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ORIGINAL PAPER

Combining gastric and ileal segments, does it overcome segment-related complications? An experimental study on rats

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Abstract Bladder augmentation has revolutionized the care of children with neurogenic bladder but it is associated with certain short- and long-term complications. Using the combination of gastric and ileal segments to balance effects of these segments might be a solution for complications. A total of 39 female Spraque-Dawley rats randomly divided into four groups: ileocystoplasty (11), gastrocystoplasty (9), ileogastrocystoplasty (11) and control (8). Serum/urine electrolytes and pH values, and serum creatinine levels and urine mucus concentration were measured. Kruskal–Wallis non-parametric variance analysis was performed to compare the groups and $p < 0.05$ was accepted as significant. Metabolic alkalosis with significantly lower urine pH was observed in gastrocystoplasty group. Gastroileal group showed similar results with the ileal group in all parameters. No stone formation was detected in the sham and gastric cystoplasty groups. Metaplastic and hyperplastic changes were observed in all segments surrounding urothelium. In conclusion, combination of gastric and ileal segments does not significantly reduce the rate of metabolic impairments, stone and mucus formation. Besides it is not associated with significant improvement in histological outcome since urine is still in contact with the gastrointestinal mucosa.

Keywords Augmentation · Bladder · Rat · Iliogastrocystoplasty · Gastrocystoplasty · Iliocystoplasty

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Introduction

Bladder augmentation has revolutionized the care of children with neurogenic bladder, but remains a major surgical undertaking. Generally, one should make every effort to prevent the need to perform augmentation cystoplasty. The choice of the segment to use usually depends on the assessment of the clinical situation, 'what is anatomically available' and 'what are the particular physiologic parameters of the patient'. In general, for a healthy patient with no metabolic problems or previous surgery, the choice of segment is probably not critical. Certain approaches such as using gastric segment for metabolic acidosis and previous multiple small bowel resections and using ileal segments for high urine volume and cloacal extrophy patients can be considered [1–4].

Consequences of augmentation are many and well documented in literature. Clearly, each type of segment has its own pros and cons. Neither ileal nor gastric segment is perfect tissue for augmentation and their use to treat the functionally and structurally compromised bladders is associated with several metabolic consequences and long-term complications. The rates and severity of these complications vary, although they have a profound impact on quality of life [5–7].

Although the most commonly used option for augmentation cystoplasty is ileal segment, it is associated with several limitations. These include hypercloremic metabolic acidosis, vitamin B_{12} deficiency, stone disease, mucus production and neoplasia [1, 8]. The down side of augmentation by using stomach segments is primarily related to the metabolic activity of the gastric mucosa. Fluid, potassium and chloride losses may develop, resulting in severe dehydratation and hypochloremic, hypokalemic metabolic alkalosis. Another potentially painfull complication of gastrocystoplasty is hematuria–dysuria syndrome [3, 6]. Demucosalization of the segments had been tried in order to prevent mucosa-related adverse metabolic consequences. However, mucosal regrowth has been reported [9]. Using the combination of gastric and ileal segments to balance resorption and excretion appears to be a simple answer. Although resection of two segments is required, we hypothesized that this can potentially minimize the long-term metabolic complications, stone formation and mucus production. Although the technique does not eliminate the presence of gastrointestinal mucosa in contact with urine, effect of composite grafts on histological changes is yet to be investigated.

