Introduction

Clinical treatment of the short bowel syndrome (SBS) is a problem far from resolved. Nutritional support may be provided by the use of home parenteral and enteral nutrition\textsuperscript{1, 2}. However, continuous intravenous support is associated with complications related to catheter placement, venous thrombosis, obstruction of the superior vena cava and infection. Moreover, the regime necessary for carrying total parenteral nutrition (TPN) in the home setting causes social discomfort and psychological problems\textsuperscript{3, 4}. Small bowel transplantation, in spite of some positive results, still causes numerous complications and many unresolved issues remain\textsuperscript{5-8}.

The above data justify the necessity for new techniques of surgical treatment of the short bowel syndrome. It is obvious that the purpose of such therapy must be to enhance absorptive capacity, either by increasing the available surface area of absorption or by slowing small intestine transit. Numerous procedures have been used to achieve these objectives; however no single method has thus far been shown to be safe and effective enough.

Original

A new method for surgical treatment of the short bowel syndrome


The Experimental Pathology Department, N.V. Sklifosovsky First Aid Research Centre, Moscow, Russia; * Department of Physiology, University of León, Spain and ** Service of Surgery, Hospital of León, Spain.

Abstract

This study was aimed to investigate the electrophysiological and morphological characteristics resulting from the structural and functional transformation of gastric tissue transplanted to the small intestine. Twelve adult mongrel dogs were studied up to 3 years. Gastric transplants preserved its main microstructure and minimal compensatory-adaptive processes developed in the mucosa and muscle layers of the graft. A significant influence on the electrical activity of the small intestine was observed, with a 10% reduction of the slow wave frequency (SWF) in the proximal and distal jejunum adjacent to the graft after meals. The SWF of the gastric graft itself, however, corresponded to the frequency of the native stomach, did not depend and was not associated with adjacent intestinal areas. In summary, the stomach graft transplanted to the small intestine keeps the properties of gastric tissue, there are functional adaptations to conditions of digestion in the small intestine and the graft has minimal effects on intestinal motility.

(\textit{Nutr Hosp} 2001, 16:133-139)


UN NUEVO MÉTODO PARA EL TRATAMIENTO QUIRÚRGICO DEL SÍNDROME DE INTESTINO CORTO

Resumen

El objetivo del estudio consistió en investigar las características electrofisiológicas y morfológicas derivadas de la transformación estructural y funcional del tejido gástrico transplantado al intestino delgado. Se estudió a doce perros cruzados adultos durante un máximo de 3 años. Los trasplantes gástricos conservaron su microestructura principal, y la mucosa y las capas musculares del tejido experimentaron procesos de compensación y adaptación. Se observó una influencia notable de la actividad eléctrica del intestino delgado y una reducción del 10% de la frecuencia de ondas lentas (SWF) en las partes proximal y distal del yeyuno adyacentes al tejido después de las comidas. No obstante, la SWF del propio injerto gástrico se correspondía con la frecuencia del estómago nativo, no dependía de las regiones intestinales adyacentes ni se encontraba asociada a ellas. En resumen, el injerto de estómago transplantado al intestino delgado conserva las propiedades del tejido gástrico, se produce una adaptación funcional a las condiciones de la digestión del intestino delgado y el injerto apenas repercute en la motilidad intestinal.

(\textit{Nutr Hosp} 2001, 16:133-139)

The use of intestinal interposition has generated more interest than any other surgical approach. In this procedure, a segment of intestine is isolated from the enteric stream and transposed, either in an isoperistaltic or, more commonly, an antiperistaltic position. Animal studies have shown conflicting results as to the efficacy of the procedure. Several investigations have reported delayed gastric emptying, slower intestinal transit and improved survival whereas others have failed to show any beneficial effect.

Colonic interposition has been used in patients with SBS, although unfavourable results appear on the long term. Attempts to increase the absorptive surface area of the small bowel have also been carried out by lengthening its segments with longitudinal dissection of the small bowel, formation of two tubes and end to end anastomoses; however, obstructions, anastomotic leak and bowel ischemia are common.

