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Reply

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We would like to thank Coeffier et al, for their interest in our recent article which delineated the mechanisms by which in vivo miR-29a/b modulates Claudin-1 and NKRF expression and leads to an alteration of intestinal permeability.[1–2] We previously reported that glutamine synthetase is a target of miR-29a and that increased miR-29a leads to decreased glutamine synthetase in small bowel and colonic intestinal mucosa of patients with diarrhea-predominant IBS (D-IBS) with increased intestinal permeability.[3] Glutamine synthetase catalyzes the conversion of glutamate and ammonia to glutamine and congenital glutamine deficiencies have been documented in children who have mutations of the glutamine synthetase gene (GLUL).[4] Patients with decreased intestinal glutamine synthetase may have low levels of available intestinal glutamine with resulting increased intestinal permeability. Glutamine is the principal fuel for enterocytes and has direct effects on intestinal integrity via tight junction proteins and decreases bacterial translocation after intestinal injury.[5] Deficiencies in glutamine may lead to increased intestinal permeability and supplementation with glutamine can reverse intestinal hyperpermeability and the accompanying gastrointestinal symptoms.

Increased intestinal permeability maybe a potential etiologic factor in D-IBS patients. Several studies have shown that D-IBS patients have increased intestinal permeability that may facilitate passage of inflammatory agents, bacteria, and toxins through the gut wall leading to sensitization of the myenteric plexus.[6,7] This may lead to a state of chronic intestinal sensitization and resulting abdominal pain.[7] Thus, therapies that reverse intestinal hyperpermeabilty in D-IBS patients such as glutamine supplementation may improve chronic gastrointestinal symptoms.

Our group has recently conducted a randomized placebo-controlled trial of glutamine in D-IBS patients with increased intestinal permeability and our preliminary results were presented at Digestive Disease Week in May 2013.[8] D-IBS patients (n = 61) were enrolled and completed the IBS Symptom Severity Score (IBS-SS) and intestinal permeability testing at baseline and following treatment and were randomized to glutamine 10 g po tid for 8 weeks or placebo 10 g po tid for 8 weeks. The glutamine group had a significant reduction in both the IBS-SS ($P < .01$) and in intestinal permeability ($P < .05$) compared to the placebo group. Analysis on each of the 5 components of the IBS-SS was done to determine the

Conflicts of interest

The authors disclose no conflicts.

percentage of changes following therapy. There was a 50%–60% decrease in abdominal pain severity and a 10%–15% decrease in abdominal pain frequency following glutamine therapy. In addition, there was a 60% improvement in satisfaction with bowel habits along with a 40% improvement in interference with quality of life. Thus, oral glutamine supplementation improves gastrointestinal symptoms and restores intestinal permeability in D-IBS patients and may be a useful therapeutic agent to treat D-IBS patients who have intestinal hyperpermeability.[8]

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