Omega-3 Fatty Acid Augmentation of Citalopram Treatment for Patients With Major Depressive Disorder

BACKGROUND

- Although pharmacotherapy is the mainstay of treatment for depression, an adequate response to a single antidepressant medication only occurs in approximately 50-75% of patients. Some data suggests that the combination of 2 antidepressant agents may double the likelihood of remission compared to monotherapy. A link between omega-3 fatty acids and mood disorders is suggested by some studies showing a lower incidence of depression among populations with a diet rich in omega-3 fatty acids. Furthermore, lower plasma levels of omega-3 fatty acids have been reported in patients with mood disorder compared to healthy individuals.

OBJECTIVE

- The objective of this study was to determine if omega-3 fatty acid supplementation of citalopram leads to greater efficacy in treatment of depression compared to antidepressant monotherapy and to determine if omega-3 fatty acid supplementation leads to an acceleration of antidepressant response at week 2 of treatment.

METHODS

- **Design** This study was a randomized, double-blind, placebo controlled, parallel study. *Duration:* 8 weeks.
- **Inclusion criteria**
  - Recruited subjects were between the ages of 18 and 65 who met DSM-IV criteria for major depression by Structured Clinical Interview for DSM Disorders (SCID) and had a 21-item Hamilton Depression Rating Scale (HAM-D) score greater than 17.
- **Exclusion criteria**
  - Diagnosis of psychotic disorders including psychotic depression and bipolar disorders
  - Current or history of drug or alcohol abuse or dependence within the previous 6 months
  - Unstable medical or neurological conditions that were likely to interfere with the treatment of depression
  - History of allergy to citalopram, omega-3 fatty acids, or shellfish
  - Previous failure of response to an adequate trial of citalopram
  - Treatment with fluoxetine or MAOIs in the previous 2 months or psychotropic medications
  - Currently on anticoagulant therapy
  - History of seizure disorder
  - Pregnancy
  - Active suicidal thoughts or other safety concerns
  - Dietary intake greater than 3.0 g of total omega-3 FA per day at baseline
- **Primary endpoints**
  - Decrease in 21-item HAM-D scores evaluated by a psychiatrist at baseline, randomization and at weeks 2,4,6, and 8.
- **Secondary endpoints**
  - Secondary measures of efficacy involved changes in several other depression rating scales including the Beck Depression Inventory (BDI), the Montgomery-Asberg Depression Rating Scale (MADRS), the Clinical Global Impression Scale (CGI), and the Patient's Global Improvement Scale (PGI).
- **# enrolled per group:** 42 subjects were randomized to 2 study arms. 20 subjects received citalopram + omega-3 and 22 received citalopram + placebo.
- **Drug Regimen:** At the end a 1 week run-in phase, subjects still with a HAM-D score greater than 17 were block randomized by sex to receive citalopram 20mg daily. Half of the subjects also received omega-3 fatty acids and the other half received placebo. Subjects were instructed to take citalopram in the morning and two omega-3 or placebo capsules twice daily with meals. All subjects remained on citalopram 20mg daily until week 4 of the study, after which the dose could be increased to 40mg/day if HAM-D scores had decreased less than 25% and adverse effects were not a concern.
- **Power:** 80% power to detect a decrease in HAM-D scores with an effect size ranging between 0.8-1 at α=0.05.

- **Data Handling:** Intent-to-treat analysis

RESULTS:

- **Number of patients completing study:** 33 total patients completed the study. 18 patients in treatment group and 15 in placebo group.
- **Primary outcome measure:** there was significantly greater improvement over time in HAM-D scores among subjects in the omega-3 FA group compared to placebo (p=0.008). Significant differences were noted between the treatment groups at study week 4, week 6, and week 8 (p=0.005, p=0.008, p=0.004)
- **Secondary outcome measures:** There was also statistically significant improvement in remission status in the omega-3 group compared to placebo (p=0.018). There were "trends" for group vs. time interaction for BDI scores and MADRS scores (p=0.018).
- **Authors Conclusions:** Omega-3 fatty acid supplementation of citalopram produced a significantly greater reduction in HAM-D scores compared to citalopram treatment alone. There was no evidence of acceleration of antidepressant response with the addition of omega-3 fatty acid.

STRENGTHS

- Randomized, double-blind, placebo controlled, parallel study.
- Good rationale for conducting study
- No conflicts of interest
- Appropriate inclusion/exclusion criteria

WEAKNESSES

- Small number of subjects
- Large dropout rate (especially in placebo group)
- Heterogeneity of subjects at baseline
- Possible inappropriate dose and duration of therapy of omega-3 fatty acid
- Recruitment of subjects by advertisement/physician referral
- Did not determine if blinding was successful
- Possible non-adherence to treatment regimens

CONCLUSIONS

- Based on this study alone, it should not be recommended to add omega-3 fatty acids to citalopram for the treatment of depression. Even though the results of this study showed statistical significance when omega-3 fatty acids were added to citalopram, key limitations prevent the usefulness of this study's results in clinical practice. These key limitations include small sample size, large dropout rate, and a large variability of subjects at baseline. Omega-3 fatty acids are inexpensive, have very few adverse reactions, and may be useful in patients with concurrent cardiovascular disease. If omega-3 fatty acids were tested in a larger study in patients with similar characteristics, omega-3 fatty acids may be a safe and effective treatment option in patients not achieving remission of depression with antidepressants.

Reference: Gertsik, Lev MD; Poland, Russell E. PhD; Bresee, Catherine MS; Rapaport, Mark Hyman MD. Omega-3 Fatty Acid Augmentation of Citalopram Treatment for Patients With Major Depressive Disorder. Journal of Clinical Psychopharmacology. 32(1), Feb 2012, p 61–64.

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