

# Baclofen Cuts Alcohol Use in Cirrhosis Patients

BY JOHN R. BELL  
Associate Editor

Alcohol-dependent persons with cirrhosis of the liver who were treated with baclofen, a  $\gamma$ -aminobutyric acid-B receptor agonist, were more than six times as likely to cease their alcohol use as were patients who took a placebo, according to a study.

The trial is the first "in which effectiveness and safety of an anticraving drug has been investigated in individuals with advanced liver disease," wrote Dr. Giovanni Addolorato of the Catholic University of Rome, and colleagues. They reported results for 84 alcohol-dependent patients with a diagnosis of cirrhosis who were randomly assigned in equal number to a 12-week regimen of either baclofen or placebo.

The baclofen dosage was 5 mg three times daily for the first 3 days and 10 mg three times daily thereafter. Mean patient age was 49 years in both groups. Patients were seen weekly for the first month, then every 2 weeks until the end of the study (Lancet 2007;370:1915-22).

**At 12 weeks, 30 (71%) of the 42 patients in the baclofen group were abstinent from alcohol, compared with 12 (29%) of the 42 patients in the placebo group (odds ratio 6.3).**

At 12 weeks, 30 (71%) of the 42 patients in the baclofen group were abstinent from alcohol, compared with 12 (29%) of the 42 patients in the placebo group (odds ratio 6.3).

In addition, those given baclofen showed improvements in measures of liver function, including ALT, bilirubin, international normalized ratio,  $\gamma$ -glutamyltransferase, and albumin. The drug was also associated with a greater number of nondrinking days than was placebo (63 days vs. 31 days), as well as a lower rate of relapse to heavy drinking at 60 days (19% vs. 45%).

Treatment with baclofen also reduced alcohol cravings, as measured with the obsessive-compulsive drinking scale.

Baclofen was not associated with any hepatotoxicity. There were no incidents of encephalopathy or hyperammonemia and no serious events leading to discontinua-

tion of the drug. Tolerability was reported as fair, with headache, tiredness, vertigo, and sleepiness reported in small numbers of patients in both groups.

These results "suggest that baclofen, because of its anticraving action and safety, could have an important role for treatment of alcohol-dependent patients with advanced liver disease," the researchers wrote. They cautioned that further studies are needed to establish optimal treatment duration and longer-term tolerance.

In a commentary accompanying the report, Dr. James C. Garbutt of the University of North Carolina at Chapel Hill, and Barbara Flannery, Ph.D., of RTI International, Baltimore, called the findings "surprisingly robust" and of potentially great clinical importance, given the routine exclusion of alcoholic patients with cirrhosis from trials of anticraving drugs because of the concern about hepatotoxicity (Lancet 2007;370:1884-5).

They also noted that the higher dropout

rate in the placebo group (31%) versus the baclofen group (14%) is of interest, because it may have skewed the results in favor of baclofen, given that these were assumed to be because of relapse, and thus affected the primary end point.

The study authors declared no financial conflict of interest. The study was supported by the Italian Ministry for University, Scientific, and Technological Research, and by the European Research Advisory Board. ■



## Indications and usage

Levemir is indicated for once- or twice-daily subcutaneous administration for the treatment of adult and pediatric patients with type 1 diabetes mellitus or adult patients with type 2 diabetes mellitus who require basal (long-acting) insulin for the control of hyperglycemia.

## Important safety information

Levemir is contraindicated in patients hypersensitive to insulin detemir or one of its excipients.

Hypoglycemia is the most common adverse effect of all insulin therapies, including Levemir. As with other insulins, the timing of hypoglycemic events may differ among various insulin preparations. Glucose monitoring is recommended for all patients with diabetes. Levemir is not to be used in insulin infusion pumps. Any change of insulin dose should be made cautiously and only under medical supervision. Concomitant oral antidiabetes treatment may require adjustment.

