Diabetes & Metabolism 37 (2011) 274–281

Review

Post-bypass hypoglycaemia: A review of current findings

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Received 19 January 2011; received in revised form 18 April 2011; accepted 28 April 2011
Available online 14 June 2011

Abstract

Gastric bypass is one of the most efficient strategies for long-term weight loss and reduction of the comorbidities associated with morbid obesity. Of the complications secondary to gastric bypass, hypoglycaemic episodes have so far been poorly studied. The present study is a comprehensive report of the fewer than 100 cases described in the literature. It shows that strict diagnostic criteria should be applied to differentiate true intense neuroglucopenic symptoms associated with low glucose values (< 2.8 mmol/L) from the more frequent symptoms of the dumping syndrome and those occurring in the context of lower-than-normal plasma glucose concentrations. The pancreatic beta-cell hyperfunction initially deemed responsible for hypoglycaemic episodes because of frequent islet abnormalities is described and reappraised in this report. The few validated therapeutic options are also discussed.

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Keywords: Hypoglycaemia; Gastric bypass; Nesidioblastosis

Résumé

Hypoglycémies après bypass gastrique : revue de la littérature.

Le bypass gastrique est une des stratégies chirurgicales les plus efficaces pour une perte de poids durable et pour la réduction des comorbidités associées à l’obésité morbide. Parmi les complications secondaires du bypass gastrique, les hypoglycémies ont été peu étudiées. Cette étude rapporte les quelques cas (moins de 100) d’hypoglycémies les plus sévères décrits dans la littérature. Cette étude montre que des critères diagnostiques stricts (la triade de Whipple) doivent être appliqués pour bien faire la différence entre les symptômes neuroglycopéniques intenses associées à des glycémies le plus souvent inférieures à 2,8 mmol/L, et les symptômes moins intenses du dumping syndrome ou moins spécifiques associées à une glycémie abaissée en dessous des valeurs normales. L’hyperfonctionnalité des cellules bêta pancréatiques considérée initialement comme responsable des hypoglycémies est discutée. Les quelques options thérapeutiques sont décrites.

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Mots clés : Hypoglycémie ; Bypass gastrique ; Nesidioblastose

1. Introduction

There is now good scientific evidence to show that obesity surgery leads to sustained weight loss [1–3]. Depending on the surgical technique, 49–73% of the initial excess weight (EW) is lost after 2 years [2,3], and the proportion is around 65% after a Roux-en-Y gastric bypass (gastric bypass) [2]. More than 70% of obese diabetic patients are in remission after bariatric surgery [2], while most patients significantly reduce their antidiabetic treatment soon after the operation [4]. However, the mechanisms leading to the improvement in glucose homoeostasis have yet to be fully elucidated [2,4–6].

The long-term complications of gastric bypass are classically the consequences of nutrient malabsorption [7]. Another rare long-term complication is hypoglycaemia. Although only a few cases of intense neuroglucopenic episodes have been

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doi:10.1016/j.diabet.2011.04.003
2. Definitions

Hypoglycaemia is defined as the occurrence of adrenergic and neuroglucopenic symptoms associated with plasma glucose concentrations ≤ 50 mg/dL (2.8 mmol/L) [8]. Particular attention should be paid to neuroglucopenic symptoms, as they are critical in the definition of post-gastric-bypass hypoglycaemia (Table 1). The Whipple triad is the association of fasting hypoglycaemic symptoms, documented low plasma glucose concentrations at the time of spontaneous symptoms (< 2.8 mmol/L) and the relief of such symptoms through correction of the low glucose level [8,19]. It suggests that hypoglycaemia is organic. After gastric bypass, the threshold of plasma glucose concentration that defines hypoglycaemia varies across different sources, and is a matter of confusion in reports of hypoglycaemia following obesity surgery. Some authors use 3.3 mmol/L as the threshold, while others report glucose values below the lowest value of the normal range and, most of the time, 4.3 mmol/L. Another cause of confusion is the frequent use of the word “severe” in the literature, which has different meanings in the fields of diabetes and obesity surgery. For diabetologists, severe hypoglycaemia is defined as an episode that requires the assistance of a third party to either give oral glucose, or because the clinical presentation is severe (including coma or seizures, for example) and requires intravenous glucose [20].

