IBS Treatment with Rifaximin: When is the Science Good Enough to Support its Use in IBS?

Peter McNally, DO, MSRF, FACP, FACG

Center for Human Simulation, University of Colorado – Denver, SOM
mcnallycolorado@aol.com

Introduction:

Irritable Bowel Syndrome (IBS) is very common disorder afflicting ~20% of the US population.1,2,3 This disorder, IBS, is poorly understood and believed to be caused by a complex interaction of biological, environmental and psychological systems, figure 1.4,5,6,7,8,9,10 The diagnosis of IBS is based upon the presence of clinical criteria and the absence of abnormal “red flags” determined by history and physical findings and focused screening laboratory tests, figure 2.11 The lack of a clear biologic marker for IBS and the diverse interaction of many dysfunctional systems in IBS have made it very difficult to scientifically confirm the efficacy of drug(s) for the treatment of IBS.12

A common symptom of IBS is abdominal bloating and pain. Pimentel, Di Stefano and many others have conducted studies with IBS subgroups and repeatedly shown that a short course of antibiotic therapy is effective in ameliorating these symptoms and improving global symptom scores.13,14,15 In this edition of www.VHJOE.org, we reviewed the results of a recently published double blind placebo controlled study that examined the efficacy of Rifaximin therapy for 14 days in 1260 IBS patients.
without constipation. This study was conducted with parallel study groups of over 600 patients in each study, Target 1 (n=623 pts) and Target 2 (n=637 pts). The primary and secondary study end points evaluated were Rifaximin vs. Placebo for improvement in global IBS symptoms and IBS-related bloating. All study patients met Rome II criteria for IBS without constipation. Patients were randomized to receive Placebo or Rifaximin 550 mg po tid for 14 days. The study patients were evaluated for both drug efficacy and safety, Figure 3. During the ten week post treatment follow up, the Rifaximin group exhibited clear, sustained improvement in global IBS symptoms, Figure 4. Individual IBS symptoms of bloating, abdominal pain, stool consistency were also shown to numerically and statically improve with Rifaximin. During the 12 week study period, the Rifaximin treatment group did not identify obvious concerns for adverse related events.

Discussion:

IBS is a disorder of great morbidity for those patients suffering from its symptoms and a significant economic burden in lost worker productivity and health care costs. A recent American College of Gastroenterology, Evidence-Based Position Statement on Management of IBS showed that only few therapies for IBS have certifiable grade “1” evidence for efficacy, Table 1. Furthermore, some of the most effective treatments for IBS that include Alosetron (IBS-D) and Tegaserod (IBS-C & IBS-M) are associated with rare, but serious side effects of intestinal ischemia and cardiac arrhythmias, respectively. Both of these FDA approved agents have been voluntarily withdrawn from the US marketplace by their manufacturer.

Although, the findings of Pimentel, et al, confirm the efficacy of Rifaximin (550 mg p.o. tid for 14 days) to improve symptoms in IBS patients without constipation, Rifaximin has not been approved by the Food and Drug Administration (FDA) for use in these patients. FDA Concerns that Rifaximin treatment of IBS patients for 14 days would not exhibit durable benefit, making retreatment necessary, influenced the FDA to disapprove the application of Rifaximin for use among IBS patients without constipation. Although this decision by the FDA is well intentioned, it is difficult to understand why Rifaximin was not approved for use in IBS patients without constipation. Rifaximin is clearly effective and safe in these patients. This “non-systemic” antibiotic is uniquely “immune” to the development of bacterial resistance,
and thus far not associated with the development of antibiotic related diarrhea, i.e., Clostridium difficile diarrhea. Further support of Rifaximin safety, would be the current FDA approval for chronic daily use of Rifaximin among patients with cirrhosis complicated by hepatic encephalopathy and complications significant adverse events have not been identified.\textsuperscript{20,21}

Unfortunately, the lack of other proven and effective treatments for this disorder, may force physicians to resort to treatment of IBS patients with other less expensive, less effective, and less safe broad spectrum antibiotics that are known to have potential side effects and prone to the development of microbial resistance and Clostridium difficile diarrhea.\textsuperscript{22} Hopefully, Salix Pharmaceuticals (Morrisville, North Carolina) will continue to push forward with the studies required by the FDA, so that these IBS patients without constipation will have an effective and FDA approved treatment for their disorder.

The author welcomes patients, scientists, and physicians to sign into the www.VHJOE.org website and blog on IBS.

\textit{Erratum: The incorrect version of this manuscript was originally published 1 September 2011 and removed on 19 September 2011. The correct, peer reviewed and accepted manuscript was reposted online 2 October 2011.}

### References:


