Brief Report

Corticosteroid-Sparing Effect of Rifaximin, a Nonabsorbable Oral Antibiotic, in Active Ulcerative Colitis: Preliminary Clinical Experience

Mario Guslandi, MD, Patrizia Giollo, MD, and Pier Alberto Testoni, MD

Gastroenterology Unit, S. Raffaele University Hospital, Milan, Italy

ABSTRACT

Background: The role of enteric flora in the pathogenesis of inflammatory bowel disease constitutes the rationale for the use of antibiotics as adjuvant agents in the treatment of ulcerative colitis (UC) and Crohn's disease.

Objective: The aim of this study was to assess, in a preliminary fashion, the efficacy of the nonabsorbable antibiotic rifaximin in the treatment of exacerbation of UC in patients with a history of poor corticosteroid tolerance.

Methods: This open-label pilot study was conducted in the Gastroenterology Unit, S. Raffaele University Hospital (Milan, Italy). Male and female patients aged 18 to 65 years with an established diagnosis of left-sided UC who were experiencing a clinical relapse during maintenance treatment with mesalamine and with a history of poor tolerance to corticosteroid therapy were included in the study. They received rifaximin 400 mg BID for 4 weeks while continuing to receive mesalamine 2.4 g/d. Disease activity before and after treatment was assessed using Rachmilewitz's Activity Index (RAI). A final RAI score <6 was considered clinical remission.

Results: Ten patients (9 men, 1 woman; mean [SD] age, 48.1 [12.3] years [range, 23–64 years]) participated in the study. The RAI decreased in all patients. Rifaximin treatment induced clinical remission in 7 patients (70%). No adverse effects were reported.

Conclusions: Due to our study design, no definitive conclusions can be drawn. However, our preliminary data suggest that rifaximin may be beneficial in the treatment of active UC, obviating corticosteroid therapy in most cases. (*Curr Ther Res Clin Exp.* 2004;65:292–296) Copyright © 2004 Excerpta Medica, Inc.

Key words: ulcerative colitis, mesalamine, rifaximin, corticosteroids.

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INTRODUCTION

It is now well recognized that enteric flora play a pathogenetic role in inflammatory bowel disease (IBD).¹⁻³ It has been found that in genetically predisposed patients with immunologic dysregulation, bacteria trigger and maintain intestinal inflammation, and that the concentration of intestinal bacteria in IBD is higher than normal in these patients and increases progressively with the severity of the disease.² Other investigators³ have proposed a breakdown in the qualitative balance between protective and harmful bacteria (dysbiosis) as one of the potential mechanisms involved in ulcerative colitis (UC) and Crohn's disease.

Clinical studies⁴ using antibiotics as adjuvant therapy in the medical treatment of IBD have yielded promising results, but long-term administration of drugs such as metronidazole and ciprofloxacin hydrochloride is accompanied by systemic adverse effects (AEs).

Rifaximin (a derivative of rifampicin), a locally acting antibiotic that is virtually unabsorbed after oral administration,⁵ has been shown to be effective in the treatment of intestinal disorders (eg, diverticulitis, traveler's diarrhea). An open-label pilot study⁶ has suggested that rifaximin 200 mg TID promotes clinical improvement in patients with Crohn's disease.

The aim of the present preliminary study was to assess the efficacy of rifaximin as an alternative therapeutic approach in patients undergoing an exacerbation of UC who should avoid corticosteroid therapy.

PATIENTS AND METHODS

Study Design

This open-label pilot study was conducted in the Gastroenterology Unit, S. Raffaele University Hospital (Milan, Italy). Approval for the study protocol was obtained from the hospital institutional review board.