Materials and methods

The study was performed with a certificate approved by the Animal Research Center Central Ethical Committe. Initially 46 rats were involved in the study. A total of 11 rats that died during the first week were replaced. All cytoplasty groups consisted of 12 rats and control group consisted of 10 rats. Survivors were followed for 6 months. One from ileal, three from gastric, one from gastoileal cytoplasty and two from control groups died within 2–5 weeks postoperatively. Therefore, totally 39 female Sprague–Dawley rats weighing between 135 and 210 g were included and were randomly distributed to the investigated groups: ileocystoplasty group 11 rats, gastrocystoplasty group 9 rats, Ileogastrocystoplasty 11 rats and control group 8 rats. Solid food was withheld the night before surgery. Following the intraperitoneal administration of ketamine (mixed with atropin and phenothiazine) for anesthaseia, operations were performed through a midline incision using an operating microscope with 3.2 times magnification. In all cystoplasty groups, bladders were opened in the sagittal plane. In ileocystoplasty group a 1.5-cm segment of ileum was isolated with its vascular pedicle intact and detubularized in its anti mesenteric border. The continuity of the bowel was reestablished by an end to end anastomosis with 7-0 polyglactin running suture.

For gastrocystoplasty group, a triangular section along the great curvature, consisting both anterior and posterior walls was isolated based on gastroepiploic vessels. Stomach was closed with 6-0 polypropylene suture. All augmentation segments were irrigated with saline before cystoplasty. The patches were anastomosed to the bladder with running7-0 polyglactin suture. The control group underwent laparotomy, bladders were opened and closed with the same suture material. The abdominal wall and skin were closed with absorbable suture. Postoperatively, rats were returned to cages separately and were unrestricted to water and standard rat chow. Rats were examined daily. Those that died during the first week of gestation were replaced. The survivors were followed for 6 months and those that died after 1 week were not replaced.

At the postoperative 30th, 90th and 180th days, each rat were kept in metabolic cages (Columbus Instruments self standing rat metabolic cage) for 24 h. Serum/urine electrolytes, pH values and serum creatinine levels were measured. Urine mucus concentration was measured by a simple technique previously described by George et al. [10] and the results were expressed as μg/ml.

After collecting the urine samples at 6th month for 24 h, animals were sacrificed and the bladders were extracted and fixed in 10% buffered formalin. In all groups, representative 4-μ sections were examined with hematoxylin and eosin and periodic acid-Schiff staining. Histological examinations were performed by uropathologists with special emphasis on changes and location (graft or bladder site).

Statistical analysis was performed by SPSS version 15.0. Kruskal–Wallis non-parametric variance analysis was performed to compare the groups and $p < 0.05$ was accepted as significant.

Results

Metabolic alkalosis with significantly lower urine pH were observed in gastrocytoplasty group. Gastroileal group showed similar results with the ileal group in all parameters. These two groups were found to have significantly lower serum pH and higher urine pH values compared to the control group ($p < 0.05$). Mucus production was significantly higher in groups with ileal patches compared to control and gastrocystoplasty groups.

Mean and standart deviation values of the groups for serum pH, urine pH, serum creatinin, serum chloride and mucus production parameters are given in Table 1. The comparison of the parameters is given in Fig. 1. Multifactorial variance analysis is performed to compare the four groups in between. Comparison of control, gastric and ileal cystoplasty groups with gastroileal cystoplasty group for statistical significance is summarized in Table 2. Gastrocystoplasty group was found to show statistically significant difference from the iliocystoplaty group in all parameters ($p < 0.05$). When compared with the control group, significant difference was observed in all parameters except the serum creatin levels ($p > 0.05$). Iliocystoplasty group is found to show significant difference in all parameters compared with the control group ($p < 0.05$).

At the end of 6 months, all rats were evaluated for stone formation. No stone formation was detected in the control and gastric cytoplasty groups. Five of 11(45%) and 6 of 11(54%) in the ileal and iliogastrocytoplasty groups,

Table 1 Mean and standard deviation values of the groups for serum pH, urine pH, serum creatinin, serum chloride and mucus production parameters

