

Methadone at Therapeutic Levels Linked to SCD

BY BRUCE JANCIN
Denver Bureau

DENVER — Methadone in therapeutic doses appears to be associated with increased risk of sudden cardiac death, Dr. Carmen Socoteanu reported at the annual meeting of the Heart Rhythm Society.

This observation from a prospective case-control study has important public health implications in light of how widely the drug is prescribed for chronic pain control and opioid addiction, added Dr. Socoteanu of Oregon Health and Science University, Portland.

She reported on 22 consecutive cases of sudden cardiac death (SCD) featuring therapeutic blood levels of methadone. The cases were evaluated by the state medical examiner with detailed autopsies as part of the ongoing Oregon Sudden Unexplained Death Study sponsored by the Centers for Disease Control and Prevention.

Controls comprised 106 consecutive cases of SCD with no evidence of methadone

on toxicology screening during the same 4-year period. Individuals with evidence of recreational drug use or any drug overdose, including a blood methadone level of more than 1 mg/L, were excluded.

The mean age of individuals with therapeutic blood levels of methadone deemed to have experienced SCD was 37 years, compared with 42 years for controls.

Among controls, a specific cardiac cause of SCD was identified in 60% of cases. In contrast, a cardiac cause could be identified

in only 5 of 22 methadone users, or 23%, leaving therapeutic use of methadone as the only identifiable potential etiology of SCD in the great majority of cases.

Dr. John P. DiMarco commented that he would take home a key lesson from the study: a reminder that noncardiac drugs can cause arrhythmias and cardiac death.

When physicians think about proarrhythmic drugs, they tend to focus on antiarrhythmic agents and other cardiac medications. That's particularly true of

cardiologists. But methadone is an IKr potassium channel blocker that prolongs the QT interval and can cause torsades de pointes, noted Dr. DiMarco, professor of medicine and director of the electrophysiology service at the University of Virginia, Charlottesville.

Late last year, the Food and Drug Administration issued a public health advisory and ordered methadone labeling changes because of the mounting evidence of serious adverse events. ■

Race Drives Path Of Peripartum Cardiomyopathy

NEW ORLEANS — Full recovery of left ventricular function is significantly less likely in black patients than in white patients with peripartum cardiomyopathy, Dr. Sorel Goland said at the annual meeting of the American College of Cardiology.

There are other intriguing racial differences in the clinical profiles of patients with peripartum cardiomyopathy (PPCM). Black patients are significantly younger at diagnosis, more likely to have gestational hypertension, less likely to present with symptoms prior to delivery, and they tend to have worse outcomes, according to Dr. Goland of the University of Southern California, Los Angeles.

She presented a retrospective study involving 52 black and 104 white women with PPCM. Baseline left ventricular ejection fraction averaged 28% in both groups, with half of all patients having an ejection fraction of 25% or less. But only 18% of black patients experienced complete recovery of left ventricular function as defined by an ejection fraction of at least 50%, compared with 61% of white patients.

Mean age of the black women at diagnosis of PPCM was 26 years, compared with 30 years in white patients. Two-thirds of black patients had gestational hypertension, as did 46% of whites. More than 80% of black women had PPCM symptoms after delivery, compared with half of white women. Black patients also had a significantly greater mean left ventricular end diastolic diameter, both at diagnosis and last follow-up, an average of roughly 2 years later.

The combined end point of death or cardiac transplantation occurred in 31% of black patients, a significantly higher rate than in whites, Dr. Goland reported.

—Bruce Jancin



Discover **Levemir**®:
a long-acting basal insulin
with a light touch

Levemir: for your patients who need a safe and effective way to improve A1C control

With proven reductions in A1C and FPG levels over time, Levemir can help your patients get to goal with up to 24 hours of glycemic control. Patients with diabetes can experience a consistent blood glucose response from injection to injection. Less weight gain was observed with Levemir in 12 of 12 clinical trials.* And Levemir is available in the Levemir® FlexPen®. FlexPen® is the world's #1 selling prefilled insulin pen.† So start your patients with diabetes on Levemir, and help them experience the light side of basal insulin.

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 should not be diluted or mixed with any other insulin preparations. 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. Any change of insulin dose should be made cautiously and only under medical supervision. Concomitant oral antidiabetic treatment may require adjustment.

Levemir is not to be used in insulin infusion pumps. Inadequate dosing or discontinuation of treatment may lead to hyperglycemia and, in patients with type 1 diabetes, diabetic ketoacidosis. 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 and NPH insulin 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.

Reference: 1. IMS Health, IMS MIDAS [12 months ending September 2005]. Please see brief summary of Prescribing Information on adjacent page. FlexPen and Levemir are registered trademarks of Novo Nordisk A/S. © 2006 Novo Nordisk Inc. 131007 September 2006


insulin detemir (rDNA origin) injection
Lighter years ahead