Eradication of Small Intestine Bacterial Overgrowth (SIBO) by Rifaximin: A Systematic Review and Meta-analysis

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Background: Small intestinal bacterial overgrowth (SIBO) is a condition caused by an increased number and/or abnormal type of bacteria (i.e. oropharyngeal or colonic type bacteria) in the small bowel. Eradication of SIBO relies on antibiotic therapy that must cover both aerobic and anaerobic enteric bacteria. Rifaximin is a poorly absorbable antibiotic, with a broad spectrum of antibacterial activity, covering Gram-positive and Gram-negative microorganisms, both aerobes and anaerobes.
Aim: To perform a systematic review and meta-analysis of clinical trials using rifaximin to eradicate SIBO.
Methods: MEDLINE, EMBASE, the Cochrane Central Register of Controlled Trials as well as abstract from the Digestive Disease Week, the American College of Gastroenterology Meeting, the United European Gastroenterological Week as well as Asian Pacific Digestive Week were searched up to November 2012. Case series, open label studies, cross-over and randomized controlled trials (RCTs) in adult patients with proven SIBO, treated with rifaximin, were eligible. Hydrogen (glucose or lactulose) breath test was used to diagnose the bacterial overgrowth and repeated after therapy to assess eradication. Risk of bias for RCTs was assessed as described in the Cochrane handbook. The proportion of individuals eradicated was combined from all studies to give a pooled eradication rate using a random effects model in order to provide a more conservative estimate.
Results: Twenty-eight studies were identified containing 921 subjects, meeting the pre-specified entry criteria and treated for SIBO. Only 4 studies were RCTs: 2 compared rifaximin to systemic antibiotics (namely tetracycline or metronidazole), and 2 compared different doses of rifaximin. All RCTs were at unclear or high risk of bias. To diagnose and follow-up the patients 16 studies used the hydrogen-glucose breath test and 12 the hydrogen-lactulose breath test. Doses of rifaximin used ranged from 600 to 1650 mg daily. Pooled eradication rate was 67.0% (95% CI: 59.1 to 69.8) with evidence of heterogeneity [Q-value: 123,714, df(Q) = 27; $p < 0.0001$; $I^2 = 78.17$]. Eradication rate was dose-dependent ($r=0.999$, $p=0.019$). In the 2 RTCs comparing rifaximin to other antibiotics, the pooled eradication rates for rifaximin was 64.1% vs. 41% for other antibiotics with a difference of 22.7% (95% CI: 7.4 to 37; $p= 0.0032$). Pooled prevalence of adverse events was 10.3% (95% CI: 7.3 to 14.2), with no evidence of dose-dependent effect ($r=0.841$, $p=0.158$).
Conclusions: Rfaximin is effective and safe for treating SIBO, with an efficacy that appears to be dose-dependent. However, large and well-performed RCTs are needed to substantiate these findings and establish the optimal regimen (daily dose and duration) of therapy.