	Gastroileal		Gastric		Ileal		Control	
	Mean	SD	Mean	SD	Mean	SD	Mean	SD
Serum pH								
Month 1	6.65	0.25	8.14	0.40	6.38	0.33	7.26	0.13
Month 3	6.85	0.33	8.10	0.34	6.57	0.47	7.27	0.12
Month 6	6.77	0.30	7.76	0.46	6.43	0.25	7.18	0.12
Urine pH								
Month 1	7.10	0.24	3.86	0.80	7.29	0.57	7.23	0.43
Month 3	6.97	0.42	4.08	0.70	7.26	0.31	7.02	0.55
Month 6	6.90	0.36	4.12	1.08	7.40	0.36	7.11	0.51
Serum creatinin								
Month 1	1.40	0.43	0.91	0.32	1.12	0.27	1.0	0.20
Month 3	1.49	0.39	0.95	0.20	1.52	0.43	0.95	0.33
Month 6	1.48	0.49	1.05	0.13	1.58	0.36	1.10	0.30
Serum chloride								
Month 1	97.6	9.65	78.2	12.8	109.5	11.1	99.0	7.78
Month 3	93.7	12.2	69.5	5.07	116.1	11.1	113.8	10.5
Month 6	101.1	8.3	72.0	7.71	111.4	12.4	104.1	4.70
Mucus production								
Month 1	691	63.6	177	90.3	588	165.1	N/M	N/M
Month 3	682	233.2	178	106.4	617	177.3	N/M	N/M
Month 6	604	243.2	159	54.3	654	11.3	N/M	N/M

N/M not measured

respectively, developed stones. All stones were analyzed and recorded as magnesium ammonium phosphate (struvite) stones (Fig. 2).

Vital gastrointestinal mucosa (an intestinal patch that did not decrease in size with a non-necrotic pink intestinal mucosa macroscopically) was found in all augmented bladders. Histopathological examination demonstrated urothelialization of the graft with native transitional epithelium extending over the junctional line. Metaplastic and hyperplastic changes were observed in all segments surrounding urothelium (Fig. 3).

Discussion

Use of non-urinary tissue to function as a urine reservoir has been a good way of treatment of patients with impaired bladder function or capacity. In this study, effects of gastric, ileal and gastroileal urinary reservoirs on metabolic outcomes were investigated and compared.

All intestinal segments used to date have advantages and disadvantages in surgical and metabolic aspects depending on anatomical and physiological properties of the segment used. Ileal segments are generally surgically available and easy to use which also mediate reservoirs with sufficient capaciy and acceptable mucus production. On the other hand, the mesentery can be relatively short that results in surgical difficulty in bringing the segment to the pelvis. Metabolic consequences releated to reabsorbtion of ions result in metabolic acidosis. Vitamin B12 and folate deficiency are important disadvantages together with risks of infection and stone formation [1, 2].

Gastric augmentation has the advantages of production of more soluble mucus and causing less infection [4, 11]. But it results in hypochloremic, hypokalemic metabolic alkalosis, which is the mainstay of its use in patients with renal function impairment. Although this complication is rarely signficant, it can be marked in cases of dehydratation. Another disadvantage of use of gastric segments is the difficulty of harvesting that is associated with larger abdominal incisions [5, 12].

Balanced augmentation using stomach and small bowel had been proposed by some authors with the idea of possible balancing of ion loss and ion resorption that can prohibit metabolic impairment. Lockhart et al. [11] reported alternative gastroileal pouch in patients who are not suitable for ileal urinary reservoirs. Although their study was limited due to the low number of patients and

