Egyptian Journal of Surgery Vol. (22), No. (2), April, 2003

EARLY HISTOPATHOLOGICAL CHANGES IN THE STOMACH FOLLOWING GASTRIC RESTRICTIVE OPERATIONS (EXPERIMENTAL STUDY)

By
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Background: *The gastric restrictive operations are the gold standard for obesity surgery, but, little is known about the histological changes that occur in the distal pouch of the stomach and pyloric antrum.*
Methods: *The present study was conducted on 33 adult New Zealand Albino rabbits randomly classified into 3 groups. Group A, comprised 3 rabbits underwent laparotomy only (control group). Group B, comprised 15 rabbits underwent vertical banded gastroplasty.. Group C, comprised 15 rabbits underwent gastric partition and bypass operation.*
Results: *On gross examination, by laparotomy, at the end of the second and fourth weeks, there was no change in the size of the stomach with minimal adhesions between it and the surroundings in group A (control group), and extensive adhesions in groups B and C. But after six weeks there was an increase in the proximal small gastric pouch (by 1-3 ml, a mean of 1.9 ml) in group C only. On histopathological examination using light and scanning electron microscopy, the proximal small gastric pouch in groups B and C, showed hemorrhagic patches in mucosa, submucosa and musculosa and loss of surface epithelial cells, which disappeared after 4 weeks. The distal gastric pouch and pyloric antrum 4 weeks after the operation showed nuclear hyperchromatosis of the lining mucosal cells, loss of normal mucosal glandular architecture,and scattered areas of mucosal necrosis. Six weeks after the operation, we found, scattered areas of squamous metaplasia, intestinal metaplasia with goblet cells, and areas of surface epithelial hypertrophy in groups B and C only.*
Conclusion: *The gastric restrictive operations produce histopathological changes in the distal pouches of the stomach and pyloric antrum, varying from gastritis up to intestinal metaplasia. So it is preferable to indicate the operations only in few patients, where morbid obesity is a pathological state and is very difficult to treat by non-surgical means. Long term follow up study is needed to prove the possibility of malignant transformation in these metaplastic tissues.*

Key words: Histopathological, gastric, obesity, experimental.

INTRODUCTION

Morbid obesity represents a serious health problem in the industrialized countries, annual costs of about 17.5 to 20 billion Euro result from treating cardiac and circulatory problems, diabetes mellitus, hyperuricaemia, and illnesses of the locomotor apparatus, all of which are illnesses accompanying morbid obesity.(1) According to the World Health Organization report in 1998 more than 50% of the American population are overweight, and about 20% of the children and adolescents are obese.(2) In morbid obesity conservative therapeutic measures are successful in only 10 – 15% of cases,and surgical methods can achieve a permanent reduction in body weight(3).

Although jejunoileal bypass was popular for the treatment of morbid obesity during the nineteen seventies, it has been abandoned, because of malabsorption that occurs. Gastric restrictive surgery (gastric partitioning operations) has been evolved over the past decade, as the treatment of choice for morbid obesity to reduce food intake, by limiting the reservoir capacity of the stomach (4).

There are several variations of gastric restrictive procedures for morbid obesity. The aim of all methods is to construct a small upper gastric pouch, since it has been shown that there is a relationship between pouch size and subsequent weight loss(5).

Gastric restrictive operations were evaluated in multiple applied researches as regard to weight reduction, operative and postoperative complications as, gastric ulceration, and dilatation of proximal pouch, widening of the stoma, and slipping of gastric band by many authors [6,7,8,9].

The aim of this work is to study experimentally the histopathological changes that can occur in the stomach after gastric restrictive operations.

PATIENTS AND METHODS

The present study was conducted on 33 adult New Zealand Albino rabbits, which were housed in central animal house, Department of Physiology, Faculty of Medicine, Tanta University, which maintained their environment at controlled temperature, and relative humidity. The rabbits weight was ranged from 1900 to 2100 grams with a mean of 2035 grams, all were males. The rabbits were randomly classified into 3 groups, group A: included 3 rabbits as control group, group B: included 15 rabbits subjected to vertical banded gastroplasty and group C: included 15 rabbits subjected to gastric bypass with gastrojejunostomy.

