

# Improvement in Ulcerative Colitis Symptoms After Use of Fish Oil Enemas

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Recent studies have demonstrated improved clinical response, sustained remission, and decreased dependence on corticosteroids in patients with ulcerative colitis (UC) after supplementing their therapy with oral omega-3 (n-3) fatty acids.<sup>1</sup> We report a case of a 75-year-old woman with active colitis who experienced improvement in her symptoms after adding to her treatment n-3 fatty acid supplements delivered via rectal enema.

## Case Report

A 75-year-old Hispanic woman with a 7-year history of distal UC presented with bloody, loose stools that had recently worsened. At the time, her stool frequency remained 1–2 times daily, but the consistency of the stool was loose and mixed with blood in each movement. In addition, the patient complained of mild cramp-like lower abdominal pains and an occasional sensation of incomplete evacuation. The patient was on long-standing UC maintenance therapy of mesalamine 2.0 g daily, as well as mesalamine enemas 2–3 times weekly, and she reported that she was highly compliant with her medications. Her last colonoscopy had been 2 years earlier and demonstrated grade III colitis from the rectum to the proximal sigmoid colon. Pathologic findings had included chronic active inflammation and focal cryptitis in the rectum.

Although the conventional recommendations of changes to her medication were made, the patient opted to independently try a novel supplement to her treatment. Remaining on the current treatment regimen, the patient self-administered an additional enema daily of 3 g of fish oil. The over-the-counter preparation of fish oil she used was marketed as an oral gel-cap liquid supplement with eicosapentaenoic acid (EPA) 540 mg, docosahexaenoic

acid (DHA) 360 mg, and vitamin E 3.3 IU, according to the package labeling. The liquid portion was separated from the gel cap and administered locally by the patient, without dilution in a solvent.

The patient's symptoms resolved within 3 weeks of starting this supplemental therapy. Subsequent colonoscopy demonstrated normal-appearing colonic mucosa in the rectum to 35 cm from the anus, as well as mild colitis in the descending colon. Histopathology revealed normal mucosa in the rectum and chronic active colitis in the proximal colon.

## Discussion

N-3 fatty acids found in fish oil are long-chain fatty acids containing two or more double bonds.<sup>1</sup> Mammals cannot produce n-3 fatty acids, and so the acids are defined as “essential” and are only available by exogenous ingestion. A number of placebo-controlled studies have shown improved clinical response and decreased need for corticosteroids in symptomatic UC patients who were administered oral n-3 supplements.<sup>2–5</sup> Although no studies or case reports have examined clinical response of n-3 products administered rectally in humans, Yuceyar and associates investigated the protective role of n-3 fatty acid enemas in the trinitrobenzene-induced colitis model in rats.<sup>6</sup> They found significant reductions in leukotriene levels in tissues exposed to n-3 enemas, but failed to demonstrate a decrease in pathologic tissue damage.

The mechanism by which n-3 fatty acids are believed to reduce inflammation results from the incorporation of the polyunsaturated fat components of EPA and DHA into the arachidonic acid precursors of inflammatory mediators. Incorporation of these products leads to increased production of 3-series prostoglandins and thromboxanes and 5-series leukotrienes, which have reduced inflammatory potential.<sup>7,8</sup> Interleukin-1B and tumor necrosis factor production may also be reduced by the presence of n-3 fatty acids.<sup>9</sup> Thus, the propagation of inflammatory pathways are diminished.

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Although structurally unrelated to n-3 fatty acids, short-chain fatty acid (SCFA) enemas have shown efficacy in treating diversion colitis,<sup>10</sup> but not in UC.<sup>11</sup> The mechanism by which SCFA improves diversion colitis is entirely different from the anti-inflammatory mechanism of n-3 fatty acids. SCFA is believed to act as a direct metabolic energy source for epithelial cells. Deprivation of SCFA in a diverted bowel segment leads to inflammation.

## Conclusion

This case report presents a case of UC in which the patient experienced significant improvement in symptoms after starting n-3 enemas and showed clear evidence of locally diminished rectal colitis on examination and histopathology. These events were either directly due to the use of n-3 enemas or represented an additional benefit of n-3 fatty acids in the induction of local remission, as her other therapies remained the same. Given prior research that oral supplementation of n-3 fatty acids is effective in UC, there is reason to believe that local rectal therapy may be of use in distal disease. Controlled studies are, therefore, warranted to investigate this possibility further. In vitro experiments may determine whether n-3 fatty acids work via systemic effect after intestinal absorption or via local contact with the gut mucosa.

