Omega-3 Treatment of Childhood Depression: A Controlled, Double-Blind Pilot Study

Hanah Nemets, M.D.
Boris Nemets, M.D.
Alan Apter, M.D.
Ziva Bracha, M.D.
R.H. Belmaker, M.D.

Objective: Major depressive disorder in children may be more common than previously thought, and its therapeutics are unclear. Because of success in a previous study on omega-3 fatty acids in adult major depressive disorder, the authors planned a pilot study of omega-3 fatty acids in childhood major depression.

Method: Children who entered the study were between the ages of 6 and 12. Ratings were performed at baseline and at 2, 4, 8, 12, and 16 weeks using Children's Depression Rating Scale (CDRS), Children's Depression Inventory (CDI), and Clinical Global Impression (CGI). Children were randomized to omega-3 fatty acids or placebo as pharmacologic monotherapy. Twenty-eight patients were randomized, and 20 completed at least 1 month's ratings.

Results: Analysis of variance showed highly significant effects of omega-3 on symptoms using the CDRS, CDI, and CGI.

Conclusions: Omega-3 fatty acids may have therapeutic benefits in childhood depression.

Major depressive disorder is a common and recurrent disorder in children. It is frequently accompanied by poor psychosocial outcome, comorbid conditions, and high risk of suicide and substance abuse, indicating the need for treatment. The prevalence of major depressive disorder is estimated to be approximately 2%–4% in children (1). Several randomized, controlled studies have shown a 50% to 60% response to both selective serotonin reuptake inhibitors and placebo (2, 3). However, these studies included a majority of adolescent children, and the efficacy of biological treatment of prepubertal childhood depression is almost unknown. We found omega-3 fatty acids to be effective in adult depression as an add-on therapy (4). We therefore performed a controlled study of omega-3 fatty acid in childhood depression, restricting our study to children between the ages of 6 and 12.

Results

Twenty-eight children were randomized for the study. Of these 28, 20 completed at least 1 month's ratings and were included in the data analysis. Of the eight who dropped out before 1 month, five were on placebo and three were on omega-3. Among the three children of the omega-3 group, the only reason for dropout before 1 month was noncompliance. Reasons for dropout before 1 month in the placebo group were 1) appearance of precocious puberty leading to an endocrine workup in one patient, 2) noncompliance in two patients, 3) nonresponse in one patient, and 4) manic episode in another patient.

Of the 20 children who entered data analysis, 10 received placebo and 10 received omega-3. There were...
seven boys and three girls in the placebo group and eight boys and two girls in the omega-3 group. Mean age in the omega-3 group was 10.0 (range: 8–12.0) and 10.3 in the placebo group (range: 8–12.5). Children had been depressed for a mean of 3.5 (SD=1.3) months in the omega-3 group and 3.3 (SD=1.6) months in the placebo group. This was a first depressive episode in all cases. In the omega-3 group, there were two children with comorbid attention deficit hyperactivity disorder, one with obsessive-compulsive disorder, one with separation anxiety, one with dysthymia, and one with chronic tics. In the placebo group, there were three children with attention deficit hyperactivity disorder, one with panic disorder, one with separation anxiety, and two with dysthymia. Concurrent medications on stable dose for at least 6 months were two children on methylphenidate in the omega-3 group and three children in the placebo group.

Figure 1 shows the CDRS scores in the 20 patients who completed at least 1 month, with the last value carried forward. The effect of omega-3 is highly significant. Among the children on omega-3 treatment, seven out of 10 had a greater than 50% reduction in CDRS scores. Of those on placebo, zero out of 10 had a greater than 50% reduction in CDRS scores (p=0.003, Fisher’s exact test). Four out of 10 children in the omega-3 group met the remission criteria of Emslie and colleagues (2) of a CDRS score <29 at study exit; no subject in the placebo group met this criteria (p=NS).

The self-rating CDI results were similar to those of the CDRS. The “N” in the placebo group was 8 because two patients were unable to complete the self-rating scale or did so with errors. Two-way repeated-measures analysis of variance of treatment over time showed a statistically significant interaction (F=3.4, df=5,80, p<0.005). In addition, there was a significant main effect of treatment (F=5.5, df=1,16, p<0.04) and time (F=7.6, df=5,80, p<0.001).

CGI results were also highly significant. Two-way repeated-measures analysis of variance of treatment over time showed a statistically significant interaction (F=10.0, df=5,90, p<0.0001). There was a significant main effect of treatment (F=27.0, df=1,18, p<0.001) and time (F=28.3, df=5,90, p<0.0001). The omega-3 group and the placebo group were significantly different at week 8 (least significant difference post hoc test, p=0.014), week 12 (least significant difference post hoc test, p=0.003), and week 16 (least significant difference post hoc test, p=0.002).

