

Gastrointestinal complications of gastrocystoplasty

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Abstract

The cases are reported of five children with chronic renal failure who underwent gastrocystoplasty for a variety of urological disorders. Gastrocystoplasty comprises the transplantation of a vascularised segment of stomach to the bladder to form an augmented neobladder. The patients had gastrointestinal complications after the operation, including considerable weight loss in all five patients, accompanied by marked failure to thrive in four of the five patients, and food aversion, feeding intolerance, dumping syndrome, delayed gastric emptying, and oesophagitis in two patients. Three of the five patients developed severe abdominal pain and haemorrhagic cystitis secondary to gastric acid secretion in the neobladder from the transplanted gastric pedicle. Nutritional and pharmacological interventions were used to manage the gastrointestinal problems. Explanations are offered for the pathophysiology of the observed complications of gastrocystoplasty. It is believed that the use of this procedure in infants and children, particularly those with chronic renal failure and uraemia, warrants caution until successful long term follow up and experience with this procedure have been reported.

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Gastrocystoplasty is a technique that uses a vascularised segment of the stomach to replace or augment the urinary bladder. The more common use of ileal, caecal, jejunal, and colonic segments for this purpose has been well described.^{1,2} Two major series have been reported for the use of gastrocystoplasty in children.^{3,4} Bladder augmentation is most often used after cystectomy in adults who have tuberculosis of the bladder or bladder carcinoma,¹ and in children who have urodynamic dysfunction (such as neurogenic bladder or bladder outlet obstruction).^{1,5-7} The most common urodynamic disorder in children that requires bladder augmentation is a trabeculated, low compliance bladder, which often occurs in boys with posterior urethral valves and chronic vesicoureteral reflex.⁸

Owing to the potential metabolic disturbances⁹ and nutritional consequences of using bowel segments,¹⁰ the use of stomach segments for bladder augmentation has been suggested. Although this technique has been studied in two types of animal model,¹¹ the complications of this operation in children and adults have not been described. This paper describes the gastro-

intestinal complications after gastrocystoplasty in five children and addresses the management of these patients.

Case reports

Gastrocystoplasty, as a form of bladder augmentation and an alternative to more conventional bladder augmentation techniques, was performed on five children with different urological dysfunctions at The Hospital for Sick Children, Toronto, Ontario, from 1987 to 1991. This operation comprised 5% of the total of 90 bladder augmentations performed at our institution during this period. These five children (three boys, two girls) ranged in age from 20 to 84 months. All five children had chronic renal impairment, and two were receiving haemodialysis at the time of the operation. The patients reported no underlying gastrointestinal or nutritional symptoms before gastrocystoplasty. All five patients had failure to thrive four to six months after gastrocystoplasty.

PATIENT 1

A 10 month old girl with urogenital sinus anomaly, cloacal extrophy, dysplastic kidneys, and a small bladder, which led to her initial bladder augmentation, a gastrocystoplasty, subsequently developed intermittent acidosis and alkalosis, and continued to have a low compliance, low volume bladder necessitating a second bladder augmentation, this time an ileocystoplasty. Nissen fundoplication was also performed during the ileocystoplasty because she developed refractory gastro-oesophageal reflux after gastrocystoplasty. Four months after the operation she developed cyclic vomiting, dumping syndrome, and food aversion. Investigations included an upper gastrointestinal series, a technetium-99 gastric emptying scan, a feeding study with fluoroscopy, preprandial and postprandial blood glucose monitoring, and upper endoscopy with biopsy sampling. Table 1 lists the findings and therapeutic interventions.¹² After treatment, her dumping syndrome and food aversion resolved, and the patient showed appropriate weight gain.

PATIENT 2

A 54 month old boy with a small non-compliant bladder, who was receiving haemodialysis for renal failure secondary to posterior urethral valves, became anephric at gastrocystoplasty. After the operation he had severe abdominal pain, dysuria, haematuria, and hyperchloraemic

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Table 1 Renal function, weight before and after surgery, and findings and treatment after gastrocystoplasty

Data	Patient 1	Patient 2	Patient 3	Patient 4	Patient 5
Glomerular filtration rate (ml/min/1.73 m ²)*	35	<10 (pre-nephrectomy)	<10	17	45
Weight (kg) before/after† surgery	7.9/7.4	12.6/11.6	18.0/17.0	15.5/14.7	17.8/16.0
Findings	Rapid gastric emptying, postprandial hyper/hypoglycaemia, endoscopy showed short straight stomach and antrum absent, normal biopsy samples	Haemorrhagic cystitis acidic intrabladder pH	Normal to rapid gastric emptying, small stomach, narrow deformed antrum, mild gastritis, severe oesophagitis	Haemorrhagic cystitis, acidic intrabladder pH	Haemorrhagic cystitis, acidic urine pH
Treatment	Small frequent feedings by mouth, addition of cornstarch and medium chain triglyceride oil, continuous nasogastric overnight feeds, daytime nasogastric bolus feeds	Bladder irrigation with bicarbonate, ranitidine, omeprazole	Short term total parenteral nutrition, cisapride and ranitidine	Bladder irrigation with bicarbonate, ranitidine	Omeprazole