Inadequate dosing or discontinuation of treatment may lead to hyperglycemia and, in patients with type 1 diabetes, diabetic

ketoacidosis. Levemir should not be diluted or mixed with any other insulin preparations. Insulin may cause sodium retention and edema, particularly if previously poor metabolic control is improved by intensified insulin therapy. Dose and timing of administration may need to be adjusted to reduce the risk of hypoglycemia in patients being switched to Levemir from other intermediate or long-acting insulin preparations. The dose of Levemir may need to be adjusted in patients with renal or hepatic impairment.

Other adverse events commonly associated with insulin therapy may include injection site reactions (on average, 3% to 4% of patients in clinical trials) such as lipodystrophy, redness, pain, itching, hives, swelling, and inflammation.

Whether these observed differences represent true differences in the effects of Levemir, NPH insulin, and insulin glargine is not known, since these trials were not blinded and the protocols (eg, diet and exercise instructions and monitoring) were not specifically directed at exploring hypotheses related to weight effects of the treatments compared. The clinical significance of the observed differences in weight has not been established.

## For your patients with type 2 diabetes, start once-daily Levemir®

Levemir helps patients with diabetes achieve their A1C goal.<sup>1,2</sup>

- 24-hour action at a once-daily dose<sup>3,4</sup>
- Provides consistent insulin absorption and action, day after day<sup>3,5,6</sup>
- Less weight gain<sup>7†</sup>

**References:** 1. Meneghini LF, Rosenberg KH, Koenen C, Meriläinen MJ, Lüddeke H-J. Insulin detemir improves glycaemic control with less hypoglycaemia and no weight gain in patients with type 2 diabetes who were insulin naive or treated with NPH or insulin glargine: clinical practice experience from a German subgroup of the PREDICTIVE study. *Diabetes Obes Metab*. 2007;9(3):418-427. 2. Hermansen K, Davies M, Derezinski T, Ravn GM, Clauson P, Home P, for the Levemir Treat-to-Target Study Group. A 26-week, randomized, parallel, treat-to-target trial comparing insulin detemir with NPH insulin as add-on therapy to oral glucose-lowering drugs in insulin-naïve people with type 2 diabetes. *Diabetes Care*. 2006;29(6):1269-1274. 3. Klein O, Lyngø J, Endahl L, Damholt B, Nosek L, Heise T. Albumin-bound basal insulin analogues (insulin detemir and NN344): comparable time-action profiles but less variability than insulin glargine in type 2 diabetes. *Diabetes Obes Metab*. 2007;9(3):290-299. 4. Phillis-Tsimikas A, Charpentier G, Clauson P, Ravn GM, Roberts VL, Thorsteinsson B. Comparison of once-daily insulin detemir with NPH insulin added to a regimen of oral antidiabetic drugs in poorly controlled type 2 diabetes. *Clin Ther*. 2006;28(10):1569-1581. 5. Data on file. Novo Nordisk Inc, Princeton, NJ. 6. Heise T, Nosek L, Rønn BB, et al. Lower within-subject variability of insulin detemir in comparison to NPH insulin and insulin glargine in people with type 1 diabetes. *Diabetes*. 2004;53(6):1614-1620. 7. Data on file. NDA21-536. Novo Nordisk Inc, Princeton, NJ.

## Substance Abuse Survey Findings Out

The Substance Abuse and Mental Health Services Administration has released the findings of the 2006 National Survey of Substance Abuse Treatment Services, an annual census of treatment facilities that provides data on the location and nature of alcohol and drug abuse treatment services in the United States. Almost 13,800 facilities participated in the 2006 survey. Copies of the report can be ordered, free of charge, by calling 877-726-4727 and requesting inventory number SMA06-4296. ■



Please see brief summary of Prescribing Information on adjacent page.

FlexPen and Levemir are registered trademarks of Novo Nordisk A/S.  
© 2007 Novo Nordisk Inc. 133236

September 2007