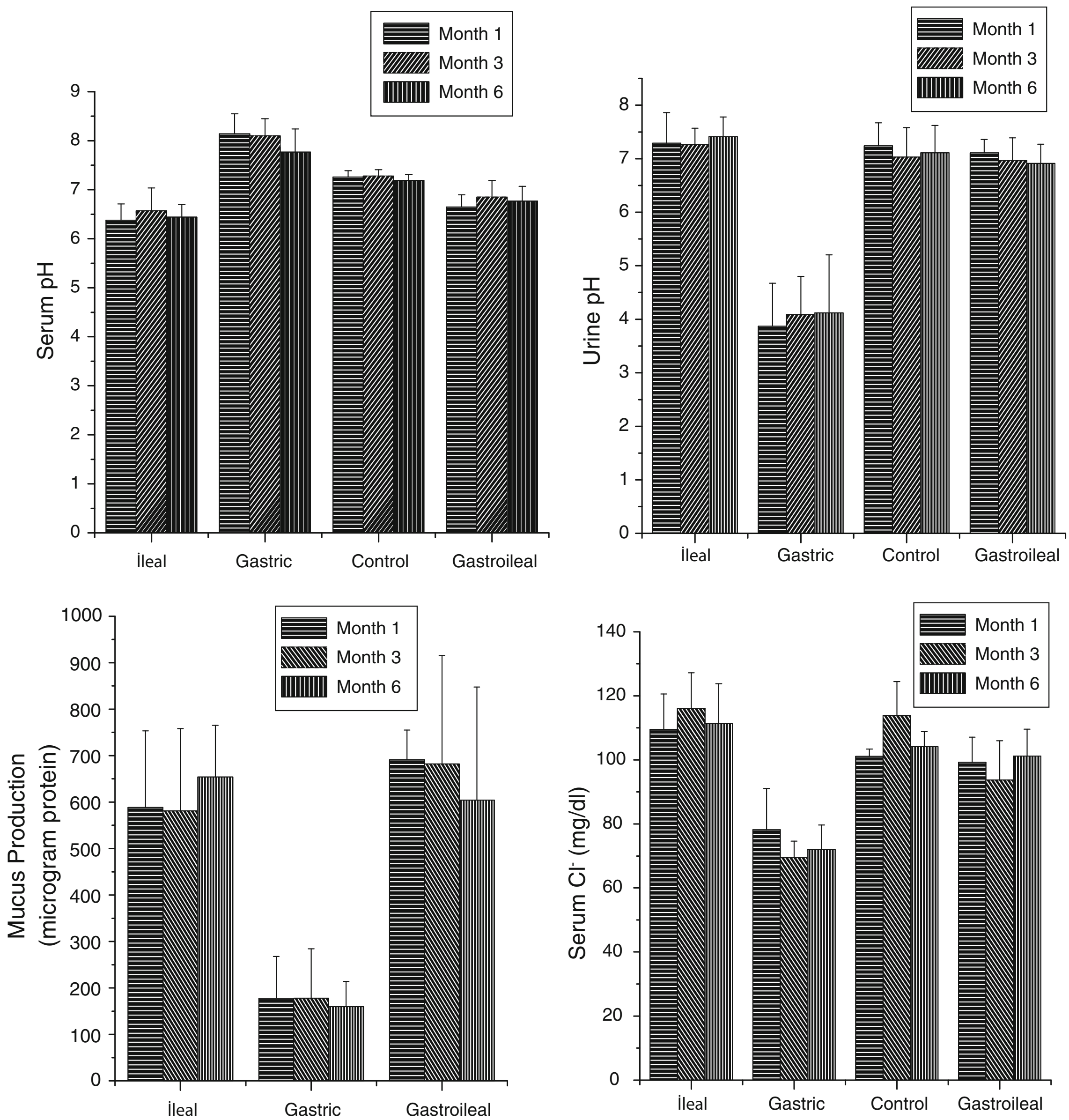

Fig. 1 Comparison of the groups for serum pH, urine pH, serum chloride and mucus production parameters

short-term follow-up period, they have suggested gastroileal reservoirs as an alternative solution. Mclaughlin et al. [12] found favorable results with the combination of gastric and ileal segments. They have reported transient hyponatremia only in one of the seven patients. Consequently in some of the challenging patients, the combined use of stomach and ileum was defined as a safe and effective alternative.

