

- Topics:** Depression, bipolar disorder, mania, omega-3 fatty acids, docosahexaenoic acid (DHA), eicosapentaenoic acid (EPA), long chain polyunsaturated fatty acids (LC-PUFAs), fish, fish oil
- Objective:** To determine if omega-3 LC-PUFA supplementation improves depressive symptoms and health related quality of life (HRQoL) in depressed elderly patients.
- Background:** Previous intervention trials have measured symptom improvements in adults with bipolar disorder and in children with depression when provided with omega-3 LC-PUFAs in combination with their standard drug treatment. Studies have also shown that omega-3 LC-PUFAs can reduce mania in young children with bipolar disorder and in juveniles with mania and depression when combined with other therapies. However, to date no study has investigated the effects of omega-3 LC-PUFAs on depression in the elderly.
- Method:** This eight week, randomized, double-blind, placebo-controlled trial included 46 depressed elderly women, aged 66-95 years from a nursing home in Pavia, Italy. Twenty-two women were treated with 2.5 g/day of an omega-3 supplement containing 1.67 g/day of EPA and 0.83 g/day of DHA while 24 patients were treated with paraffin oil placebo for 8 weeks. All patients met the Diagnostic and Statistical Manual of Mental Disorders 4<sup>th</sup> edition criteria for major depression or dysthymia. Body composition and nutritional status were also determined including body weight, height, BMI, body fat content by skin fold, and Mini Nutritional Assessment. The following tests were completed on both groups before and after treatment for 8 weeks.
- Primary endpoint** – Depressive Symptoms determined by the Geriatric Depression Scale (GDS)
  - Secondary endpoint** – HRQoL using the Short-Form 36-Item Health Survey (SF-36) to assess quality of life; body composition; nutritional status.
  - Red blood cell (RBC) fatty acids
- Findings:**
- The mean GDS was significantly lower (33%) at 8 weeks compared to baseline in the Omega-3 group ( $p < 0.017$ ). The response rate was 45.5% in the Omega-3 group and 8.3% in the placebo group. The remission rate was 40.9% in the omega-3 group and 16.7% in the placebo group.
  - The physical and mental components of the SF-36 were significantly increased in the intervention group ( $p < 0.001$ ).
  - There were no changes in body composition or nutritional status from the start of the study until the end.
  - Fatty acid analysis confirmed that compliance was good. There was a significant increase in EPA and DHA in the intervention group with no change in placebo. DHA significantly increased from 3.22 % up to 4.06% ( $P < 0.05$ ).
  - Omega-3 and placebo treatments were both well tolerated with no serious adverse event observed over the eight weeks of the study.
- Conclusion:** Supplementation with omega-3 LC-PUFAs relieved depressive symptoms and improved quality of life in depressed elderly female patients.
- Relevance to:** Efalex Active 50+
- Reference:** Rondanelli M, Giacosa A, Opizzi A, Pelucchi C, Vecchia C et al. Effect of omega-3 fatty acid supplementation on depressive symptoms and on health-related quality of life in the treatment of elderly women with depression: a double-blind, placebo-controlled, randomized clinical trial. *Journal of the American College of Nutrition* 2010;29(1):55-64.

**PRESS RELEASE****Omega-3 LC-PUFAs reduce mania and depression in elderly patients with bipolar disorder<sup>1</sup>.**

A recent double-blind intervention study has shown that supplementation with 2.5 g/d of long chain omega-3 fatty acids (LC-PUFAs) for 2 months significantly reduces depression and improved quality of life in elderly patients with major depression<sup>1</sup>. The study was a collaboration between the Department of Applied Health Science, University of Pavia, Pavia, and The Department of Gastroenterology and Nutritional Science, Institute for Pharmacological Research, Institute of General Physiology and Biochemistry, University of Milan, Milan, Italy.

Depression is one of the most frequently missed diagnoses. It often occurs in association with cardiovascular disease and chronic inflammatory diseases, and is observed in 50% of elderly patients with dementia. It is now believed that increased depressive disorders in recent years may be due to decreased intake of omega-3 fatty acids relative to omega-6. Several studies have shown that many depressed patients have significantly lower dietary intake and serum levels of LC-PUFAs including docosahexaenoic acid (DHA) and eicosapentaenoic acid (EPA) primarily obtained in the diet from fish<sup>2,3</sup>. These fatty acids play a major role in brain function.

