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Original

Simultaneous dynamic study of gastric emptying and changes of serum levels of gut hormones in patients after peptic ulcer surgery

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Abstract

BACKGROUND: The aim was to examine the influence of different modalities of peptic ulcer surgery on the gastric emptying (GE) pattern and related serum level changes of selected gut hormones.

MATERIAL AND METHODS: Fifty eight subjects were examined. In 48 of them peptic ulcer surgery was performed at least six months before the examination: Billroth I (B1) in 11, Billroth II (B2) in 16, B1 with the selective vagotomy — Harkins 1 (H1) in 9 and B2 with the selective vagotomy — Harkins 2 (H2) in 12. Ten healthy volunteers (C) were also examined.

RESULTS: The results of gastric emptying showed that the lag phase duration was inversely related to the GE rates, and the GE pattern was linear in both controls (C) and in operated patients, except in B2 group, in which the GE pattern was exponential. In comparison with C group, GE was slower in B1, H1 and H2 groups, and faster in B2 group. The plasma gastrin values in C group, showing two peaks, were higher in relation to other groups. In relation to C group, higher values of motilin were obtained in patients after the selective vagotomy. The plasma somatostatin values recorded in B1 and H1 groups, showing the marked peaks, were higher in relation to C group. In relation to C group the highest plasma neurotensin values were obtained in B2 group.

CONCLUSIONS: In order to understand entirely the influence of peptic ulcer surgery on the GI function, further research of the role of specific hormones and neuropeptides is needed, which would enable more precise selection of the therapy in order to prevent postvagotomy and postgastrectomy syndromes.

Key words: gastric emptying, scintigraphy, gastrointestinal hormones

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Introduction

Peptic ulcer surgery may seriously alter gastric emptying rates and most frequently results in retardation of solid phase transit. Specific alterations occur in symptomatic patients, with symptoms of postgastrectomy and postvagotomy sequelae [1]. Postgastrectomy syndrome occurs from the second week after operation. It includes signs and symptoms of recurrent or anastomotic ulcer, bowel action, and nutritional deficiencies postprandial syndromes (late postprandial hypoglycemia and dumping syndrome) – a condition that occurs when food moves too fast from the stomach into the small intestine, associated with nausea, pain, weakness, and sweating. Postvagotomy syndrome includes delayed stomach emptying.

Gastrointestinal hormones are peptides secreted by the gastrointestinal mucosa, that, together with other hormones and transmitters, control all gastrointestinal functions. Also, many hormones

or peptides found in the gastrointestinal tract and endocrine pancreas are known to influence the motor function of the gastrointestinal tract, including the stomach. The peptides released from these organs that are shown to influence the gastric motility include, among others, gastrin, motilin, somatostatin and neurotensin.

Gastrin stimulates antral motility. Gastrin is the strongest stimulator of gastric acid secretion as well as of gastrointestinal motility. Its secretion is also influenced by the vagus nerve, directly or indirectly. Vagal, cholinergic preganglionic fibres transfer signals to the G-cells via non-adrenergic, non-cholinergic postganglionic neurons. These enteric neurons liberate gastrin-releasing peptide to the gastrin producing G-cells. An indirect vagal route to the G-cells is via postganglionic cholinergic enteric neurons to somatostatin cells that are located close to the G-cells. When these enteric neurons release acetylcholine, the response of the somatostatin cells is the inhibition of somatostatin release. Somatostatin inhibits G-cell secretion by paracrine action. The result of both vagal inputs to the G-cells is gastrin release.

Motilin triggers phase 3 activities of the gastric antrum and upper small intestine in the interdigestive period. Although it stimulates gastric and upper intestinal motility to enhance gastric emptying, it is yet to be decisively determined whether or not its action is physiological. It is partly released under vagal stimulation. Somatostatin is a strong, universal inhibitor — both blood-born and paracrine. When gastric acid, fats, and hyperosmolar solutions have entered and distended the duodenum, enterogastrones (GIP, somatostatin, CCK, and secretin) are released and suppress gastric acid secretion and motility of the stomach. Somatostatin was shown to inhibit ileal motility. In addition, it modulates human interdigestive motility by shortening the interdigestive motility cycle when it is given intravenously in physiological doses. It stimulates oesophageal body contraction and decreases lower oesophageal sphincter pressure. Neurotensin decreases lower oesophageal sphincter pressure and delays gastric emptying and intestinal transit time.

The aim of the study was to examine the influence of different modalities of peptic ulcer surgery on gastric emptying (GE) patterns, and on the serum level changes of selected gut hormones during GE.