The criteria for Whipple’s triad need to be rigorously applied if a correct diagnosis is to be made, as post-gastric-bypass patients may have many non-specific symptoms. Through the discipline of applying Whipple’s triad in the evaluation of hypoglycaemia, regardless of whether it occurs in the fasting or post-prandial period, the recognition of additional disorders causing endogenous hyperinsulinaemic hypoglycaemia has been possible [8].

The dumping syndrome is a frequent complication of gastric surgery. This refers to symptoms and signs that occur when food reaches the small bowel too quickly. Previously frequently seen after gastric surgery for ulcer or cancer, it is nowadays one of the most frequent complications after gastric bypass (affecting 15–20% of patients, according to Yecht et al. [21], and perhaps 70%, according to Hsu et al. [22]), as the stoma between the gastric pouch and jejunum permits a too-rapid entry of large, unprocessed, food particles into the bowel. An early component of the dumping syndrome comprises both intestinal and vasomotor symptoms appearing within minutes after the start of a meal (Table 1). Late dumping syndrome, occurring between 1 and 3 hours after the beginning of a meal, is hypoglycaemia (Table 1) without the intense neuroglucopenic symptoms [23], similar to reactive hypoglycaemia.

In the literature on post-bypass hypoglycaemia, different presentations have been documented. There are some rare cases of severe episodes associated with major neuroglucopenic symptoms, and there are also other, less severe cases without major signs that are probably much more frequent and easier to treat. Finally, there is some debate over the occurrence of asymptomatic low plasma glucose values after a glucose challenge or meal test.

3. Description of the most severe cases of post-bypass hypoglycaemia

Outside of the context of bariatric surgery, Service et al. [24] have described cases of non-operated-on patients suffering from postprandial hypoglycaemia attributed to a non-insulinoma pancreatic ganglioneuromatous hypoglycaemic syndrome. In these patients, hypoglycaemia had the features of organic hypoglycaemia except for the unusual postprandial timing, and occurred without insulinoma and without the genetic mutations associated with the syndrome. Imaging studies of the pancreas (transabdominal, endoscopic, intraoperative ultrasound and computed
<table>
<thead>
<tr>
<th>Number of cases</th>
<th>Age (years)</th>
<th>Gender</th>
<th>BMI presurgery</th>
<th>Diabetes presurgery</th>
<th>Weight loss (kg)</th>
<th>Weight regain (kg)</th>
<th>Time to symptoms (months)</th>
<th>Documented lowest glucose value (mmol/L)</th>
<th>Severe neuroglucopenia</th>
<th>Reference</th>
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<tbody>
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<td>3</td>
<td>56.3 ± 7.8</td>
<td>2 F 1 M</td>
<td>49.3 ± 10.2</td>
<td>None</td>
<td>69 ± 26.5</td>
<td>7.2 ± 3.4</td>
<td>25 ± 11</td>
<td>1.6</td>
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<td>Bantle et al. [27]</td>
</tr>
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<td>1</td>
<td>34</td>
<td>F</td>
<td>NA</td>
<td>All</td>
<td>NA</td>
<td>NA</td>
<td>12</td>
<td>2.6</td>
<td>Unknown</td>
<td>Alvarez et al. [46]</td>
</tr>
<tr>
<td>8</td>
<td>41.1</td>
<td>7 F 1 M</td>
<td>54.7 ± 3.0</td>
<td>3 out of 8</td>
<td>62</td>
<td>NA</td>
<td>6–60</td>
<td>1.9</td>
<td>All patients</td>
<td>Kim et al. [40]</td>
</tr>
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<td>9</td>
<td>38.4 ± 10.8</td>
<td>8 F 1 M</td>
<td>NA</td>
<td>6 out of 9</td>
<td>NA</td>
<td>NA</td>
<td>21 ± 19</td>
<td>2.4 ± 0.2</td>
<td>Not all patients</td>
<td>Mathavan et al. [45]</td>
</tr>
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<td>42.9 ± 10.4</td>
<td>8 F 1 M</td>
<td>47.7 ± 9.3</td>
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<td>49 ± 14.7</td>
<td>NA</td>
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<td>NA</td>
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<td>NA</td>
<td>All</td>
<td>NA</td>
<td>32</td>
<td>10</td>
<td>2.5</td>
<td>None</td>
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</tr>
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<td>43.6</td>
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<td>16</td>
<td>2.8</td>
<td>None</td>
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<td>NA</td>
<td>15 ± 7.9</td>
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<td>1.8</td>
<td>Unknown</td>
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<tr>
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<td>44</td>
<td>NA</td>
<td>8.7</td>
<td>35 ± 25</td>
<td>1.8 ± 0.1</td>
<td>7 out of 12</td>
<td>Z’Graggen et al. [14]</td>
<td></td>
</tr>
<tr>
<td>2</td>
<td>42.5 ± 10.6</td>
<td>2 F</td>
<td>NA</td>
<td>None</td>
<td>71.6 ± 27.3</td>
<td>NA</td>
<td>30 ± 8</td>
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<td>All patients</td>
<td>Clancy et al. [13]</td>
</tr>
<tr>
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<td>48</td>
<td>10 F 2 M</td>
<td>51.1</td>
<td>None</td>
<td>54.8</td>
<td>37</td>
<td>NA</td>
<td>2.8</td>
<td>All patients</td>
<td>Goldfine et al. [26]</td>
</tr>
<tr>
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<td>45</td>
<td>25 F 2 M</td>
<td>47</td>
<td>NA</td>
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<td>17–264</td>
<td>2.8</td>
<td>Unknown</td>
<td>Rumilla et al. [12]a</td>
<td></td>
</tr>
</tbody>
</table>