One promising field is the increase of intestinal absorptive area by growing new intestinal mucosa. Growth of neomucosa has been demonstrated on colonic serosal patches or abdominal wall pedicle flaps in experimental animals. One potential approach to the surgical treatment of SBS could be the transposition of gastric tissue in tubular form into the initial part of the small intestine. This model would allow the simultaneous achievement of two objectives: increase of the absorptive surface of the small bowel and decrease of the gastric acid hypersecretion often observed after massive resection of small bowel. The favourable outcome in patients with SBS who have undergone subtotal gastrectomy and vagotomy supports the validity of this model.

In this study we describe the electrophysiological and morphological characteristics resulting from the structural and functional transformation of gastric tissue transplanted to the small intestine.

**Methods**

**Surgical technique**

Twelve adult mongrel dogs weighing 21 to 27 kg were used. Animals were anaesthetised by intravenous fentanyl citrate-droperidol (0,1 ml/kg) and succinylcholine chloride (0,5 ml) administered every 90 minutes.

Surgery was performed in two stages (fig. 1): formation of a gastric pedicled graft and implantation of the graft end-to-end into the dissected initial part of the jejunum at a distance of 30 cm distal from the Treitz ligament.

In four animals a fistula was implanted in the gastric transplant for morphological control during the second stage of operation. In five dogs, four bipolar electrodes were placed in the subserous layer of the gastric stump, the graft, and the jejunum adjacent to the graft located proximally (10 cm) and distally (10 cm) relatively to the transplant. Axes of electrodes were directed along the small intestine. Additionally, one electrode was fixed to the duodenum in one of the dogs.

The control group included three dogs. Three bipolar electrodes were implanted into the stomach, duodenum and the initial part of the jejunum at a distance of 30 cm distal from the Treitz ligament. The electrodes were fixed to special subcutaneous 12-pin connectors on the back of the animals, thus allowing free movement. After 1-4 months of recovery and 1 to 3 years later each animal had recordings of mioelectrical activity.

At 1-4 months mucosal bioplates of the "transplant" were taken through the implanted fistula. At 1.5 and 3 years, laparotomy was performed and some pieces of the transplant and jejunal fragments above and below it were dissected. Samples were studied by hematoxylin-eosin, Van Gison staining and PAS-reaction for mucus determination.

**Electromiography**

Electrodes "PEG-8" (1,2 mm diameter, 5 mm apart, Co-Cr-Ni-Mc-Ta alloy) were connected to an amplifier. The output signals were transformed to digital form and entered in an IBM PC AT computer. A fast Fourier transform (FFT) algorithm was used to obtain the frequency power spectra of electrical signals. The Fourier analysis is a mathematical technique to describe a nonsinusoidal periodic waveform as the sum of several sinusoidal waveforms. The FFT method can provide a power spectrum that gives the frequencies of stomach and small intestine and displays the intensity of all frequency components in the signals. The significant frequency components appear as large peaks on the basal frequency. Studies of spike activity were carried out by visual inspections of recorded signals and processing on nonlinear filtering algorithm.

**Results**

**Electrophysiology**

Slow waves were demonstrable in all the studied areas of the gastro-intestinal tract in control animals.
The spectrum analysis showed a slow wave frequency (SWF) of 0.05-0.1 Hz, 0.30-0.32 Hz and 0.27-0.29 Hz, in the stomach, duodenum and jejunum, respectively. The frequency gradient of SW in the small bowel was in the oral direction. SWF and SW gradient did not show any change after meals.

During the 1st month after transposition, large peaks with a frequency of 0.08 Hz (typical for the stomach), appeared in the gastric stump and the graft. The power spectrum (fig. 2) in the signal of the graft displayed the fundamental SWF (0.08 Hz) together with an integer multiple harmonic of the fundamental SWF (0.16 Hz and 0.24 Hz). In contrast to the controls, an increase of the SWF (0.30-0.32 Hz) was observed in the jejunum above the graft while the SWF distal to the graft tended to decrease (0.20-0.23 Hz).

