Case Study: Management of Type 2 Diabetes After Bariatric Surgery

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PRESENTATION

J.B. is a morbidly obese man with a medical history significant for type 2 diabetes diagnosed at 40 years of age and combined hyperlipidemia with severe hypertriglyceridemia. His diabetes was originally treated with oral agents for ~ 4 years. Subsequently, his glycemic control worsened, and his hemoglobin A_{1c} (A1C) ranged between 10 and 12%. During this time, he was also diagnosed with hypertension and obstructive sleep apnea. After hospitalization for mild diabetic ketoacidosis at 44 years of age, he was started on insulin therapy. At that time, he weighed 264 lb, and his BMI was 37 kg/m^2.

During the next 2 years, J.B. required increasing doses of insulin and, because of his significant insulin resistance, was switched to the more concentrated U500 regular insulin formulation. With this therapy, his A1C decreased to < 7%. Previously, he had failed pharmacological and lifestyle changes to lose weight, including low-fat diets, fenfluramine/phentermine, phentermine, and sibutramine. Because of multiple medical issues that could improve with weight loss, he was referred to the bariatric surgery clinic. At that time, his diabetes regimen included U500, 30 units at breakfast and lunch and 70 units at dinner (the equivalent of 150 and 350 units of regular insulin, respectively), and metformin, 1,000 mg twice daily. His weight had increased to 374 lb and his BMI to 52 kg/m^2.

J.B. had a hand-assisted laparoscopic roux-en-Y gastric bypass. He was discharged home 2 days after surgery on a new diabetes regimen of glargine insulin, 30 units at bedtime, and lispro insulin, 20 units before meals, which was about one-seventh of his total preoperative insulin dose. Despite good glycemic control postoperatively, he developed a wound infection, which responded well to outpatient oral antibiotics. Three weeks after surgery, his average blood glucose was 115 mg/dl, with rare blood glucose measurements > 200 mg/dl, and he had lost 37.4 lb. Over the next 4 months, he lost 103.4 lb, and his insulin sensitivity continued to improve. He was gradually weaned off insulin therapy.

One year after surgery, J.B. had lost 143 lb, and his A1C was 6.6% only taking metformin, 500 mg twice daily. His hypertriglyceridemia had also improved. Preoperatively, he was treated with fenofibrate and atorvastatin, and his triglycerides ranged from 400 to 1,200 mg/dl. One year after surgery, off medications, his triglycerides had decreased to 150–300 mg/dl, secondary to weight loss alone.

QUESTIONS

1. What is U500 regular insulin?
2. Is gastric bypass effective at improving type 2 diabetes for morbidly obese patients?
3. What are the dietary restrictions after gastric bypass?
4. What are some approaches to treating diabetes after gastric bypass?

COMMENTARY

U500 regular insulin is a highly concentrated (500 units/ml) formulation of regular insulin. At this concentration, it behaves differently than the more common U100 regular insulin. Specifically, it has a prolonged duration of action and provides a five times more potent dose than U100 regular insulin. With three to four injections a day, it behaves as basal insulin in addition to providing prandial coverage secondary to the peak of insulin action. It is used for patients with severe insulin resistance who would otherwise require very large doses of U100 regular insulin.

The prevalence of obesity continues to rise to concerning levels. It is well established that obesity increases the rate of death from all causes[1] and that obesity-related comorbidities cause more than 2.5 million deaths per year worldwide.[2] In 1991, the National Institutes of Health–recommended guidelines for bariatric surgery included a BMI > 35 kg/m^2 with comorbidities or a BMI > 40 kg/m^2 without comorbidities. Bariatric surgery is becoming more common, with an estimated 130,000 procedures in 2005. The most common procedure is gastric bypass (80–90%).[3] Meta-analysis has shown that bariatric surgery is more effective than lifestyle changes or pharmacological therapies for weight loss and in decreasing obesity-related comorbidities.[4]

In the Swedish Obesity Study[5] the incidence of diabetes after surgery compared to conventional management of obesity was significantly lower at 2 and 10 years, 1 versus 8% and 7 versus 24%, respectively. Similar improvement was seen also with hypertriglyceridemia and hypertension.