Operative technique:

The rabbits were kept food fasting for 24 hours and water fasting for 12 hours. Animals were anaesthetized with 50 mg. /kg. ketamine subcutaneously, and placed in the supine position on the operative table .The abdomen was cleansed with povidone iodine 10% .An upper midline incision was done for all rabbits and stomach was explored. Three rabbits (group A) underwent laparotomy only and the abdomen was then closed. Fifteen rabbits (group B) underwent vertical banded gastroplasty using two rows of polypropylene O sutures taken vertically starting from the left side of the gastro-esophageal junction, parallel to lesser curvature, to a point near to midbody of the stomach above the pyloric antrum, for creation of a small gastric pouch (5-10 ml), and then banding its outlet along the lesser curvature using a mesh collar (0.5 by 1 cm) to prevent it from dilatation. Fifteen rabbits (group C), underwent gastric bypass by transecting the stomach to perform a proximal small pouch (5-10 ml) and then reconstructing a side to side gastrojejunostomy with a stoma of 1 cm diameter. The distal part of the stomach was closed.

Postoperatively, the animals were kept individually in wire-bottomed cages, at a suitable room temperature, and were given the same standard diet. Each of them was weighed every 2 days. One rabbit of group A, 4 of group B and 4 of group C, were sacrificed 2 weeks after the operation .One rabbit of group A, 5 rabbits of group B and 4 of group C were sacrificed 4 weeks after the operation .One rabbit of group A, 5 rabbits of groups B and C were sacrificed 6 weeks after operation, and their abdomen were examined grossly. Specimens from the different parts of the stomach (closed and open parts of the body and pyloric antrum)were taken . After washing with saline, every specimen was divided into two parts, one for light microscopy and the other for scanning electron microscopy examination. Every part was put in a suitable preservative (formol saline and Carnoy's fixative for light microscopy and Karnovsky's fixative for scanning electron microscopy). Haematoxylin and eosin stain was done to study the general histological features, Masson's trichrome stain to study the changes in connective tissue and collagen fibers, Periodic acid Schiff's (PAS) reaction to demonstrate the PAS positive materials.

RESULTS

Gastric restrictive operations were done on 33 rabbits with an average weight of 2035 gm (ranging from 1900-2100 gm). No difficulties were met during the operations. At early postoperative period, one rabbit of group B, and two of group C were died within 48 hours. Postmortem laparotomy revealed anastomotic leak in rabbits of group C and no obvious cause in the rabbit of group B.

The weight loss was evaluated by weighing the rabbits every 2 days. In rabbits of group A, there was insignificant loss of body weight during the first postoperative week (average from 30 to 80 gm with a mean of 68 gm), but the weight gradually increased during the period of follow up. In rabbits of groups B, and C, there was an average weight loss of about 100 –150 gm during the first postoperative week (a mean of 117 gm), loss of about 90 to 150 gm during the second and the third weeks (a mean of 114 gm), loss of about 50-90 gm during the fourth , fifth and sixth weeks (a mean 72 of gm). There was insignificant changes in weight loss between groups B and C (where P<:0.005).

On gross examination by laparotomy at the end of the second and fourth weeks, there was no change in the size of the stomach with minimal adhesions between it and the surroundings in group A (control group) and extensive adhesions in groups B and C. At the end of the six week, there was an increase in the size of the proximal small gastric pouches by 1-3 ml (a mean of 1.9 ml) in group C only.

In the control group, the wall of the stomach was consisted of mucosa, submucosa, musculosa and serosa .The wall of the pyloric antrum had the same layers of the body except that the glands were highly tortuous and the inner circular muscle layer was apparently thick (Fig.1)

Two weeks after the operations. By light microscopic examination, the proximal small pouches of the stomach in groups B and C showed hemorrhagic patches in mucosa, submucosa, and musculosa and loss of surface epithelial cells with inflammatory cellular reaction in the mucosa (Fig. 2). The distal pouches and the pyloric antrum in groups B and C showed gastric pits hyperplasia which was manifested by increased pit depth, glandular corkscrew appearance of the glands, increase connective tissue in the basal part of the mucosa, submucosa and all other layers (Fig. 3) and increase PAS positive reaction both in the surface epithelial cells and in the mucous neck cells. Scanning electron microscopy of the proximal gastric pouches in groups B and C showed increase in mucus production with red blood cells detected in the gastric pits and bacterial infection in the form of diplococci, but the distal pouches and pyloric antrum showed a large number of rod shaped bacteria.

Four weeks after the operations. By light microscopic examination, of the proximal small gastric pouch of groups B and C, there were areas of cellular loss in the midgland region of the mucosa, and disappearance of mucosal, submucosal, and musculosal hemorrhagic areas. In distal pouches of the stomach and pyloric antrum we found dysplastic changes as , nuclear hyperchromasia of the lining mucosal cells, loss of normal mucosal glandular architecture and moderate PAS positive reaction. By scanning electron microscopy, in the proximal small pouches of all groups (B, C) we found amalgamated gastric glands, widened gastric pits with aggregation of mucus in their mouths. In the distal stomach pouches and pyloric antrum, there were scattered areas of mucosal necrosis and ulcerations, the floor of these ulcerative areas presented necrotic debris and fibrous tissue.