*Approximate glomerular filtration rate calculated with the Schwartz method; values given are for before the gastrocystoplasty (reference normal value at this institution >100 ml/min/1.73 m²).¹³

†Four to six months after gastrocystoplasty.

alkalosis. Investigations included cystoscopy, and intragastric and intrabladder pH measurements. His suprapubic pain was consistently associated with a bladder pH of less than 2, and the resolution of symptoms was associated with an increase in bladder pH (table 2). He initially received ranitidine and intrabladder bicarbonate irrigation, but the pH decreased two hours after bicarbonate irrigation and his symptoms resumed (tables 1 and 2). Sucralfate bladder irrigation was not successful because of intrabladder concretions. Treatment with omeprazole gave a resolution of symptoms, maintenance of normal intrabladder pH, and an increase in intragastric pH (table 2), with an increase of gastrin in serum samples to 3105 ng/l (reference range 0–75 ng/l). He has gained weight appropriately, but has required maintenance treatment with omeprazole for symptomatic relief despite renal transplantation and a glomerular filtration rate of 74 ml/min/1.73 m².

PATIENT 3

A 62 month old boy with a small non-compliant bladder, who was receiving haemodialysis for renal failure secondary to posterior urethral valves, underwent an unsuccessful gastrocystoplasty and subsequent ileocystoplasty. He subsequently developed food aversion, nausea, vomiting, and early satiety, in addition to hypoalbuminaemia (albumin concentration 24 g/l) without significant proteinuria. Investigations included upper gastrointestinal series and

upper endoscopy with biopsy sampling (table 1). The patient gained weight adequately after therapeutic intervention and had no additional gastrointestinal disorders at follow up.

PATIENT 4

Four months after gastrocystoplasty for a neurogenic bladder this 80 month old boy with Vater association developed abdominal pain and haematuria. Investigations included cystoscopy and intrabladder pH measurements (tables 1 and 2). This patient did not receive omeprazole as he found his symptoms tolerable with ranitidine and intrabladder bicarbonate irrigation (table 2). Six months after treatment had begun it was discontinued without recurrence of symptoms.

PATIENT 5

A 40 month old girl with urogenital sinus anomaly, high cloacal anomaly, anomalous ureteric implantation, small kidneys, and a small bladder, underwent gastrocystoplasty during genitourinary tract reconstruction. Three months after her gastrocystoplasty, she developed severe lower abdominal pain and bladder spasm, with symptoms intensifying 30 minutes to one hour postprandially. Neither cystoplasty nor other investigations were performed. Omeprazole (10 mg/day) successfully resolved her symptoms; her urine pH three days after treatment with omeprazole was 4.2. A pH

Table 2 Intrabladder and intragastric pH before and after treatment

pH	Patient 2 (anuric)	Patient 4
Intrabladder pH* before treatment	0.5–2.0 with GI and GU symptoms‡	1.0–1.5 with GI and GU symptoms‡
Intrabladder pH one hour after bladder irrigation with bicarbonate	5.5–8.0 without symptoms	6.0–7.5 without symptoms
Intrabladder pH two hours after bladder irrigation with bicarbonate	1.5–2.0 with GI and GU symptoms	2.5–3.0 with minimal symptoms
Intrabladder pH after treatment with omeprazole	5.0–7.0 without symptoms	Not applicable
Intragastric pH† after treatment with omeprazole	4.5–6.0	Not applicable

*Intrabladder pH obtained by catheterisation.

†Intragastric pH obtained by nasogastric tube.

‡GI=gastrointestinal; GU=genitourinary.

value for urine free of omeprazole has not been obtained. She is still being treated with omeprazole for symptomatic relief after two unsuccessful attempts to discontinue the drug.