After 1 and 2 years following the transposition, the SWF remained unchanged in all the studied areas of the gastro-intestinal tract. Action potentials recorded from the graft after two years of transposition are shown in fig. 3. In contrast, by 3 years following transplantation, no differences in the SWF from the different areas could be appreciated. It is interesting that feeding caused a decrease in the SWF (10%) of the jejunum proximal and distal to graft. The SWF of the graft was not changed after meals.

Four different types (fig. 4, table I) of electrical activity were observed when comparing the SWF between duodenum and jejunum in the controls and between duodenum and proximal jejunum to the graft in transplanted animals. The classification arises from the theory of synchronization of coupled auto-oscillators applied to small bowel.

1. Synchronization. Frequencies are the same and phase lags are constant (fig. 4A).
2. Non-synphase oscillations. Frequencies can be

![Power spectrum of the electrical signal of the graft after the first month.](image)

![Electrical activity of the graft (slow waves and action potentials) after the second year.](image)

![Basic types for synchronization of the electrical activity measured in mv (vertical axis) between duodenum (top bars) and proximal jejunum (bottom bars) adjacent to the graft (after the 3th year).](image)

<table>
<thead>
<tr>
<th>Table I</th>
</tr>
</thead>
<tbody>
<tr>
<td>Types of electrical activity observed when comparing the SWF between duodenum and jejunum in the controls and between duodenum and proximal jejunum to the graft in transplanted animals (Percent from total values)</td>
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</tbody>
</table>

<table>
<thead>
<tr>
<th>Electrical activity</th>
<th>Transplant fasted state</th>
<th>Transplant fed state</th>
<th>Control fasted state</th>
<th>Control fed state</th>
</tr>
</thead>
<tbody>
<tr>
<td>1. Synchronization</td>
<td>56.2%</td>
<td>24.7%</td>
<td>98.8%</td>
<td>94.7%</td>
</tr>
<tr>
<td>2. Non-synphase oscillations</td>
<td>35.9%</td>
<td>37.5%</td>
<td>11.2%</td>
<td>0%</td>
</tr>
<tr>
<td>3. Quasistochastic oscillations</td>
<td>7.9%</td>
<td>5.7%</td>
<td>0%</td>
<td>5.3%</td>
</tr>
<tr>
<td>4. Alternative synchronization</td>
<td>0%</td>
<td>32.1%</td>
<td>0%</td>
<td>0%</td>
</tr>
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distinguished and phase lags are changed within each period (fig. 4B).

3. Quasistochastic oscillations. Oscillations in duodenum are relatively stable but show large variations in jejunum (fig. 4C).

4. Alternative synchronization. Similar to type 1 but with changes in the phase lag (fig. 4D).

As shown in table 1, type 1 dominated throughout the duodenum and proximal jejunum during the fasted and fed states and occupied over 90% of the total recording time in the control group. Furthermore, the gastric graft implantation resulted in various types of electrical activity. Type 1 dominated only during the fasted state and occupied 56.2% of the total recording time. The most striking feature after meals was the presence of type 4.

In all cases, SW oscillations in the graft did not synchronize with oscillations of the upper part of an intestine. This was supported not only by frequency differences but also by randomness of distribution for phase lags of the recorded signals.

Morphology

Signs of gradual transformation of the structure of the gastric epithelium were observed. During the first month after transposition, gastric pits lengthened, their lumen deformed and dilated and some of them became branched and covered with a high cylindrical mucin-secreting epithelium. Cystic dilatations of single gastric glands were seen. Mucin-secreting function of the glands was preserved as confirmed by positive PAS-reaction (Fig. 5). “Gross gastric folds” were formed by branching of gastric pits.

During the next months (1 to 4) a tendency to the atrophy of gastric glands was observed. Epithelium covering the gastric pits formed deep “papillae” and there was a decrease of secretion and focal atrophy of glands. Mucus was present in fundic glands. The lamina propria of the gastric mucosa was moderately infiltrated by round-cell epithelium.

