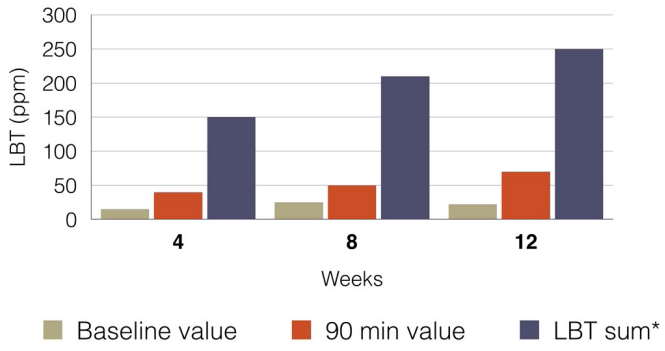
KRESSER INSTITUTE FOR FUNCTIONAL AND EVOLUTIONARY MEDICINE

# Gut: Treatment Protocols - SIBO, Part 1

Hey, everybody, it's finally time to talk about treatment protocols. We're going to begin with SIBO.

SIBO is probably the most complex and nuanced treatment protocol that we're going to talk about, so I'd like to discuss three general considerations to begin with. The first is the duration of the treatment, which should correlate with breath test results, and we'll talk more about that in a moment. The second is that treatment depends on whether hydrogen, methane, or both are Elevated, and the third is that retesting is crucial, and this is true for all treatment protocols, not just SIBO.




**Mean values of the lactulose breath test *(LBT)* according to treatment duration.** Between the group treated for 4 weeks and that for 12 weeks, statistically significant differences were found in the hydrogen value at 90 min ($P < 0.05$) and its sum ($P < 0.05$). The baseline values were not significantly different among all groups.

*LBT sum means a sum of lactulose hydrogen breath test data during 90 min.

**Adapted from:** Bae S et al. J Korean Med Sci. 2015 Jun;30(6):757-62

Treatment duration with rifaximin is often seven to 14 days, but this isn't really matched with the lactulose breath test results; it's just a period of time that was chosen at one point that everyone has stuck with. But a study in Korea from clinics that treat SIBO there found that treatment success was not surprisingly correlated with lactulose breath test results. They did a retrospective study and found that patients with hydrogen values at 90 minutes of 35 parts per million required four weeks of treatment to normalize their breath test results and improve symptoms. Patients with hydrogen values of 50 parts per million at that same 90-minute interval required eight weeks of treatment to normalize breath tests and symptoms, and patients with 72

parts per million or above of hydrogen at 90 minutes required 12 weeks, so that's a full three months of treatment to normalize their breath test.

And then they looked at another measure, which was the sum of hydrogen values, so the sum of all the hydrogen values leading up to the 90-minute time point. So patients with a sum of 151 parts per million required four weeks, those with a sum of 209 parts per million required eight weeks, and those with a sum of 253 parts per million required 12 weeks. So those are just two different ways of looking at it, and the sum would be relevant in cases where perhaps the distribution of values was a little bit different. So if they had higher values at baseline, for example, or lower values at 90 minutes, it's still going to catch those patients.

These researchers also found that symptoms improved before breath test results normalized, so that's something that's very important to realize. Most people felt better after four weeks of treatment, but their breath tests were still abnormal, and some still needed the full 12 weeks of treatment in order to normalize the breath tests. And that's crucial because I believe that one of the primary reasons for the high rates of recurrence that we see with SIBO treatment is that patients are not treated long enough, whether they're treated with rifaximin or botanical protocols, and the patient feels better with a shorter period of treatment, but the SIBO hasn't been treated fully and it will just come back, and that's why we see recurrence rates of up to 45 percent in these treatment protocols. So there aren't any similar studies correlating duration of treatment and hydrogen breath test values with botanical protocols, but we found in our practice that similar tailoring of duration of the treatment is necessary, and we use these same cutoffs as a general guide, which we'll talk about more later.