In a long-term prospective study, Austin et al. [13] evaluated the metabolic impact of gastrointestinal composite reservoirs. The serum bicarbonate and pH levels were significantly higher in the postoperative measurements but urine pH levels did not differ compared to preoperative measurements. The authors concluded that use of composite resevoirs have long-term metabolic advantage over other intestinal reservoirs and may be beneficial in patients compromised by either pre-existing metabolic acidosis or the short bowel syndrome. They also evaluated the role of gastrointestinal composite urinary reservoir's metabolic impact in myelomeningocele and extrophy patients [14] and confirmed the beneficial role of composite reservoirs in patients with pre-existing metabolic acidosis and short bowel syndrome. In a multi-institutional study, the safety and effectiveness of gastrointestinal composite reservoirs are intensified and authors emphasized this option only for patients who are not suitable for standard intestinal reservoirs [15]. In a recent study, DeFoor et al. [16] reported the long-term results of composite reservoirs.

Table 2 Comparison of control, gastric and ileal cystoplasty groups with gastroileal cystoplasty group

	Gastric S. Sign.	Ileal S. Sign.	Control S. Sign.
Serum pH			
Month 1	+	+	+
Month 3	+	−	+
Month 6	+	+	+
Urine pH			
Month 1	+	−	−
Month 3	+	−	−
Month 6	+	+	−
Serum creatinin			
Month 1	+	−	+
Month 3	+	−	+
Month 6	+	−	+
Serum chloride			
Month 1	+	−	−
Month 3	+	+	−
Month 6	+	−	−
Mucus production			
Month 1	+	−	N/M
Month 3	+	−	N/M
Month 6	+	−	N/M

