

## Lactulose in Cirrhosis Patients with Minimal Hepatic Encephalopathy

Results of a study examining the effects of lactulose treatment in cirrhosis patients with minimal hepatic encephalopathy (MHE) were published in a recent issue of *Hepatology*. Led by Radha K. Dhiman, MD, Department of Hepatology, Postgraduate Institute of Medical Education and Research in Chandigarh, India, researchers conducted a study identifying 61 patients with MHE due to abnormal scores (a Z score less than  $-2$ ) on 2 or more of 6 neuropsychological tests assessing their mental state. To determine the impact of MHE on daily activities, the patients were also given a sickness impact profile (SIP) questionnaire covering 12 groups, such as sleep/rest, eating, work, home management, social interaction, and emotional behavior. Patients were then divided into two nonblinded groups: 31 patients received lactulose treatment for 3 months, and 30 patients received no treatment.

The mean number of abnormal neuropsychological tests decreased significantly in patients in the lactulose-treated group, who went from 2.74 at baseline (95% confidence interval [CI] 2.40–3.08) to 0.75 after 3 months (95% CI 0.36–1.16) compared to patients in the untreated group, who went from 2.47 at baseline (95% CI 2.19–2.74) to 2.55 after 3 months (95% CI 2.16–2.94), with a multivariate analysis of variance for time and treatment of  $P=.001$ .

The mean total SIP score also improved among patients in the lactulose-treated group, who went from 10.39 (range, total score 0 [best] to 100 [worst]) at baseline (95% CI 9.36–11.43) to 3.77 after 3 months, (95% CI 2.52–5.02) compared with patients in the untreated group, who went from 10.36 at baseline (95% CI 8.98–11.73) to 10.39 after 3 months (95% CI 8.36–12.42), with a multivariate analysis of variance for time and treatment of  $P=.002$ . Improvement in health-related quality of life was associated with improvement in psychometry.

The authors concluded that lactulose improved both cognitive function and health-related quality of life in cirrhosis patients with MHE, but noted that “whether treatment also prevents or delays progression to overt HE and improves prognosis remains to be determined.”

## Vaccine Patch for Travelers' Diarrhea

The journal *Vaccine* recently published results from a double-blind challenge study of a vaccine patch for travelers' diarrhea. The study, led by Robin McKenzie, MD, Assistant Professor of Medicine at The Johns Hopkins University School of Medicine, enrolled 27 patients who

received 3 doses of the Iomai enterotoxigenic *Escherichia coli* (ETEC) vaccine and 20 patients who received a placebo. Patients were then given a dose of *E. coli* larger than expected under normal foreign travel conditions and were monitored closely to assess stool frequency, weight, and antibiotic and intravenous fluid use.

Similar numbers in both the vaccine and control groups met the definition of moderate-to-severe illness, but patients who received the vaccine had significantly fewer loose stools ( $P=.04$ ) and lower mean weights of their loose stools ( $P<.05$ ). In addition, patients who did not receive the vaccine became ill more quickly and were more likely to require intravenous fluids, with 40% of the control group receiving fluids compared with only 14% of the vaccine group ( $P=.03$ ).

Members of the vaccine group also saw increases in immunoglobulin (Ig)A and IgG antibodies, which are associated with protection against ETEC. After three doses, all patients had a 4-fold increase in serum IgG and 97% had a 4-fold increase in IgA.

The Iomai vaccine uses transcutaneous immunization technology to deliver it to the immune system via a patch affixed to the skin. A phase III trial of the vaccine is planned for the coming year.

## Fewer Upper GI Events Associated With Etoricoxib Compared to Diclofenac

Results from a prespecified upper gastrointestinal (GI) safety analysis of the MEDAL (Multinational Etoricoxib and Diclofenac Arthritis Long-Term) Program comparing the investigational selective cyclooxygenase-2 (COX-2) inhibitor etoricoxib (Arcoxia, Merck) and diclofenac, a widely prescribed nonsteroidal anti-inflammatory drug (NSAID), were published in a recent issue of *The Lancet*. Although etoricoxib has been approved in several European countries, its US Food and Drug Administration (FDA) approval is still pending.

A pooled intent-to-treat analysis was performed of results from three double-blind randomized comparisons of etoricoxib (60 or 90 mg daily) and diclofenac (150 mg daily) in 34,701 patients with osteoarthritis or rheumatoid arthritis of the knee, hip, hand, or spine, who were at least 50 years of age. Upper GI clinical events (bleeding, perforation, obstruction, or ulcer) and the subset of complicated events (perforation, obstruction, witnessed ulcer bleeding, or significant bleeding) were investigated. Investigators also assessed these outcomes in patients who were taking concomitant proton pump inhibitors (PPIs) or low-dose aspirin. The average therapy duration was 18 months.