Material and methods

Fifty eight subjects were examined — 10 healthy volunteers (C) and 48 patients following peptic ulcer surgery (performed at least 6 months before studying): 11 — Billroth I (B1), 16 — Billroth II (B2), 9 - B1 with the selective vagotomy — Harkins 1 (H1) and 12 — B2 with the selective vagotomy — Harkins 2 (H2).

A high density test meal was prepared by subcapsular injections of ^{99m}Tc-S-colloid (total radioactivity 37 MBq) into chicken liver, which was thereafter boiled (for 20 minutes), minced and mixed with 220 g of beef stew having standard composition.

Immediately after ingestion of the test meal followed by 200 ml of water, dynamic imaging of the gastric region in supine position, lasting 120 minutes, was performed using a gamma-camera with LEAP collimator, and dedicated computer (1 frame/min.; matrix size 64 × 64). The lag phase duration (min) and emptying rates (%) at the 30th, 60th, 90th and 120th minutes were determined from the gastric time-activity curve corrected for ^{99m}Tc decay.

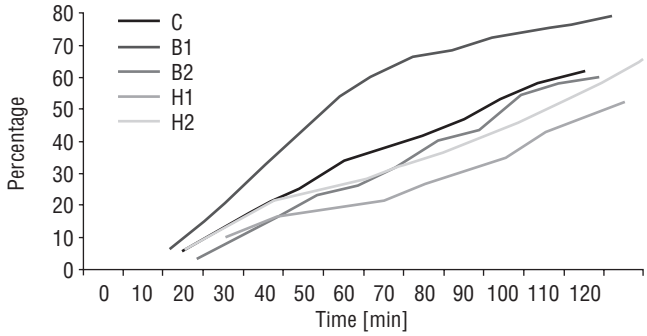


Figure 1. The mean values of gastric emptying as a function of time in the different groups of patients studied.

The blood samples were drawn from the cubital vein just before the test meal, as well as at the beginning and every 10 minutes until the end of GE imaging. The serum levels of gastrin, motilin, somatostatin and neurotensin were determined in the collected blood samples using RIA techniques.

Statistical analysis was performed using dual way analysis of variance.

Results

The results of gastric emptying showed that the lag phase duration was reversely related to GE rates, and the GE pattern was linear in both controls and operated patients, except in B2 group in which the GE pattern was exponential. GE was slower in patients after B1 ($p < 0.05$) as well as H1 and H2 operations ($p < 0.01$), but faster in B2 group ($p < 0.01$) in comparison with controls (Figure 1).

Mean plasma gastrin levels were lower in all groups other than in healthy volunteers ($p < 0.01$), in whom two peaks occurred (Figures 2AB).

In all groups the plasma motilin values showed peaks during the first 60 minutes. Higher values were obtained in patients after selective vagotomy ($p < 0.01$) (Figures 3AB).

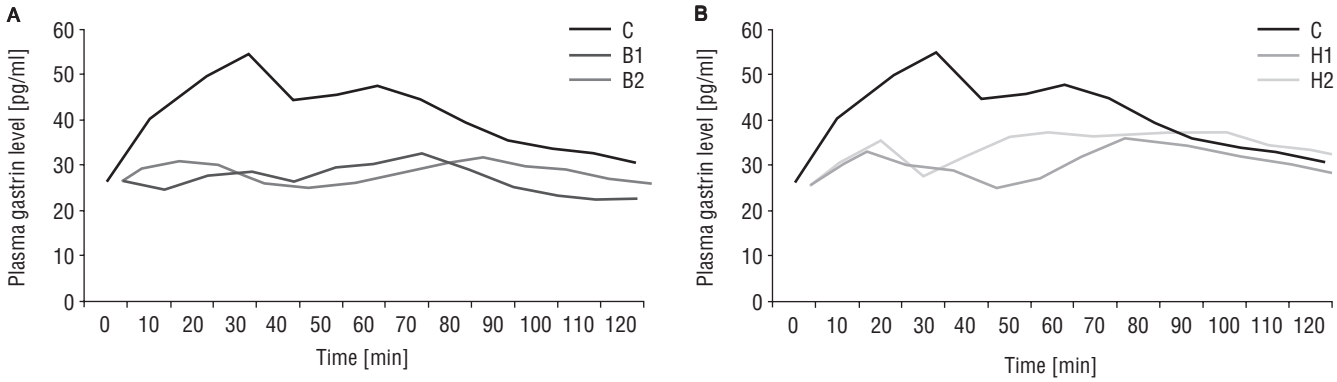
The plasma somatostatin values recorded in B1 and H1 groups, showing the marked peaks in both, were higher compared to C group ($p < 0.01$) (Figures 4AB).