So the second principle is that treatment should be based on whether hydrogen is elevated, methane is elevated, or both are elevated. It doesn't matter quite as much with botanicals as it does for drug treatment, though we do make some changes, but with pharmaceuticals you will have to tailor the treatment based on this.

Retesting after treatment is absolutely essential. Without it, you have no idea what's going on. If the patient doesn't feel better, it could be because the treatment wasn't successful, or it could be that it was, but SIBO wasn't causing their symptoms, and without retesting, you cannot know the answer to this question. You need to explain to patients upfront that retesting is a crucial part of the treatment protocol. Prepare them for it in advance and let them know that they may need multiple retests depending on the success of the treatment. This is one big advantage of the Biohealth SIBO test. It provides results usually in 48 to 72 hours, which makes it much easier to make treatment decisions with retesting.

So, let's move on to talking about antimicrobials. I'm going to start with the botanical treatment. A study in 2014 compared botanical therapy to treatment with rifaximin, which is the drug of choice. This was an open-label trial; subjects were given the option of rifaximin at 1,200 milligrams per day, which is less than the current recommended dose by Dr. Pimentel. So they were given that option of rifaximin at 1,200 per day for 30 days, or two capsules each day of

four different botanical formulas for 30 days. At the end of the 30-day period, 46 percent of people who were taking the botanicals had a normal lactulose breath test versus 34 percent of rifaximin. So the botanical protocol was 85 percent more likely to produce normal lactulose breath test results, although that was not statistically significant. Fourteen of 44 rifaximin non-responders were offered the botanical protocol at that point, and 57 percent of those non-responders had a normal lactulose breath test after that. Ten of the non-responders were then offered a triple antibiotic protocol, and 60 percent responded, which is, as you can see, not much different than the botanical protocol. There were some adverse effects reported in the rifaximin arm, but none were reported in the botanical arm.

So this is a really remarkable study, and it shows us essentially that botanical protocols are equivalent or better than rifaximin treatment, at least at 1,200 milligrams a day. The crossover nature of this study was particularly helpful, because even rifaximin non-responders, 57 percent of them ended up responding to the botanical protocol, and we've definitely seen that in our practice, where patients come to us having already done rifaximin. They're doubtful that botanicals will help because they perceive drugs to be more effective, but we explain this study to them and, in some cases, they go ahead and do the botanicals and they have better results. And you'll note also, as I mentioned at the end there, that the adverse effects were not noted at all with the botanical protocol, though they were with rifaximin. Our experience with that is a little bit different; we do definitely see some adverse effects in both cases, but I think they're more related to a Herxheimer die-off reaction than to any adverse effects of the medications themselves.

As you can see, botanical therapy is at least as effective and maybe more effective with fewer side effects. Rifaximin efficacy was low in this study. I'm not sure why, but the overall efficacy of rifaximin in meta-analysis is about 50 percent. That is obviously not great. It's a flip of a coin. But this may be because the dose and duration of rifaximin treatment was not high enough and not matched with the severity of the lactulose breath test results in those patients. Rifaximin is not approved by the FDA for treatment of SIBO. It is only approved for hepatic encephalopathy and IBS-D or IBS with diarrhea. A one-month supply of rifaximin, if paid out-of-pocket at 1200 mg at a typical pharmacy, is over $1,200. However, there is a cash pay option of ordering rifaximin direct from Australia Center for Digestive Disorders. It's still expensive, but it's about a third of the cost that the patient would have to pay at a local pharmacy, somewhere between $300 and $400 typically.

It's important to note that at the time of this recording they only accept prescriptions from MDs and DOs, not from nurse practitioners and physician assistants. Also, SIBO tends to be a recurrent issue in a subset of patients. This means that they may need treatment more than once, and taking botanicals repeatedly over time, I think, is probably safer than taking rifaximin repeatedly, even though it's relatively safe as an antibiotic. Finally, another benefit of the botanical protocol is that we can use roughly the same protocol with minor tweaks for elevated hydrogen and methane and even suspected hydrogen sulfide production.