**Table 2**

Summary of case reports.

F: female; M: male; NA: not available.

a Probably includes the six cases described by Service et al. [9].

tomography [CT] imaging) were uniformly negative. Pancreactectomy was required, and histopathological explorations demonstrated nesidioblastosis. The same authors reported the first cases of post-bypass hypoglycaemia, the description of which was similar to their initial one [9]. Although the definition of severe post-bypass hypoglycaemia varies among authors, all agree that it occurs after a meal [9,25–27].

The clinical presentations of these patients are summarized in Table 2. Most reports have been of small series of patients, and the total number is about 80–90, considering that there may be multiple publications of the same patients. Some features of these observations are similar to those of patients included in the meta-analysis by Buchwald et al. in 2009 [2], which analyzed weight changes and diabetes remission after bariatric surgery. The age (44 vs 40 years in Buchwald), preoperative body mass index (BMI; 48 vs 47.9 kg/m²) and proportion of diabetic patients before surgery (23% vs 22%) are all comparable. More patients with hypoglycaemia were women (88% vs 80%). It is also noteworthy that the weight loss after surgery was greater in hypoglycaemic patients (56.5 kg, or 82–86% of excess weight loss, while the figures were 41 kg and 65% in the meta-analysis [2]). It is also worth noting that the excess weight losses were recalculated from estimated heights and that, therefore, these values give a trend and should not be considered actual values. Neuroglucopenic signs were present in 72% and absent in 11% of the patients. However, it was not possible to address this question in 17% of the studied patients. The neuroglucopenic symptoms ranged from very severe (car accidents, seizures, loss of consciousness) to milder ones (blurred vision, confusion, disorientation, lightheadedness, dizziness). The lowest glucose concentration (some in plasma and some capillary) documented at the time of symptoms was very low (weighted mean: 2.3 mmol/L). By definition, most authors considered hypoglycaemia as <2.8 mmol/L, while others chose 2 mmol/L [14], 3.3 mmol/L [26] or 3.9 mmol/L [25]. The mean time elapsed between surgery and the first symptom was 29 months, and ranged from 1 to 264 months. Very few patients (n=4) had symptoms before 12 months. The time lag in the Swedish registry study was 32 months (range 12–178) [28]. Weight regain was a matter of little importance (n = 16 patients) and amounted to 8.5 kg [14,27,29].