Discussion

Although bladder augmentation with part of the gastrointestinal tract was described nearly 100 years ago,⁵ descriptions of the sequelae of this procedure, particularly gastrointestinal tract complications, have been difficult to find. Furthermore, bladder augmentation effects on nutritional status have only recently been reported showing no long term changes in vitamin B-12, carotene, and albumin concentrations.¹⁰ Metabolic complications after enterocystoplasty, such as chronic acidosis and rickets, have been described in children,¹⁴ and hyperchloraemic metabolic acidosis and diminished acid challenge capacity have been described in children and animal models of bladder augmentation.^{9 11}

Using a canine bladder augmentation model, Piser *et al* showed a net reabsorption of chloride, ammonia, phosphate, and sodium in animals who underwent colcystoplasty compared with those who underwent gastrocystoplasty.¹¹ Guan *et al*, using Long-Evans rat species, studied the short and long term effects of ileal, colonic, and gastric segment cystoplasties.¹⁵ They found that all voiding parameters, renal function, and biochemical profiles remained normal; levels of mucus production in the neobladder were higher in patients with gastrocystoplasty and colcystoplasty than in those with ileocystoplasty; and uroepithelialisation of the graft occurred, with native transitional epithelium extending over the junctional margin of the graft and covering the enteropatch mucosa as seen at necropsy.

The effect of chronic renal failure on bladder augmentation with stomach rather than sigmoid colon segments has been reviewed in the canine study by Kennedy *et al*.¹⁶ Their results indicate that gastrocystoplasty is a superior technique for the treatment of the azotaemic canine. These animals tolerated significantly greater acid loading and did not have the hyperchloraemic acidosis and weight loss of the other animals who underwent enterocystoplasty.

Reports of bladder augmentation in children, including gastrocystoplasty, have not addressed the gastrointestinal complications that seem physiologically inherent in this procedure. Adams *et al*, in the largest series to date, described 10 patients undergoing gastrocystoplasty who had no sequelae or complications.¹⁷ Follow up however, occurred only at one and three months, less than the average follow up interval (five months) for our series, at which time complications became apparent and clinically significant. In addition, Adams *et al* did not measure glomerular filtration rate, a more accurate indicator of renal function, making less clear the degree of renal compromise existing in their patients before and after gastrocystoplasty.¹⁷

Two studies of animal models reported that the use of stomach segments is a viable alterna-

tive and has functioned well, causing no gastrointestinal complications or genitourinary problems.^{15 16} Others, using a canine model, have shown that urine, or some component of urine, appears to suppress antral gastrin secretion as measured by serum gastrin concentrations and antral G cell hyperplasia.^{7 18} Lau *et al* showed that 4% aqueous peptone solution instilled into exteriorised antral pouches caused a significant increase in mean serum gastrin concentrations, compared with little or no change in mean serum gastrin with a 4% aqueous peptone solution in concentrated dog urine.¹⁸ Muraishi *et al*, however, reported a markedly decreased postprandial urine pH (2.4-4.2) in six dogs undergoing gastrocystoplasty at six months' follow up.¹⁹ More importantly they found that histological erosions developed in the bladder remnant in five dogs, and an ulcer in the native bladder remnant in the sixth dog. Tiffany *et al* reported severe hypergastrinaemia after the operation that led to the development of gastric ulcers in dogs undergoing gastrocystoplasty.²⁰ Renal function was not addressed in these studies.

Based on our findings for patients 2, 4, and 5 in our series, we believe that their native bladder epithelium lacked some form of cytoprotection against the normal acid production of the transplanted gastric segment. Cystoscopy in two of these patients showed haemorrhagic cystitis of the native bladder, but not of the transported gastric segment, probably the consequence of acidic urine.

Epidermal growth factor, or urogastrone, a normal constituent of canine and human urine, has been shown to inhibit gastric acid secretion after parenteral administration and is required for ongoing urinary tract epithelial growth. Horikoshi *et al* have shown that decreased production of epidermal growth factor and local differences of epidermal growth factor concentrations may be contributing factors to the development of dysplastic mesonephric tissue and also to normal urinary tract epithelialisation.²¹ It may be important to ensure quality urine production before gastrocystoplasty to provide adequate epithelialisation of the neosegment from the surrounding native bladder epithelium and thus protect it from acid secretion. Inadequate amounts, low concentrations, or inactivation of growth factors, or lack of some other factors may have contributed to the bladder pathology.^{22 23} Lack of cytoprotection may explain why patients 2 and 4, who had comparable glomerular filtration rates, developed similar cystoscopic and clinical findings, compared with patient 1, who had a significantly better glomerular filtration rate and who developed none of the observed complications. Patient 5, however, was symptomatic and had clinical evidence of haemorrhagic cystitis and an acid urine pH early in the course of her treatment, despite a glomerular filtration rate similar to that of patient 1. The difference in quality of urine production in patients 1 and 5, resulting in one patient developing symptoms and the other not, may eventually be explained when the cytoprotection factors in urine can be evaluated.

