

Weight Loss Sustained After Bariatric Surgery

BY DAMIAN McNAMARA

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PEDIATRIC ACADEMIC SOCIETIES

DENVER – Bariatric surgery resulted in significant weight loss at 1 year in a study of 890 morbidly obese adolescents who had the procedure at a designated center of excellence.

“This is one of the first reports of a national scope ... revealing the prevalence

estimates of weight loss among adolescent patients,” Dr. Nestor de la Cruz-Munoz said at the meeting. “Bariatric surgery has the potential to be a safe and effective treatment option for significant weight loss in U.S. adolescents, irrespective of gender.”

Fewer than 1% of bariatric surgery cases in the country are being done on adolescents, and “very little is known about the short-term and long-term outcomes

in terms of weight and associated health consequences in these patients,” said Dr. de la Cruz-Munoz, a bariatric surgeon at the University of Miami.

To find out more, he and his coworkers evaluated all patients aged 11-19 years old who had bariatric surgery from June 2007 through October 2010 in the prospective BOLD (Bariatric Outcomes Longitudinal Database) registry.

Weight decreased from a mean 138 kg

at baseline to 110 kg at 1 year in these 890 patients. Baseline mean z score changed from 2.86 to 2.31, and the weight percentile of these adolescents (compared with the general population) decreased from 99.6% to 97.1%. In addition, the body mass index z score decreased from 2.6 to 2.11 during this time. Assessments were also done at 6 months post surgery in all patients. “All of those [changes] were statistically significant,” Dr. de la Cruz-Munoz said.

“Bariatric surgery results in significant weight loss among morbidly obese multiethnic adolescents at 1 year post surgery, for both boys and girls,” he said.

Broken down by sex, the mean baseline weight was 162 kg for boys and 129 for girls. The mean z score decreased from 3.52 to 2.77 for boys and from 2.64 to 2.12 for girls. “The weight percentages for boys started at about as high as you can get (99.95%) and ended up at 98.7%,” Dr. de la Cruz-Munoz said.

At the same time, weight percentages for girls decreased from 99.46% to 95.97%. The BMI z score decreased from a baseline 3.15 in boys to 2.57 at 1 year. For girls, this measure decreased from 2.42 to 1.92. Again, all these changes were statistically significant.

“The most rapid weight loss was in the first 6 months,” he said.

One patient died from cardiac failure 5 months after surgery, resulting in a mortality rate of 0.11% in the cohort. In all, 141 postoperative adverse events were reported. Nausea and vomiting were the most common (13%), followed by vitamin D deficiency (8%).

Gastric bypass was the most common type of bariatric surgery in these adolescents, performed in 454 patients (51%). Gastric banding was a close second and was performed in 436 patients (49%). No gastric sleeve procedures were done in this age group during this time.

Consistent with adult data, about 80% were females; mean age was 18 years, and 69% were white, 15% Hispanic, 11% black, and 5% other.

There are now more than 375,000 patients in the BOLD registry, so adolescents represent only 0.7%. The independent, nonprofit Surgical Review Corporation (SRC) administers the American Society for Metabolic and Bariatric Surgery Center of Excellence (BSCOE) program. The SRC developed BOLD in 2007 to help ensure compliance with the BSCOE program. There are 440 facilities currently designated as centers of excellence, with 758 surgeons; approximately 100 additional facilities have provisional status, Dr. de la Cruz-Munoz said.

Dr. de la Cruz-Munoz is a member of the SRC’s surgical review committee and a consultant for Ethicon Endo-Surgery Inc. ■

To watch an interview with Dr. de la Cruz-Munoz, scan this QR code with a smartphone.



• *Insulin initiation and intensification of glucose control*

Intensification or rapid improvement in glucose control has been associated with a transitory, reversible ophthalmologic refraction disorder, worsening of diabetic retinopathy, and acute painful peripheral neuropathy. However, long-term glycemic control decreases the risk of diabetic retinopathy and neuropathy.

• *Lipodystrophy*

Long-term use of insulin, including LANTUS, can cause lipodystrophy at the site of repeated insulin injections. Lipodystrophy includes lipohypertrophy (thickening of adipose tissue) and lipoatrophy (thinning of adipose tissue), and may affect insulin absorption. Rotate insulin injection or infusion sites within the same region to reduce the risk of lipodystrophy. [See *Dosage and Administration (2.1)*].

