Brazilian Journal of Medical and Biological Research (1997) 30: 1257-1266
ISSN 0100-879X

Gastroduodenal resistance and neural mechanisms involved in saline flow decrease elicited by acute blood volume expansion in anesthetized rats

J.R.V. Graça[1], F. de-A.A. Gondim[1], D.I.M. Cavalcante[1], J. Xavier-Neto[2], E.L.M. Messias[1], M.C.V. Rego[1], J.A.P. Marques[1], A.A. Santos[1] and F.H. Rola[1]

[1]Departamento de Fisiologia e Farmacologia, Universidade Federal do Ceará, Fortaleza, CE, Brasil
[2]Laboratório de Biologia Molecular, Instituto do Coração (INCOR), Faculdade de Medicina, Universidade de São Paulo, São Paulo, SP, Brasil

Abstract

We have previously demonstrated that blood volume (BV) expansion decreases saline flow through the gastroduodenal (GD) segment in anesthetized rats (Xavier-Neto J, dos Santos AA & Rola FH (1990) *Gut*, 31: 1006-1010). The present study attempts to identify the site(s) of resistance and neural mechanisms involved in this phenomenon. Male Wistar rats (N = 97, 200-300 g) were surgically manipulated to create four gut circuits: GD, gastric, pyloric and duodenal. These circuits were perfused under barostatically controlled pressure (4 cmH_2O). Steady-state changes in flow were taken to reflect modifications in circuit resistances during three periods of time: normovolemic control (20 min), expansion (10-15 min), and expanded (30 min). Perfusion flow rates did not change in normovolemic control animals over a period of 60 min. BV expansion (Ringer bicarbonate, 1 ml/min up to 5% body weight) significantly ($P<0.05$) reduced perfusion flow in the GD (10.3 ± 0.5 to 7.6 ± 0.6 ml/min), pyloric (9.0 ± 0.6 to 5.6 ± 1.2 ml/min) and duodenal (10.8 ± 0.4 to 9.0 ± 0.6 ml/min) circuits, but not in the gastric circuit (11.9 ± 0.4 to 10.4 ± 0.6 ml/min). Prazosin (1 mg/kg) and yohimbine (3 mg/kg) prevented the expansion effect on the duodenal but not on the pyloric circuit. Bilateral cervical vagotomy prevented the expansion effect on the pylorus during the expansion but not during the expanded period and had no effect on the duodenum. Atropine (0.5 mg/kg), hexamethonium (10 mg/kg) and propranolol (2 mg/kg) were ineffective on both circuits. These results indicate that 1) BV expansion increases the GD resistance to liquid flow, 2) pylorus and duodenum are important sites of resistance, and 3) yohimbine and prazosin prevented the increase in duodenal resistance and vagotomy prevented it partially in the pylorus.

Key words
- Blood volume expansion
- Gastroduodenal resistance
- Duodenum
- Pylorus
- α-Blockers
- Vagotomy

Correspondence
F.H. Rola
Departamento de Fisiologia e Farmacologia
Universidade Federal do Ceará
Rua Coronel Nunes de Melo, 1127
Caixa Postal 3157
60430-270 Fortaleza, CE
Brasil
Fax: 55 (085) 243-9333
E-mail: gondimfranc@sec.secrel.com.br

This work was presented at the IX and X Annual Meetings of the Federação de Sociedades de Biologia Experimental, Caxambu, MG, Brasil, 1994 and 1995, and at the 5th United European Gastroenterological Week, Paris, France, 1996, and reported in abstract form (1).

Research supported by CNPq, CAPES, UNIMED and UFC. Publication supported by FAPESP.

Received January 10, 1997
Accepted August 19, 1997

Introduction

There is increasing evidence indicating that the gastrointestinal (GI) tract is an active regulator of the homeostatic response to volume imbalance, i.e., acute blood volume changes modify the GI motor function (1-7) as well as its permeability to salt and water (8,9).

The overall GI response to volume imbalance is unknown, but it can be significant, since the human gut can handle about 20 l of fluid daily (10). Several lines of evidence

also indicate that decreased jejunal absorption elicited by increased uretero-pelvic pressure may be important to manage increased body fluid volume (11). Besides changing absorption and secretion (8,9), the integrated GI response to a volume challenge could conceivably involve adjustments in the relationship between luminal fluid and epithelial surface area, as well as in motor patterns which could maximize net absorption or secretion after blood volume (BV) retraction and expansion, respectively.

In this respect, we first demonstrated that gastric and jejunal compliances are modified by acute volemic changes (2,3). We have also observed that gastroduodenal (GD) resistance to the liquid flow is increased after BV expansion in rats and dogs (4,5). In the present study we utilized a rat model (4) to further detail the GD resistances (stomach, pylorus and duodenum) and the neural mechanisms involved in the GD flow decrease due to BV expansion.

Material and Methods

Surgical procedures

Male Wistar rats (200-300 g) were fasted for 24 h and allowed free access to water before surgery. The animals were anesthetized with urethane (1.2 g/kg, intraperitoneal) and a cannula was inserted into the trachea to ensure free breathing. The right carotid artery and the left jugular vein were cannulated with a polyethylene tube (PE 50) for mean arterial pressure (MAP) measurements and to perform BV expansion, respectively. The design and methodology employed were essentially the same as described by Xavier-Neto et al. (4), which have been extensively utilized in other studies (4,5,12). The abdomen was opened through a midline incision and the gastroduodenal segment was handled to create four different perfusion circuits (Figure 1).