It is worth noting that at least two of these patients had insulinoma presenting as postprandial hypoglycaemia, but with a positive fast-growing or easily identifiable tumour of the pancreas [9,30]. It should also be noted that a few patients had these symptoms before surgery, although a low glucose concentration had not been demonstrated [13,26].

4. Prevalence

The prevalence of post-bypass hypoglycaemia with severe symptoms is low. Kellogg et al. [25] reported 14 cases out of 3082 procedures (0.36%) performed over the years. Marsk et al. [28] studied the registries of the Swedish health system, and analyzed the prevalence of hospitalizations for hypoglycaemia and for confusion, syncope, epilepsy or seizures attributed to hypoglycaemic episodes both before and after the dates of bariatric surgery. The prevalence before bariatric surgery was similar to that in the general population, whereas the prevalence was increased after bariatric surgery, reaching 0.2–1% of the operated-on patients (depending on symptoms). The increased prevalence was specific to the gastric-bypass procedure, as it was not observed after gastric banding or vertical banded gastroplasty. Whether diabetic patients were included or not in the analysis did not make a difference.

5. Metabolic changes

5.1. Postprandial changes in glucose homeostasis after gastric bypass

After gastric bypass, early, major and transient postprandial glycaemic rises have been described [26,31–33], albeit not by all authors [34,35]. A corresponding rise in plasma insulin concentrations may or may not occur, although plasma insulin is systematically low at 90 minutes after a meal or glucose load test. However, GLP-1 responses to a glucose load are dramatically increased [36–38]. This information was obtained by comparing patients after a gastric bypass to patients before surgery (matched for either their initial BMI or BMI after surgery), or following a restrictive procedure but without an intestinal bypass (such as gastric banding or sleeve gastrectomy). Glycaemic profiles obtained with a continuous glucose monitoring system (CGMS) over many days confirm these early, important and transient postprandial glycaemic rises [29,39].

5.2. Postprandial changes in glucose homeostasis in hypoglycaemic patients

In cases of severe hypoglycaemia, an early and transient plasma glucose peak is also observed [25,26,40]. Insulin concentrations following a glucose challenge (as a liquid meal providing 40–80 g of maltodextrin or up to 75 g of a glucose solution) suggest an inadequate hyperinsulinaemia. The same observations have been made in asymptomatic patients [26,40].

Important information has also been obtained from a comparison of symptomatic and asymptomatic gastric-bypass patients. Although fasting glucose and insulin values did not differ between the symptomatic and asymptomatic patients [26,40], they were usually lower than in the controls (matched for preoperative BMI or for BMI at the time of symptoms). This illustrates the dramatic improvement in insulin sensitivity elicited by weight loss, and the specific metabolic improvements induced by gastric bypass.

Table 3 presents the glucose and hormonal concentrations after a carbohydrate load in patients with true severe hypoglycaemic episodes with neuroglucopenic symptoms. Peak glucose concentrations were either similar [40] (after a 75-g glucose solution) or lower (after a meal test providing 40 g of maltodextrin) [26] in symptomatic compared with asymptomatic patients. The corresponding insulin concentrations were also similar [26,40]. Goldfine et al. [26] suggested that the peak insulin response was out of proportion to glucose concentration, as the insulin-to-glucose molar ratio was much higher in
symptomatic than in asymptomatic patients. Close inspection of Table 3, however, refutes this argument, as it is possible that the ratio was increased because the patients simply had lower glucose concentrations (they received the lowest of the carbohydrate loads in these experiments).

