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Critical Analysis of Bariatric Procedures in Prader-Willi Syndrome

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Abstract

Prader-Willi syndrome (PWS) is a complex genetic disorder localized to chromosome 15 and is considered the most common genetic cause of the development of life-threatening obesity. Although some morbidities associated with PWS, including respiratory disturbance/hypoventilation, diabetes, and stroke, are commonly seen in obesity, others such as osteoporosis, growth hormone deficiency, and hypogonadism, and also altered pain threshold and inability to vomit, pose unique issues. Various bariatric procedures have been used to cause gastric stasis, decrease gastric volume, and induce malabsorption, with poor results in PWS patients in comparison with normal obese individuals.

Keywords

Prader-Willi syndrome; Bariatric procedures; Postoperative issues

Prader-Willi syndrome (PWS) is a complex genetic disorder localized to chromosome 15 and is considered the most common genetic cause of the development of life-threatening obesity. An estimated 350,000 to 400,000 people are affected by the condition, which presents with early hypotonia, feeding difficulties, and poor weight gain. During childhood, children manifest impaired satiety, growth failure secondary to growth hormone deficiency, and excessive weight gain, which can lead to morbid obesity if intake is not carefully monitored (1). Life expectancy beyond 50 to 60 years of age is unusual among individuals with PWS; excessive weight may contribute to mortality (2). Although some morbidities associated with PWS, including respiratory disturbance/hypoventilation, diabetes, and stroke, are commonly seen in obesity, others such as osteoporosis (3,4), growth hormone deficiency, hypogonadism, altered pain threshold, and inability to vomit pose unique issues. Various methods aside from strict dietary monitoring have been used unsuccessfully for weight control in PWS, prompting exploration of bariatric procedures to promote weight

loss. We chose to review the available published data on the safety and efficacy of bariatric procedures in PWS.

METHODS

A retrospective review was performed on published cases of 60 PWS patients (35 male, 15 female) who underwent bariatric surgery. Among these patients, 49 were identified through a MEDLINE (1974–2006) search using the key words “Prader-Willi syndrome” and “bariatric surgery” (5–23). The remaining 11 patients underwent bioenteric intragastric balloon placement for 6 months and were reported in abstract form at the 2006 National Prader-Willi Syndrome Association meeting in Buffalo, NY (24). Patient age, demographics, year of publication, body mass index (kg/m^2), preoperative medical conditions, preoperative laboratory data, type of bariatric procedure performed, and outcomes were listed. Percent weight loss was defined as the difference in preoperative and postoperative weight divided by the preoperative weight. Several of the reported series included a control group of obese patients without primary endocrine abnormalities. These patients were also incorporated in our analysis.

RESULTS

The mean age (SD) of the individuals with PWS at the time of bariatric procedure was 19.7 ± 6.4 years. Twenty-eight percent of patients had a deletion confirmed by genetic testing (fluorescence in situ hybridization), 5% had uniparental disomy confirmed by chromosome 15q microsatellite studies, and in 67% the diagnosis of PWS was based on consensus diagnostic criteria published by Holm et al (25). The mean preprocedural body mass index ($n = 42$) was $51.6 (\pm 10.1) \text{ kg}/\text{m}^2$. Preprocedural medical conditions were reported in 19 of 60 (31%) of individuals with PWS, including hypercholesterolemia (8/19, 42%), type 2 diabetes mellitus or hyperglycemia (6/19, 31.5%), hypertension (4/19, 21%), nonalcoholic fatty liver (3/19, 15.7%), and cardiac or respiratory insufficiency (3/19, 15.7%) (5,12,13,15,18,20,22).