Group A (Figure 1A): gastroduodenal perfusion (N = 9). A polyethylene cannula (O.D. = 3 mm, I.D. = 1.5 mm) was introduced into the gastric fundus *per os* and fixed with a ligature around the cervical esophagus, while another cannula (O.D. = 4 mm, I.D. = 2 mm) was inserted into the duodenum through a fistula and the tip was then positioned 2.5 cm from the pylorus and fixed with a ligature.

Group B (Figure 1B): gastric perfusion (N = 10). A polyethylene cannula (O.D. = 3 mm, I.D. = 1.5 mm) was placed in the proximal portion of the stomach as in group A and a second cannula (O.D. = 4 mm, I.D. = 2 mm) was positioned in the gastric antrum through a fistula located in the duodenum 1.0 cm from the pylorus and fixed with a duodenal ligature.

Group C (Figure 1C): pyloric perfusion (N = 10). A polyethylene cannula (O.D. = 3 mm, I.D. = 1.5 mm) was placed in the stomach immediately before the pylorus through a fistula located in the gastric fundus region. A second polyethylene cannula (O.D. = 4 mm, I.D. = 2 mm) was advanced through a duodenal fistula, and the tip was positioned immediately after the pylorus, approximately 1 cm after the first cannula. To avoid twisting, the cannulas were exteriorized through two lateral abdominal incisions.

Group D (Figure 1D): duodenal perfusion (N = 9). The proximal duodenum received an oral cannula through a fistula (O.D. = 4 mm, I.D = 2 mm) which was positioned 1 cm beyond the pylorus. A second duodenal cannula (O.D. = 4 mm, I.D = 2 mm) was also fixed 3 cm below the oral cannula. Both cannulas were fixed with a ligature around the duodenum.

Perfusion system

Figure 1 shows that both the oral and aboral free ends of the cannula were connected to the bottom of liquid reservoirs (barostats). The system was filled with isotonic saline (0.9 g% NaCl) and an oral to