Indeed, there is evidence to suggest that beta-cell and insulin responses to a glucose challenge are impaired after gastric bypass. The early and transient glucose peaks, which are much higher than those in non-operated-on patients or in patients with a restrictive procedure (gastric banding or sleeve gastrectomy) [41], are only possible if the insulin response is inadequate, thus allowing the glucose concentration to increase. Kim et al. [42] demonstrated that the insulin response to a graded intravenous glucose challenge was lower in symptomatic patients than in various controls. This was also the case in the asymptomatic patients studied by Vidal et al. [32], and in patients following a bilipancreatic diversion [43].

Hypoglycaemia could also result from a difference in insulin sensitivity between symptomatic and asymptomatic patients, as suggested by Kim et al. [40] and Goldfine et al. [26].

In addition, plasma GLP-1 concentrations are increased after a meal [26], and even more so in hypoglycaemic patients, whereas gastric inhibitory polypeptide (GIP) is similar in symptomatic and asymptomatic patients [26]. There are no other incretin data comparing symptomatic and asymptomatic patients.

Taken altogether, these arguments may be interpreted in different ways. One interpretation is that hypoglycaemic episodes are secondary to hyperinsulinaemia that, in turn, results from beta-cell hyperplasia or hyperfunction (see below). Another is that the primary problem is beta-cell failure, which allows glucose concentrations to reach high values. Because of a deficiency in counterregulatory hormones, or because the secretion of insulin occurs too late after the glycaemic peak, some patients present with low glycaemic concentrations at the same time as too-high insulin concentrations. This latter observation has been made by several authors [9,25–27,40,42,44–46]. Although little is known of the counterregulatory hormones, glucagon concentrations have been reported to vary across studies [5,26,32], as has ghrelin [37,47,48], being either increased, decreased or unchanged after surgery.

### 6. Mild hypoglycaemia

Many post-bypass patients present with asymptomatic hypoglycaemic episodes. Hanaire et al. [29] showed that 50% of post-gastric-bypass patients present with CGMS readings of < 3.3 mmol/L, while Goldfine et al. [26] reported that 33% of asymptomatic patients have a post-meal glucose concentration of < 3.3 mmol/L. Kim et al. [40] also reported that 33% of the patients studied displayed values < 2.8 mmol/L after a 75-g glucose solution whether they were symptomatic or asymptomatic. Likewise, around 10% of the non-operated-on patients displayed similarly low values after a glucose challenge [40]. Scavini et al. [49] found that 3–4% of patients with gastric banding displayed asymptomatic hypoglycaemia after a 75-g glucose load.

Two remaining questions are why are so few patients symptomatic, when so many display low plasma glucose concentrations after a glucose load, and why do they sometimes not display the same symptoms as in real life when given a 75-g glucose load and on reaching values < 2.8 mmol/L [40]?

Some of these patients could present exactly like patients with the late dumping syndrome. It has also been shown that, in such patients, low glucose (< 2 mmol/L) [14] and high GLP-1 concentrations [16,17], but with no neuroglucopenic symptoms, may be observed. The dumping syndrome was described in its two phases for years, when gastric surgery for ulcer disease and cancer involved procedures similar to gastric bypass.

### 7. Pathological observations

The initial observations led to the concepts of beta-cell hyperplasia, beta-cell hyperfunction and nesidioblastosis [9,13,14,44,45]. There is no doubt that when pancreatectomy was performed, abnormal islet cells were found. Vella and Service [8] referred to an evaluation of 37 additional patients, with documented endogenous hyperinsulinaemic hypoglycaemia in the postprandial period, all of whom had previously undergone Roux-en-Y gastric-bypass surgery. Most of the resected specimens exhibited islet hypertrophy with nesidioblastosis, and some also had one or more functioning insulinomas. Some of the published cases were true nesidioblastosis with hypertrophy of islets, hypertrophy of beta cells within islets, islet cells “budding” from ducts, ductoinsular complexes and scattered...
complexes of endocrine cells within the pancreatic parenchyma [45].

There has been some debate over how to demonstrate islet hypertrophy and nuclear beta-cell hypertrophy [18,39,46]. Using similar pancreatic samples, Patti et al. [44] and Meier et al. [10] came to different conclusions, with the former suggesting that islet cells were truly enlarged compared with “normal” controls, while the latter suggested that islet cells were not hypertrophied compared with samples from obese patients.

