

# Improving Mood Also Helps Glycemic Control

*HbA<sub>1c</sub> levels were 'significantly lower than baseline' during the depression-free interval of maintenance.*

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Contributing Writer

Glycemic control, body mass index, and diabetes self-care improved significantly in type 2 diabetics with major depressive disorder who used bupropion for both acute and maintenance therapy, a two-phase open-label study found.

"Our study affirms the importance of depression management in diabetic patients in its potential to improve glycemic control, even though the mechanisms involved are not fully understood," wrote study authors Patrick J. Lustman, Ph.D., of the Washington University School, St. Louis, and colleagues. "This advantage could lead to better outcomes, measured not only in quality of life but also in reduced or delayed onset of complications."

The researchers evaluated data from a two-phase (acute and maintenance) open-label depression treatment trial in type 2 diabetics with major depressive disorder to determine whether treatment with bupropion hydrochloride extended release (Wellbutrin XL) affected glycemic control.

They assessed whether hemoglobin A<sub>1c</sub> (HbA<sub>1c</sub>), described as an "aggregate measure of glycemic control over the 120-day period before testing," improved with treatment and whether mood, diabetes self-care, and anthropometric changes also affected a change in HbA<sub>1c</sub>.

Of the 93 patients enrolled, 75 completed the acute 10-week bupropion treatment (mean dosage 334 mg/day). Of the 18 patients who discontinued treatment during the acute phase, 6 withdrew because of side effects, with increased anxiety being the most common. Those patients who withdrew were more likely to be black and older at depression onset; however, there were no significant between-group demographic differences

among those completing the acute phase.

Of the 75 patients who completed the acute phase, 63 (84%) had remittance from their depression and therefore were eligible to continue with maintenance therapy. Of that group, 8 patients (13%) discontinued treatment prematurely. The remaining 55 patients (87%) went on to complete the full 24-week maintenance phase; no one in that group suffered a recurrence.

Compared with their baseline values, patients who had relief from depression also significantly improved their adherence to diet and exercise regimens during the 10-week acute phase and 24-week maintenance phase. Glucose testing adherence was not significantly affected throughout the study (Diabetes Care 2007;30:459-66).

"Depression remitted in 68% of those who started bupropion treatment and in 84% of those who completed the acute phase," the authors wrote.

For the 55 patients who completed the maintenance phase, "changes from baseline over the maintenance interval were significant for weight and [body mass index]; total body fat mass showed a trend toward significance, and, in this instance, the reduction in percent body fat was also significant," the authors found.

The overall HbA<sub>1c</sub> decrease from baseline during the acute phase was a mean of -0.5, and this effect "was completely attributable to changes in the subset showing remission ... as the change in those who did not show a remission was minimal and insignificant," they continued. These levels "remained significantly lower than baseline (-0.7) during the depression-free interval of maintenance," the researchers noted.

This two-phase study was funded by the National Institutes of Health and GlaxoSmithKline Inc., the manufacturer of Wellbutrin XL. ■

# Brittle Diabetes May Be a Sign Of Psychiatric, Organic Illness

BY NANCY WALSH  
New York Bureau

NEW YORK — True brittle diabetes is a rarity, with characteristic blood glucose lability, frequent hospitalizations, and life disruption often reflecting underlying psychiatric or organic disease, according to Dr. Irl B. Hirsch.

Diagnosis and management of this potentially lethal condition present significant challenges, as was shown in several cases Dr. Hirsch presented at a meeting sponsored by the American Diabetes Association.

One case involved a 23-year-old woman who presented with a 15-year history of type 1 diabetes in 2000. She had been on an insulin pump for 5 years, and her hemoglobin A<sub>1c</sub> (HbA<sub>1c</sub>) levels ranged from 9% to 12%.

As a teenager she had had an eating disorder and had multiple hospitalizations for diabetic ketoacidosis. In the previous 2 years she had been hospitalized twice for gastroparesis, and had developed severe peripheral neuropathy and osteoporosis.

By 2002 she developed nonproliferative retinopathy and proteinuria. "All those years of poor control were already catching up with her at age 25," said Dr. Hirsch, professor of medicine in the division of metabolism, endocrinology, and nutrition at the University of Washington, Seattle.

In 2004 she had an unplanned pregnancy and was hospitalized for 4 months, delivering the child 3 months prematurely. Her glucose was well controlled while she was in the hospital, but subsequently HbA<sub>1c</sub> became elevated once again, reaching 10.4%.