The dissection of the transplant after 1.5 year revealed the preservation of a folded gastric mucosa, of rosy color, with no ulceration or hemorrhagy. The mucosa of the graft formed deep micropapillae. Mucin-secreting function decreased at the site of anastomosis.

In the wall of the gastric tubular transplant implanted in the small bowel mucosal folds were grossly hypertrophical, because of branching and lengthening of gastric pits, micropapillae were formed, covered with high cylindrical mucin-secreting epithelium, which was verified by PAS-reaction. In the lamina propria a moderate lymphocyte and histocyte infiltration was observed. The architecture of the gastric glands was preserved with presence of main and parietal exocrinocytes. In submucosal and muscular layers of the gastric transplant there was evidence of oedema and separation of muscle fibres (fig. 6).

Fig. 5.—Microphotograph of the mucosal biopate of the graft from the body of the stomach after the first month. (a) General view (H & E, 0.2x); (b) Deformation and branching of the gastric pits; (H & E, 10x).

Fig. 6.—Macropreparation of the graft after 1.5 years. General view.

Within the anastomotic zone (between the gastric transplant and the small bowel) a single gastric pit lengthened throughout the bulk of the mucosa; it has dendritic form associated with preserved structure of gastric glands and of intestinal mucosa villi. Covering columnar epithelium decreased the mucin-secreting capacity (fig. 7).

The small bowel mucosa preserved its architecture. Intestinal villi were foliated, they adjoin closely, covered with high columnar epithelium, though with decreased mucin secretion, seen as a dark narrow fine strip. The muscular layer was featured by edema, smooth muscle cell distrophy and focal necrobiosis. Coagulation necrosis of smooth muscle cells, preferentially of inner muscular layer of the bowel wall without signs of associated inflammatory infiltration was present.

Histological evaluation of long-term effects gastric tube implanted into a small bowel in 3 years revealed preserved architecture of the gastric wall, which consisted normally of mucosa, submucosal layer, muscle layer and serosa (fig. 8).
It turned out that thickness of mucosa appeared to be normal, gastric pits occupied about one quarter of it, covered with one-rowed plasmatic epithelium. Mucin-secreting function of the latter was preserved, PAS-reaction being positive. Some gastric pits closely adjoined. In the lamina propria under covering epithelium there was weak focal lymphocyte infiltration, capillaries being moderately dilated and filled with blood. The gastric proglads occupied the major part of the bulk of mucosa, located in aggregates in form of tubules and opened into the gastric pits. At the base of the gastric pits PAS-positive cells were located. In the muscularis plate a moderate lymphoid infiltration associated with the formation of solitary lymphoid follicules was seen. In the submucosal layer there were fine collagen filament; some small arteries with collapsed lumina and moderately dilated venulae, their lumen filled with free located red cells. Smooth muscle cells of the inner and middle muscle layers presented foci of dystrophy. Dystrophic changes of gastric smooth cells might be connected with adaptation of muscle fibers to the bowel peristalsis.

In general, the results obtained suggest that morphological alterations in the gastric transplant are consistent with compensatory and adaptive transformation. These changes initiate and localize in gastric pits that form micropapillae resembling small bowel villi. The mucin-secreting function of the covering epithelium of gastric pits is not disturbed and the gastric glands preserve their structure.

Discussion

The various surgical approaches to the treatment of SBS patients still remain controversial. Long term TPN is associated to several complications. The lack of oral feeding may cause intestinal mucosa atrophy, and development of a malabsorption syndrome that increases the risk of unfavourable outcome. Surgical transplantation is recommended in some cases when TPN is not feasible or grave complications develop in SBS patients. However, in spite of accumulated positive clinical experience, numerous obstacles remain, including technical difficulties, graft rejection and impaired graft function as most common complication. Use of immunosupressors such as cyclosporine, FK-506 and prostaglandine El has allowed in the last years successful small bowel transplantation plus liver transplantation.