Buchwald et al.[2] reported that, of patients with diabetes who undergo bariatric surgery, ~76% have complete resolution and another 10% have improvement of their diabetes. These authors reported that 15.3% of bariatric surgery patients have type 2 diabetes, and as many as ~25% have biochemical tests suggesting pre-diabetes. Considering the estimated number of procedures above, nearly 20,000 diabetes patients had bariatric surgery in 2005, with most having resolution and many others improvement of the disease. The time course to resolution of diabetes is not addressed specifically, but patients lose most of their weight in the first year postoperatively.

Multiple authors have looked at long-term outcomes in patients after bariatric surgery. MacDonald et al.[6] compared type 2 diabetic patients who had bariatric surgery to type 2 diabetic patients who were referred for surgery but did not have it because of personal reasons or because their insurance company refused to cover the procedure. The authors reported that patients who underwent surgery had a 9-year mortality rate of 9% compared to 28% over 6.2 years for those who did not have the surgery.[6] A larger observational study compared 1,035 bariatric surgery patients to 5,746 severely obese control subjects. The surgical patients had significantly less cancer, cardiovascular disease, endocrinological disease, and infectious disease and fewer hospitalizations. Furthermore, the surgery group's risk of mortality was reduced 89%.[7]

Multiple reasons account for an improvement in diabetes control after gastric bypass—mainly significant weight loss and reduced dietary intake. There are multiple phases to the post–gastric bypass diet.[8] High-protein, low-fat, low-carbohydrate foods are recommended, which contributes to improved glycemic control. Secondary to the nature of the surgery, patients are very susceptible to dumping syndrome, which can be provoked by high-fat, high-carbohydrate foods.

The postoperative diet includes:

- Phase 1: Clear liquids. While in the hospital, dietary intake includes water and noncarbonated, carbohydrate-free clear liquids, with no more than 30 ml per hour the first day. On the second day, patients gradually increase their volume to 4 oz per hour if tolerated.
- Phase 2: Full liquids. After patients leave the hospital, they start the second phase, which lasts 7–10 days. This includes 4–8 oz per waking hours of liquids no thicker than tomato juice. At this stage, patients receive 400–600 kcal/day.
- Phase 3: Pureed diet. If the second phase is tolerated, patients advance to the puree phase for 4 weeks. Patients eat three meals a day consisting of foods that must be pureed to the texture of baby food. No more than 4 oz is consumed at a time, and foods must be taken in slowly (no faster than 30 minutes per 4 oz).
- Phase 4: Soft diet. This phase lasts for 2–3 months and includes three meals per day with up to 6 oz per meal.
- Phase 5: Regular diet. In the final phase, it is recommended that patients eat three meals a day, once again eating slowly and chewing food well. Low-fat, low-calorie foods are recommended. At this time, calorie intake is 1,200–1,500 kcal/day.

Progression through these phases varies on an individual basis. Great importance is given to satiety, and patients are asked to stop eating when full. If patients do not follow these recommendations, they are at risk for complications, including anastomotic leaks, which can require reoperation. Initially after surgery, it is common for patients to lose 15–20 lb per month, a rate that slows down with time. Postoperatively, patients' physical activity level is increased gradually based on tolerability. Patients' weight, dietary intake, and activity level change regularly; therefore, they require frequent follow-up for diabetes, especially during the first year after surgery.

Tight glycemic control with intensive insulin therapy has been shown to reduce morbidity and mortality for surgical patients.[9] For patients seen preoperatively, we strive to get good glycemic control at that time in keeping with these data. After surgery, patients are followed closely because their insulin sensitivity can fluctuate rapidly. Initial outpatient follow-up is < 2 weeks after surgery, as patients transition to the third diet phase. During the first 6–8 weeks postoperatively, patients return to the clinic every 2 weeks and fax their blood glucose monitoring results to the clinic on a weekly basis. It is not uncommon for regimens to be changed weekly. However, if patients have complications, such as wound infections, their insulin resistance may temporarily increase.