Increased beta-cell nuclear size was, however, a consistent feature. Indeed, it is a surrogate marker of beta-cell function, raising the question of the origin of the hyperfunction. It may be that beta-cell hyperfunction is secondary to the insulin resistance that prevails in morbidly obese patients and which fails to wind down even when patients lose weight [10,26]. There is probably an increased insulin response that is out of proportion to insulin sensitivity [40], thereby predisposing patients to hypoglycaemia (see metabolic changes above). Another often-cited proposition is that beta-cell changes are secondary to increased GLP-1 concentrations, which are multiplied 5- to 10-fold after gastric bypass [42]. GLP-1 concentrations are also increased in patients with the dumping syndrome [16,17]. Given that GLP-1 promotes beta-cell hypertrophy in rodents and that it slows down apoptosis in humans, the concept of non-regulated GLP-1-induced beta-cell hyperfunction was proposed to explain hyperinsulinaemia and hypoglycaemic episodes [8]. However, it was recently shown that GLP-1 may not be responsible for islet-cell changes. Carpenter et al. [50] reported that long-term exposure of rodents or monkeys to a GLP-1 analogue at very high doses did not lead to pathological changes in islets. Also, in contrast to insulinoma, hyperinsulinaemic hypoglycaemia after gastric bypass is not accompanied by overexpression of GLP-1 receptors in pancreatic tissue samples [11]. This, therefore, suggests that the pathobiology of insulinoma and of post-gastric-bypass hypoglycaemia may be distinct [9,11,30]. Similarly, Rumilla et al. [12], on analyzing the largest series published so far, suggested that pancreatic samples display overexpression of IGF-2, IGF-1 receptor alpha and transforming growth-factor receptor beta 3. These findings suggest that the increased production of growth factors and growth-factor receptors may contribute to the development of neoplasia in adults with post-bypass hypoglycaemia.

8. Therapeutic options

None of the therapeutic options are supported by strong evidence-based arguments. All authors agree that dietary modifications should be attempted first. Kellogg et al. [25] found that a diet low in carbohydrates applied for a month improved symptoms in 83% of patients. More precisely, six out of 12 patients were dramatically improved, three were mildly improved and two were unchanged. It is, however, difficult to adhere to low-carbohydrate diets, and Kellogg et al. believed that the two failed patients had difficulty sticking to the diet. Dietary changes involve splitting the daily food intake into five or six small meals, avoiding high glycaemic-index (GI) carbohydrates and taking steps against preparations that increase GI (for example, toast instead of wholewheat bread). Also, meals should be taken in a quiet environment, with sufficient time allowed to chew the food properly.

A surgical option to reduce food intake was proposed by Z’Graggen et al. [14]. Given the fact that patients regained weight, ate larger portions, and had reduced satiety and increased hunger, they proposed a reduction of the size or banding of the gastric pouch. Although the report is of only a few cases, some features are interesting. Five of the nine patients had severe neuroglucopenic symptoms before the operation, whereas none of the nine had a recurrence of symptoms after 4–18 months of follow-up. Mortality was also low (0), especially in comparison to that with pancreatectomy (1–5%) [14].

 Undoing the gastric bypass has been tested without success [13,44]. This is intriguing, as one recent report of feeding a patient through a tube in the gastric remnant led to the disappearance of symptoms [52] and normalization of the metabolic features associated with gastric bypass, as similarly seen in diabetic patients [15].

There are also reports of pharmacological treatments, but without strong evidence that they work. In patients with postprandial hypoglycaemia attributed to non-insulinoma pancreaticogenous hypoglycaemic syndrome, Won et al. [18] gave diazoxide at various doses. None of the patients had had gastric bypass, although four of the 10 patients had undergone gastrectomy for ulcer disease. After 34–40 months, the patients’ symptoms were controlled, and their insulin and C-peptide responses to a meal test were decreased.