The highest plasma neurotensin values were obtained in B2 group ($p < 0.01$), and in H1 and H2 groups (Figures 5AB).

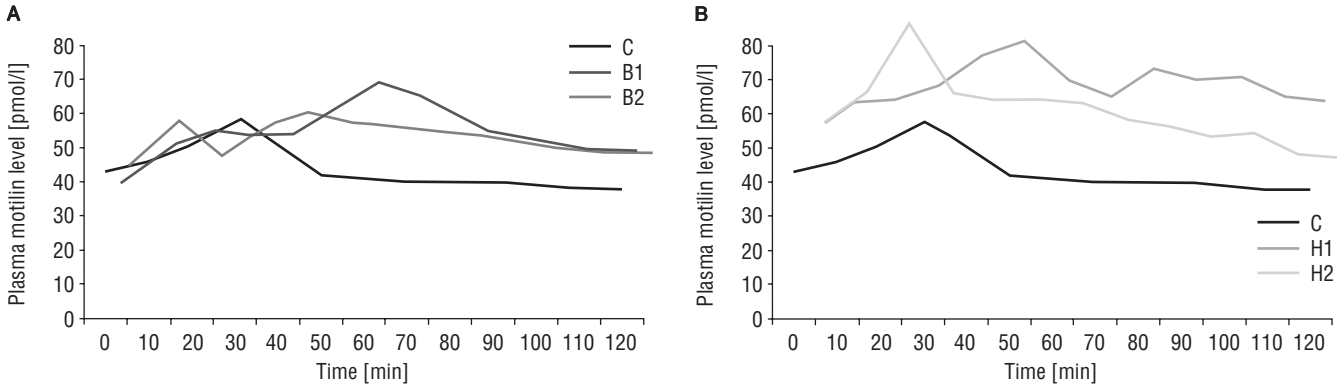
Discussion

The dynamic scintigraphic examination in this study was performed to enable accurate measurement of both the lag phase duration and gastric emptying rate. The high density test meal was chosen to provoke possible latent gastric motoric disturbances.

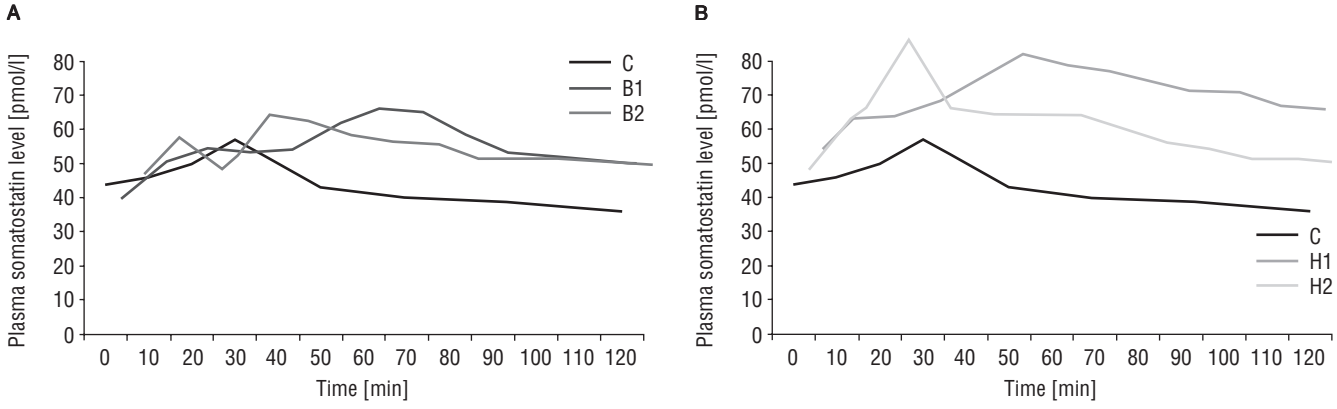
The results of gastric emptying showed that the lag phase duration was reversely related to GE rates, and the GE pattern was linear in both controls and operated patients, except in B2 group in which the GE pattern was exponential. In relation to C group, GE was slower in B1 ($p < 0.05$), H1 and H2 groups ($p < 0.01$), and faster in B2 group ($p < 0.01$). The slower GE in operated patients, except B2 group, could be explained by massive gastric motility disorders (H1, H2) and by decreased anastomotic patency (B1, H1). Faster GE in B2 group could be a conse-



Figures 2AB. The average curves of plasma gastrin level changes during gastric emptying.



