

Sleeve Gastrectomy for Childhood Morbid Obesity: Why Not?

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In this issue, Dan and colleagues describe use of vertical sleeve gastrectomy (VSG) for treatment of a 6-year-old girl with morbid obesity, Blount's disease, and social stigmatization. The report suggests that caregivers lacked understanding of basic energy balance concepts and were complacent with cultural norms encouraging overfeeding. Once the child's problems came to medical attention, nutritional education and dietary intervention were attempted but were reportedly unsuccessful. According to these authors, the healthcare team was satisfied that all available treatment options had been attempted and failed, and surgery was deemed the only option and was medically necessary.

This commentary is written as a cautionary note. While it is true that desperate situations often require extraordinary interventions, there are nonetheless numerous concerns about this report. On a factual level, the case report itself provides too little evidence that adequate baseline clinical investigations were performed to evaluate factors contributing to severe obesity at such a young age. A complete work-up may have revealed a syndromic form of early onset severe obesity that may have changed clinical decision-making. For instance, if there was excessive insulin secretion in response to a provocative challenge, some would have considered a trial of octreotide or even truncal vagotomy initially. The report does indicate a failed short preoperative trial of leptin therapy, although there is no information about genotyping performed or details of

the treatment trial. Finally, there are minimal postoperative outcome data presented and very short term follow-up.

Perhaps more importantly, the report could be interpreted as justifying the use of VSG in young children. This could lead to tragic consequences. Aside from demonstrating what *can be done* for morbid obesity at a very young age, the report fails to present a balanced discussion of how VSG may adversely affect growing children. A critical analysis of why developmental (age) limits are necessary when considering irreversible treatment options (like VSG) is warranted. Throughout this article, the word "children" is used to indicate that stage of development prior to adolescence or puberty.

There is enthusiasm in the surgical community for VSG, a procedure which involves no foreign body, needs no adjustments, and likely avoids malabsorption of many micronutrients. The enthusiasm is in part justified by early clinical trial results in adults. The studies have not yet elucidated possible long-term nutritional risks of the procedure however. There is also no evidence available as yet to estimate safety, effectiveness, or durability in growing children; on the contrary, there is good reason to believe VSG may be contraindicated.

So what are some potential problems with VSG in children? Surgeons often intervene surgically for conditions that threaten the life and health of a young child, but very few traditional pediatric operations *depend on the motivated volitional participation of a patient* for "success." In contrast, successful and safe bariatric surgery requires active participation and understanding and consent of both patient and any relevant caregivers. While *adolescents* are increasingly seeking bariatric surgery for justifiable health reasons, most *children* are not fully capable of participating in weight loss surgery treatment decisions, nor comprehending and adhering to the critically important dietary and

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activity plan needed postoperatively for life-long success [1]. Most children lack decisional capacity to participate in decisions about complex, elective, and irreversible surgical procedures. On a pragmatic level, children do not purchase, prepare, or serve their own food and are dependent on caregivers' knowledge and ability to provide access and support for healthy behaviors and physical activity. Therefore, it is entirely appropriate to withhold bariatric surgical treatment in cases where parents are not "savvy to basic dietary principles" until the patient and family have demonstrated an ability to adhere to medical and nutritional recommendations.

There are physiologically relevant concerns about VSG in a skeletally immature child. We know that people who have undergone subtotal gastrectomy can develop iron and vitamin B12 deficiency related to reduced acid and intrinsic factor production, respectively. Thus, while VSG is not as aggressive as subtotal gastrectomy, anemia, neurologic, and neurocognitive sequelae of iron and vitamin B12 deficiency could result long term in the absence of life-long vitamin supplementation. We know very little if anything about consequences of these deficiencies starting at age six. In the absence of some evidence of safety derived from studies of more mature individuals, it is not possible to justify this intervention in children.