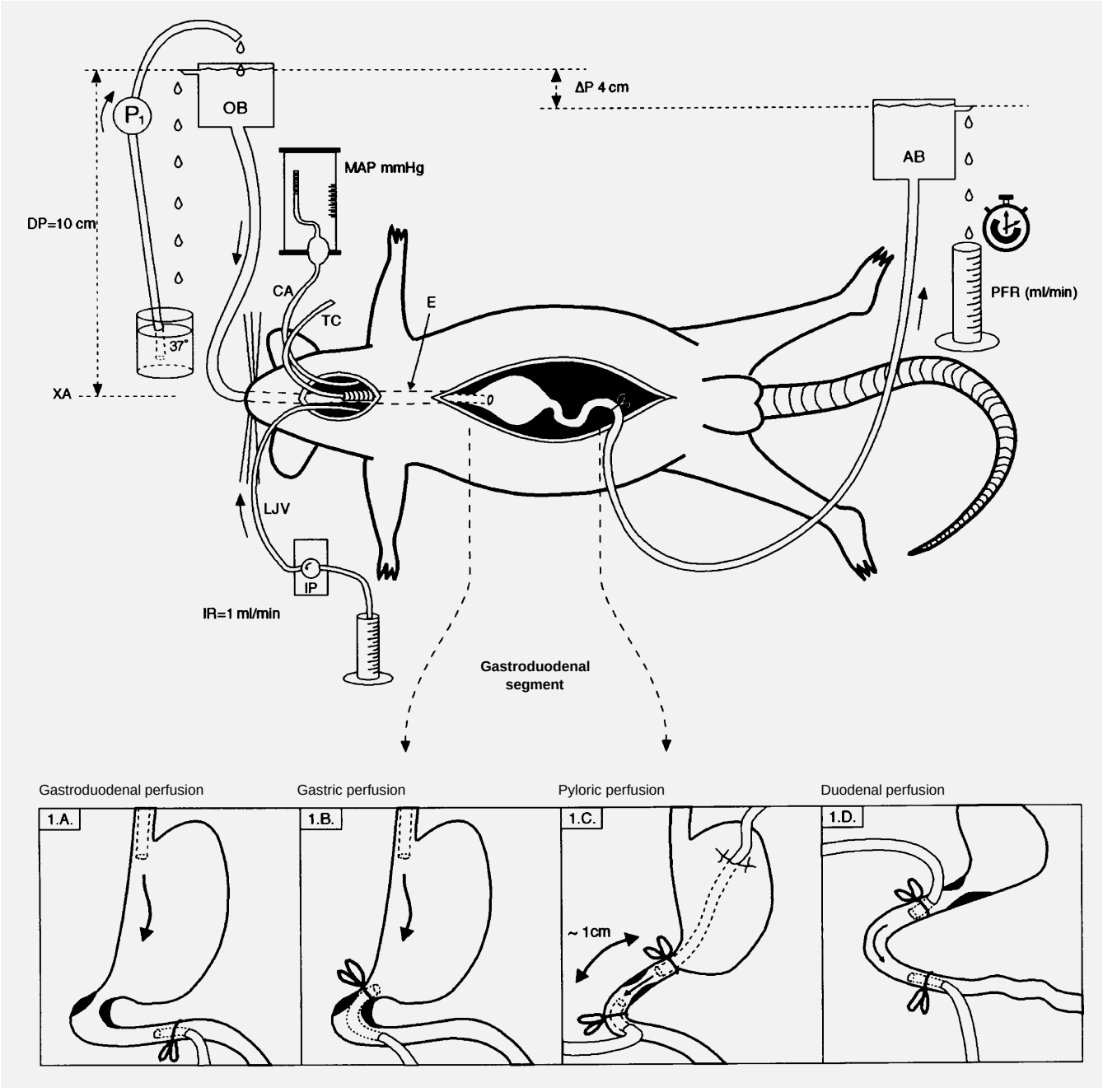

Figure 1 - Schematic representation of the communicating vessel system designed to perfuse at a constant pressure the gastroduodenal segment as a whole and its gastric, pyloric and duodenal portions in anesthetized rats. CA refers to carotid artery, MAP to mean arterial pressure, LJV to left jugular vein, IP to infusion pump, IR to infusion rate, PFR to perfusion flow rate, TC to trachea and E to esophagus. Four gut perfusion circuits were surgically created: *1.A.*, gastroduodenal; *1.B.*, gastric; *1.C.*, pyloric and *1.D.*, duodenal. OB and AB refer to oral and aboral barostats and XA to xiphoid appendix. The oral barostat level was kept constant by pumping back (P1) the saline flowing out of it by leakage. The aboral barostat level was also kept constant by leakage. In this system the only resistance which could vary was the gut circuit being perfused. DP is the distance from the barostat level to the xiphoid appendix and ΔP the gradient of pressure created by the difference in height between the oral and aboral barostats.

aboral flow was driven by a constant gradient of 4 cmH_2O in all groups. This gradient was established by setting the liquid level of the oral barostat connected to the gastric cannula (in groups A, B and C) or to the oral duodenal cannula (in group D) 10 cm above the xiphoid appendix, while keeping the liquid level of the aboral barostat 6 cm above the xiphoid appendix. The liquid level of the oral barostat was kept constant by pumping back the liquid flowing out of it by leakage. The liquid level of the aboral barostat was also kept constant by leakage.

The perfusion temperature was maintained at 37ºC by previously circulating the saline solution through a heated water bath. The perfusion saline volume flowing off the aboral barostat perfusion was collected and measured every 2 min as perfusion flow (PF) rate (in ml/min). In this communicating vessel system the only resistance which could vary was the segment being perfused, and in the steady state the liquid flowing out of the aboral barostat reflects the resistance of the perfused segment.

Cardiovascular parameters

MAP was measured with an Hg manometer connected to the carotid cannula and zeroed with the normal *ictus cordis*. Central venous pressure (CVP) was determined by positioning a PE 50 catheter in the right atrium via the jugular vein, before and after 5% expansion in a separate group of anesthetized animals (N = 5). The PE 50 catheter was connected to a water manometer also zeroed with the normal *ictus cordis*. Intracardiac samples were also collected for hematocrit determination in this group.

BV expansion

BV was expanded according to the protocol of Humphreys and Earley (13). Briefly, the animals were infused *iv* with Ringer bicarbonate solution (Na^+ = 140 mM, K^+ = 4 mM, Cl^- = 124 mM, HCO_3^- = 20 mM) at a rate of 1 ml/min up to a volume equivalent to 5% body weight.

Experimental design

PF rates and MAP levels were recorded every 2 min throughout the experiment in all groups. After 20 min (control period) the animals had their BV expanded by an *iv* infusion of Ringer bicarbonate solution at a rate of 1 ml/min up to a volume equivalent to 5% body weight, which was completed within about 10 to 15 min (expansion period). After expansion the animals were observed for an additional period of 30 min (expanded period). All groups had appropriate non-expanded, normovolemic time controls. In these experiments PF rates and MAP levels were measured for 60 min in the absence of BV expansion.

Neural mechanism investigation

After the first set of experiments, when we determined that pylorus and duodenum were the two main GD resistance sites activated by BV expansion, we selected the pyloric and duodenal circuits to start the neural mechanism investigation. After measuring pyloric and duodenal PF rates and MAP levels for 20 min (normovolemic control period), atropine sulfate (0.5 mg/kg; Sigma Chemical Co., St. Louis, MO), prazosin chloride (1 mg/kg; Pfizer, Guarulhos, SP), yohimbine hydrochloride (3 mg/kg; Sigma), propranolol hydrochloride (2 mg/kg; Sigma) or hexamethonium bromide (20 mg/kg; Sigma) was administered *iv*. Bilateral cervical vagotomy was also performed in another group. PF rates were monitored for 10 (prazosin and yohimbine) to 30 min (bilateral cervical vagotomy, atropine, propranolol or hexamethonium) (drug control period). After the drug control period, BV expansion with Ringer bicarbonate *iv* infusion in a volume up to 5% body weight was

performed and the PF rates and MAP levels were monitored during the expansion (10-15 min) and expanded periods (30 min).

Statistical analysis

Data are reported as means ± SEM. One-way analysis of variance of repeated measures (ANOVA) and the Dunnett's test were used to compare different groups (Sigma Stat for Windows, version 1.0, Copyright 1992-1994, Jandel Corporation (San Rafael, CA). Comparisons between experimental groups and their respective time controls were made using equivalent time periods. Statistical differences were considered to be significant at $P<0.05$.

