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Dietary Supplementation with Fish Oil in Ulcerative Colitis

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Objective: To determine the efficacy of fish oil supplementation in patients with active ulcerative colitis.

Design: Multicenter, randomized, double-blind, placebo-controlled, crossover trial with 4-month treatment periods (fish oil and placebo) separated by a 1-month washout.

Setting: Four gastroenterology divisions.

Patients: Twenty-four patients with active ulcerative colitis entered the study. Five dropped out, and one was noncompliant. Eighteen patients completed the study. All patients had active disease as manifested by diarrhea and rectal inflammation.

Interventions: Treatment with prednisone and sulphasalazine was continued. Fish oil supplementation consisted of 18 Max-EPA (eicosapentaenoic acid) capsules daily (eicosapentaenoic acid, 3.24 g; and docosahexaenoic acid, 2.16 g). Placebo supplementation consisted of 18 identical capsules containing isocaloric amounts of vegetable oil.

Measurements: Patients were evaluated at study entry and after each diet period. Evaluations included a review of symptoms, flexible sigmoidoscopy, rectal biopsy, and rectal dialysis to measure prostaglandin E2 levels and leukotriene B4 levels.

Results: Fish oil supplementation resulted in a significant decrease in rectal dialysate levels of leukotriene B4 from 71.0 to 27.7 pg/mL (average change, -43.3 pg/mL; 95% CI, -83 to -3.6). Significant improvements were seen in acute histology index (average change, -8.5 units from a baseline of 10.5 units; CI, -12.9 to -4.2) and total histology index (average change, -8.5 units from a baseline of 14.80; CI, -13.2 to -3.8) as well as significant weight gain (average weight gain, 1.74 kg; CI, 0.94 to 2.54). No significant changes occurred in any variable during the placebo period. Seven patients received concurrent treatment with prednisone. During the fish oil supplementation period, the mean prednisone dose decreased from 12.9 mg/d to 6.1 mg/d and rose from 10.4 mg/d to 12.9 mg/d during the placebo diet period (P > 0.20).

Conclusions: Four months of diet supplementation with fish oil in patients with inflammatory bowel disease resulted in reductions in rectal dialysate leukotriene B4 levels, improvements in histologic findings, and weight gain.

Prostaglandin E2, a metabolite of arachidonic acid through the cyclooxygenase pathway, is a product of many cell types including enterocytes and macrophages (1, 2). Prostaglandin E2 increases vascular permeability, dilates blood vessels, and down-regulates immune functions (3). Leukotriene B4, a metabolite of arachidonic acid through the 5-lipoxygenase pathway, is formed primarily by inflammatory cells including neutrophils, macrophages, and mast cells (4). Leukotriene B4 is a potent neutrophil chemotactic agent (5); the primary role of leukotriene B4 in inflammation is thought to be the recruitment of neutrophils from the circulatory system and into the inflamed tissue.

Increased levels of prostaglandin E2 and leukotriene B4 are found in patients with ulcerative colitis. Inflamed colonic mucosa from patients with ulcerative colitis has an increased synthetic capacity for both these compounds and lipid extracts of mucosa from surgical resections in patients with ulcerative colitis contain 50-fold more leukotriene B4 than do lipid extracts of normal mucosa (6). Rectal dialysates from patients with ulcerative colitis contain markedly elevated levels of leukotriene B4 and prostaglandin E2 (7). The levels of these compounds in rectal dialysates correlate with the severity of disease measured clinically, endoscopically, or histologically (7). Prednisolone treatment of patients with ulcerative colitis reduces leukotriene B4 and prostaglandin E2 concentration in the rectal dialysates and results in clinical improvement (8). A specific role for leukotriene B4 in the pathogenesis of ulcerative colitis is suggested by the finding that leukotriene B4 is the main neutrophil chemotactic factor in the mucosa of patients with ulcerative colitis (9). A recent preliminary report showed that a specific, orally administered 5-lipoxygenase inhibitor was found to be effective in the treatment of ulcerative colitis (10).

Although arachidonic acid (20:4 n-6) is the usual substrate for both the cyclooxygenase and 5-lipoxygenase pathways, some other polyunsaturated fatty acids are also potential substrates. Among these alternative substrates is eicosapentaenoic acid (EPA), which is commonly present in fish oil. Eicosapentaenoic acid (20:5 n-3) is metabolized through the cyclooxygenase pathway to prostaglandins and thromboxanes of the 3 series (11) and by the neutrophil 5-lipoxygenase pathway to leukotriene B4, which is 30 times less potent than leukotriene B4 as a neutrophil chemotactic agent (12-14). Long-term ingestion of large amounts of fish oil increases the EPA content of neutrophils, increases leukotriene B4 production, and decreases leukotriene E5 production (15). Dietary fish oil supplementation has...