Besides small intestine transplantation, intensive search is in progress in an attempt to surgically increase the absorptive surface area using the remaining small bowel fragment or intact parts of the digestive tract, colon in particular. However, at the time being, no procedure has proved to be both safe and effective to justify a recommendation for its clinical use.

In view of the experimental and clinical experience we made an attempt to increase the absorptive surface area of the small bowel by lengthening the resected intestine with interposition of tubular grafts taken from the greater curvature of the stomach in chronic long-term experiments (1 to 3 year) in dogs. This animal model foresees atwo stage surgical interventions: the graft formation and the implantation of the graft.
into the intestinal defect 2-3 month later. Long-term control of the graft was carried out by observation of the electrical activity and morphological adaptations in the transplanted gastric tissue.

As it is known tubular gastric grafts are most often used in reconstruction of esophagus. In this technique, a significant impairment of blood circulation in the gastric graft, restoration of acid production and substantial microstructural transformation are common. These changes are characterized by mucosal atrophy (irregular epithelial desquamation and proliferation), the thinning of the muscle layer and the thickening of the submucosal layer. Nevertheless, many patients could benefit from the transplanted esophagus.

Gastric tissue is often used in pediatric urology to cover the bladder defect. However, this graft, very convenient as muscular patch, is not adequate because of its preserved acid secretion. Artificial bladder sphincters constructed of gastric tissue have been successfully utilized in dogs. Histological investigations revealed well preserved and native cells of the stomach and a phenomenon of hyperplasia directed from the gastric flap to the bladder after 12 months.

The present study demonstrated that electrical activity of the gastrointestinal tract changes significantly after the transplantation of a stomach part in small intestine. Pandolfo et al. have also reported an altered motility pattern of the jejunum in cancer patients with esophago-gastro-plasty after esophagectomy. A large difference of SW frequencies between the upper and lower parts of the intestine was observed both in fasted and fed conditions. External innervation was kept in our model. Therefore the development of a frequency jump in parts adjacent to the nervous system (that can not be observed in control animals) indicates that the main role in SW propagation is exerted by the smooth muscle tissue.

After meals, a 10% reduction of the SW frequency both in the jejunum proximal and distal to the graft was observed, while frequency in the graft remained constant. Changes took place before a real inflow of chyme in the graft tube; that is, the reaction could be initiated by the preserved external innervation and the humoral control. Only one minute after starting of oral feeding, the transition in the abnormal synchronization regime between duodenum and proximal jejunum adjacent to the graft was set up and the intensification of the spike activity was noted in the small intestine. Most probably, feeding stimulates secretion not only in the gastric stump, but in the gastric graft as well, and the graft releases a quantity of HCl that increases the electrical activity in the adjacent part of the small intestine. This coincides with the finding that an injection of HCl into the duodenum intensifies the activity of both duodenum and the proximal part of the jejunum. The response here found would be caused by the penetration of gastric secretion from the graft into the small intestine and duodenum. In fact, transplantation of the small bowel does not cause a decrease in the SWF.

The SWF of the gastric graft corresponds to the frequency of the native stomach, does not depend upon and is not associated with adjacent parts of intestine. This is consistent with the data of other authors who reported an absence of coordination (synchronization) between the intact duodenum and the transplanted jejunouileum after an autotransplantation. It is also known that contractions recorded in the graft after a heterotransplantation do not depend upon a myoelectrical activity of the native bowel.

The present study also demonstrated that in the period of three years the morphological criteria of adaptation of the gastric tissue implanted into the small intestine mainly concerned the epithelium covering the gastric pits. These appeared substantially lengthened, dilated and distorted with “pseudovilli” formation, though the mucin-secreting function of the gastric graft was preserved. Apparently, muscle layers dystrophy of the graft serves the purpose of adaptation to the propulsive action of the small intestine.

In summary, the stomach graft transplanted to the small intestine keeps the properties of gastric tissue, there are functional adaptations to conditions of digestion in the small intestine and the graft has minimal effects on intestinal motility. Increases of the absorptive surface area with tubular gastric grafts constitute an open alternative to surgical therapy of SBS.

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References