The randomized, double-blind, placebo-controlled trial included 46 depressed elderly women, aged 66-95 years from a nursing home in Pavia, Italy. Twenty-two women were treated with 2.5 g/day of an omega-3 supplement containing 1.67 g/day of EPA and 0.83 g/day of DHA while 24 patients were treated with paraffin oil placebo for 8 weeks. All patients were diagnosed with depression using standardized tests. Before and after treatment, each patient was assessed for body composition, nutritional status, depressive symptoms determined by the Geriatric Depression Scale (GDS), quality of life using the Short-Form 36-Item Health Survey (SF-36) and red blood cell (RBC) fatty acids.

After treatment, there was a significant 33% improvement in depression scores in the omega-3 group compared to placebo. The response rate was 45.5% in the Omega-3 group and 8.3% in the placebo group, while the remission rate was 40.9% in the omega-3 group and 16.7% in the placebo group. Quality of life significantly improved in the omega-3 group compared to placebo. There were no changes in body composition or nutritional status from the start of the study until the end and RBC fatty acid analysis confirmed that compliance was good. In addition, omega-3 and placebo treatments were both well tolerated with no serious adverse event observed over the eight weeks of the study.

Results of this study confirm the results of various previously published population and intervention studies. Hibbeln showed that as intake of omega-3 LC-PUFAs decreased the prevalence of depression increased across 13 countries<sup>4</sup>, and Tanskanen et al reported a higher prevalence of depressive symptoms in Finnish people who ate fish less often<sup>5</sup>.

Previous intervention studies have shown that in adolescents with bipolar disorder omega-3 LC-PUFAs can reduce mania and depression beyond the levels achieved with conventional medications<sup>6</sup> and can improve symptoms of depression<sup>7</sup> in children and bipolar disorder in adult<sup>8</sup> when taken together with standard drug treatments. Studies have also shown they can improve mania symptoms in young children with bipolar disorder when given singly<sup>9</sup>. Although all of these studies are preliminary investigations, the combined strength of the consistent improvements suggests that larger scale, randomised, double-blind, placebo controlled clinical trials are a necessity for this condition in all age groups.

**References:**

1. Rondanelli M, Giacosa A, Opizzi A, Pelucchi C, Vecchia C et al. Effect of omega-3 fatty acid supplementation on depressive symptoms and on health-related quality of life in the treatment of elderly women with depression: a double-blind, placebo-controlled, randomized clinical trial. *Journal of the American College of Nutrition* 2010;29(1):55-64.
2. Hakkarainen R, Partonen T, Haukka J, Virtamo J, Albanes D et al. Is low dietary intake of omega-3 fatty acids associated with depression? *Am J Psychiatry* 2004;161:567-569.
3. Conklin SM, Manuck SB, Yao JK, Flory JD, Hibboln JR et al. High omega-6 and low omega-3 fatty acids are associated with depressive symptoms and neuroticism. *Psychosom Med* 2007;69:932-34.
4. Hibbeln JR. Fish consumption and major depression. *Lancet* 1998;351:1213.
5. Tanskanen A, Hibbelin JR, Tuomilehto J, Uutela A, Haukkala A et al. Fish consumption and depressive symptoms in the general population in Finland. *Psychiatr Serv* 2001;52:529-531.
6. Clayton EH, Hanstock TL, Hirneth SJ, Kable CJ, Garg ML, Hazell PL. Reduced mania and depression in juvenile bipolar disorder associated with long chain w-3 polyunsaturated fatty acid supplementation. *Eur J Clin Nutr* 2009;63:1037-1040.
7. Nemets H, Nemets B, Apter A, Bracha Z, Belmaker RH. Omega-3 treatment of childhood depression: a controlled, double-blind pilot study. *Am J Psychiatry* 2006; 163:1098-1100.

8. Stoll AL, Severus WE, Freeman MP, Rueter S, Zboyan HA, Diamond E et al. Omega-3 fatty acids in bipolar disorder: a preliminary double-blind placebo-controlled trial. *Arch Gen Psych* 1999;56:407-412.
9. Wozniak J, Biederman J, Mick E, Waxmonsky J, Hantsoo L, Best C et al. Omega-3 fatty acid monotherapy for pediatric bipolar disorder: a prospective open-label trial. *Eur Neuropsychopharmacol* 2007;17:440-447.