Results

Effect of BV expansion on GD, pyloric, duodenal and gastric PF rates and MAP levels

Figure 2 shows the changes in GD, gastric, pyloric and duodenal perfusion flows during the experiments in time control animals and in animals submitted to BV expansion (up to 5% body weight) after the 20-min

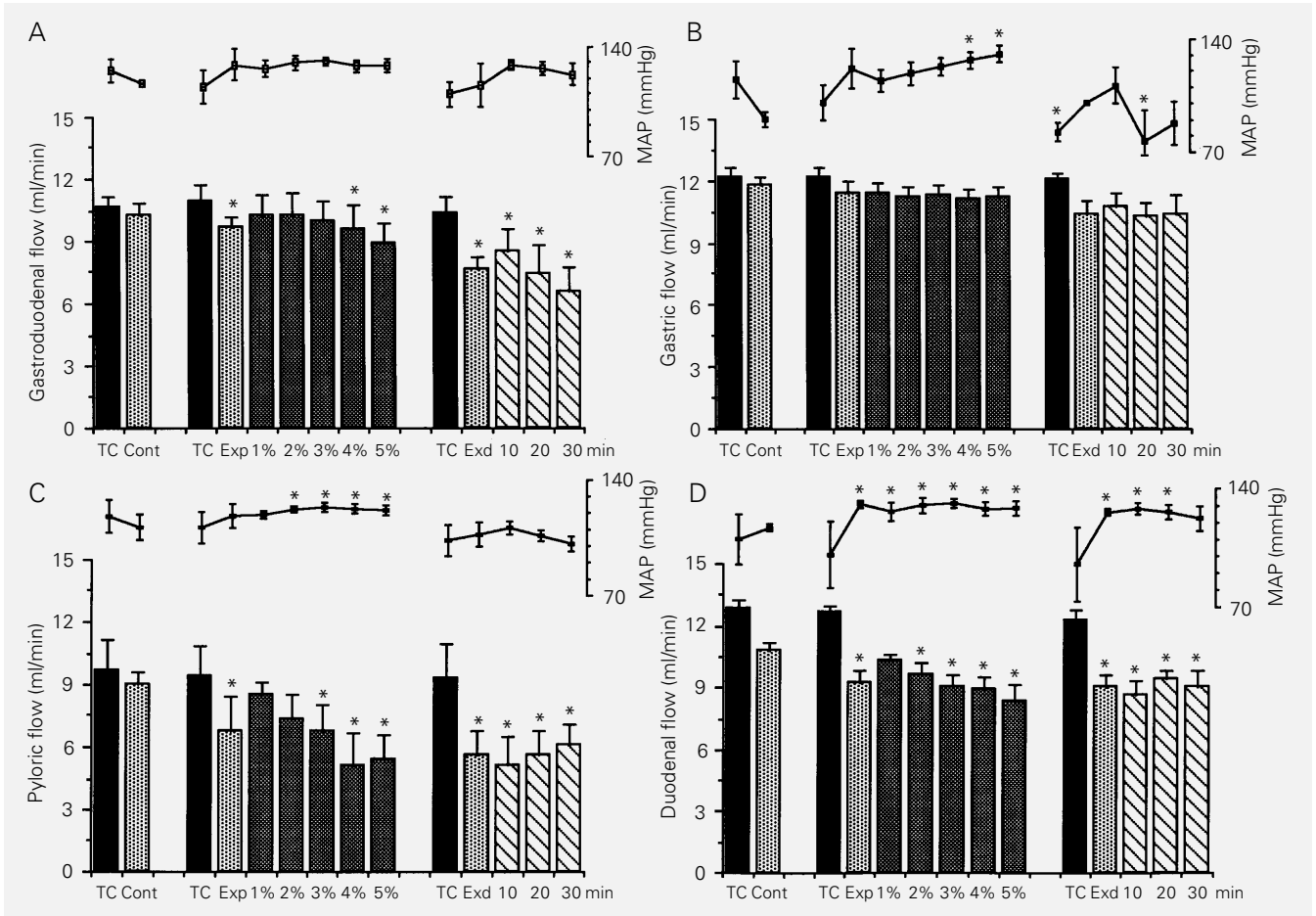

Figure 2 - Modifications in gastroduodenal (A), gastric (B), pyloric (C) and duodenal (D) perfusion flow (PF) rates and mean arterial pressure (MAP) in normovolemic time controls and in animals submitted to blood volume (BV) expansion. TC (black bars) refers to time control animals (N = 5, 5, 5 and 4 for GD, gastric, pyloric and duodenal PF rates, respectively) during the 60-min observation period, which was divided into three parts (corresponding to the control, expansion and expanded periods of experimental animals). The control (Cont), expansion (Exp) and expanded (Exd) periods were also divided in experimental animals (N = 5 for each circuit). Expansion was divided into five parts according to the amount of volume infused (up to 1, 2, 3, 4 and 5% of body weight). The expanded period was divided into three parts: 10, 20 and 30 represent the PF rates in the first 10, middle 10 and in the last 10 min of the 30-min expanded period. Vertical lines represent the SEM. *$P<0.05$ compared to control levels (Dunnett's test).

normovolemic control period.

