Rifaximin Improves Restless Legs Syndrome Associated With Small Intestinal Bacterial Overgrowth

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INTRODUCTION

- Restless legs syndrome (RLS) is compelling urge to move legs at night and is often associated with discomfort
- RLS causes insomnia, negative daily functioning, and poor quality of life
- RLS has been reported as a symptom condition in diseases associated with small intestinal bacterial overgrowth (SIBO) such as irritable bowel syndrome (IBS), Crohn’s disease, and celiac disease

• Prospective multicenter study found 45% of patients with Crohn’s disease (32 of 71) had RLS (see poster P505 by Wierink et al presented at this meeting)
• Treatment of RLS with dopamine agonists, ropinirole (Giacomelli et al, Research Triangle Park, NC), is only marginally more effective than placebo, with only 60% of ropinirole-treated patients achieving much or very much improvement in global symptoms compared with 40% of patients who received placebo

- Rifaximin is a broad-spectrum, gastrointestinal (GI)-targeted antibiotic with low systemic absorption (≤0.1%) that is effective for treatment of SIBO
- Rifaximin has been effectively used as reducing RLS symptoms in patients with IBS
  - In prospective clinical trial of 12 patients with IBS and RLS, 77% of patients reported ≥50% improvement of RLS symptoms following treatment with 1200 mg of rifaximin for 10 days

OBJECTIVES

- To evaluate efficacy of rifaximin for treatment of patients with idiopathic RLS and SIBO
- To evaluate prevalence of GI symptoms in idiopathic RLS and effect of rifaximin in patients with RLS and SIBO

METHODS

Inclusion criteria

- Patients were either previously diagnosed with idiopathic RLS or neurologist had RLS diagnosis confirmed using international RLS (IRLS) diagnostic criteria and abdominal lactose breath test (LBT)
- Patients were screened by nurse coordinator using LBS score to document that all patients had severity score ≥3
  - Set of 10 questions rated on scale that assessed frequency of symptoms and severity of RLS
  - Impact on sleep, mood, and activity of daily living
  - Each question on scale ranged from 0 (no impact) to 4 (very severe impact)

Study design

- Prospective, open-label, single-center study conducted from November 2007 to March 2008
- Rifaximin (Xifaxan®; Salix Pharmaceuticals, Inc, Montville, NJ) 400 mg 3 times daily for 10 days followed by rifaximin 400 mg every other day for 20 days
- Assessments
  - Lactulose breath test
  - Hydrogen and methane excretion measured every 20 minutes for 120 minutes after ingestion of 10 g of lactulose
  - Abnormal result was defined as increase in hydrogen and/or methane excretion ≥2 ppm

RESULTS

- Of 21 patients with RLS who were screened, 6 had normal LBT and were excluded
- One patient with abnormal LBT result was diagnosed with Helicobacter pylori – associated gastritis in workup for iron deficiency and was also excluded
- Total number of 14 patients with RLS and concurrent SIBO received rifaximin treatment

Parameter Patients (N=14)

| Mean ± SD | 54.3 ± 16.5 |
| Mean Male/Female | 6/8 |
| Mean duration of RLS + SIBO | 8.6 ± 7.5 |
| GI disorder, n(%) | IBS 6 (43), Eclampsia 3 (21), Crohn’s disease 1 (7) |
| Mean duration of GI disorders + SD | 16 ± 13 |
| LBT result, n (%) | High hydrogen excretion 8 (57), High methane excretion 4 (29), Hydrogen + methane excretion 2 (14) |
| Mean baseline RLS severity score + SD | 23.1 ± 6.2 |
| Mean baseline IRLS severity score + SD | 23.1 ± 6.2 |
| Abdominal pain | 2.8 ± 1.6 |

- Sixty-four percent (9 of 14) of patients with RLS and SIBO reported slight, moderate, or marked global improvement of RLS symptoms following rifaximin treatment

- Improvement

- No improvement

DISCUSSION AND CONCLUSIONS

- GI disturbances may be common in patients with idiopathic RLS
- In this small, prospective, open-label study, rifaximin 1200 mg for 10 days followed by 400 mg every other day for 20 days substantially improved both RLS and GI symptoms
- These results provide additional evidence of link between SIBO and RLS
- Breath testing for SIBO may be a diagnostic tool in patients with RLS, and antibiotic therapy with small intestine–targeted antibiotic appears to be warranted
- Randomized, double-blind, placebo-controlled trial is currently underway in patients with RLS and antibiotic therapy with small intestine–targeted antibiotic appears to be warranted

- Abdominal pain and bloating scores improved in majority of patients (Figure 3)