Fish oil reduced relapse and maintained remission in Crohn disease


Objective
To determine the effectiveness of an enteric-coated fish oil preparation for maintaining remission in patients with Crohn disease.

Design
1-year, randomized, double-blind, placebo-controlled trial.

Setting
Gastroenterology outpatient clinic in Italy.

Patients
78 patients (age range 18 to 67 y, 50% men) who had Crohn disease and were in clinical remission but at high risk for relapse as judged by laboratory criteria, including at least 1 of serum α2-acid glycoprotein concentration > 130 mg/dL, serum α2-globulin concentration > 0.9 g/dL, or erythrocyte sedimentation rate > 40 mm/h. Exclusion criteria were age < 18 or > 75 years; receipt of mesalamine, sulfasalazine, or corticosteroids in the previous 3 months or immunosuppressive drugs in the previous 6 months; or previous resection of > 1 m of bowel. 91% of patients completed the study.

Intervention
Patients were allocated to fish oil, three 500-mg enteric-coated capsules (n = 39), or placebo, 60% caprylic acid and 40% capric acid (n = 39), 3 times/d. The capsule coating was designed to resist gastric acid for 30 minutes to allow release of fish oil into the small intestine. Compliance was assessed by pill count.

Main outcome measures
Relapse rate and remission rate. Relapse was defined as an increase of ≥ 100 points over baseline on the Crohn Disease Activity Index and a score > 150 for > 2 weeks.

Main results
Treatment with fish oil led to fewer relapses than did placebo (28% vs 69%, P < 0.001). (This absolute risk reduction of 41% means that 2 patients would need to be treated (NNT) with fish oil for 1 year (compared with placebo) to prevent 1 additional patient from having a relapse,

95% CI 2 to 5; the relative risk reduction was 59%, CI 32% to 77%.)* More patients who received fish oil were still in remission at 1 year than were patients who received placebo (59% vs 26%, P = 0.003) (absolute risk improvement 33%; NNT 3, CI 2 to 9; relative risk improvement 130%, CI 31% to 325%)*. 4 patients (10%) withdrew because of diarrhea in the fish oil group compared with 1 patient (3%) in the placebo group, but the ~7% difference did not reach statistical significance (CI −21% to 4%, P = 0.17)*.

Conclusion
An enteric-coated fish oil preparation reduced relapse and maintained remission in patients with Crohn disease that was clinically inactive but was accompanied by an increase in serum levels of markers of inflammation.

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*Numbers calculated from data in article.


Commentary
The study by Belluzzi and colleagues was a randomized, controlled trial of an enteric-coated fish oil preparation in outpatients with Crohn disease in clinical remission. A high relapse rate (69%) in the placebo group was predicted by elevated serum levels of markers of inflammation. The efficacy of fish oil for preventing relapse was greater than that reported for 5-aminosalicylates, metronidazole, or corticosteroids. The number of patients who were clinically eligible but were excluded because of negative laboratory tests was not stated. If few patients were excluded by laboratory criteria, the results of the study are more generalizable to patients who have Crohn disease that is in remission.

The treatment showed a trend toward an increased incidence of diarrhea but had no other substantial side effects. Co-intervention with antidiarrheal agents was not permitted (A. Belluzzi, Personal communication). A previous small, unblinded study by Maté and colleagues (1) also suggested that fish oil or a diet high in fish was effective. A crossover study of fish oil by Lorenz and colleagues (2) included 29 patients with Crohn disease and 10 with ulcerative colitis. Although it failed to show efficacy in Crohn disease, the study was limited by both power considerations and the crossover design that had relatively short treatment periods.

The results of the study by Belluzzi and colleagues should be confirmed and extended to patients with active disease. This treatment will be attractive to many patients, particularly those with a preference for "natural remedies," those who have had surgery, and those who have experienced side effects from conventional drugs. The cost is also likely to be less than that of high doses of 5-aminosalicylates, the most widely used agents for relapse prevention.

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References