Finally, in the summer of 2006, she had a kidney-pancreas transplant. "So the question is, does she have brittle diabetes?" Dr. Hirsch asked.

A diagnostic work-up determined that she had underlying celiac disease, with an important clue being the osteoporosis. "When you see osteoporosis in a young person you have to think about calcium absorption," he said. "Celiac disease often goes hand in hand with type 1 diabetes."

These patients can have extremely irregular blood glucose patterns because their food absorption is so erratic, he added.

A further concern to keep in mind with a patient such as this is that between one-third and one-half of all teenage girls with type 1 diabetes will withhold insulin at some time for weight loss. "Unfortunately, this is a very effective and dangerous way to lose weight," Dr. Hirsch said.

A second case involved a 30-year-old man who had nine hospitalizations during the first half of 2006 because of se-

vere gastroparesis. "We solved this case with the help of our friends at the Mayo Clinic," Dr. Hirsch said.

The patient was diagnosed with cannabis hyperemesis syndrome, a condition associated with long-term cannabis use that is characterized by cyclical episodes of vomiting in a susceptible patient.

"When he stopped smoking he also stopped coming to the hospital, but when he started smoking again the hospitalizations recurred," he said.

The likely mechanism for this little-known phenomenon is a slowing of gastric emptying caused by the cannabis. "This patient does not have brittle diabetes when he's not smoking dope," he said.

A third case involved a 29-year-old woman with a 20-year history of type 1 diabetes and an HbA<sub>1c</sub> of 12% despite being on an insulin pump. She worked as a bank teller, and was not married.

This patient had frequent hospitalizations for pyelonephritis during the previous 10 years, although none for diabetic ketoacidosis.

"These patients are very good at taking just enough insulin to stay out of really bad ketoacidosis, even though they're ketotic most of the time," Dr. Hirsch said.

In 2001 she switched from the insulin pump to glargine and lispro, with no change in HbA<sub>1c</sub>.

She denied having depression and refused evaluation by a psychiatrist or psychologist.

In 2002 she developed mucormycosis and was hospitalized for 2 weeks and released on home intravenous antibiotics.

"One week after discharge the mother found the patient dead at home. The home antibiotics had never been opened," he said.

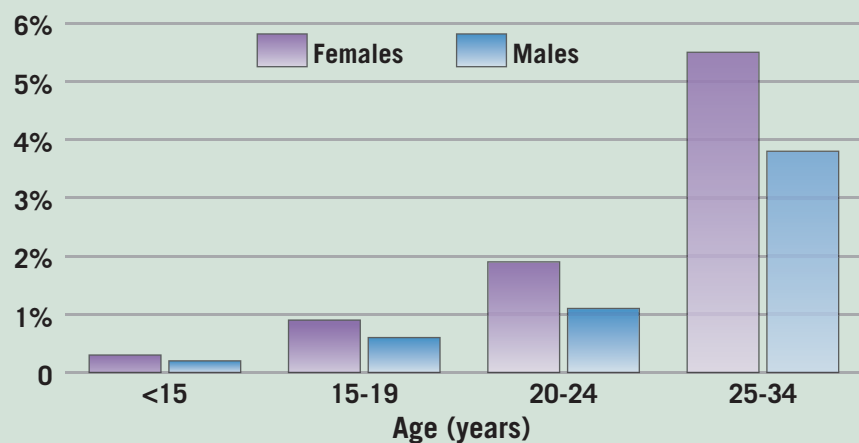
Like many patients with uncontrolled or brittle diabetes, this patient had severe major depression. With no family support, she was totally incapable of taking care of the diabetes and too depressed and overwhelmed even to take the antibiotics. "This is as difficult a case as you can get," he said.

It can be quite dramatic how poorly some of these patients do, Dr. Hirsch continued. In one series where 20 patients whose mean age was 19 were followed for 8 years, 2 of the patients died. In another series of 33 patients followed for a decade, 5 were lost, and of the remaining patients, 19% died from diabetic ketoacidosis, hypoglycemia, or end-stage renal disease.

"What you want to do when you present cases to a group like this is talk about really tough patients and how everybody lived happily ever after. That doesn't often happen with brittle diabetes," he said. ■

## DATA WATCH

### Diabetes Prevalence Higher in Females Than Males Among Native Americans and Alaska Natives



Source: 2004 data, Centers for Disease Control and Prevention