Figures 3AB. The average curves of plasma motilin level changes during gastric emptying.



Figures 4AB. The average curves of plasma somatostatin level changes during gastric emptying.

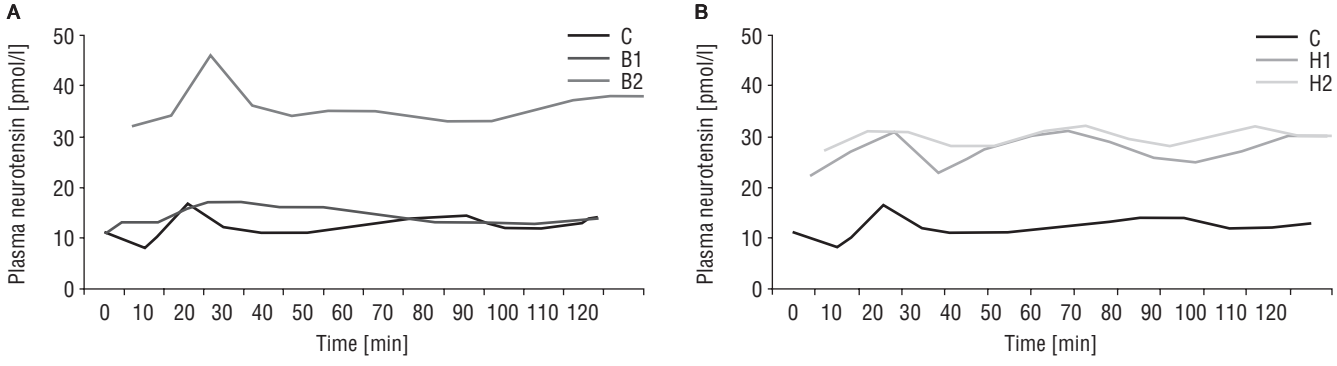


Figure 5AB. The average curves of plasma neurotensin level changes during gastric emptying.

quence of increased anastomotic patency (large stoma) and lack of the duodenal inhibitory activity. In addition to our results, Smout [2] claims that increased GE can be explained by the exclusion of physiological means of the transit of food through the duodenum, which excludes the activity of its mechano-, osmo- and chemoreceptors. Other authors have also tried to find out the relationship between the surgical procedures performed and the rate of gastric emptying. So, according to Stier et al [3], the transit in a jejunal pouch follows a linear decreasing function and is significantly slower compared to the exponential passage of the jejunostomy. Both patterns remain still significantly accelerated compared to the physiological ranges of gastric emptying. Contrary to our results, motility disturbances were not observed more frequently in patients with either moderately or severely impaired vagal function than in patients with normal vagal function. Stasis in the Roux limb was seen even more frequently in patients with a normal vagal function than in patients with a severely impaired vagal function [4]. Metzger et al [5], emphasized the value of metoclopramide (a stimulant of gastric motility) in patients with chronic gastric retention after vagotomy and gastric resection, unexplained by mechanical obstruction or stomal ulceration. Also, Petrov et al [6] proved the value of dynamic scintigraphy of the stomach for studying evacuative function of the resected stomach.

The second part of our results concerns the measurement of the gastric hormone levels in patients after gastric surgery. El-Salhy et al [7] evaluated the effects of left and right unilateral cervical vagotomy on the content of several neuroendocrine peptides in different parts of the murine gastrointestinal tract, known to receive vagal innervation (among others: gastrin, motilin, somatostatin and neurotensin). The neuroendocrine peptide concentration was affected after both left and right vagotomy, and the changes in the concentrations occurred in all the gastrointestinal segments investigated, namely antrum, small and large intestine. However, these changes varied, depending on which side was vagotomised and the interval after vagotomy It is suggested, furthermore, that the contradictory results obtained earlier on the effect of vagotomy on the gastrointestinal peptides may depend on differences in the vagotomy methods used and on differences in observation time after vagotomy.