Mathavan et al. [45] used the strategy of starting treatment with verapamil and/or diazoxide before switching to octreotide. However, nine out of 15 patients were refractory to this treatment. Kellogg et al. [25] reported on two cases treated with acarbose, one of which saw symptom-relief. Hanaire et al. [29] and Moreira et al. [52] had two positive results with acarbose, one of which saw symptom-relief. Hanaire et al. [29] described the case of a woman who became free of symptoms after 20 months of treatment with nifedipine. Halperin et al. [54] tried glucagon, based on the hypothesis that it would increase hepatic glucose output. The patient did not improve, despite the expected insulin secretagogue action of glucagon.

Pancreatectomy has been an option for patients who are resistant to diet and/or medical treatment, with the calcium provocation test used for the localization of insulin production within the pancreas to guide conservative surgery [45]. It appears that the 80% pancreatectomy, recommended for idiopathic neoplasia, is not sufficient in many cases, thus leading to near-complete pancreatectomy [13,44,45] that, in turn, exposes patients to perioperative mortality and diabetes. In some cases, distal pancreatectomy has been sufficient, as seen in the case of Alvarez et al. [46] and in four cases from Z’Graggen et al. [14], with asymptomatic patients 4–18 months after surgery. In Mathavan et al.’s [45] series, nine patients underwent 80% pancreatectomy, and all reported marked relief of symptoms. However, two required near-complete pancreatectomy and, over
time, seven of the nine patients experienced symptoms again. In Rumilla et al.’s [12] series, eight out of 27 patients still had ongoing mild symptoms after pancreatectomy (the extent of which was not reported). Vella and Service [8], from the same team as Rumilla et al. [12], referred to the evaluation of 37 additional patients with documented endogenous hyperinsulinaemic hypoglycaemia in the postprandial period who had previously undergone Roux-en-Y gastric-bypass surgery. Because of the severity of their symptoms, 23 of these patients underwent gradient-guided pancreatic resection, and around 60% of their pancreatic tissue was removed. Twenty-one patients remained symptom-free.

9. Conclusion

There are true cases of severe neuroglycopenic hypoglycaemia after gastric bypass. The symptoms can be serious, as car accidents have been described. However, such cases are rare and should not be considered in the same light as the more frequently seen mild or asymptomatic hypoglycaemic episodes after similar surgery. Nevertheless, thorough exploration of these patients is warranted to demonstrate low glucose concentrations, which are often very low (mean: 2.3 mmol/L). An in-hospital prolonged fasting test is useful for ruling out insulinoma (rarely associated with postprandial hypoglycaemia), and to confirm that insulin concentrations are decreased. Calcium provocation angiography may also be considered.

A provocative meal challenge should be discussed, as not all patients present with symptoms and low plasma glucose values [26,40]. Furthermore, diabetes does not protect against post-gastric-bypass hypoglycaemia, as the prevalence was the same in previously diabetic and non-diabetic patients.

The first line of treatment is dietary, which is certainly effective in cases of the dumping syndrome and reactive hypoglycaemia. However, it may not be effective for the most severe cases.

The pathophysiology of post-bypass hypoglycaemia has not yet been fully elucidated. If hyperinsulinaemia results from beta-cell hyperplasia and hyperfunction, it appears logical to look for treatments that can slow the process to avoid pancreatectomy. Pancreatectomy remains a therapeutic option, albeit with the concern that it can put patients at increased risk of diabetes and persistent symptoms in some cases. If hyperinsulinaemia is an inadequate and delayed response to early and high glycaemic rises, then pancreatectomy should not be performed, and other means of controlling glucose homeostasis after meals need to be evaluated. Finally, the cross-fertilization of concepts and therapeutic options from the fields of diabetes and nutrition should be encouraged to propose new hypotheses and mechanisms, to ensure that the diagnosis is accurate and to choose the most effective treatments.

Funding

No funding for research or publication.

Disclosure of interest

The authors declare that they have no conflicts of interest concerning this article.

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