Six weeks after the operations. By light microscopy, we found, in the proximal small gastric pouch of groups B and C, areas of cellular loss in the midgland region similar to that present in the fourth-postoperative week. In the distal pouches of the stomach and pyloric antrum we found scattered areas of squamous metaplasia in the surface epithelium of their mucosa (Fig 4), and intestinal metaplasia with goblet cells seen among the surface epithelial cells (Fig 5). By scanning electron microscopy, in the proximal small pouches of groups B and C we found increased vacuoles in mucous neck cells but in the distal gastric pouches and pyloric antrum, there were surface epithelial hypertrophy with finger like intestinal villi protruding from the surface epithelial cells (Fig 6).

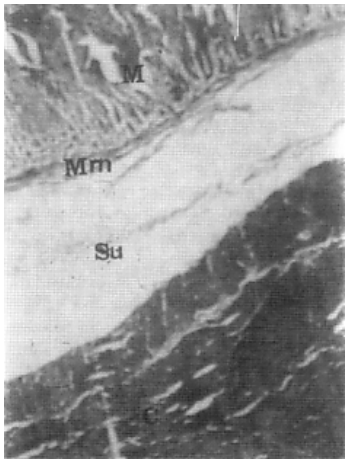

Fig.(1): Transverse section in the pyloric antrum of the stomach in control rabbit (Group A) showing the mucosa (M),muscularis mucosa(Mm),submucosa(Su)and inner circular muscle layer(C), 4weeks after laparotomy.

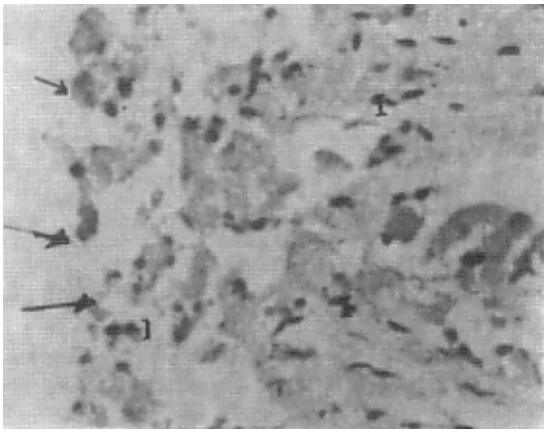

Fig.(2): Transverse section (magnified micrography) in proximal pouch of the stomach 2 weeks after the operation (group C), showing loss of the surface epithelial cells (arrows) and inflammatory cellular infiltration(I) .

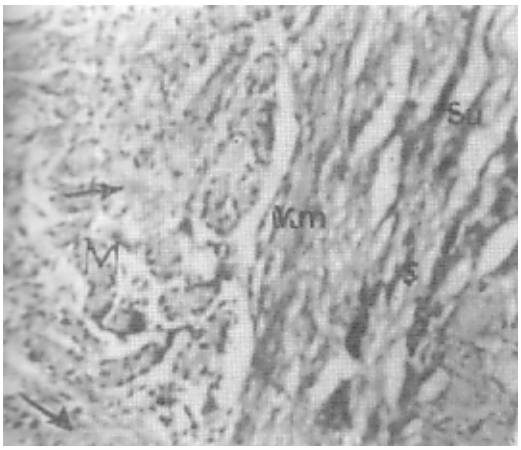

Fig.(3): Transverse section in the pyloric antrum 4 weeks after operation (group B) showing marked increase in the amount of connective tissue in the mucosa (M) and submucosa (Su).

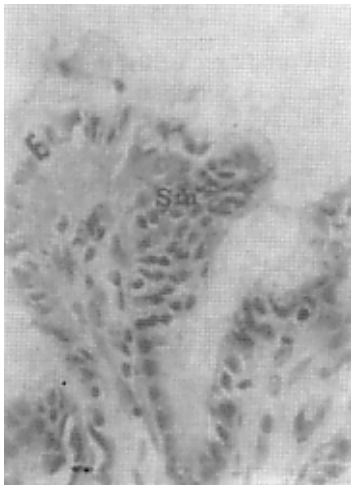

Fig.(4): Transverse section in the pyloric antrum 6 weeks after the operation (group C) showing areas of surface columnar epithelial cells (E) and squamous cells (Sm).