There were no clinically relevant side effects reported. No patient reported a fishy taste when asked specifically. Debriefing of the blind revealed a random guess rate by both patient and clinician.

Discussion

The very small placebo effect in this study is unusual for studies of childhood depression (2, 3) but is similar to our previous study of omega-3 in adult depression (4). In the adult study, we speculated that the placebo effect may have been due to low expectations for omega-3 in recurrently depressed and “experienced” patients; however, the children in this study had been ill for a much shorter period of time than the previously studied adults.

The previous study in adults used eicosapentanoic acid, the precursor of docosahexaenoic acid. The present study used a combination of eicosapentanoic acid and docosahexaenoic acid that is commonly available as an over-the-counter preparation. It should be noted that not all studies of omega-3 fatty acids in depression in adults have been positive (6, 7). The reasons for this discrepancy are unclear, but baseline dietary differences in different populations may be involved (8). The present study is the first, to our knowledge, of omega-3 treatment in prepubertal childhood depression.

Received May 11, 2005; revision received Aug. 24, 2005; accepted Oct. 18, 2005. From the Faculty of Health Sciences, Ben Gurion University of the Negev, Israel; and Schneider Children’s Medical Center, Tel Aviv University, Tel Aviv. Address correspondence and reprint requests to Dr. Belmaker, Beer-Sheva Mental Health Center, PO Box 4600, Beer-Sheva, Israel; belmaker@bgu.ac.il (e-mail).

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References

Brief Report

Omega-3 Polyunsaturated Essential Fatty Acid Status as a Predictor of Future Suicide Risk

M. Elizabeth Sublette, M.D., Ph.D.
Joseph R. Hibbeln, M.D.
Hanga Galfalvy, Ph.D.
Maria A. Oquendo, M.D.
J. John Mann, Ph.D.

Objective: Low levels of docosahexaenoic acid, a polyunsaturated fatty acid, and elevated ratios of omega-6/omega-3 fatty acids are associated with major depression and, possibly, suicidal behavior. Predicting risk of future suicidal behaviors by essential fatty acid status merits examination.

Method: Plasma polyunsaturated fatty acid levels in phospholipids were measured in 33 medication-free depressed subjects monitored for suicide attempt over a 2-year period. Survival analysis examined the association of plasma polyunsaturated fatty acid status and pathological outcome.

Results: Seven subjects attempted suicide on follow-up. A lower docosahexaenoic acid percentage of total plasma polyunsaturated fatty acids and a higher omega-6/omega-3 ratio predicted suicide attempt.

Conclusions: A low docosahexaenoic acid percentage and low omega-3 proportions of lipid profile predicted risk of suicidal behavior among depressed patients over the 2-year period. If confirmed, this finding would have implications for the neurobiology of suicide and reduction of suicide risk.

Depressive disorders are associated with low levels of omega-3 plasma polyunsaturated fatty acids and elevated omega-6/omega-3 ratios (1–5), while augmentation with omega-3 plasma polyunsaturated fatty acids is reportedly therapeutic (6). However, there is disagreement regarding a possible link between plasma polyunsaturated fatty acid status and suicidal behavior (7–9). In the present study, we sought to prospectively determine whether plasma polyunsaturated fatty acid status is related to suicide attempt.

Method

Adult subjects (N=33) seeking treatment for depression gave written informed consent, approved by our institutional review board, and met criteria for a major depressive episode. Axis I diagnoses were based on the Structured Clinical Interview for DSM-IV. Subjects were excluded for neurological or medical disease or substance dependence and were off antidepressant medications for at least 14 days prior to baseline assessments. The 24-item Hamilton Depression Rating Scale and the Beck Scale for Suicidal Ideation measured depression and suicidal thoughts. Lifetime aggression was assessed using the Brown-Goodwin Aggression History. A suicide-attempt history was also obtained. Baseline fasting plasma polyunsaturated fatty acid composition was analyzed using gas chromatography, and percentages of total phospholipid fatty acids were determined for docosahexaenoic acid (22:6n-3), eicosapentaenoic acid (20:5n-3), arachidonic acid (20:4n-6), and omega-6/omega-3 ratio. Subjects received naturalistic psychopharmacological inpatient (8 weeks) or outpatient (6 months) treatment from the research team, followed by community-based treatment. Research evaluations were performed at 3, 12, and 24 months by raters unaware of the subjects’ plasma polyunsaturated fatty acid status.

Demographic/clinical attributes at study entry were tested for associations with plasma polyunsaturated fatty acid levels using Student’s t test, Pearson’s r, or Spearman’s rho correlations.