• *Weight gain*

Weight gain can occur with insulin therapy, including LANTUS, and has been attributed to the anabolic effects of insulin and the decrease in glucosuria.

• *Peripheral Edema*

Insulin, including LANTUS, may cause sodium retention and edema, particularly if previously poor metabolic control is improved by intensified insulin therapy.

• *Allergic Reactions*

Local Allergy

As with any insulin therapy, patients taking LANTUS may experience injection site reactions, including redness, pain, itching, urticaria, edema, and inflammation. In clinical studies in adult patients, there was a higher incidence of treatment-emergent injection site pain in LANTUS-treated patients (2.7%) compared to NPH insulin-treated patients (0.7%). The reports of pain at the injection site did not result in discontinuation of therapy.

Rotation of the injection site within a given area from one injection to the next may help to reduce or prevent these reactions. In some instances, these reactions may be related to factors other than insulin, such as irritants in a skin cleansing agent or poor injection technique. Most minor reactions to insulin usually resolve in a few days to a few weeks.

Systemic Allergy

Severe, life-threatening, generalized allergy, including anaphylaxis, generalized skin reactions, angioedema, bronchospasm, hypotension, and shock may occur with any insulin, including LANTUS and may be life threatening.

• *Antibody production*

All insulin products can elicit the formation of insulin antibodies. The presence of such insulin antibodies may increase or decrease the efficacy of insulin and may require adjustment of the insulin dose. In phase 3 clinical trials of LANTUS, increases in titers of antibodies to insulin were observed in NPH insulin and insulin glargine treatment groups with similar incidences.

6.2 Postmarketing experience

The following adverse reactions have been identified during post-approval use of LANTUS.

Because these reactions are reported voluntarily from a population of uncertain size, it is not always possible to estimate reliably their frequency or establish a causal relationship to drug exposure.

Medication errors have been reported in which other insulins, particularly short-acting insulins, have been accidentally administered instead of LANTUS [See *Patient Counseling Information (17) in the full prescribing information*]. To avoid medication errors between LANTUS and other insulins, patients should be instructed to always verify the insulin label before each injection.

7. DRUG INTERACTIONS

A number of drugs affect glucose metabolism and may require insulin dose adjustment and particularly close monitoring.

The following are examples of drugs that may increase the blood-glucose-lowering effect of insulins including LANTUS and, therefore, increase the susceptibility to hypoglycemia: oral anti-diabetic products, pramlintide, angiotensin converting enzyme (ACE) inhibitors, disopyramide, fibrates, fluoxetine, monoamine oxidase inhibitors, propoxyphene, pentoxifylline, salicylates, somatostatin analogs, and sulfonamide antibiotics.

The following are examples of drugs that may reduce the blood-glucose-lowering effect of insulins including LANTUS: corticosteroids, niacin, danazol, diuretics, sympathomimetic agents (e.g., epinephrine, albuterol, terbutaline), glucagon, isoniazid, phenothiazine derivatives, somatropin, thyroid hormones, estrogens, progestogens (e.g., in oral contraceptives), protease inhibitors and atypical antipsychotic medications (e.g. olanzapine and clozapine).

Beta-blockers, clonidine, lithium salts, and alcohol may either potentiate or weaken the blood-glucose-lowering effect of insulin. Pentamidine may cause hypoglycemia, which may sometimes be followed by hyperglycemia.

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

The signs of hypoglycemia may be reduced or absent in patients taking sympatholytic drugs such as beta-blockers, clonidine, guanethidine, and reserpine.

8. USE IN SPECIFIC POPULATIONS

8.1 Pregnancy

Pregnancy Category C: Subcutaneous reproduction and teratology studies have been performed with insulin glargine and regular human insulin in rats and Himalayan 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 Units/day (0.008 mg/kg/day), based on mg/m². In rabbits, doses of 0.072 mg/kg/day, which is approximately 2 times the recommended human subcutaneous starting dose of 10 Units/day (0.008 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, five fetuses from two litters of the high-dose group exhibited dilation of the cerebral ventricles. Fertility and early embryonic development appeared 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.

8.3 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.

8.4 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 (2.3) 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.

8.5 Geriatric Use

In controlled clinical studies comparing LANTUS to NPH insulin, 593 of 3890 patients (15%) with type 1 and type 2 diabetes were ≥65 years of age and 80 (2%) patients were ≥75 years of age. The only difference in safety or effectiveness in the subpopulation 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 dosing, 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.

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Bridgewater, NJ 08807

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