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V. Ortiz · S. Goldenberg

Hypergastrinemia following gastrocystoplasty in rats

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Abstract Gastrocystoplasty has been previously described as an effective method of bladder augmentation or replacement. Twenty-four female Wistar rats were divided into three groups of eight animals each: control (G1), partial gastrectomy with the gastric body (G2) and gastrocystoplasty with the gastric body (G3). The period of observation was 2 months and the parameter assessed was serum gastrin. Increases in serum gastrin were seen in 62.5% (5/8) of rats in group 2 and in 50% (4/8) of rats in group 3. Our results suggest that, in rats, hypergastrinemia is induced by the partial surgical removal of the gastric body and is not due to gastrocystoplasty.

Key words Gastrocystoplasty · Gastrin · Gastric body · Bladder augmentation

The concept of using a segment of the stomach as a bladder substitute was first introduced by Sinaiko [21] in 1956. The advantages of this approach include protection against hyperchloremic acidosis, reduced mucus production and a low urinary pH with decreased urine infection rates [14]. However, the procedure has been used in children and has shown some complications: hypochloremic alkalosis, hyperaciduria, ulcers and perforation of the gastric segment and hypergastrinemia [2, 4, 5, 11, 15, 18]. The disadvantages and complications of gastrocystoplasty with the gastric body in the short and long term are not well known, and any malignant potential has not yet been established. We therefore conducted a study of gastrocystoplasty with the gastric body in rats, by monitoring the serum gastrin.

V. Ortiz (✉)
Rua Gaivota, 988 apto. 11, São Paulo, 04522.032 Brazil

V. Ortiz · S. Goldenberg
Department of Surgery, Division of Surgical Research, Escola Puulista de Medicina, São Paulo, Brazil

Materials and methods

Twenty-four female adult Wistar rats (EPM1) each weighing 180–220 g were randomly allocated into three groups: group 1 ($n = 8$) control, group 2 ($n = 8$) partial gastrectomy with the gastric body and group 3 ($n = 8$) gastrocystoplasty with the gastric body. All animals were anesthetized with an intraperitoneal injection of sodium pentobarbital (30 mg/kg body wt.). The operation was performed using the operating microscope. In groups 2 and 3 a full midline incision was made and the stomach was carefully isolated. In the rat, the gastric fundic portion is nonglandular with a squamous epithelium and is identified by a limiting ridge. The antrum is distal and is sharply delimited from the body by its lighter color and thinner wall. The short gastric vessels were divided along the greater curvature as far as the limiting ridge. The right gastroepiploic vessels were divided at the transition line between the body and antrum. A vascularized segment based along the greater curvature was obtained and the stomach was closed using 6/0 polypropylene suture. The isolated gastric patch measured approximately 1.0 × 0.7 cm. The bladder was bisected with a generous longitudinal incision.

In group 2, the gastric patch was removed and the bladder closed with a running 6/0 chromic catgut suture. In group 3, the gastric patch was kept vascularized by the left gastroepiploic artery and was anastomosed to the bladder with a running suture with 6/0 chromic catgut (Fig. 1). The abdominal wall and skin were closed with absorbable suture. Group 1 served as control. Rats were returned to their cages with unrestricted access to water and standard rat chow pellets.

Two months postoperatively, following a fasting period of 18 h, rats were weighed and then anesthetized with intraperitoneal pentobarbital. The abdomen was opened and the rats exsanguinated by aortic puncture. The serum was collected and frozen at −20 °C for determination of gastrin, using radioimmunoassay (antibody rabbit ×gastrin/Cholecystokin). The Kruskal-Wallis test was used for statistical analysis and $P < 0.05$ was considered significant.