## References

1. Belluzzi A, Boschi S, Brignola C, et al. Polyunsaturated fatty acids and inflammatory bowel disease. *Am J Clin Nutr*. 2000;71:339S-42S.
2. Seidner DL, Lashner BA, Brzezinski A, et al. An oral supplement enriched with fish oil, soluble fiber, and antioxidants for corticosteroid sparing in ulcerative colitis: a randomized, controlled trial. *Clin Gastroenterol Hepatol*. 2005;3:358-369.
3. Hawthorne AB, Daneshmend TK, Hawkey CJ, et al. Treatment of ulcerative colitis with fish oil supplementation: a prospective 12 month randomized controlled trial. *Gut*. 1992;33:922-928.
4. Stenson WF, Cort D, Rodgers J, et al. Dietary supplementation with fish oil in ulcerative colitis. *Ann Intern Med*. 1992;116:609-614.
5. Aslan A, Triadafilopoulos G. Fish oil fatty acid supplementation in active ulcerative colitis: a double-blind, placebo-controlled, crossover study. *Am J Gastroenterol*. 1992;87:432-437.
6. Yuceyar H, Ozutemiz O, Huseyinov A, et al. Is administration of n-3 fatty acids by mucosal enema protective against trinitrobenzene-induced colitis in rats? *Prostaglandins Leukot Essent Fatty Acids*. 1999;61:339-345.
7. Belluzzi A. n-3 fatty acids for the treatment of inflammatory bowel diseases. *Proceed Nutr Soc*. 2002;61:391-395.
8. Sharon P, Stenson WF. Enhanced synthesis of leukotriene B<sub>4</sub> by colonic mucosal inflammatory bowel disease. *Gastroenterology*. 1984;86:453-460.
9. Endres S, Ghorbani R, Kelly VE, et al. The effect of dietary supplementation with n-3 fatty acids on the synthesis of interleukin-1 and tumor necrosis factor by mononuclear cells. *N Engl J Med*. 1989;320:265-270.
10. Harig JM, Soergel KH, Komorowski RA, Wood CM. Treatment of diversion colitis with short-chain fatty acid irrigation. *N Engl J Med*. 1989;320:23-28.
11. Breuer RI, Soergel KH, Lashner BA, et al. Short chain fatty acid rectal irrigation for left-sided ulcerative colitis: a randomised, placebo controlled trial. *Gut*. 1997;40:485-491.

# Review

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Throughout history, the fish has symbolized different things in different cultures and religions. In Greek mythology, Aphrodite, the goddess of love and beauty, rose from the foam of the sea, and pisces (“the fish”) represented her and her son Eros. In Roman mythology, Venus is the equivalent of Aphrodite; in the painting “The Birth of Venus” by Botticelli, Venus is standing on a shell floating in the sea by the beach. In the Hindu text *Bhagavata Purana*, the god Vishnu first descends in the form of a fish. The Celts referred to the fish as “the Great Mother,” and early Christians associated the fish with fertility, birth, and feminine sexuality. In Christianity, the symbol of a fish signifies salvation and evangelism. In addition, the fish is part of traditional meals on religious holy days. Gefilte fish is part of the traditional meal eaten by Jews on Sabbath and holy days, and in the Catholic church, fish is eaten during Lent.

In the twentieth century, the benefits of a fish diet began to be investigated when epidemiologic studies in the early 1970s conducted by Dyerberg and Bang among the Inuit population in western Greenland showed a relatively low incidence of heart disease and a high incidence of hemorrhagic stroke.<sup>1</sup> There were also significant differences in the lipoprotein profile of the Inuit population in western Greenland compared to an age-matched Danish population and also compared to the lipoprotein profile of Inuits living in Denmark.<sup>2</sup> At the time of the study, the typical diet of the Inuit population in western Greenland was fish, whale, seal, walrus, and other sea animals—in other words, a diet high in protein and fat and low in carbohydrates. In contrast to the low incidence of heart disease in western Greenland, there was a high incidence of heart disease in Danish and other European populations, even though during that time their diet was also high in protein and fat. The difference between the typical diet of the Inuit population in western Greenland and the diet in the Danish population is that the former is rich in long-chain omega-3 fatty acids with a high ratio of unsaturated to saturated fatty acids. Omega-3 fatty acids are polyunsaturated fatty acids (PUFA) found in ocean fish, sea mammals, and vegetable oils such as primrose

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