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## Fish Oil May Reduce Psychosis in High-Risk Individuals

Pauline Anderson

February 3, 2010 — Omega-3 fatty acids may prevent the transition from a subthreshold psychotic state to full-blown psychosis, new research suggests.

The study showed a 22.6% difference in risk of progression to psychosis in vulnerable young people taking a 12-week course of fish oil supplements compared with those taking a placebo. The benefits of the supplements were sustained up to 1 year.

The fish oil intervention "may at least delay, but probably prevent, the onset of schizophrenia, and that's just great news," lead study author G. Paul Amminger, MD, Oxygen Research Centre, Centre for Youth Mental Health, University of Melbourne, Australia, told *Medscape Psychiatry*.

In contrast to antipsychotic drugs, fish oil supplements prevent cell deterioration in the brain and lower levels of damaging triglycerides, said Dr. Amminger. The supplements are made of a "natural substance" that is publicly acceptable and offers benefits to general, as well as mental, health, he added.

The study is published in the February issue of the *Archives of General Psychiatry*.

The randomized, double-blind, placebo-controlled trial included 81 patients aged 13 to 25 years who met validated criteria for being at risk for psychosis and who were referred to the psychosis detection unit of the Department of Child and Adolescent Psychiatry, Medical University of Vienna, Austria.

Patients were randomized to receive 4 placebo or 4 long-chain omega-3 polyunsaturated fatty acid capsules daily for 12 weeks. The treatment capsules contained eicosapentaenoic acid (EPA) and docosahexaenoic acid (DHA) and vitamin E. The amount of fish oil used in the study was in the range of the recommended daily dose. The look-alike placebo capsules contained coconut oil.

Subjects did not take antipsychotic medications or mood stabilizers during the study but could take antidepressants.

As part of the study protocol, participants were offered 9 sessions of psychological and psychosocial interventions. The study's "state-of-the-art comprehensive treatment package" included support to cope with symptoms and assistance with school or work-related problems, said Dr. Amminger.

Researchers assessed subjects weekly for 4 weeks and then at 8 and 12 weeks and again at 6 and 12 months. They used the Positive and Negative Syndrome Scale (PANSS) to determine conversion to psychotic disorder. Nonproject psychiatrists independently confirmed the diagnosis.

### Sustained Effect

At the end of the 12-month study, researchers found that the cumulative conversion rates to psychotic disorder were 4.9% in the fatty acid group and 27.5% in the placebo group. The 22.6% difference in risk of progression to psychosis between the 2 groups had a confidence interval of 4.8% to 40.4%.

The omega-3 group had significantly lower PANSS positive, negative, general, and total scores at 12 weeks, 6 months, and 12 months than the control group. For example, the total change in PANSS score from baseline to 12 months was  $-15.7$  in the treatment group compared with  $-4.4$  in the placebo group.

The researchers were somewhat surprised that the effect of omega-3 fatty acids extended beyond the cessation of the intervention. "We were expecting a washout effect after we stopped the medication, but we didn't see it and the effect was sustained," said Dr. Amminger.

The improvements in scores were reflected in blood levels, he said. "We were also able to show that in the group that received omega-3 supplements, the increase in red blood cell levels of DHA and EPA correlated with the functional improvement."

There was a marked but similar reduction in depressive symptoms in the placebo and treatment groups, possibly because of a high placebo response rate in this young population or because of the psychosocial interventions provided during the study.

### **Well Tolerated**

Although there were a few digestive issues early in the study, the fish oil capsules were generally well tolerated. "I would expect more digestive problems if we had treated at higher doses," said Dr. Amminger.

The rate of adverse effects, including concentration difficulties and tension or inner unrest, was higher in the placebo group. The mean rate for adherence with study medication was 81.4% in the omega-3 group and 75.4% in the placebo group.

The current study adds to the growing body of evidence pointing to the protective qualities of fish oils in mental health. A recent study in people with established schizophrenia who were treated with omega-3 supplements showed that these patients needed lower doses of antipsychotics. Epidemiologic studies show that countries where the diet is rich in fish, such as Japan, Norway, and Iceland, have lower levels of schizophrenia.

