Inpatient Cause of Death In Cirrhosis Shifts to Sepsis

BY ALICIA AULT
Associate Editor, Practice Trends

SAN DIEGO — Sepsis has become a leading cause of death for hospitalized patients with cirrhosis, according to a retrospective cohort study.

Overall mortality from cirrhosis is high, but mortality due to variceal bleeding is declining, Dr. Suraj Naik reported at Digestive Disease Week.

He and his colleagues hypothesized that as treatment of variceal bleeding has improved, the leading cause of in-hospital mortality for cirrhotic patients has shifted.

They studied two specific time periods at Parkland Memorial Hospital in Dallas: 1983-1985 and 2003-2005. Patients were identified by ICD9 codes for any and all causes of cirrhosis. The condition was defined by clinical history, physical findings, and laboratory measures. The cause of death was defined by diagnoses in clinical data and death summaries.

In 1983-1985, there were 610 patients admitted to Parkland with confirmed cirrhosis; 163 (27%) died in-hospital. In 2003-2005, there were 1,187 patients admitted and 241 (20%) died in-hospital. The two cohorts were matched in gender, race, and age (the average age was 50 years in the first group and 53 years in the later group). In 1983-1985, the most common cause of death was variceal bleed (49 patients, or 8%), followed by sepsis (43 patients, or 7%), and liver failure/hepatorenal syndrome (14 patients, or 2%). In 2003-2005, the most common cause of death was sepsis (97 patients, or 8%), followed by variceal bleed (31 patients, or 3%) and liver failure (23 patients, or 2%).

Overall mortality decreased from the first to the second cohort by 22%, and death due to variceal bleeding decreased by 57%.

Mortality due to sepsis increased by 50% in the second cohort, and led to death three times as often as in the earlier cohort, said Dr. Naik of the University of Texas at Dallas.

The etiology of cirrhosis changed from the earlier cohort to the later, with alcohol as a factor in 88% of patients in the first group and only 46% of the second, more recent group.

Dr. Naik said that it was not clear how many patients in each group also had hepatitis C, although he believed that it was a majority.

The most frequent causes of infection in these patients were pneumonia, bacteremia, and spontaneous bacterial peritonitis.

The study results suggest that clinicians should be more aware of the danger of infection in patients with cirrhosis, Dr. Naik said.

He reported no disclosures. ■

Hepatitis C Treatment Response Is Impaired in Latino Patients

BY HEIDI SPLETE
Senior Writer

SAN DIEGO — A Latino population had a significantly lower sustained virologic response to the standard treatment for hepatitis C virus, compared with a non-Latino population, suggesting that targeted treatments based on race and genetics may be keys to better management of chronic hepatitis C, according to data from a prospective study presented at the annual Digestive Disease Week.

Hepatitis C virus (HCV) is common in the Latino population, and data from previous studies have shown that Latinos have a more rapid progression to chronic HCV and cirrhosis, Dr. Maribel Rodriguez-Torres said in an interview.

Latinos are the largest minority population in the United States, so this represents a potentially huge number of patients with severe liver disease, she noted.

Dr. Rodriguez-Torres of the Fundacion de Investigacion de Diego in San Juan, P.R., and her colleagues compared pooled data in a multicenter, open-label study of 269 Latino adults with HCV and 300 non-Latino adults with HCV. Patients in both groups received the standard HCV treatment of 180 mcg of peginterferon α-2a (Pegasys) weekly and 1000-1200 mg of ribavirin daily based on body weight. Hoffmann-La Roche Inc., manufacturer of Pegasys and the Copegus formulation of ribavirin, sponsored the study.

After 6 months, 49.3% of the non-Latino patients had achieved a sustained virologic response (SVR), compared with 33.5% of the Latinos, a statistically significant difference. The almost 16% lower SVR suggests that more studies are needed to determine how best to treat HCV in the Latino population, the investigators noted.

"The standard treatment is capable of curing 40%-51% of people with HCV, but we want to have the highest possible cure rates for all populations," said Dr. John Vierling of Baylor College of Medicine, Houston, who moderated a discussion of the findings.

"We need to optimize the treatment we have," Dr. Rodriguez-Torres commented. Data from ongoing studies suggest that using higher doses or perhaps a longer duration of the standard therapy in treatment-resistant patients with higher viral loads and higher body mass indexes may improve outcomes, she explained.

"The most important next step is to make Latinos a priority in clinical research for HCV," she added.

Dr. Rodriguez-Torres disclosed that he had received funding from Hoffmann-La Roche. ■

Prucalopride Eased Chronic Constipation; More Data Sought

BY MARY ANN MOON
Contributing Writer

The selective 5-hydroxytryptamine receptor agonist prucalopride improved the rate of spontaneous, complete bowel movements in patients with severe chronic constipation, researchers reported.