The bariatric procedures performed are shown in Fig. 1. Among individuals with PWS, 54% underwent biliopancreatic diversion (BPD), 29% gastric bypass, 18% placement of a bioenteric intragastric balloon, 5.4% jejunioileal bypass, 3.6% gastropasty, 3.6% vertical banded gastropasty, 1.8% silicone band gastropasty, and 1.8% truncal vagotomy with division of the major nerve trunks slightly above the diaphragm. The 6-month average weight loss results ($n = 9$ PWS patients) were reported as 4.2% for PWS patients after gastric bypass or gastropasty ($n = 7$) and 7% in obese control individuals ($n = 16$), 14% weight loss for PWS patients after bioenteric intragastric balloon placement ($n = 9$) (weight was regained once the balloon was removed), 19% weight loss for PWS patients after BPD ($n = 1$), and 19.3% for PWS patients with jejunioileal bypass ($n = 1$) (6,13,16,24). The average 12-month weight loss results ($n = 15$ PWS patients) were 6.5% with gastric bypass ($n = 6$), 27.6% with BPD ($n = 5$), 40% with jejunioileal bypass ($n = 2$), and 24.2% with vagotomy ($n = 1$) (6,8,11,13,15,16,17). The 24-month follow-up data after bariatric surgery was available for 5 PWS patients. In comparison with preoperative weight, weight loss at 2 years ranged from 0% to 40% with BPD ($n = 3$) to 4% with gastropasty ($n = 1$) and 2%

weight gain after bariatric procedure were available for 11 PWS patients; the average weight loss results from gastric bypass were 2.4% (n = 9) and 3.5% gain above preoperative weight after vertical banded gastroplasty (n = 2). By contrast, obese control patients lost 10.3% of their preoperative weight 5 years after gastric bypass (n = 9) and 25% of their preoperative weight 5 years after vertical banded gastroplasty (n = 1) (7,19).

A variety of postoperative issues were reported among the PWS patients who underwent bariatric procedures. Among the 3 PWS patients who underwent jejunoileal bypass, there were serious sequelae in 2 of 3 patients (1 death, 1 with an early wound infection followed by deep vein thrombosis with pulmonary embolus); the third patient had persistent fatty liver despite a 33-kg weight loss at 1 year (8,10,16). Among those with PWS who underwent gastric bypass, 2 patients required splenectomy at the time of bariatric surgery, 1 had a postoperative wound infection, and 63% of patients had poor response in weight after the procedure. One PWS patient died 50 months after gastric bypass as a result of congestive heart failure attributed to weight regain. Subsequently, 47% of PWS patients required surgical revision after gastric bypass (6,7,9). For gastroplasty, the majority of PWS patients experienced initial weight loss, then regained weight, including 1 patient who did not lose weight and died 3 years postoperatively of influenza. Another PWS patient had progressive weight gain after gastroplasty and a return of impaired glucose tolerance with snacking (found on barium swallow to have pouch dilatation) (18,19). The only reported PWS patient who underwent laparoscopic silicone gastric banding died 45 days postoperatively, which was attributed to GI bleeding (21). Among the 11 PWS patients who underwent bioenteric balloon placement, complications were reported in 5 individuals (45%) including death from gastric perforation 22 days after balloon placement (1), suspected gastric perforation (abdominal pain and vomiting) 25 days after balloon placement (1), acute gastric dilation after Gatorade ingestion (1), and abdominal pain with diarrhea (2) (24). The rate of gastric dilation and perforation among the PWS patients (27%) is far greater than the reported experience of gastric perforation and dilation among a series of 2515 non-PWS patients (0.278%) (26). After BPD, nearly half of the PWS patients experienced initial weight loss followed by regain within 2 to 5 years after the procedure. Complications reported after BPD included diarrhea attributed to bile acids, bone demineralization/severe osteopenia, nutritional anemia (iron, B₁₂, folate), and hypoalbuminemia/protein malnutrition (15,17,20). In the series of BPD in PWS patients reported by Marinari et al (22), 2 patients died 6 years and 9 years postoperatively; 1 of the 2 patients had regained weight after BPD and died of respiratory failure exacerbated by obesity.