Neutralisation of acid urine provided relief in all patients. Bladder irrigation with bicarbonate alleviated symptoms, but its effect was short lived and the procedure time consuming. Patients 2 and 4 had inadequate relief of symptoms with H₂ blockers and required treatment with omeprazole. Omeprazole is the first of a new class of drugs that inhibit gastric secretion by altering the activity of hydrogen/potassium ATPase.^{24 25} This drug has been used in a variety of patients for whom hyperacidity is a major problem (for example, Zollinger-Ellison syndrome) and who have been refractory to more conventional H₂ blockers or antacids.²⁶

Studies have implicated the long term use of omeprazole in gastric carcinoma in rats, secondary hypergastrinaemia, and hyperplasia of enterochromaffin cells.²⁴ In one study of the long term effects of gastrocystoplasty in rats,²⁷ follow up 18 months after the operation showed prominent histopathological changes of the bladder in the gastrocystoplasty group, ranging from atrophy of glands in the gastric patch, to tumours of the mucosal surface. Patients who are at risk for development of cancer because of immunosuppression after renal transplant may develop dysplastic changes in the bladder epithelium from long term exposure to an acid environment. We therefore believe that any patient undergoing gastrocystoplasty should be monitored with regular cystoscopy. Furthermore, these patients may also require long term treatment with omeprazole, which may further enhance their risk of developing a malignancy.

Patients with chronic renal failure may be at greater risk for gastrointestinal complications from gastrocystoplasty. Uraemia and chronic renal failure have often been reported as causes of gastrointestinal symptoms such as nausea, vomiting, anorexia, and poor weight gain. These symptoms may be aggravated by gastric surgery.²⁸

Descriptions of the animal model of gastrocystoplasty report the surgical excision of only a small segment of stomach from the gastric antrum to form the augmented neobladder.³ Too small a gastric flap often results in inadequate bladder augmentation. Conversely, the larger the gastric segment the greater the risk for developing gastrointestinal complications.^{4 7 29} Therefore, patient size and age may be important factors in assessing suitability for this procedure.

Gastrectomy, which alters gastric motility and changes gastric compliance, probably resulted in the symptoms experienced by patients 1 and 3, namely, vomiting, dumping syndrome and food aversion,^{30 31} nausea and early satiety, and failure to thrive. The dumping syndrome of patient 1 was eventually alleviated by the addition of medium chain triglyceride oil and cornstarch to Peptamen (Carnation) delivered through a nasogastric tube to delay gastric emptying.¹³ The severe oesophagitis observed in patient 3 was probably avoided in patient 1 by the antireflux procedure (Nissen fundoplication) performed after the gastrocystoplasty. We are not, however, advocating this as a concurrent procedure in all patients undergoing

gastrocystoplasty as Nissen fundoplication may be accompanied by complications such as rapid gastric emptying and dumping syndrome.³⁰ The food aversion of patient 3 was probably due to severe oesophagitis.^{30 32} With conventional treatment (cisapride, ranitidine, and a high carbohydrate, low fat diet), we were able to alleviate his symptoms.

In summary, there are considerable gastrointestinal complications associated with gastrocystoplasty. As a result of the complications observed in all of our patients who have undergone gastrocystoplasty, we believe that the use of this procedure for bladder augmentation in infants and children, particularly those with chronic renal failure, warrants caution. Future research should focus on animals with previously induced chronic renal failure. Only after long term follow up and more extensive experience with gastrocystoplasty in children will we be able to evaluate the viability of gastrocystoplasty as an alternative to more conventional techniques for bladder augmentation.

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All Greek

Here's a fascinating fact for you. I bet you didn't know that Greek eggs contain eight or nine times as much docosahexaenoic acid (DHA) as standard American supermarket eggs (Artemis P Simopoulos and Norman Salem, Jr, *American Journal of Clinical Nutrition* 1992;55:411-4). But then, when the fatty acid has a name like that, they would, wouldn't they? And if the author's name had been Simopollochkov they'd probably have been Russian eggs.

Studies have shown that infant formulas are lacking in such long chain polyunsaturated fatty acids which are present in human milk. DHA may be an essential nutrient as there is evidence that babies who don't get enough of it have deficient functioning of the retinal rods. Eggs are used as a source of fatty acids for infant formulas but their content of DHA varies according to how the hens were fed. American supermarket eggs were found to have a low content, eggs from hens fed on flax or on fishmeal contained more, but free range (Greek) eggs contained most of all. Other studies have shown that in plants, eggs, fish, and meat the wild or free varieties have a greater content of certain fatty acids than the cultivated or restrained. So that's another one up for the Greens. Infant feeding is so complex it's a wonder that any of us grow up to have an ounce of sense or even grow up at all (see Archivist 1991:1290).

ARCHIVIST