PF rates for normovolemic time controls were quite stable throughout the experiments (60 min) in all the perfusion circuits studied. PF rates for the first 20, middle 10 and last 30 min of time control experiments were 10.6 ± 0.5, 10.9 ± 0.8, 10.4 ± 0.7; 12.2 ± 0.4, 12.2 ± 0.4, 12.1 ± 0.3; 9.7 ± 1.4, 9.4 ± 1.4, 9.3 ± 1.6 and 12.8 ± 0.4, 12.6 ± 0.3, 12.3 ± 0.4 ml/min for GD, gastric, pyloric and duodenal perfusion, respectively ($P>0.05$ for all groups). MAP levels were also quite stable throughout the experimental period in time control animals.

We can also see in Figure 2 that BV expansion significantly decreased the GD, pyloric and duodenal saline flow rates. The gastric perfusion circuit did not respond to BV expansion. In the GD and pyloric segments, decreases in flow started during expansion and were fully developed after expansion was completed. In the duodenal segment the effect of expansion was already maximal during the expansion period and remained as such until the end of the experiment. PF rates in the three periods (normovolemic control, expansion and expanded) were 10.3 ± 0.5, 9.7 ± 0.5, 7.6 ± 0.6, $P<0.05$; 11.9 ± 0.4, 11.4 ± 0.6, 10.4 ± 0.6, $P>0.05$; 9.0 ± 0.6, 6.8 ± 1.6, 5.6 ± 1.2, $P<0.05$, and 10.8 ± 0.4, 9.2 ± 0.6, 9.0 ± 0.6 ml/min, $P<0.05$, for GD, gastric, pyloric and duodenal perfusion, respectively. The mean PF rate decreases during the expanded period in the GD, gastric, pyloric and duodenal circuits were 26.2%, 12.6%, 37.7% and 16.7%, respectively.

Figure 2 also shows that MAP levels were only transiently increased during the expansion and expanded periods in the GD, gastric and pyloric circuits. In the duodenal circuit, however, MAP levels were consistently increased during the expansion and expanded periods (from 117.0 ± 1.9, control, to 131.0 ± 1.8, expansion, $P<0.05$, and to 126.0 ± 1.8 mmHg, expanded, $P<0.05$).

Figure 2 also details the development of flow changes as a result of increased percentage of infused volume (up to 1-5% body weight). The GD flow gradually decreased during the expansion period, reaching statistical significance at 4% body weight expansion and remained below control levels throughout the expanded period. Gastric flow did not change during BV expansion. The pyloric flow also gradually decreased and attained statistical significance at 3% body weight. This effect persisted until the end of the expanded period. The duodenal flow also decreased, attaining statistical significance even earlier, when BV expansion reached 2% body weight and again the effect persisted at least until the end of the expanded period.

Mean hematocrit values decreased from 49.3 ± 1.4% in normovolemic animals to 34 ± 1.1% after 5% expansion ($P<0.05$) and CVP levels increased from 3.6 ± 1.6 to 9.6 ± 3.2 cmH_2O after 5% expansion ($P<0.05$).

Neural mechanism investigation

Table 1 shows the PF rates in drug-pretreated or vagotomized animals before, during (expansion period) and after BV expansion was completed (expanded period). Hexamethonium, atropine and propranolol had no effect on the decrease of saline flow through the duodenal or pyloric circuits during the expansion and expanded periods. However, yohimbine and prazosin prevented the decrease of duodenal flow elicited by BV expansion in both periods, but did not prevent the decrease of pyloric flow in either period (Figure 3 and Table 1). Bilateral cervical vagotomy prevented the decrease of pyloric flow during the expansion but not during the expanded period, while it had no effect on the decrease in duodenal flow (Figure 3 and Table 1). Hexamethonium, atropine, propranolol, yohimbine and prazosin reduced MAP levels ($P<0.05$) while bilateral cervical vagotomy did not modify them.

Discussion

We have previously observed that gastric and jejunal compliances are modified by acute volemic changes in anesthetized dogs (2,3). In addition, we further demonstrated that the gastroduodenal resistance to liquid flow was modified by acute volemic changes: BV expansion decreased the gastroduodenal flow while retraction increased it (4,5). Recently, we have also extended these observations to the lower GI tract, i.e., the ileocolonic segment (6). This evidence leads us to speculate about the possible coupling between GI tract motility and intestinal water and sodium flux to correct the body fluid imbalance observed under these volemic conditions.

The present study confirms our previous findings in the rat (4) showing that BV expansion reduces saline flow through the GD segment perfused under barostatically controlled conditions. However, it further details the sites of resistance (pylorus and duodenum) and the neural mechanisms involved. In addition, it extends our observations to a less severe experimental protocol of BV expansion, since BV expansion was up to 5% body weight instead of the 10% expansion previously performed (4). The rat model utilized (4) appears to be an adequate experimental model to investigate the gastroduodenal resistances, with stable time controls and high reproducibility.

In the barostatically controlled system used in the experiments, changes in flow

Table 1 - Mean perfusion flow rates (duodenal and pyloric flows, ml/min) and mean arterial pressure (MAP, mmHg) levels in the animals submitted to bilateral cervical vagotomy or intravenous injection of yohimbine (3 mg/kg), prazosin (1 mg/kg), propranolol (2 mg/kg), atropine (0.5 mg/kg) or hexamethonium (10 mg/kg).