DISCUSSION

Prader-Willi syndrome has been classified as the most common genetic cause of the development of life-threatening obesity resulting from a defect in satiety, with onset during early childhood. Abnormalities in the feedback from gut peptides, including ghrelin, may contribute to the satiety defect; autonomic dysfunction may also play a role in impaired satiety (27,28). Medical problems among obese individuals with PWS present unique challenges despite similarities to weight-related medical issues among morbidly obese individuals without PWS. Individuals with PWS experience weight-related morbidities such as respiratory disturbance/hypoventilation and stroke that are similar to those in obese

individuals without PWS. Unlike other obese populations, those with PWS have a higher degree of insulin sensitivity, along with unique medical issues such as an underlying growth hormone deficiency, hyperlipidemia, osteoporosis (pathologic fractures), a decreased ability to vomit (risking toxicity from emetics), abnormal pain threshold, and potential for the development of gastric dilation/necrosis (29). Although 42 (69%) of patients had no reported preprocedural medical conditions, it cannot be assumed that these patients had no complications associated with PWS. Moreover, it is not entirely clear whether the availability of these data would have changed the overall conclusions reached on the value of bariatric surgery in this unique genetic disorder.

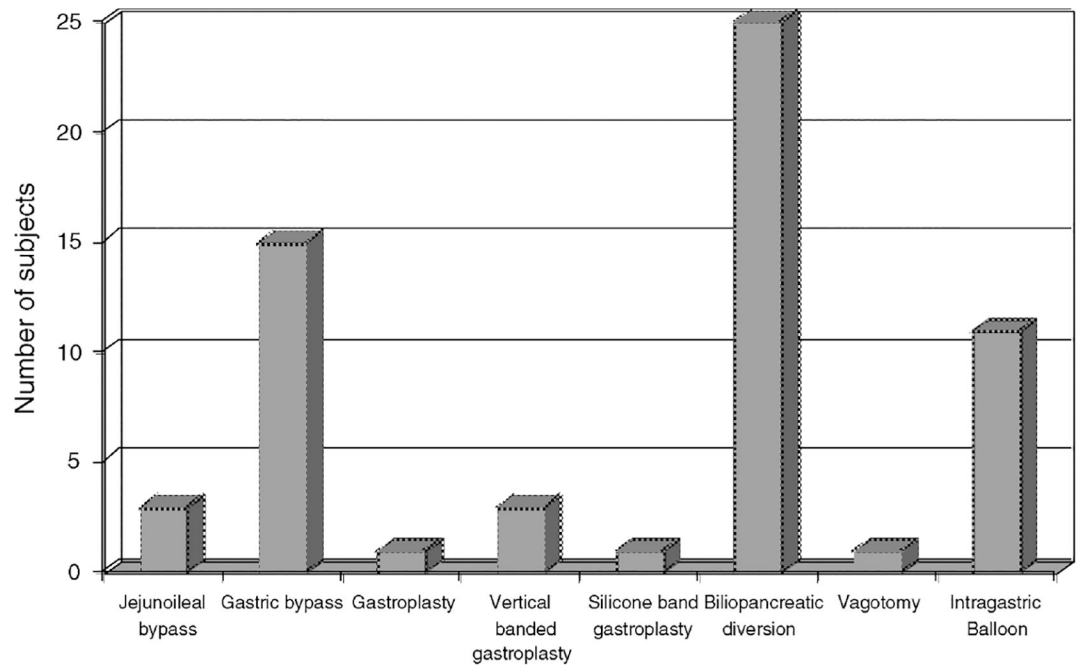
A variety of methods aside from energy restriction (with supplementation of vitamins and minerals), treatment of growth hormone (to improve linear growth and improve lean body mass), and strict supervision of access to food within the environment have been used to control the development of obesity, with disappointing results.

In summary, a variety of bariatric techniques have been implemented, including truncal vagotomy without pyloroplasty to create gastric stasis and create satiety, gastroplasty and endoscopic balloon placement to decrease gastric volume, and malabsorptive procedures ranging from gastric bypass to BPD. Although small case series have reported short-term success with bariatric surgery, the results of this retrospective review suggest that there is little justification for subjecting PWS patients to the potential risks of surgical interventions. Rather than the limited weight reduction observed in PWS patients after bariatric surgery, we would support an alternative approach, including the use of supervised reduced-energy diets with vitamin/mineral supplementation, restricted access to food, and a daily exercise regimen.

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**FIG. 1.**

Types of bariatric procedures performed on individuals with Prader-Willi syndrome.