Preventing Infection in Cirrhotics With Gastrointestinal Hemorrhage

Dear Sir:

We were impressed with the findings of Soriano et al. regarding the efficacy of norfloxacin-induced selective intestinal decontamination (SID) in preventing bacterial infection in cirrhotics with gastrointestinal hemorrhage. The number of patients needed to be treated (NNT) with norfloxacin to prevent one infection is only 3.7 (95% confidence interval, 2.4–7.8), which represents a clinically meaningful effect. The corresponding NNTs for bacteremia treated (NNT) with norfloxacin to prevent one infection is only 5.4 (95% confidence interval, 3.5–11) and urinary tract infection (5.4; 95% confidence interval, 3.5–11) are impressive and clinically meaningful as well.

In deciding whether to incorporate SID into our everyday care of patients, we wondered about two issues. First, because a significant number of infections were in the urinary tract, what criteria were used for diagnosis? Second, did the benefits of SID accrue to any particular patient subgroup, specifically, Child-Pugh subgroups? Previous research has suggested that Child-Pugh class C patients may derive significant benefit from SID. Although post hoc analysis might lack the power to detect a clinically meaningful difference and must be viewed cautiously and validated prospectively, it would be interesting to know in order to target certain subgroups for SID, at least initially. Further study of this treatment should be conducted with these subgroups in mind and hopefully will corroborate the findings of Soriano et al.

THOMAS F. IMPERIALE, M.D.
EDWARD J. ESBER, M.D.
Case Western Reserve University at MetroHealth Medical Center
2500 MetroHealth Drive
Cleveland, Ohio 44109


Bowel Rest and Elemental Diet in Crohn's Disease

Dear Sir:

The comment by Bernstein and Shanahan on the treatment of Crohn’s disease with elemental diet deserves further analysis. They state that bowel rest is unlikely to be an important mechanism for the action of this type of treatment because total parenteral nutrition (TPN) has not been shown to be effective in controlled studies and give five references. Dickinson et al. only included 3 patients with Crohn’s disease in the control group, and Lochs et al. included patients with a Crohn’s Disease Activity Index of <150 in both groups. McIntyre et al. studied 16 patients, all of whom responded to treatment, resulting in difficulty assessing which was the better treatment, and Matuchansky’s article was a review. In the study by Greenberg et al., there were 17 patients treated by TPN; 5 had a fistula and 7 had an inflammatory mass (both more frequent than in the group treated with partial parenteral nutrition [PPN] and oral diet), yet clinical remission still occurred more frequently in the TPN group (71% vs. 60%). A recent study of fecal stream diversion in Crohn’s disease provides strong support for the effect of bowel rest.

Bernstein and Shanahan also refer to three comparative studies finding elemental diet therapy equivalent to steroid therapy and two studies in which elemental diet therapy was inferior to steroid therapy. They do not refer to the recent controlled nonrandomized study finding elemental diet therapy superior to steroid therapy. It is also interesting that Vivonex (using protein only as amino acids) was used in two of the studies finding elemental diet therapy equivalent to steroid therapy and Elenital (also using protein only as amino acids) was used in the study finding elemental diet superior to steroid therapy. Survivmed (containing whey, soy, meat hydrolysate, and amino acids) and Peptisorb (80% oligopeptide using protein hydrolysate) were used in the two studies in which elemental diet was inferior to steroid therapy. Flexical (containing hydrolyzed casein and amino acids) was used in the other study finding elemental diet therapy equivalent to steroid therapy. The response of Crohn’s disease to monomeric or polymeric diet therapy may vary according to the protein content of the formulation administered.

ALEX MORAN, M.R.C.P.
Department of Gastroenterology
East Birmingham Hospital NHS Trust
Bordesley Green East
Birmingham B9 5ST, England

April 1993

Reply. We appreciate Dr. Moran's letter in response to our Selected Summary. His comments actually reinforce our message: (1) there is no conclusive evidence for a primary therapeutic role of bowel rest or elemental enteral diet therapy in Crohn's disease, and (2) studies controlling for the natural history of the disease and the large placebo effect associated with its treatment are needed.