The results showed that overall upper GI clinical events were significantly lower with etoricoxib than with diclofenac in a broad patient population (hazard ratio [HR] 0.69, 95% CI 0.57–0.83;  $P=.0001$ ). The rates of uncomplicated GI events were significantly lower with etoricoxib than with diclofenac (HR 0.57, CI 0.45–0.74;  $P<.0001$ ). However, there was no significant difference in the rates of complicated upper GI events between etoricoxib and diclofenac (HR 0.91, CI 0.67–1.24;  $P=.561$ ).

“The significant difference in overall upper GI clinical events demonstrated between etoricoxib and diclofenac was driven by uncomplicated symptomatic ulcers,” said Loren Laine, MD, MEDAL Steering Committee Co-chair and Professor of Gastrointestinal & Liver Diseases at the University of Southern California. Dr. Laine stated that the difference in the results between complicated and uncomplicated events could potentially relate to diclofenac’s lack of antiplatelet effect.

These results were maintained in patients taking PPIs for GI protection and in patients taking low-dose aspirin (<100 mg daily) for cardiovascular protection for at least 75% of the study. PPIs were used concomitantly by 13,862 (40%) patients and low-dose aspirin by 11,418 (33%) patients. Treatment effects did not differ significantly in these individuals.

## New Index For Measuring Liver Fibrosis

A study to find a noninvasive and less expensive alternative to liver biopsy when diagnosing fibrosis found that an index of routinely available blood tests can accurately predict significant fibrosis in hepatitis C patients, according to a recent issue of *Hepatology*. This new series of markers, called FibroIndex, was found to more accurately diagnose fibrosis than two other commonly used indices, the Forns index and the aspartate aminotransferase-to-platelet ratio index (APRI).

Led by Masahiko Koda, MD, of Tottori University in Tottori, Japan, the study included 402 patients with chronic hepatitis C who were scheduled to undergo a liver biopsy between April 1994 and March 2004. Blood samples were collected within 3 days of biopsy. Patients who had previously been diagnosed with cirrhosis were not included. The researchers identified platelets, aspartate aminotransferase, and gamma globulin as independent predictors of fibrosis and used them to construct the FibroIndex equation.

Results from the study showed that FibroIndex was more accurate in predicting significant or severe fibrosis than the Forns index or APRI. By determining cutoff values to identify the absence or presence of

significant fibrosis, the study found that 101 patients could have avoided liver biopsy. In addition, FibroIndex was applied to a subgroup of 30 patients treated with interferon who underwent a second biopsy more than 1 year after treatment. Changes in FibroIndex were found to correlate with changes in fibrosis, although the Forns index and APRI did not show this correlation. FibroIndex was also accurate in patients with normal levels of alanine aminotransferase, one third of whom had significant fibrosis.

The researchers noted that the blood tests for the predictors used by FibroIndex are routinely available in most hospitals and laboratories, making it an accessible and inexpensive tool for determining fibrosis.

They also noted that the sensitivity of FibroIndex was limited, which may be due to variation found in laboratory tests. Nevertheless, they concluded that fewer liver biopsies would be needed with FibroIndex during follow-up and that FibroIndex would help gather longitudinal data on liver fibrosis progression.

### In Brief

**Pre-endoscopy serologic testing, in combination with biopsy of high-risk cases, detected all cases of celiac disease,** according to a prospective study. The use of this tool may aid endoscopists in targeting patients who need duodenal biopsy. (*BMJ*. 2007;334:729.)

**COX-2 inhibitors and NSAIDs reduce the incidence of colonic adenomas,** according to a systemic review by the US Preventive Services Task Force. NSAIDs also reduce the incidence of colorectal cancer. However, because these agents are associated with serious cardiovascular events and GI harms, the balance of benefits to risk does not favor chemoprevention in average-risk individuals. (*Ann Intern Med*. 2007;146:376-389.)

**Covered self-expandable metal stents (SEMS) are an effective treatment for distal biliary obstructions** caused by pancreatic carcinoma, according to a study. Their prolonged patency and removability makes them an attractive option for biliary decompression, regardless of resectability, and the strategy of initial covered SEMS placement may be the most cost-effective strategy in these patients. (*Endoscopy*. 2007;39:319-324.)