Whereas gastric physiologists have for decades known that the glandular stomach has functions that go well beyond initiation of digestion and micronutrient absorption, it is only in the last few years that we have begun to learn about the central importance of ghrelin, a small peptide hormone produced predominantly by endocrine cells of the oxyntic mucosa of the stomach. Removal or bypass of the acid-producing portion of the stomach profoundly decreases circulating ghrelin concentrations in rodents and humans [2, 3]. Like other hormones, ghrelin has a diurnal rhythm, likely plays a major role in the neuroendocrine and metabolic response to changes in nutritional status, and developmentally, acts as a major anabolic hormone. Ghrelin has a strong growth hormone (GH)-releasing action on somatotroph cells within the adenohypophysis portion of the pituitary gland [4]. When administered exogenously, the most significant response to ghrelin is pituitary GH release [5]. Gastrectomized rodents demonstrate weight loss (lean and fat mass), an observation that can be reversed with exogenous ghrelin replacement [6]. All of these observations suggest an important role for ghrelin in somatic growth that is almost certainly relevant to growing children.

Furthermore, ghrelin has manifold other effects within the endocrine system, as it is also associated with changes in appetite, prolactin, adrenocorticotropin hormone, aldosterone, and cortisol production. So one critical question that emerges is whether the endocrine system of a developing child, that is dependent upon normal production

of GH and numerous other hormones, has the capacity to adapt to a significant and chronic reduction in ghrelin levels following VSG. Do we know the developmental importance of early interruption of components of the gut–hypothalamic–pituitary axis? The answer to this question is unknown at present and unknowns raise considerable doubt as to the appropriateness of elective VSG in childhood.

Finally, a 6-year-old status-post VSG could be at significant risk of developing metabolic bone disease. The endocrine mechanism is likely complex and may involve variable calcium and/or vitamin D intake, and absorption. Indeed, recent data suggest that ghrelin deficiency may be related in some fashion to post-gastrectomy osteomalacia. Ghrelin potentially stimulates osteoblasts in vitro which provides a link to a role of ghrelin in bone formation [7]. Serum ghrelin concentration also strongly predicts bone mineral density in normal adolescent girls [8] and obese children [9], suggesting an important role for this hormone in normal acquisition of bone mineralization in childhood.

So if we understand that VSG potentially reduces ghrelin availability, and appropriate ghrelin production is needed for proper skeletal development and mineralization, then this evidence suggests that VSG in childhood represents a greater long-term risk for osteomalacia than other modern weight loss procedures. Perhaps more importantly, other non-human data demonstrate that gastrectomy-induced reduction in bone mass is not salvaged with ghrelin replacement [6]. These findings would further argue for avoiding VSG in a growing child.

Treatment decisions for pediatric obesity are never easy. However, particularly for children, we must not lose sight of the fact that treatment paradigms should be developmentally appropriate, and perhaps staged, beginning with conservative, safer, and potentially reversible options. Most children do not exhibit severe weight-related comorbidities that are associated with significant mortality and morbidity in the short term. For the vast majority of morbidly obese children therefore, the risk: benefit ratio of resectional weight loss surgery is extremely difficult to assess. Can we be confident that the profound weight loss seen following VSG outweighs the long-term risk of iatrogenic endocrine injury, especially when the obesity-related health risks for a child are not often forcing a surgical intervention?

The role of VSG in the bariatric surgery armamentarium is being defined. There is justified enthusiasm. Almost certainly it has a role in the treatment of morbid obesity, and compared to other procedures, it likely has more advantages than disadvantages for appropriately selected patients. But defining the optimal or safe age for use of this operation requires more rigorous study. Irreversible weight loss surgery in a growing child who cannot conceptualize nor understand the life-long consequences of surgery is

179 hazardous. This position is particularly relevant to entero-
 180 endocrine surgery, where significant knowledge gaps are
 181 present and where long-term consequences are as yet
 182 poorly understood. With time and more research, a better
 183 understanding of the role of this and other operations in the
 184 management of pediatric obesity will be possible.

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