Scientists believe that dysfunctional fatty acid metabolism may cause psychosis. Lack of fatty acids may cause oxidative stress that leads to cell degeneration. Low levels of unsaturated fatty acids may also explain the decreased sensitivity to pain or temperature among people with schizophrenia, said Dr. Amminger.

Although the mechanism is unclear Dr. Amminger speculated that omega-3 fatty acids may alter membrane fluidity and receptor responses, or they may interact with the dopamine and serotonergic systems. It is also possible that they may increase glutathione in the temporal lobe to protect neurons from oxidative stress. "What we are doing with this treatment is replacing those unsaturated fatty acids, which may help stabilize the cell and keep it alive," said Dr. Amminger.

Dr. Amminger believes there is enough evidence to recommend that fish oil capsules be added to standard antipsychotic medication in patients with established psychosis.

And fish oil supplements may be an excellent intervention in a young population at risk for psychosis. The "state-of-the-art opinion" is that young people who may be hearing voices or feeling that someone is trying to read their mind, but who do not meet criteria for a psychotic disorder, should not take antipsychotic medication unless they are very bothered by the symptoms, become aggressive, or are at risk of self-harm, said Dr. Amminger.

"It's not that they're psychotic and have lost touch with reality at this stage — the intensity and frequency is not at the threshold of a psychotic disorder."

## **Drugs Stigmatizing**

The rationale for this approach is that taking antipsychotics is stigmatizing, and the drugs are often unacceptable to young people because of severe adverse effects that can include metabolic changes, sexual dysfunction, and weight gain, he said.

About 60% to 70% of patients recover from symptoms with a nondrug approach that includes providing family support and assistance with coping with symptoms.

Dr. Amminger suspects that adding fish oil supplements to this standard treatment can help get these young people through a crucial period without a psychotic breakdown. "My theory is that if you get people through this most vulnerable phase, which is pretty much defined by the presence of those subthreshold attenuated symptoms, then they stabilize."

An additional benefit of omega-3 fatty acids is that they lower triglyceride levels. This is important because many antipsychotic medications can rapidly double triglyceride levels, said Dr. Amminger.

Omega-3 fatty acids may be beneficial for other brain-related disorders, including Alzheimer's disease (AD). Dr. Amminger is excited about the possibility that fatty acids may eventually prove effective in diabetes where oxidative stress also plays an important role. His preliminary analysis of these data shows that the lipid metabolism abnormalities in people who progress to psychosis are similar to those in individuals with diabetes.

"People probably have different vulnerabilities, based on their genetic makeup and environmental influences, that put them at greater risk for diabetes, AD, depression, or psychosis. This is more of a general principle here, but I think it's highly likely that fish oil supplements have a mechanism which is beneficial not just for schizophrenia, but rather in a broader way."

It's unclear whether omega-3 fatty acids are effective in treating psychosis beyond 12 months, but Dr. Amminger and his colleagues are planning a 3-year follow-up of the patients in the study.

## **Tremendously Exciting**

Commenting on the study findings, Felice Jacka, PhD, research fellow at the University of Melbourne, said the research is based on "terrific thinking." "The idea that you could intervene with a natural treatment that really has no side effects and is commonly available, cheaply available, and readily used is tremendously exciting," Dr. Jacka told *Medscape Psychiatry*.

Omega-3 fatty acids strengthen the signal-to-noise ratio in the brain that has become impaired in psychosis, so signals are less influential in terms of what a patient is focusing on and noise becomes stronger, said Dr. Jacka. These fatty acids also reduce neuroinflammation and oxidative stress, which also improve signaling.

Dr. Jacka speculated that fish oils may be particularly effective in young people but perhaps less so after transition to a full-blown psychosis because metabolic disturbances and inflammation have progressed to the point that it might be more difficult for fatty acids to be properly incorporated into cell membranes.

She agreed that fish oils are beneficial not just for mental illnesses. "Omega-3 fatty acids in general are absolutely essential to virtually every aspect of human health."

*The study authors and Dr. Jacka have disclosed no relevant financial relationships.*

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