European **Rev**iew for **Med**ical and **Pharmacol**ogical **Sci**ences 2015; 19: 1121-1123

Letter to the Editor

Remission of type 2 diabetes after bariatric surgery

Dear Editor,

Type 2 diabetes is one of the fastest growing epidemics worldwide and is closely associated with obesity. The disease has been historically considered a relentless and progressive clinical condition due to ongoing and irreversible beta-cell failure. This knowledge has been recently challenged by a growing body of evidence that its remission, defined as normal glycemia and glycated hemoglobin levels without medications, can be achieved after bariatric surgery[1]. Although weight loss by diet and physical activity in addition to proper medical treatments should cause amelioration of glycemic control, it is unrealistic to expect that a patient will experience diabetes remission with any combination of drugs and lifestyle measures. The remission of diabetes has been noted by every bariatric surgeon who has been involved in the care of morbidly obese and diabetic patients since the beginning of the use of intestinal bypass. A meta-analysis of studies on various bariatric surgical procedures involving morbidly obese and diabetic patients showed an overall rate of remission of 78% among the various procedures. Type 2 diabetes remission occurred in 50% of patients who underwent laparoscopic adjustable gastric banding, 80% of those who underwent gastric bypass, and 95% of those who underwent biliopancreatic diversion[2]. In the early years diabetes remission was considered a consequence of reduced caloric intake and subsequent weight loss. Indeed, return to euglycemia and normal insulin levels are often observed within days after surgery suggesting the presence of an intrinsic mechanism of bariatric surgery[2]. Gastric bypass with its single anastomosis variant (minigastric bypass) and biliopancreatic diversion reroute food through the upper small bowel activating mechanisms of diabetes control independent of weight loss. In fact, type 2 diabetes is seen to improve or even revert to normal soon after gastric bypass or biliopancreatic diversion well before any significant weight loss has taken place[3]. This observation prompted scientist to investigate the effects of bariatric surgery on diabetic patients with BMI < 35 kg/m^2. A recent randomized trial, belonging to Lee et al[4], comparing a purely restrictive procedure (sleeve gastrectomy/SG) versus a restrictive/malabsorptive procedure (single anastomosis gastric bypass/SAGB) has shown persistent improved glucose outcomes as measured by the HbA1c up to 5 years after surgery in mildly obese (BMI range 25-35 kg/m^2; mean 30 kg/m^2) and poorly controlled type 2 diabetic patients. Still, 60% of patients undergoing SAGB experienced complete remission of diabetes (HbA1c < 6%) at fifth year after bariatric procedure. Conversely, only 30% of patients undergoing SG experienced at the same time improvement of glucose metabolism with mean HbA1c values < 7%. This study supports an increased usage of gastric bypass surgery in the treatment of non-severely obese type 2 diabetic patients. For the first time in 2012 Mingrone et al[5] published their original results on diabetes remission after bariatric surgery. They compared optimized conventional medical therapy with two bariatric procedures (GB and BPD) in morbidly obese patients with type 2 diabetes. Their results clearly showed how bariatric surgery is far more effective than medical therapy in the control of hyperglycemia in such patients. Similar results were obtained by Schauer et al[6] who compared GB and SG versus intensive medical therapy.

The underlying mechanism of diabetic remission after bariatric surgery is intriguing and still not fully understood. The most well-known mechanism is a rapid decrease of insulin resistance which is mainly related to caloric restriction and consequent weight loss. This mechanism is certainly working after any procedure or treatment reducing food intake as restrictive bariatric procedures. Diabetes reversal after malabsorptive bariatric surgery seems to be correlated with a new anatomical connections between the stomach and small intestine, thereby a change in the normal pathway for food, suggesting that the intestine itself plays a role in the pathogenesis of type 2 diabetes. The term "enteroinsular axis" arises from the fact that the gastrointestinal tract plays a role in controlling glucose metabolism. In fact, glucose ingestion stimulates insulin secretion 50% more than glucose infusion even in the presence of similar circulating levels of glucose[7]. After purely restrictive procedures as laparoscopic gastric banding or sleeve gastrectomy the mechanism of glucose metabolism improve-

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ment or remission seems to be essentially related to weight loss. Consequently, in severely obese and diabetic patients whatever bariatric procedure able to induce weight loss will be successful and indicated. After bariatric procedures as gastric bypass and biliopancreatic diversion, which both exclude the duodenum and a variably long portion of jejunum from food transit by creating a gastroenteroanastomosis, diabetes improvement or remission occurs within 1 month of the operation in more than 75% of patients before any significant weight loss occurred and without any food restrictions in patients who underwent biliopancreatic diversion. Two main hypotheses have been proposed to explain the early effects of malabsorptive surgery on diabetes: the hindgut and the foregut hypothesis[7,8]. The hindgut hypothesis states that the rapid delivery of nutrients to the distal small intestine (ileum) enhances the release of hormones such as GLP-1 (glucagon-like peptide-1), which has been shown to improve glucose metabolism stimulating insulin secretion and suppressing glucagon secretion. The foregut hypothesis states that the exclusion of the proximal small intestine reduces or suppresses the secretion of still unknown anti-incretin hormones with a consequent improvement of glucose metabolism control. Malabsorptive bariatric surgery has a better glycemic control for type 2 diabetes but there are some disadvantages arising from long-term micro- and macro-nutrient malnutrition. Chronic iron deficiency anemia, osteoporosis and protein malnutrition are only some of the clinically relevant long-term complications to be kept in mind before deciding which type of surgery to adopt. Identifying preoperative predictors of diabetes remission is critical for determining which patients will benefit from surgery and understanding mechanism of diabetes resolution could help surgeons to choose appropriate bariatric procedures. Purely restrictive procedures as sleeve gastrectomy or adjustable gastric banding may be considered in patients with newly onset diabetes, presumable good islet cell preservation and high C-peptide levels. Diabetic patients with poor endocrine pancreatic reserve, long history of diabetes disease (more than 5-10 years), and low levels of C-peptide could benefit from bariatric procedures able to induce an incretin effect as gastric by-pass and biliopancreatic diversion.

Obviously, randomized study comparing all available bariatric procedures in obese and no-obese patients with type 2 diabetes are, more and more, necessary to clearly tailor bariatric surgery to patient.

However, it is interesting and somehow revolutionary that today after 30 years of bariatric surgery both a consensus meeting[9] and the International Diabetes Federation[10] have recommended consideration of bariatric surgery for control of type 2 diabetes.

Conclusions

We stated that bariatric surgery is superior to any medical treatment to induce diabetes remission in severe and mildly obese patients, the question is: "Is it ethically correct not to offer bariatric surgery as valid therapeutic option to severely and, even more, to mildly obese patients with type 2 diabetes?".

Conflict of Interest

The Authors declare that there are no conflicts of interest.

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