Addition of Rifaximin Shows Value in Intercepting Complications of Cirrhosis

Complications are more likely in cirrhotic patients with ascites and Model for End-Stage Liver Disease (MELD) scores of 12 or greater plus international normalized ratios (INRs) of 1.2 or greater. Rifaximin (Xifaxan, Salix) therapy, however, may ameliorate risk. These were the findings of a post hoc analysis presented by Steven L. Flamm, MD, of Northwestern Feinberg School of Medicine in Chicago, Illinois during a poster session at the 64th annual meeting of the American Association for the Study of Liver Diseases (AASLD), which took place on November 1 to 5, 2013. The study, which included 299 patients with hepatic encephalopathy in remission, sought to identify baseline characteristics for the risk of complications of cirrhosis and the role of rifaximin in preventing complications.

Patients received, in randomized double-blind fashion, either rifaximin, at a dosage of 550 mg twice daily, or placebo and were stratified according to baseline MELD scores, INRs, and the presence or absence of ascites. MELD scores were higher in patients with ascites and other complications. Rifaximin, however, reduced the risk of complications in patients with ascites (hazard ratio [HR], 0.58; \( P = .045 \); 42% relative risk [RR] reduction) or a high MELD score of 12 or greater plus an INR of 1.2 or greater (HR, 0.40; \( P < .001 \); 60% RR reduction). Further, compared with placebo, rifaximin was associated with greater risk-reduction ratios in patients who did not have ascites (\( P = .001 \); 65% RR reduction) and MELD scores of less than 12 and INRs of less than 1.2 (76% RR reduction).

In a similar presentation, a team from the Oregon Health and Science University in Portland showed that rifaximin specifically reduced the incidence of spontaneous bacterial peritonitis (SBP) in patients with cirrhosis-associated ascites. In this study, described by Susanne Shokoohi, MD, in a poster session during the AASLD meeting, researchers followed 139 patients to observe the effect of short-term rifaximin therapy (1200 mg/day for 15 days) on psychologic and cerebral hemodynamic function and blood ammonia levels.

At the end of the treatment period, a significant improvement in psychometric test scores, compared with baseline scores, was seen, particularly in the Trail Making Test B (mean, 111±74 vs 123±77 seconds; \( P < .05 \)) and Digit Symbol Test (mean, 31±12 vs 27±9 seconds; \( P < .05 \)). A significant reduction in the portacaval anastomosis resistive index (mean, 0.57±0.08 vs 0.61±0.07; \( P < .05 \)) and a trend toward reduction in the portacaval anastomosis pulsatility index (\( P = .06 \)) on transcranial Doppler imaging were also observed, and blood ammonia levels after treatment were lower than baseline levels, but the difference was not statistically significant, said Dr Caracciolo.

The researchers concluded that short-term rifaximin therapy could be useful in improving psychometric test scores and cerebral hemodynamic parameters in cirrhotic patients with minimal hepatic encephalopathy and that the mechanism of action might be reduction in production of gastrointestinal toxins. Dr Caracciolo added that the results suggest that the effects of cerebrovascular resistance seen in hepatic encephalopathy may be functional and reversible.
**Vitamin D Deficiency May Be Unrelated to the Development of Fatty Liver Disease**

Although vitamin D deficiency is common in persons with nonalcoholic fatty liver disease (NAFLD) and nonalcoholic steatohepatitis (NASH), it appears to be an independent condition and not directly related to development of NAFLD or NASH, according to Dr Fernando Bril of the University of Florida in Gainesville, who reported on research by a multicenter team from Gainesville and San Antonio, Texas during a poster session at the AASLD meeting.

Dr Bril and coresearchers recruited 235 patients, 57% of whom had type 2 diabetes, and assessed plasma vitamin D levels and other measures of bone metabolism, fasting plasma glucose and insulin, insulin resistance, total body fat, and liver fat (using magnetic resonance imaging and spectroscopy), and they performed a liver biopsy in 151 patients.

The team found a vitamin D deficiency (≤20 ng/mL) in 70% of the study cohort. Compared with study participants who were not vitamin D–deficient, these patients had a higher body mass index (34.0 vs 32.1 kg/m²; \(P=.01\)) and percentage of liver fat (21.4% vs 16.7%; \(P=.04\)); however, other parameters, including degree of insulin resistance, aspartate aminotransferase and alanine aminotransferase levels, liver histology, and fibrosis scores, were similar, and no significant correlations between body mass index, total body fat, liver fat, liver histology, steatosis, inflammation, ballooning, fibrosis, or insulin resistance could be found. These findings led Dr Bril and colleagues to conclude that vitamin D levels are not associated with liver fat accumulation or the histologic severity of NASH and are also not associated with insulin sensitivity. Rather, a sedentary lifestyle may be the common factor between vitamin D deficiency and obesity, the latter of which is associated with metabolic syndrome and NAFLD.

**Restless Leg Syndrome Common in Patients with Hepatic Encephalopathy and Decompensated Cirrhosis**

Although the prevalence of restless leg syndrome (RLS) in the general population is about 10%, it was found to be 67% in a group of patients with decompensated cirrhosis and hepatic encephalopathy in a study performed by a multicenter team based in New York City. The study, presented by Patrick Basu, MD, of Columbia University School of Physicians and Surgeons during a poster session at the AASLD meeting, included 108 participants who were divided into 3 groups: group A (n=36) included patients with decompensated cirrhosis, group B (n=36) included patients with noncirrhotic chronic liver disease, and group C (n=36) included healthy controls. All study participants received rifaximin at a dosage of 550 mg twice daily for eradication of small intestinal bacterial overgrowth, and groups A and B underwent neuropsychometric and flicker testing for minimal and overt hepatic encephalopathy and sleep testing for RLS.

It was found that 67% of the patients with decompensated cirrhosis had RLS compared with 3% of patients with noncirrhotic liver disease and 6% of healthy controls. Eighty percent of patients with decompensated cirrhosis also had overt hepatic encephalopathy and esophageal varices. Dr Basu noted that larger studies are warranted to further explore the relationship between RLS and cirrhosis complicated by hepatic encephalopathy and portal hypertension.