Cont refers to the control period before drug injection, Drug to the drug control period before expansion, Exp to the expansion period after drug injection and Exd to the expanded period after drug injection. Data are reported as means ± SEM of 4 animals in each group. *P<0.05 *vs* drug control period (Dunnett's test).

	Pylorus				Duodenum			
	Cont	Drug	Exp	Exd	Cont	Drug	Exp	Exd
Yohimbine								
Flow	14.1 ± 0.6	13.6 ± 0.6	12.2 ± 0.6*	8.8 ± 1.4*	12.2 ± 1.0	9.3 ± 0.7	11.0 ± 1.0	11.8 ± 0.8
MAP	112.9 ± 3.6	95.6 ± 4.5	116.1 ± 6.5	106.9 ± 4.7	114.6 ± 7.3	92.4 ± 8.9	102.9 ± 10.9	100.8 ± 6.3
Prazosin								
Flow	25.8 ± 1.1	22.1 ± 1.2	17.5 ± 1.5*	10.9 ± 2.3*	23.6 ± 0.8	25.0 ± 1.0	28.1 ± 1.8	21.5 ± 1.0
MAP	136.0 ± 6.9	100.0 ± 7.7*	103.0 ± 3.6*	99.5 ± 10.9*	116.5 ± 2.1	73.2 ± 13.0*	73.8 ± 7.0*	60.5 ± 13.5*
Propranolol								
Flow	26.3 ± 2.1	21.6 ± 1.5	13.7 ± 2.4*	11.7 ± 2.9*	32.6 ± 1.2	30.5 ± 1.7	28.1 ± 1.8*	27.6 ± 2.4*
MAP	105.9 ± 8.9	90.1 ± 7.2*	107.6 ± 9.0	111.7 ± 10.3	128.9 ± 8.1	100.1 ± 7.3*	133.8 ± 3.9	135.4 ± 4.5
Atropine								
Flow	11.8 ± 0.6	8.6 ± 0.5	4.1 + 1.6*	2.5 + 0.9*	28.9 ± 0.2	28.9 ± 0.9	24.5 ± 1.7*	22.7 ± 1.6*
MAP	115.6 ± 7.4	92.9 ± 19.3*	103.5 ± 7.3	106.2 + 8.1	117.8 ± 2.3	90.5 ± 5.0*	113.9 ± 7.1	109.1 ± 7.5
Hexamethonium								
Flow	13.0 ± 0.7	11.0 ± 1.1	8.1 ± 1.7*	7.2 ± 1.1*	27.2 ± 0.8	26.7 ± 1.0	23.5 ± 1.7*	24.2 ± 1.7*
MAP	122.8 ± 4.0	82.5 ± 10.0*	105.8 ± 7.5*	100.3 ± 5.9*	114.0 ± 5.5	58.9 ± 11.7*	80.4 ± 13.7*	71.8 ± 12.5*
Vagotomy								
Flow	26.2 ± 2.3	27.7 ± 2.1	24.6 ± 2.3	22.0 ± 0.7*	28.9 ± 0.1	30.5 ± 0.8	26.5 ± 1.0*	25.7 ± 1.5*
MAP	114.3 ± 10.2	104.1 ± 8.4	103.7 ± 12.9	106.6 ± 16.6	117.8 ± 2.3	98.5 ± 7.4	109.0 ± 4.7	105.0 ± 6.1

rates through the perfused segments may be due to alterations in resistance, capacitance or both. An increase in capacitance is a rather unlikely mechanism to explain flow reduction during BV expansion, since the volumetric capacity of the perfused segments (GD, gastric, pyloric and duodenal) is clearly lower than the amount of fluid used in the perfusion system (perfusion minute flow). Furthermore, in this experimental model, capacitance changes would have been transient and not long-lasting to determine the persistence of the decrease in the flow rates during both the expansion and expanded periods, as we observed. The increased resistance instead of the increased capacitance hypothesis is further supported by our own results showing that BV expansion is associated with reductions rather than with increases in gastric (2) or intestinal compliances (3).

The decrease in GD, pyloric and duodenal flow rates elicited by BV expansion (up to 5% body weight) seems to be a slowly progressing process, therefore being basically different from the fast effect previously reported by Xavier-Neto et al. (4). However, when we separately analyzed the evolution of flow rate changes against the percentage of BV expansion, we observed that the effect of BV expansion on the PF rates develops quickly, attaining statistical significance after infusion of volumes equivalent to 2 or 3% body weight in the duodenal and pyloric perfusions, respectively.

