The rollercoaster of post-bariatric hypoglycaemia

Bariatric surgical procedures induce substantial and sustained weight loss and improve or normalise obesity-related comorbidities, including type 2 diabetes. Surgery is superior to medical treatment for weight loss and diabetes, improves glycaemic control, reduces need for drugs, and improves lifespan.1 Although surgical benefits are achieved with low operative mortality, long-term intestinal and nutritional complications can occur.

One challenging and sometimes severe complication of bariatric surgery is post-bariatric hypoglycaemia.2 Patients with hypoglycaemia can present with non-specific symptoms, including a mixture of adrenergic, cholinergic, and neuroglycopenic features. Hypoglycaemia unawareness and neuroglycopenia can result in severe consequences, including impaired cognition, falls, motor vehicle accidents, loss of consciousness, and seizures. Mild, often unrecognised, hypoglycaemia can contribute to increased appetite and weight regain after surgery.

Diagnosis of post-bariatric hypoglycaemia requires documentation of low venous glucose concurrent with symptoms, with symptom relief by glucose correction (Whipple’s triad). This is especially important because adrenergic and cholinergic symptoms (palpitations, light-headedness, and sweating) experienced during hypoglycaemia share substantial overlap with symptoms of dumping syndrome experienced by some post-bariatric patients. Typically, dumping-related symptoms occur very early (30 min) after eating, are not associated with concurrent hypoglycaemia, and are most prominent in the early postoperative period, resolving over time. By contrast, hypoglycaemia typically occurs 1–3 h after meals, with first symptoms developing more than 1 year postoperatively. Confirmation of hypoglycaemia, either during a spontaneous or meal-provoked episode, is crucial to distinguish these aetiologies.

Once hypoglycaemia is documented, it is important to assess the pattern and severity of hypoglycaemia. Post-bariatric hypoglycaemia typically occurs postprandially, concurrent with inappropriately high concentrations of plasma insulin. Glucose concentrations typically remain stable after overnight or prolonged fasting. If history or diagnostic testing suggest fasting hypoglycaemia, clinicians must consider additional causes for hypoglycaemia, including drug treatments, alcohol, other hormonal factors (eg, adrenocortical hormone deficiencies), or autonomous insulin secretion from an insulinoma, and if indicated, undertake diagnostic fasting in the hospital setting.

Patients with severe post-bariatric hypoglycaemia undergo profound changes in glycaemic patterns in the postprandial state. Early after meals, glucose concentrations increase rapidly, often to greater than 200 mg/dL (11·1 mmol/L), thereby triggering insulin secretion, which in turn contributes to rapid decline in glucose and subsequent hypoglycaemia.2,3 Thus, the initial aim of treatment is to reduce postprandial glucose surges by restricting intake of high-glycaemic-index carbohydrates and slowing carbohydrate absorption with α-glucosidase inhibition with acarbose. Collectively, these approaches can reduce insulin secretion, but often yield only modest benefits in patients with severe post-bariatric hypoglycaemia. Long-term approaches targeting either incretin or insulin secretion—eg, octreotide, diazoxide, or calcium channel blockade—can be effective for some patients with post-bariatric hypoglycaemia. Personal continuous glucose monitoring helps patients to predict and detect hypoglycaemia before neuroglycopenia develops.4 Gastric restriction or banding (to slow gastric emptying) or gastrostomy tube feeding into the bypassed stomach can provide improved glucose stability for those requiring intensified approaches. Partial pancreatectomy was initially used to reduce insulin secretion, but is not uniformly successful and is no longer routinely recommended.

Incretin hormones probably contribute to glucose-dependent insulin secretion. Postprandial glucagon-like peptide 1 (GLP-1) is increased 10-fold in post-bypass patients, is even higher in those with post-bariatric hypoglycaemia, and is inversely associated with postprandial glucose concentration.5 Short-term pharmacological blockade of the GLP-1 receptor attenuates insulin secretion in patients with post-bariatric hypoglycaemia.3 Although these findings emphasise the importance of altered food delivery patterns and secretion of intestinal peptides as crucial contributors to hypoglycaemia, additional mechanisms might contribute to altered metabolism.

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Figure: Potential mechanisms contributing to post-bariatric hypoglycaemia

In post-bypass patients, food quickly transits to the intestine, and plasma glucose rises rapidly. Chronic intestinal and neural adaptations, including altered intestinal and bile acid metabolism, contribute to the triggering of excessive postprandial incretin and insulin secretion. These insulin-dependent mechanisms, together with increases in insulin-dependent glucose disposal, converge to increase risk for hypoglycaemia in the postprandial state.

Several key questions remain. Can hypoglycaemia be prevented? Can we identify patients at the highest risk for this complication during the preoperative assessment? Until we better understand genetic and environmental factors, clinicians should be vigilant for possible hypoglycaemia. More broadly, we do not yet know whether hypoglycaemia, whether symptomatic or completely asymptomatic, could contribute to chronic weight regain, or be detrimental to long-term cognitive function. Longitudinal studies are crucial to address these key questions. Until findings from such studies are reported, clinicians should be vigilant for possible hypoglycaemia.
Comment

other factors that can increase risk, it seems prudent to carefully balance the risk versus the benefits of surgical approaches for individual patients, especially in people without type 2 diabetes or those with a history of possible hypoglycaemia uncovered during preoperative assessment. For individuals deemed to be at increased risk for hypoglycaemia, clinicians might consider favouring procedures that do not irreversibly change intestinal anatomy or function (eg, gastric banding). In the long term, it will be essential to identify mechanisms responsible for weight loss and metabolic improvement after bariatric surgery to develop surgical or pharmacological approaches that maximise weight loss and resolution of diabetes, yet minimise risk of hypoglycaemia and other nutritional or metabolic complications.

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6 Patti ME, Li P, Goldfine AB. Insulin response to oral stimuli and glucose effectiveness increased in neuroglycopenia following gastric bypass. Obesity (Silver Spring) 2015; 23: 798-807.