Regimens need to be adjusted immediately after surgery. Frequently, patients whose diabetes is controlled with oral agents do not require any antidiabetic agents by the time they leave the hospital. Commonly, all oral agents are stopped because patients can only take medications that can be crushed and do not tolerate medications that have any gastrointestinal symptoms (i.e., metformin, or α-glucosidase inhibitors). Metformin should be stopped a few days before surgery because of the risk of lactic acidosis. Clinicians must be careful that the diabetes regimen does not put patients at risk for hypoglycemia because patients' ability to correct hypoglycemia is restricted because of food intake restrictions. For patients who are on insulin, adjustments are made immediately postoperatively. This varies greatly based on degree of insulin resistance, preoperative insulin doses, and other factors, and because of this, there are no standard recommendations. Typically, basal insulin is decreased to half, and often further decreases may be needed before discharge home. When patients start caloric intake, a small meal dose of insulin is initiated as needed.

Basal-bolus insulin regimens after bariatric surgery create a challenge

because patients are advised to eat as many as six times per day initially, and eating can be unpredictable because of changes in satiety. Patients who still require significant basal and prandial doses are better served by a rapid-acting insulin analogue for prandial coverage, because this insulin offers many advantages. It can be taken multiple times a day without dose stacking (taking a dose before the last dose activity has been completed), which increases the risk of hypoglycemia. Rapid-acting analogues can also be taken 15–20 minutes after patients start eating, which can be safer for those who do not know how much they will be able to eat because of nausea and early satiety.

Another method favored by many clinicians is U100 regular insulin four times a day before eating. It can used as basal and prandial converge in this manner. The dose taken would be based on preprandial blood glucose similar to a correction scale (sliding scale). However, insulin doses start at normal blood glucose to behave as basal coverage. Because of its onset of action, regular insulin in nonsurgical patients is recommended to be taken 20–30 minutes before eating. However, after bariatric surgery, patients eat very slowly, and therefore their insulin can be taken just as they begin to eat. In our experience, patients whose diabetes is controlled on this regimen are commonly tapered off of all insulin in the first 2–3 months postoperatively.

Prandial insulin doses for a type 2 diabetic patient who has not had surgery often start at 0.2–0.4 units/kg and are adjusted based on prandial blood glucose values. After bariatric surgery, insulin sensitivity is improved, and meal sizes are smaller. Therefore, a starting dose might be half or less than half of the standard regimen. Correction dose coverage can also be initiated starting with the addition of ~ 2 units for every 50 mg/dl above 120 mg/dl their blood glucose rises, with an upper limit for this coverage. However, secondary to vast differences in insulin resistance, carbohydrate intake, and weight loss, this dosing can vary widely.

If patients have multiple elevated or any low blood glucose values, they are instructed to call so their regimen can be adjusted. After about 2 months, patients' gastric capacity improves, and, if needed, we consider restarting oral regimens while remaining mindful of the risk of hypoglycemia with ongoing improving insulin sensitivity.

Bariatric surgery is becoming more common for patients with diabetes; therefore, postoperative management of these patients is a growing concern for both endocrinologists and primary care physicians. Our facility has a surgical center for weight loss and from 2003 to 2005 performed nearly 1,000 procedures. Many of these patients are followed in our endocrinology clinic or seen postoperatively by our consult service. Although specific guidelines are not available for diabetes management after bariatric surgery and would be difficult to create based on patient variability, the approaches discussed here can provide helpful guidance for other clinicians treating this growing patient population.

CLINICAL PEARLS

- Gastric bypass is a well accepted means of weight loss for morbidly obese patients and has been proven to improve or even cure diabetes. The best outcomes come from centers that have expert surgeons who specialize in the procedure.
- After gastric bypass, diabetes improves rapidly. Because of weight loss during the first 6–12 months postoperatively, insulin sensitivity continuously improves, requiring frequent follow-up.
- Patients with diabetes treated with oral agents often cease all oral hypoglycemic agents as early as the immediate postoperative period.
- Insulin needs commonly decrease by half or lower even before patients leave the hospital.
- Close follow-up postoperatively is needed because of the high risk of hypoglycemia.
- Long-term follow-up is needed because subsequent weight gain can cause a recurrence of diabetes.

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