The relative importance of increases in pyloric *vs* duodenal resistance remains to be established. Duodenal resistance appears to

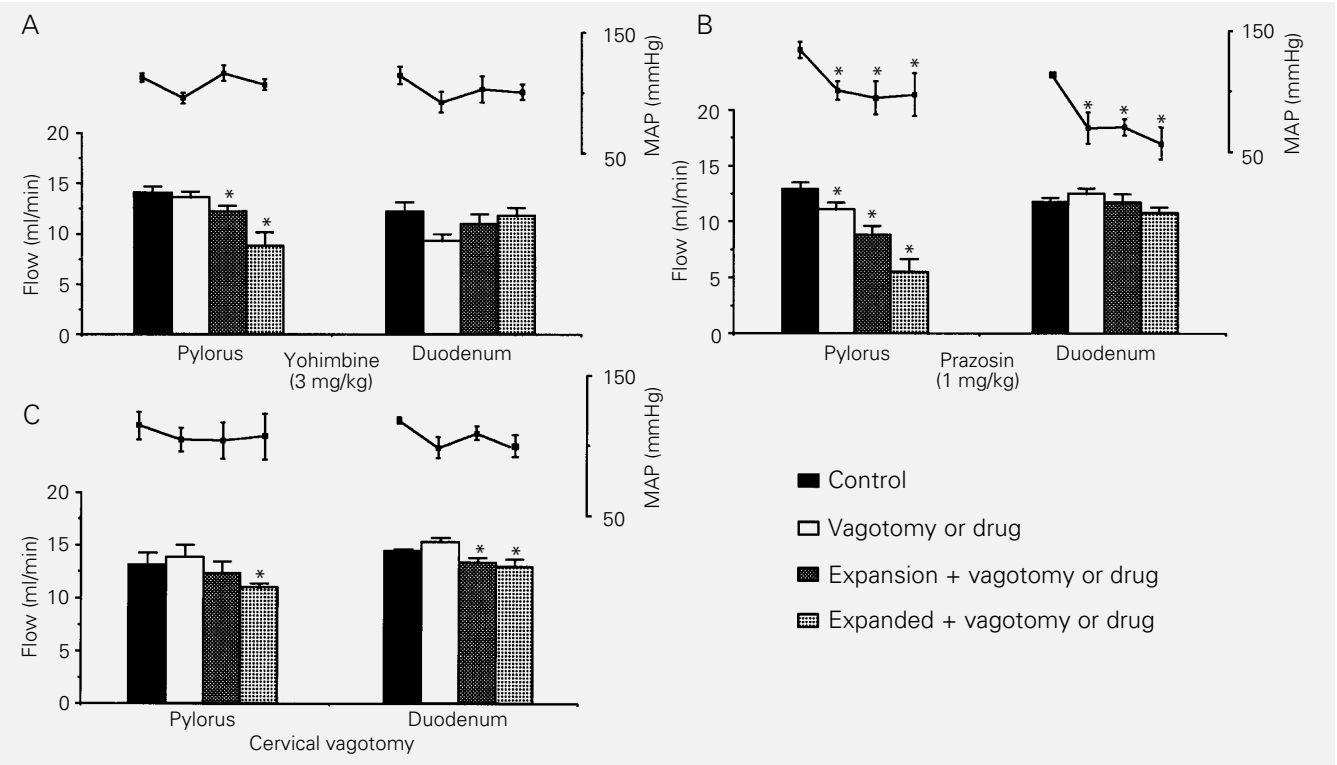

Figure 3 - Details of the effect of yohimbine (N = 5), prazosin (N = 5) and bilateral cervical vagotomy (N = 5) on the decrease in blood volume expansion-induced pyloric and duodenal perfusion flow (PF) rates and on mean arterial pressure (MAP) levels. After a 20-min normovolemic control period (control), yohimbine or prazosin was injected *iv* or bilateral cervical vagotomy was performed. After another control period (vagotomy or drug), the animals had their blood volume expanded up to 5% body weight (expansion + vagotomy or drug). This phase was followed by another 30 min of observation (expanded + vagotomy or drug). Bars represent mean PF rate in ml/min. Dots indicate MAP levels in mmHg and the vertical lines represent the SEM. *P<0.05 *vs* control levels (MAP) or *vs* vagotomy or drug levels (PF rates) (ANOVA and Dunnett's test).

be increased earlier by BV expansion (2% body weight) but, on the other hand, the increase in pyloric resistance appears to be greater. The data in Figure 2 suggest that isolated increases in duodenal resistance (as shown after 2% body weight BV expansion) are not sufficient to produce sustained reductions of flow in the GD segment. It is possible that stable reductions in GD flow are only observed when the combined contribution of pyloric and duodenal resistances is fully developed.

The flow decrease was more pronounced in the pyloric than in the duodenal circuit. This finding may be related to the peculiarities of the duodenal circuit, since coincidentally the duodenum was the only circuit where MAP levels were persistently increased, in contrast to the transient MAP changes observed in the other circuits. In fact, we also observed different patterns of MAP changes when we perfused separate parts of the ileocolonic segment, which we were unable to explain (6). The pyloric response was surprising, since we also observed that pyloroplasty did not abolish the effect of BV expansion on the gastric emptying of liquid in awake rats (14). The possible pyloric role in gastric outflow regulation is controversial, since the pylorus has not been widely accepted as an important site of resistance in the GD segment. However, our results are consistent with those of Edin et al. (12) who showed that the pylorus can act as a site of resistance to liquid flow, when barostatically perfused under controlled pressure gradients. The results also demonstrated that gastric resistance is not elicited by BV expansion. However, since the stomach was perfused as a whole, the lack of gastric response does not permit us to rule out a modification in compliance of the gastric fundus, which has mainly a reservoir function, since our experimental protocol is more apt to detect changes of resistance rather than compliance.