Patients

Male and female patients aged 18 to 65 years who experienced a clinical exacerbation of UC (based on Truelove & Witts criteria) while receiving maintenance treatment with oral mesalamine 2.4 g/d during the 3 months before the study were enrolled. Patients were required to have an endoscopically and histologically confirmed diagnosis of left-sided UC ≥ 6 months earlier. Endoscopy was not repeated at the time of inclusion because relapse was clinically evident. For ethical reasons, only patients with a history of poor tolerance to corticosteroid therapy were enrolled. In their medical history, due to steroid treatment, 4 patients (40%) had sodium retention, 3 (30%) had decompensated diabetes, 2 (20%) had severe rash, and 1 (10%) had severe dyspepsia unresponsive to proton pump inhibitors. In all cases, the patient and/or physician was reluctant to restart a course of corticosteroids, and thus provided verbal informed consent to first try a course of therapy with rifaximin while continuing

mesalamine treatment. Also, only patients with an initial score of ≥ 9 on the Rachmilewitz's Activity Index (RAI)⁷ (calculated on the basis of stool frequency, blood in the stool, general conditions, fever, abdominal pain, erythrocyte sedimentation rate, and hemoglobin concentration) were included.

Treatment

Rifaximin 400 mg BID PO was self-administered for 4 weeks while patients continued to receive mesalamine 2.4 g/d. No other oral or rectal medications were permitted during the study.

Efficacy Assessment

Clinical assessment before and after treatment was performed using the RAI.⁷ A final score of < 6 on the RAI⁷ was considered a therapeutic success (ie, clinical remission). In the event of worsening of symptoms, patients were instructed to return to the clinic to be switched to corticosteroid therapy.

Tolerability Analysis

AEs were recorded and assessed using patient interview and spontaneous reporting.

RESULTS

Ten patients (9 men, 1 woman; mean [SD] age, 48.1 [12.3] years [range, 23–64 years]) participated in the study.

Efficacy

Seven patients (70%) achieved clinical remission (score < 6 on RAI⁷); corticosteroid treatment was avoided in these patients. A reduction in the RAI,⁷ indicating partial clinical improvement, was observed in 3 patients (30%) (**Figure**).

Tolerability

All patients completed the prescribed treatment with rifaximin without reporting any AEs.

DISCUSSION

Typically, patients with an exacerbation of UC while receiving maintenance treatment with mesalamine receive a course of corticosteroids to suppress the acute inflammatory process. However, corticosteroid therapy is poorly tolerated in some patients; thus, alternative therapeutic approaches must be considered.

In view of the pathogenetic role of intestinal bacteria in IBD,^{1–3} the use of antibiotics is an option. A nonabsorbable antibiotic, such as rifaximin, which has not been associated with the systemic AEs of antibiotics such as metroni-

Figure. Individual patient values on Rachmilewitz's Activity Index⁷ before (baseline) and after 1 month of treatment with rifaximin plus mesalamine.

dazole and ciprofloxacin, is particularly attractive in this respect. Preliminary uncontrolled data on the use of rifaximin 600 mg/d in active Crohn's disease for ≤ 16 weeks was provided by Shafran et al.⁶ That study showed promising results in terms of clinical response.

However, our pilot study was different from the study by Shafran et al.⁶ in that we administered combination therapy with mesalamine plus rifaximin during active UC to try to avoid corticosteroid therapy. Despite the differences in dose and duration of rifaximin treatment and in the type of IBD studied, both pilot studies suggest that the antibiotic might be clinically useful in most patients with active intestinal inflammation. In particular, our study indicated that by adding rifaximin to the mesalamine regimen, it is possible to achieve clinical remission, as evidenced by the fact that corticosteroid treatment was avoided in 70% of patients.

Weaknesses of our study included its open-label, pilot characteristics; the lack of a control group; and the small sample size used. However, our data and those of other investigators are encouraging and warrant further controlled studies with rifaximin in the treatment of IBD.

CONCLUSIONS

Due to our study design, no definitive conclusions can be drawn. However, our preliminary data suggest that rifaximin may be beneficial in the treatment of active UC, obviating corticosteroid therapy in most cases.

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Address correspondence to: Mario Guslandi, MD, FACC, Gastroenterology Unit, S. Raffaele University Hospital, Via Olgettina 60, 20132 Milan, Italy. E-mail: guslandi.mario@hsr.it