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
  o 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
  o Diagnosis of psychotic disorders including psychotic depression and bipolar disorders
  o Current or history of drug or alcohol abuse or dependence within the previous 6 months
  o Unstable medical or neurological conditions that were likely to interfere with the treatment of depression
  o History of allergy to citalopram, omega-3 fatty acids, or shellfish
  o Previous failure of response to an adequate trial of citalopram
  o Treatment with fluoxetine or MAOIs in the previous 2 months or psychotropic medications
  o Currently on anticoagulant therapy
  o History of seizure disorder
  o Pregnancy
  o Active suicidal thoughts or other safety concerns
  o Dietary intake greater than 3.0 g of total omega-3 FA per day at baseline
• Primary endpoints
  o Decrease in 21-item HAM-D scores evaluated by a psychiatrist at baseline, randomization and at weeks 2,4,6, and 8.
• Secondary endpoints
  o 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 \( \alpha=0.05 \).
• 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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