Results

The average initial weights of groups 1, 2 and 3 were 204, 200 and 199 g, respectively. The average weights at

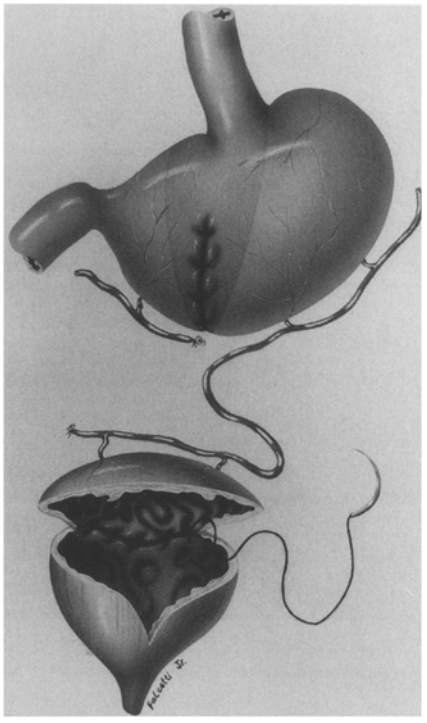

Fig. 1 Body gastric segment vascularized by the left gastroepiploic artery anastomosed to the bladder

Table 1 Mean fasting serum gastrin (pg/ml)

Group	Gastrin[a]	Range
1	143.7 ± 17.7	120–160
2	181.2 ± 44.2*	130–230
3	196.2 ± 66.9*	140–340

[a] Mean ± standard deviation
* $P > 0.05$

the time of death were 213 g (G1), 209 g (G2) and 209 g (G3) ($P > 0.05$). The mean serum gastrin levels were 143.7 pg/ml in group 1, 181.2 pg/ml in group 2 ($P > 0.05$) and 196.2 pg/ml in group 3 ($P > 0.05$) (Table 1). Although there were no statistically significant differences between the fasting serum gastrin levels, in 62.5% (5/8) of the animals of group 2 and 50% (4/8) of group 3 animals the gastrinemia was greater than 190 pg/ml.

Discussion

In recent years, there has been growing interest in the use of the stomach for urological reconstruction. Piser et al. [16] clearly demonstrated with a canine model that gastric mucosa not only acts as a barrier to the resorption of ammonium and chloride but secretes chloride. Kennedy et al. [10] demonstrated the resultant metabolic advantage of stomach over large bowel. Ryberg et al. [20] demonstrated that there was a close correlation between the amount of gastric body mucosa removed and the plasma gastrin levels. Rats subjected to 50% body gastric resection had a mean increase of approximately twofold in serum gastrin levels and a sixfold increase when 90% was resected. The G cells in the antrum produce gastrin as a result of high pH and/or food intake. The resection of large segments of the gastric body reduces the amount of parietal cells and increases the pH in the antrum [6]. Gastrin exerts trophic effects on the oxyntic mucosa, with proliferation of enterochromaffin-like (ECL) cells that contain large amounts of histamine [6, 17].

The ECL cells represents about 1% of the cells of the gastric body epithelium in the rat [6]. In isolated perfused rat stomach, gastrin was able to stimulate histamine release, which was followed by acid secretion. These findings, in several species both in vivo and in vitro, provide consistent but indirect evidence that gastrin has a direct effect on ECL cells [1, 6]. In rats, lifelong hypergastrinemia results in ECL cell hyperplasia and may give rise to the development of gastric ECL cell carcinoids [8, 9, 13].

In man, chronic atrophic gastritis with or without pernicious anemia is associated with achloridria, hypergastrinemia, ECL cell hyperplasia and an increased incidence of gastric carcinoids [3, 19]. The acid-related urinary symptoms experienced by some patients following gastrocystoplasty with the gastric body are usually controlled by acid-blocking drugs [11]. In rats, omeprazole and ranitidine decrease acid production from parietal cells and stimulate gastrin release [7, 9, 13].

These facts suggest that acid-blocking drugs can increase even more the hypergastrinemia following gastrocystoplasty with a potential induction of gastric carcinoids. A limited resection of the gastric body is recommended [2], or whenever larger body resection is done an amount of the antrum is also removed to prevent hypergastrinemia and to give a good functional result. Histopathologic changes of the bladder mucosa, in rats, after 18 months of gastric body cysto-plasty showed papillomas in 5 of 15 rats surviving long term [12]. Further investigations is required to improve our understanding of the physiopathology of basic gastrocystoplasty before it is accepted as a routine urological procedure.

It is concluded from this study that, in rats, hypergastrinemia can be expected following gastrocystoplasty with the gastric body and these findings are a result of the surgical removal of the acid-producing mucosa and are not due to the gastrocystoplasty itself.

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