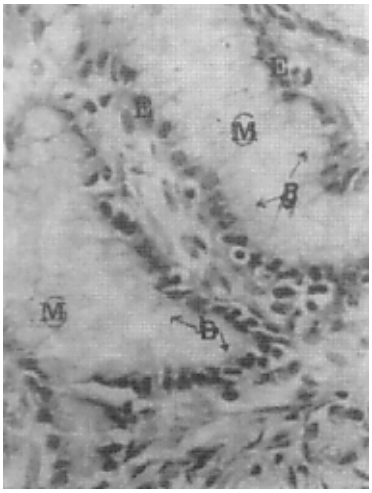

Fig.(5): Transverse section in the pyloric antrum 6 weeks after the operation (group B), showing intestinal metaplasia with scattered goblet cells (B) among the surface epithelium (E).

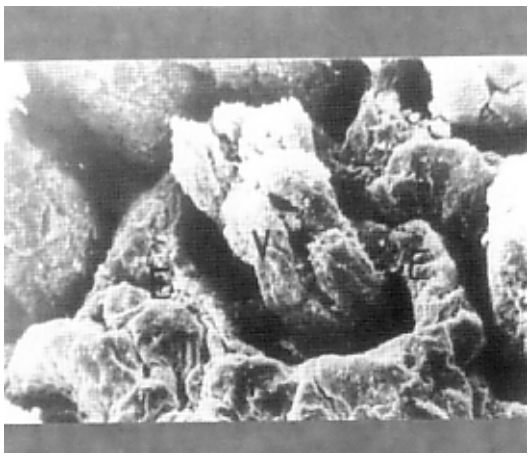

Fig.(6): A scanning electron micrograph(magnified) in the pyloric antrum 6 weeks after the operation (group C), showing hypertrophied finger like intestinal villi(V) protruding from the surface epithelium(E).

DISCUSSION

After open or laparoscopic gastric restrictive operations as a treatment of morbid obesity, the distal gastric pouches and duodenum are not readily available for radiological and endoscopic evaluation. Furthermore, little is known about the physiologic and histologic changes that occur in the stomach.[10]

In this work, inflammatory cellular reaction in the mucosa and loss of surface epithelial cells, accompanied with mucosal, submucosal and musculosal hemorrhage were found in the proximal gastric pouchs 2 weeks after the operations in groups B and C. This is coincided with the results reported by Papavramidis et al.,[11] Sipponen and Hyvarnin [12] who found gastritis and intramural hemorrhagic patches, which developed as a result of damage to gastric mucosal barrier. Robls et al.,[13] suggested

two factors could produce gastritis in patients undergoing such gastric operations, which are bacterial infection and duodenogastric reflux.

In this study, scanning electron microscopy in groups B,and C, revealed large number of rod shaped bacteria in pits of the distal gastric pouches and pyloric antrum 2 weeks after the operations and also revealed scattered areas of mucosal necrosis 4 weeks after the operations. These findings coincided with those reported by Nunn et al.,[14] , Bonvicini et al.,[15] and Price et al.,[16] as they reported that, rod shaped bacterial infection is etiologically related to postoperative gastritis and ulcerations. Magnus et al.,[17] reported areas of mucosal necrosis and absence of campylobacter pylori infection in the distal pouch of 3 males required access to the distal gastric pouches because they were suffered from repeated gastrointestinal bleeding after gastric bypass operation for obesity.

Six weeks postoperatively, in this study, the luminal surface of gastric mucosa both in the distal pouches and pyloric antrum in groups B and C by scanning electron microscopy revealed surface epithelial hypertrophy with finger like intestinal villi protruding from the surface epithelial cells with distinct topographic differences in the intestinalized and non intestinalized regions. This intestinal metaplasia was similar to that reported in human stomach studies after such operations by Winborn and Wesser [18].These squamous and intestinal metaplasia seen among the surface epithelial cells in the distal pouches and pyloric antrum of groups, B and C in our work coincided with Lin et al., [19] findings who recorded that the longer the postoperative priod, the higher the frequency of gastric metaplasia, they also suggested that, the enterogastric reflux of duodenal contents, local chronic ischemia, and inflammatory reaction have been considered responsible for these changes . Niv and Turani [20] mentioned that areas with intestinal metaplasia represented a change of mucosal pattern from gastric to intestinal type, where the normal columnar epithelial cells were converted to goblet cells.

CONCLUSION

The gastric restrictive operations produce histopathological changes in the stomach, varying from gastritis up to intestinal metaplasia. So it is preferable to indicate these operations only in few patients, where morbid obesity is a pathological state, and is very difficult to treat by non-surgical means. Long term follow up study is needed to prove the possibility of malignant transformation in these developed metaplastic tissues.

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