The hemodynamic data indicate that the effect of BV expansion on the PF rates does not correlate well with MAP level changes since reductions in liquid flow rate were maintained long after MAP returned to control levels in the pyloric and duodenal perfusion groups. CVP levels, however, were consistently increased and hematocrit values significantly decreased by BV expansion.

After establishing that the pylorus and duodenum were the main sites of resistance to saline flow activated by BV expansion, we decided to investigate the possible neural mechanisms involved in the flow decrease in these two circuits. Cholinergic pathways appear not to be involved, since atropine did not block the expansion effect. Interestingly, bilateral cervical vagotomy prevented the effect of expansion on the pylorus during the expansion period, but had no effect on the duodenum. These findings indicate that vagal pathways are necessary for the full expression of the effect of BV expansion on GI motility. However, a more precise definition of the vagal participation could not be obtained, since anesthesia *per se* interferes with vagal activity (15).

Yohimbine (an α-2 antagonist) and prazosin (an α-1 antagonist) prevented the decrease in duodenal PF rate during the expansion and expanded periods while propranolol (a ß-blocker) was ineffective. In fact, α adrenergic activation is known to mediate GI motility inhibition (16), i.e., clonidine (an α-2 agonist) delays small intestine transit in the rat (17) and reduces the amplitude of gastric phasic contractions (18). We do not know whether the effect of prazosin and yohimbine was peripheral or central. However, since hexamethonium was ineffective and expected to block a peripheral adrenergic activation, the results point to a central α-receptor activation or to an effect of prazosin and yohimbine on non-α receptors, such as imidazoline receptors, as also suggested by others (19).

In addition to a possible neural mechanism, increased CVP also leads to atrial

natriuretic peptide (ANP) release, which may interfere with GI motility and absorption. ANP increases the magnitude of spontaneous duodenal contractions (20) and reduces fluid and electrolyte absorption (21).

In summary, we conclude that 1) the GD segment appears to be a target region for volume-dependent modulation by increasing its resistance to liquid flow during and after BV expansion, 2) pylorus and duodenum are two important sites of resistance in the GD segment which are activated by BV expansion, and 3) α-adrenergic and vagal pathways appear to be involved in this phenomenon.

References

1. Da Graça JRV, Cavalcante DIM, Gondim F de AA, Oliveira GR, Rego MCV, Alencar HMP & Rola FH (1996). Neural mechanisms and gastroduodenal resistances to saline flow activated by acute blood volume expansion in awake rats. *Gut*, 39 (Suppl 3): 156 (Abstract).
2. Capelo LR, Cavalcante DM, Leitão IA, Cristino Filho G & Da-Silva EAT (1983). Modifications of gastric compliance in dogs related to changes of extracellular fluid volume: A possible physiological role. *Brazilian Journal of Medical and Biological Research*, 16: 73-76.
3. Rola FH, Santos AA, Xavier-Neto J, Cristino Filho G, Rocha CI, Santiago Jr AT, Gondim FAA, Pereira JM & Capelo LR (1989). Effects of acute volemic changes on the jejunal compliance in dogs. *Brazilian Journal of Medical and Biological Research*, 22: 523-531.
4. Xavier-Neto J, dos Santos AA & Rola FH (1990). Acute hypervolemia increases the gastroduodenal resistance to the flow of saline in rats. *Gut*, 31: 1006-1010.
5. Santos AA, Xavier-Neto J, Santiago Jr AT, Souza MAN, Martins AS, Alzamora F & Rola FH (1991). Acute volaemic changes modify the gastroduodenal resistance to the flow of saline in anaesthetized dogs. *Acta Physiologica Scandinavica*, 143: 261-268.
6. Santiago Jr AT, Gondim F de-AA, Cavalcante DIM, da-Graça JRV, de-Oliveira GR, Dos-Santos AA & Rola FH (1997). Acute extracellular fluid volume changes increase ileocolonic resistance to saline flow in anesthetized dogs. *Brazilian Journal of Medical and Biological Research*, 30: 999-1008.
7. Brummermann M & Braun EJ (1995). Effect of salt and water balance on colonic motility of white leghorn roosters. *American Journal of Physiology*, 268: R690-R698.
8. Duffy PA, Granger DN & Taylor AE (1978). Intestinal secretion induced by volume expansion in the dog. *Gastroenterology*, 75: 413-418.
9. Levens NR (1985). Control of intestinal absorption by the renin-angiotensin system. *American Journal of Physiology,* 249: G3-G15.
10. Guyton A & Hall J (1996). Digestion and absorption in the gastrointestinal tract. In: *Textbook of Medical Physiology*. 9th edn. W.B. Saunders, Philadelphia, Pennsylvania, 833-851.
11. Suzuki S, Khanchowdhury MR, Uemura N, Morita H & Hosomi H (1992). Renojejunal reflex controlling jejunal absorption of fluid and NaCl. *Journal of the Autonomic Nervous System*, 39: 219-228.
12. Edin R, Lundberg J, Terenius L, Dahlstrom A, Hokfelt T, Kewenter J & Ahlmin H (1980). Evidence for enkephalergic neural control of the feline pylorus and stomach. *Gastroenterology*, 78: 492-497.
13. Humphreys MH & Earley LE (1971). The mechanism of decreased intestinal sodium and water absorption after acute blood volume expansion in the rat. *Journal of Clinical Investigation*, 50: 2355-2367.
14. Rego MCV, Graça JRV, Gondim F de AA, