Rifaximin for the prevention of spontaneous bacterial peritonitis

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Abstract
According to a review article by Biecker et al published in a previous issue of World Journal of Gastroenterology in March 2011, intestinal decontamination with norfloxacin remains the mainstay of primary prophylaxis of spontaneous bacterial peritonitis (SBP) at the expense of development of quinolone-resistant bacteria after long-term use. In our research, the administration of a 4-wk regimen with rifaximin 1200 mg/d reduced significantly the ascitic neutrophil count in cirrhotic patients with sterile ascites in line with a significant decrease in plasma endotoxin levels. Our observations concur with recent findings, showing a significantly reduced 5-year probability of SBP in cirrhotic patients taking rifaximin.

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Key words: Rifaximin; Cirrhosis; Ascites; Spontaneous bacterial peritonitis
advantage of rifaximin is that it is virtually unabsorbable, which minimizes the antimicrobial resistance and adverse events and renders the drug safe in all patient populations. In addition, rifaximin has a better activity against gram-positive organisms than norfloxacin[3].

We investigated whether rifaximin can reduce the burden of gut flora and BT, which are the requisite effects of a drug used for SBP prophylaxis, by studying its effects on circulating endotoxin levels and AF neutrophil counts in cirrhotic patients with sterile ascites.

Sixteen cirrhotic patients with ascites with no history of previous SBP episodes who required regularly a large-volume paracentesis were included in our study. Cirrhosis was established by non-invasive and/or histological criteria; all patients were Child Pugh class C. The patients were studied at baseline and after a 4-wk regimen with rifaximin 1200 mg/d (Group 1, n = 9; alcohol/viral etiology: 7/2) or an observational period (Group 2, n = 7; alcohol/viral etiology: 5/2). Exploratory paracentesis was performed in association with each therapeutic paracentesis to exclude ascitic fluid infection. All patients were included after written informed consent was obtained from them and the local scientific-ethical committee approved the study. Criteria for inclusion were: (1) Abstinence from alcohol for at least 6 mo before inclusion; (2) Absence of clinical and laboratory signs of bacterial infections; (3) No history of variceal bleeding within the 2 wk preceding the study; and (4) No treatment with antibiotics during the last 8 wk before inclusion. For ethical reasons, only patients with AF total protein concentration >1 g/dL were studied. AF white blood cell (WBC) and neutrophil count, the proportion of neutrophils in AF (AF% neutrophils), and plasma endotoxin levels were measured at baseline and at the end of observational or treatment period. For the detection of plasma endotoxin levels, the Limulus amebocyte lysate chromogenic endpoint assay (Hycult biotech, Uden, The Netherlands) was used as instructed by the manufacturer. The Wilcoxon matched pairs test was used for comparing variations within the same group. Results were expressed as mean ± SE. Statistical significance was designated as P < 0.05.

Rifaximin caused significant reductions in AF WBC, neutrophil count, AF% neutrophil count, and plasma endotoxin levels (Table 1); the values of the abovementioned parameters decreased uniformly in all patients (Figure 1). No significant changes in the AF cytological characteristics or plasma endotoxin levels were noted in Group 2. No patient developed AF infection during the study period and no side-effects were noted by the use of rifaximin.

Our findings strongly suggest that rifaximin suppresses IBO, which in turn reduces BT and the subclinical activation of AF defence mechanisms from prior silent colonisations with bacteria in cirrhotic patients with sterile ascites. The reduction of endotoxemia by ri-

![Figure 1](image-url)
Rifaximin may further reduce BT by causing a fall in portal pressures, considering that portal hypertension induces structural abnormalities in intestinal mucosa leading to an enhanced permeability. Overall, the effects of rifaximin on IBO and BT in our study are consistent with recent findings, showing a significantly reduced 5-year probability of SBP in cirrhotic patients taking rifaximin. In conclusion, the role of rifaximin as an alternative mean of preventing SBP deserves further attention in prospective studies.

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Table 1  Ascites cytological characteristics and plasma endotoxin levels in patients after rifaximin treatment or in observational period

|                         | Group 1 (n = 9) |          |          | Group 2 (n = 7) |          |
|-------------------------|----------------|----------|----------|----------------|----------|
|                         | Baseline       | 4 wk     | P value  | Baseline       | 4 wk     | P value  |
| WBC count (per mm$^3$)  | 147.7 ± 24.1   | 107.7 ± 16.6 | 0.004   | 164.5 ± 30.2   | 175 ± 20.8 | NS       |
| Neutrophil count (per mm$^3$) | 28.4 ± 9.3 | 13.5 ± 4.3 | 0.01    | 34.6 ± 6.4     | 37.9 ± 7.2 | NS       |
| AF% neutrophils         | 17.1 ± 3       | 11.2 ± 2.1 | 0.0008  | 21.6 ± 3.5     | 22.1 ± 2.5 | NS       |
| Plasma endotoxin (EU/mL)| 3.3 ± 1.1      | 1.6 ± 0.5 | 0.03    | 2.9 ± 0.9      | 3 ± 0.8   | NS       |

Data are expressed as mean ± SE. WBC: White blood cell; NS: Not significant; AF: Ascitic fluid. Group 1: 9 cirrhotic patients with refractory ascites at baseline and after 4-wk rifaximin treatment; Group 2: 7 patients in the observational period.