Over 12 weeks of treatment in the phase III clinical trial, prucalopride also reduced the frequency and severity of abdominal and stool symptoms, and it significantly improved quality of life, compared with placebo, according to Dr. Michael Camilleri of the Mayo Clinic, Rochester, Minn., and his associates.

However, there is concern about potential cardiac risks with the drug, which is "similar in function to cisapride and tegaserod, two constipation-reducing drugs that were voluntarily removed from the market after warnings from the Food and Drug Administration about life-threatening cardiac side effects," Dr. Arthur J. Moss of the University of Rochester (N.Y.) said in an editorial comment accompanying the report.

There are additional concerns about the 9-year delay in publishing the results.

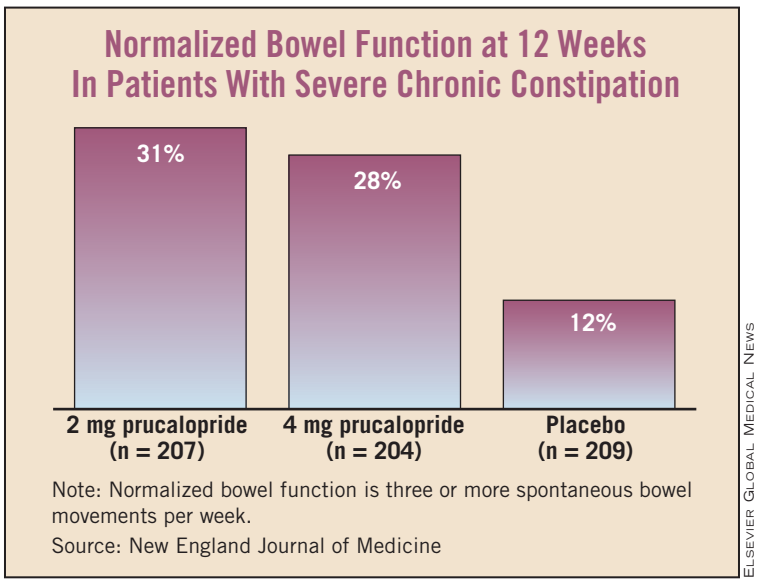
The trial was designed by Johnson & Johnson in 1998 and conducted in 1998-1999, but the final analysis was done by a Belgian company, Movetis NV, in 2007, after Movetis purchased the drug.

"It is not known why clinical trials with prucalopride were temporarily suspended around 2001, or why it took so long to bring this study to publication," Dr. Moss noted (N. Engl. J. Med. 2008;358:2402-3).

The study was conducted at 38 U.S. medical centers and involved 620 patients who had two or fewer spontaneous, complete bowel movements per week for a minimum of 6 months.

Patients had hard or very hard stools, a sensation of incomplete evacuation, or straining during defecation at least 25% of the time.

In all, 207 patients were randomly assigned to receive 2 mg of prucalopride, 204 patients received 4 mg of prucalopride, and 209 patients received placebo orally once a day for 3 months. The percentage of patients whose bowel function normalized to three or more spontaneous, complete bowel movements per week was 31% with the 2-mg dose, and 28% with the 4-mg dose of prucalopride, a difference that was not statistically significant.



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The percentages were significantly greater than the 12% of subjects in the placebo group whose bowel function normalized, Dr. Camilleri and his associates said (N. Engl. J. Med. 2008;358:2344-54).

Similarly, the percentage of patients who reported an increase in the number of spontaneous, complete bowel movements per week was 47% with 2 mg prucalopride and 47% with 4 mg prucalopride, compared with 26% with placebo, the investigators reported.

Patients in both active-treatment groups also were able to decrease their use of "rescue" laxatives by approximately half during the study.

Quality of life improved in 45% of patients taking 2 mg prucalopride and in 49% of those taking 4 mg, compared with 24% of those patients taking placebo.

Adverse events occurred in 80% of patients taking 2 mg of prucalopride, in 78% of patients taking 4 mg, and in 71% of patients taking placebo. The most frequent adverse events were abdominal pain, headache, nausea, and diarrhea.

Adverse events led to treatment stoppage in 8.2% of patients on 2 mg of prucalopride, in 8% of patients on 4 mg, and in 2% of those on placebo. Three patients discontinued treatment because of adverse events that included cardiovascular events.

"Further assessment of the cardiovascular safety of prucalopride in other trials is required to ensure that rare adverse cardiovascular effects are ruled out," the investigators said.

In his editorial comment, Dr. Moss concurred. "More complete clinical, electrophysiological, and pharmacokinetic data are required before this drug can be brought to market for the treatment of chronic constipation," he said. ■