Dr. Moran's comments about the study by Greenberg et al.2 are misleading. In that study, there was no significant difference between the group receiving TPN and the group receiving PPN plus oral diet. In the TPN group, 5 of 17 patients had fistulas and 7 of 17 patients had inflammatory masses, compared with 3 of 15 patients with fistulas and 5 of 15 patients with inflammatory masses in the PPN plus oral diet group. Clinical remission was not defined by disappearance of either fistulas or inflammatory masses, but rather by a Crohn's Disease Activity Index of <150 and ability to tolerate oral diet by day 21. The difference in remission rates between the groups was not significantly different (12 of 17 in the TPN group and 9 of 15 in the PPN plus oral diet group). Greenberg et al. conclude that "in patients with active Crohn's disease bowel rest was not a major factor in achieving remission during nutritional support and did not influence outcome during one year's follow-up."

Dr. Moran appears to misrepresent the recent study of fecal stream diversion in Crohn's disease.3 The goal of that study was to investigate the role of fecal stream in the pathogenesis of recurrent Crohn's lesions in 5 patients who underwent ileal resection. The study revealed a decrease in inflammation at the neoterminal ileum of ileostomies compared with the neoterminal ileum was restored to continuity with the colon. This study has important implications for the role of colonic flora in the recurrence of Crohn's disease but did not address the role of bowel rest.

Dr. Moran's comments on the relative merits of the protein content of individual enteral diets are inconclusive because he is not citing studies in which different diets were directly compared. Furthermore, the study by Rigaud et al.4 and others reviewed by us,1 show that polymeric diets when directly compared with elemental diets are probably equivalent in efficacy.

We stand by our conclusions, including that neither bowel rest nor elemental diets have been clearly proven to be of primary therapeutic benefit in the treatment of Crohn's disease. Certainly nutritional supplementation is beneficial in the malnourished patient.

CHARLES N. BERNSTEIN, M.D.
FERGUS SHANAHAN, M.D.
Division of Gastroenterology
UCLA School of Medicine
10333 Le Conte Avenue
Los Angeles, California 90024


ω-3 Fatty Acids and Bowel Cancer

Dear Sir:

I have read with great interest the article by Anti et al.,1 the accompanying editorial by Wargovich,2 and the summary by Spechler.3 I would like to clarify an important issue about prostaglandins.

This well-performed study has important scientific significance. However, I disagree with the interpretation that the beneficial effects of fish oil are related to decreased prostaglandin production. Furthermore, the Discussion section and Editorial implicate prostaglandins generally as a possible etiologic factor in carcinogenesis. For the benefit of readers I would like to clarify this issue. Endogenous prostaglandins, thromboxanes, and leukotrienes are formed from three major dietary fatty acid precursors. Dihomo-gamma linolenic acid is a substrate for forming prostaglandin E1, thromboxane A2, and leukotriene A4. Arachidonic acid is a substrate for forming prostaglandin E2, thromboxane A2, and leukotriene A4. Eicosapentanoic acid is a substrate for forming prostaglandin E3, thromboxane A2, and leukotriene A4.

The high dietary ingestion of fish oils is therefore associated with significant production of eicosanoids derived from eicosapentanoic acid. These eicosanoids have a physiological and pharmacological effect that differs substantially from those of arachidonic and linoleic acid-derived products. For example, Phillipson et al.4 show that the ingestion of fish oil, but not vegetable oil, induced a marked reduction in the concentration of triglyceride-rich lipoproteins in the plasma of patients with hypertriglyceridemia. A fish oil-rich diet decreases the content of arachidonic acid and increases the content of eicosapentanoic acid in the platelet membranes.5,6 Furthermore, platelet membrane eicosapentanoic acid that is released in response to agonists inhibit, the metabolism of arachidonic acid and is converted to metabolic products that inhibit platelet functions.7 Furthermore, it has been shown that diets rich in fish oil may exert anti-inflammatory effects by inhibiting the 5-lipoxygenase pathway in neutrophils and monocytes and inhibiting the leukotriene B4-mediated functions of neutrophils.8