The literature data about this topic is very controversial, and concerns mainly the effect of gastric surgery on gastrin release. In our study, the plasma gastrin values in C group, showing two peaks, were higher in relation to other groups ($p < 0.01$). Lower values obtained in all those operated have been commonly explained by the absence of the secretory active antral mucosa. Contrary to our results, according to Hoshikawa et al [1] and Hausamen et al [8], all patients after esophagogastrostomy showed hypergastrinaemia. According to Fabri et al [9], postoperative serum gastrin levels are increased after vagotomy and the degree of hypergastrinaemia does not correlate with the risk of ulcer recurrence. In addition, Sasaki et al [10] concluded that in the pathogenesis of ulcer recurrence the role of gastrin release from the residual antral mucosa seems to be limited. Friess et al [11] revealed severe primary exocrine pancreatic insufficiency with decreased gastrin, decreased late postprandial pancreatic polypeptide, and increased cholecystokinin levels in patients after total gastrectomy, which might explain why many patients with total gastrectomy have maldigestion and postoperative weight loss.

In all our groups the plasma motilin values showed peaks during the first 60 minutes. In relation to the control group, higher values were obtained in patients after selective vagotomy ($p < 0.01$). As the role of motilin was to accelerate gastric motility, the later findings could be explained by an attempt to normalize marked GE retardation (H1, H2), i.e. to overcome a relative anastomotic stenosis (H1). Similar to our results, Yang et al [12] suggests that motilin can modulate the mechanism of gastric pacing by altering gastric motility, and Mizumoto et al [13] indicated that motilin agonist EM-523 may be useful as a gastroprokinetic drug for patients with vagotomy. Also, the correlation between GE and the motilin level agrees with the investigation of Lawaetz et al [14], who found that the patients after dumping syndrome had a small decrement of motilin, so, it is logical that the ones with delayed GE had an increment. In contrast to our results, Lemoyne et al [15] found in their experiments that the release of motilin is not chronically altered by distal vagotomy, while Hanyu et al [16] concluded that vagotomy seemed to produce an effect to prevent phasic motilin release and Yoshiya et al [17] concluded that motilin secretion in the fasting state and after nutrient ingestion is not influenced by truncal vagotomy.

The plasma somatostatin values recorded in B1 and H1 groups, showing the marked peaks, were higher in relation to the controls ($p < 0.01$). According to Johansson et al [18], somatostatin stimulated the early phase of gastric motility, and our results might be explained as a compensatory result of decreased anastomotic patency, while such an effect was not necessary in other operated patients.

The highest plasma neurotensin levels were obtained in B2 group ($p < 0.01$). Since neurotensin has an inhibitory effect on GE, this might be consistent with an attempt to slow down very fast GE in those patients, which is also confirmed by the results of Lawaetz et al [13]. But, the same mechanism cannot explain the increased values obtained in H1 and H2 groups. However, Kohler et al [19] concluded that changes in intestinal transit time were responsible for the pathological increase in neurotensin release after exclusion of the duodenal passage.

Conclusions

According to our investigation, dynamic scintigraphic examination enables accurate measurement of both the lag phase duration and gastric emptying rate. In all investigated groups, the lag phase duration was reversely related to GE rates. The GE pattern was linear in healthy volunteers and operated patients, with the exception of B2 group in which the GE pattern was exponential. Slower GE in B1, H1 and H2 groups could be explained by massive gastric motility disorders and/or decreased anastomotic patency. The faster GE in B2 group could be a consequence of increased anastomotic patency (large stoma) and lack of the duodenal inhibitory activity.

Lower values of gastrin obtained in all operated patients have been commonly explained by the absence of the secretory active antral mucosa.

Motilin accelerates gastric motility, so, the highest values obtained in patients after selective vagotomy could be explained by an attempt to normalize marked GE retardation (H1, H2), i.e. to overcome a relative anastomotic stenosis (H1).

Taking into account that somatostatin stimulated the early phase of gastric motility, the increased values in B1 and H1 groups might be explained as a compensatory result of decreased anastomotic patency, while such an effect was not necessary in other operated patients.

Since neurotensin has an inhibitory effect on GE, the highest plasma neurotensin levels obtained in B2 group might be consistent with an attempt to slow down very fast GE in those patients. However, the same mechanism cannot explain the increased values obtained in H1 and H2 groups.

The dynamic scintigraphic examination is an accurate and noninvasive approach to studying disorders of the stomach function after peptic ulcer surgery. In our study, typical GE patterns and the duration of lag phase were established, as well as typical patterns in the hormone serum level changes during gastric emptying, which might explain some of the compensatory hormonal mechanisms that occur after gastric surgery. But, in order to better understand all functional consequences of each type of gastric operation, and to determine the exact role of some gastrointestinal hormones and neuropeptides in the pathogenesis of postoperative disorders, further and more specifically designated examinations are needed. More precise knowledge about this topic could allow more specific choice of surgical and/or conservative therapy in order to prevent postvagotomy and postgastrectomy syndrome.

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