Rifaximin as Treatment for Hepatic Encephalopathy: Some Considerations

Sir,

Although hepatic encephalopathy (HE) pathogenesis is not completely clarified, plasma ammonia certainly remains the key factor.[1] Therefore, current therapeutic approaches for HE treatment and prevention are based upon ammonia lowering strategies. Ammonia mainly originates in the gut, being produced by glutamine metabolism in the small bowel and by bacterial flora in the large bowel.[1] Non-absorbable disaccharides therapy is among the most used treatment for HE.[1] We read with great interest the review by Bleibel W *et al.*, recently published,[2] where therapy with rifaximin - a non-absorbable antibiotic is suggested to be superior as compared to non-absorbable disaccharides for HE treatment. However, there are no convincing data in literature clearly supporting the advantage of rifaximin over disaccharides. Indeed, in a systematic review, rifaximin has been found to be at least equally effective or superior to non-absorbable disaccharides and antimicrobials in relieving signs or symptoms observed in patients with mild to moderately severe HE.[3] However, as the authors pointed out, this review included studies with either open label or retrospective design, those with enrollement of patients with treatable precipitating factors, those with a lack of clearly described criteria for defining the efficacy of treatment, and studies not specifying the type of HE being evaluated.[3] Similarly, some methodological biases occurred in more recent studies on long-term rifaximin therapy in HE patients.[4] Moreover, rifaximin therapy failed to prevent HE in cirrhotics at high risk for its development, such as those with transjugular intrahepatic portosystemic shunt (TIPS).[5] The last but not the least, safety of long-term use of such an antibiotic in cirrhotics remains a matter for concern. Indeed, the increased rifaximin absorption in cirrhotics significantly raises its plasma concentrations in these patients with potential systemic side-effects.[4] Moreover, some cases of *C. difficile* colitis at long-term rifaximin therapy have been reported,[4] and the possibility of other bacterial resistance would suggest a note for caution for the proposed long-term rifaximin therapy in HE patients.[4]

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