clinical symptoms, but also the abnormal prostaglandin values or ratios in the menstrual blood returned to normal with this therapy. This is thus a first point of approach for the possibility of a new treatment concept for dysmenorrhea. Considering the fact that this kind of therapy is not only free of side effects, but overall and for various reasons has an altogether positive evaluation, therapy with fish oil capsules recommends itself in these cases.

Lowering Triglycerides is Especially Important for Women

Heart attack prophylaxis using fish oil has already been reported on thoroughly here. Contrary to the widely held opinion that heart attacks are mostly a male problem, epidemiological investigations show that, after menopause, heart attack is the number one cause of death among women as well. Furthermore, women who have suffered a heart attack have a poorer prognosis than men. Thus, 54 percent of men, but 66 percent of women, die within 30 days of a heart attack. There is therefore no reason to neglect the prevention and therapy of heart attacks among women.

As far as prevention is concerned, the same rules apply as for men. In addition, the cardioprotective effect of estrogen/progestin substitution might play a role in peri- and post-menopause. To be sure, the only thing that’s been confirmed is a positive influence on the lipid status. Nevertheless, direct proof that the infarct mortality is reduced is still lacking, and none is expected until completion of the so-called HERS Study in 2005. There is also an important difference between the sexes with respect to the cardiovascular risk profile. While hypertriglyceridemia as an independent risk factor for men is still disputed, its role as independent forerunner of heart attack in women is much better substantiated. This has since been confirmed by a large scale Norwegian study: more than 24,000 women aged 35 to 49 in three Norwegian groups took part in this prospective investigation. Their cardiovascular risk factors were recorded anamnestically, blood pressure, height and weight measured, total cholesterol and triglycerides determined. The time to the preceding meal was recorded as well.

During the observation period of, on average, 14.6 years, 108 women died as a result of coronary heart disease and 238 of cardiovascular diseases; 931 died in all. Independently of the cause of death, a positive correlation was found with the triglyceride level. Even when age and other risk factors were taken into account in the statistical evaluation, the neutral fat levels turned out to be independent predictors. Compared with women whose triglycerides were below...
130 mg/dl, subjects with values above 300 mg/dl had a 4.7 times higher probability of falling victim to coronary heart disease. Even the overall risk of dying was 2.3 times greater. The authors see no disadvantage in the fact that the blood samples were not taken when the stomach was empty of food. They surmise that possibly the delayed clearance of chylomicrons in atherogenesis is of crucial significance. In this respect, values determined after a meal might even be more informative. Against the background of the pronounced lipid lowering effect of n-3 fatty acids, this study is of great significance.

Although the effect of fish oil on the serum cholesterol level is relatively low, it does effect a strongly pronounced lowering of the serum triglyceride level. The higher the initial triglyceride level is, the more pronounced is the effect. Lowering of the triglyceride level starts up in its full therapeutic extent within a month and persists unchanged for at least two years.

The biochemical foundations of this effect can be explained as follows (Fig. 1): during fat resorption, in the enterocytes of the intestines, triglycerides are associated with the apolipoproteins A and B to the lipoproteins of the chylomicrons. In the blood, depending on the LDL concentration, there takes place an exchange of the apolipoproteins on the surface of the chylomicrons (A) with those of the HDL (E and C). In these complexes, fatty acids are transported into the tissues. The residue („remnant”) of the chylomicron decomposition winds up in the liver.

Inhibition of the biosynthesis of VLDL Apo B could be demonstrated in human Hep G 2 cells as well as rat hepatocytes. In vivo as well, fish oil lowers VLDL Apo B in test subjects, as well as total Apo B, Apo C III and Apo E in patients with very pronounced hypertriglyceridemia. The special pharmacological effect of fish oil on lipid metabolism also finds it expression in that fish oils prevent or at least sharply reduce increases in: triglycerides after carbohydrate ingestion; chylomicrons after fat ingestion; LDL-cholesterol and LDL Apo B after exogenous cholesterol supply.

In this connection, it is interesting that patients who are homozygous for apolipoprotein E (25 percent of the population) seem to be especially sensitive to therapy. These triglyceride lowering effects have great significance, particularly for infarct prophylaxis among women.

Thus, the n-3 fatty acids contained in fish oil are not only suited to the treatment of specific gynecological problems, they are also of great significance for infarct prophylaxis particularly for women.

References


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