S. Sign statistically significant, *N/M* not measured

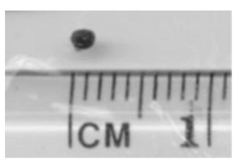

Fig. 2 Magnesium ammonium phosphate (struvite) stone

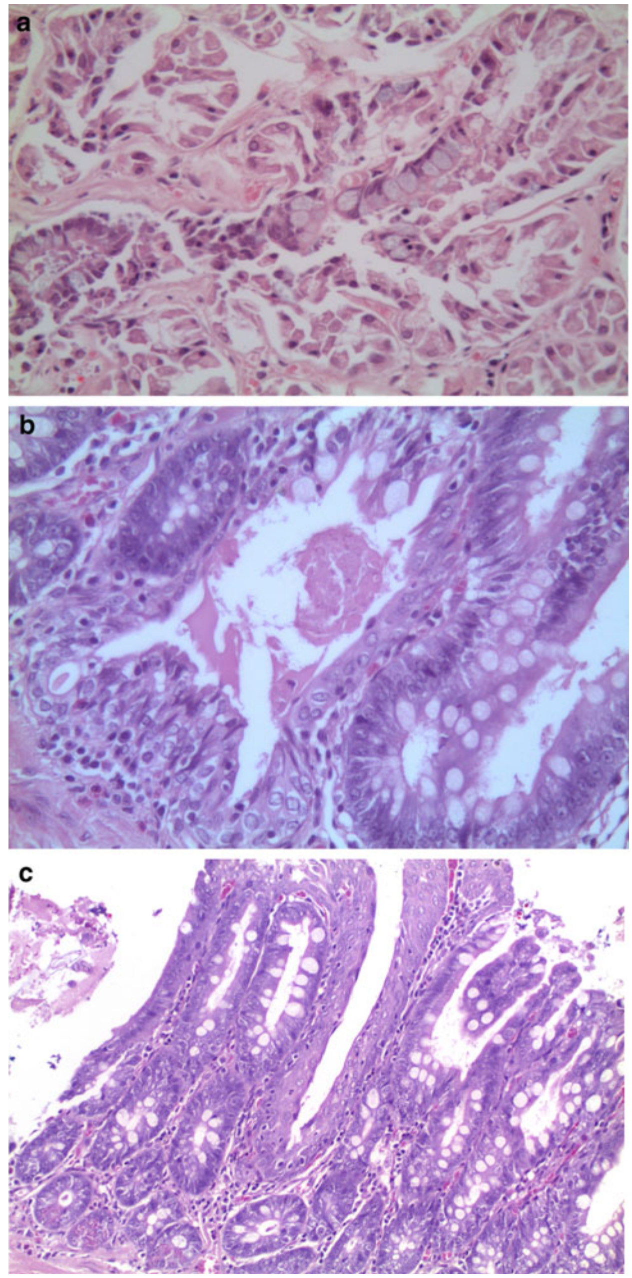

Fig. 3 **a** Focal intestinal metaplasia of gastric mucosa (HE ×40). **b** Transitional metaplasia on ileal mucosa (HE ×20). **c** Squamous metaplasia on ileal mucosa (HE ×20)

In this series of 26 patients, 8 patients developed reservoir stones, 8 patients had febrile urinary tract infection and 6 patients had metabolic acidosis in long-term follow-up.

The present study considers and compares the metabolic outcomes of gastric, ileal and composite segments. Similar to the aforementioned studies, the gastroileal segments expressed more close values to the control group than the ileal reservoirs but still there is significant difference in serum pH, urine pH and serum creatinin levels. These findings demonstrate that the gastroileal patches have tendency to behave like ileal segments rather than gastric segments and hypothetically beneficial metabolic effect of the gastric mucosa does not seem to fulfill the expectations.

The occurence of bladder stone varies between 10 and 52% of the augmentation cystoplasty cases [8, 17]. Gastric segments exhibit lower incidence of bladder stones [7, 17]. The possible reasons for this may be lower bacteriuria incidence and less mucus formation. Khoury et al. [18] demonstrated that the fluid mucus centers of these stones in a gastrointestinal urinary reservoir. In our study, we did not detect any stone formation in the gastric group. The ileal and gastroileal groups revealed similar number of stones which is higher compared to the other reports in literature. This may possibly have two explanations. First this might be releated to the metabolic features of our animal model. Second the lack of clean intermittent catheterization in our animal model which is practically impossible might have potentially ended with mucus accumulation, which serves as a biofilm that can harbor urea splitting microorganisms, thus initiating stone formation. The mucus formation was alike in the ileal and gastroileal group and this feature is harmonious with the rate of stone formation. Similar to the metabolic outcome comparison, the gastroileal reservoirs demonstrated more familiar characteristics with the ileal group.

Buson et al. [19] compared gastric, ileal and sigmoid segments histologically and transitional metaplasia was found to be more common in the gastrocystoplasty group. Also no transitional cell carcinoma was detected in the whole group at the end of 12 months. In another study with 2 years of follow-up, tumor development was observed in the gastric, ileal and colonic segments [20]. Additionally in a recent study, after 14 years of follow-up, metastatic adenocarcinoma development was observed in gastrocystoplasty patients [21]. In our study, histologically combining gastric and ileal segments revealed no significant benefit when compared to each segment used alone.

One of the major limitations of this study is the short duration of follow-up when a surgery like augmentation cystoplasty is considered. However, once rats are considered, due to the higher metabolic rates and shorter expected duration to develop complications, 6 months of follow-up seems to be sufficient but for histological changes at least 12 months of follow-up seems to be enough according to the existing literature. Additionally, housing of the animals longer than 6 months is costly and not feasible.

Conclusion

Ileum is the most common gastrointestinal segment used in augmentation cystoplasty with significant metabolic effects. To overcome these effects, combining different segments seems to be a reasonable option. However, present study concludes that combination of gastric and ileal segments does not significantly reduce the rate of metabolic impairment, stone and mucus formation. Besides, it is not associated with significant improvement in histological outcome since urine is still in contact with the gastrointestinal mucosa. Together with associated surgical disadvantages, use of combined reservoirs does not seem to be a favorable option except in selected cases.

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