Ketamine Lifted Bipolar Depression in 40 Minutes

**Major Finding:** In patients with treatment-resistant bipolar depression, an infusion of 0.5 mg/kg of ketamine significantly relieved depression within 40 minutes, an effect that lasted at least 3 days.

**Data Source:** Randomized, placebo-controlled, double-blind, crossover study involving 18 patients.

**Disclosures:** The National Institute of Mental Health and the National Alliance for Research on Schizophrenia and Depression funded the study. A patent application for the use of ketamine for depression has been submitted, listing two of the investigators among the inventors; they have assigned their rights on the patent to the U.S. government.

**LANTUS® (insulin glargine [DNA origin] injection) solution for subcutaneous injection**

The following are examples of drugs that may increase the blood-glucose-lowering effect of LANTUS in patients with diabetes who are lactating may require adjustments of their insulin doses.

**9. Use in Specific Populations**

9.1 Pregnancy

Pregnancy Category C: Subcutaneous reproduction and teratology studies have been performed with insulin glargine and regular human insulin in rats and Hanabayan rabbits. Insulin glargine was given to female rats before mating, during mating, and throughout pregnancy at doses up to 0.36 mg/kg/day, which is approximately 7 times the recommended human subcutaneous starting dose of 10 Unit/kg (0.088 mg/kg/day), based on mg/m² in rabbits, doses of 0.027 mg/kg/day, which is approximately 2 times the recommended human subcutaneous starting dose of 10 Unit/kg (0.088 mg/kg/day), based on mg/m², were administered during organogenesis. The effects of insulin-glargine did not generally differ from those observed with regular human insulin in rats or rabbits. However, in rabbits, live fetuses from two litters of the high-dose group exhibited dilatation of the cerebral ventricles. Fertility and early embryonic development appear normal.

There are no well-controlled clinical studies of the use of LANTUS in pregnant women. Because animal reproduction studies are not always predictive of human response, this drug should be used during pregnancy only if the potential benefit justifies the potential risk to the fetus. It is essential for patients with diabetes or a history of gestational diabetes to maintain good metabolic control before conception and throughout pregnancy. Insulin requirements may decrease during the first trimester, generally increase during the second and third trimesters, and rapidly decline after delivery. Careful monitoring of glucose control is essential in these patients.

9.3 Nursing Mothers

It is unknown whether insulin glargine is excreted in human milk. Because many drugs, including human insulin, are excreted in human milk, caution should be exercised when LANTUS is administered to a nursing woman. Use of LANTUS is compatible with breastfeeding, but women with diabetes who are lactating may require adjustments of their insulin doses.

9.4 Pediatric Use

The safety and effectiveness of subcutaneous injections of LANTUS have been established in pediatric patients (age 6 to 15 years) with type 1 diabetes [see Clinical Studies (14) in the full prescribing information]. LANTUS has not been studied in pediatric patients younger than 6 years of age with type 1 diabetes. LANTUS has not been studied in pediatric patients with type 2 diabetes.

Based on the results of a study in pediatric patients, the dose recommendation when switching to LANTUS is the same as that described for adults [see Dosage and Administration (2.4) and Clinical Studies (14) in the full prescribing information]. As in adults, the dosage of LANTUS must be individualized in pediatric patients based on metabolic needs and frequent monitoring of blood glucose.

9.5 Geriatric Use

In controlled clinical studies comparing LANTUS to NPH insulin, 393 of 3890 patients (15%) with type 1 and type 2 diabetes were ≥75 years of age. The only difference in safety or effectiveness in this subgroup of patients ≥65 years of age compared to the entire study population was a higher incidence of cardiovascular events typically seen in an older population in both LANTUS and NPH insulin-treated patients. Nevertheless, caution should be exercised when LANTUS is administered to geriatric patients. In elderly patients with diabetes, the initial dosage, dose increments, and maintenance dosage should be conservative to avoid hypoglycemic reactions. Hypoglycemia may be difficult to recognize in the elderly [see Warnings and Precautions (5.3)].

10. OVERDOSAGE

An excess of insulin relative to food intake, energy expenditure, or both may lead to severe and sometimes prolonged and life-threatening hypoglycemia. Mild episodes of hypoglycemia can usually be treated with oral carbohydrates. Adjustments in drug dosage, meal patterns, or exercise may be needed. More severe episodes of hypoglycemia with coma, seizure, or neurologic impairment may be treated with intramuscular/subcutaneous glucagon or concentrated intravenous glucose. After apparent clinical recovery from hypoglycemia, continued observation and additional carbohydrate intake may be necessary to avoid recurrence of hypoglycemia.

Dr. Nancy Diazgranados and her colleagues from the National Institute of Mental Health.

Ketamine was used in human and veterinary medicine since 1962, most commonly for inducing and maintaining general anesthesia, sedation in intensive care, analgesia, and treatment of bronchospasm.

When used for general anesthesia, the initial dose of intravenous ketamine is typically 1–4 mg/kg, which is substantially higher than the level used in this study.

Ketamine is thought to act as a non-competitive inhibitor of the N-methyl-D-aspartate (NMDA) receptor, which is part of the glutamatergic neurotransmitter system. Several lines of evidence have implicated the glutamatergic system in bipolar disorders.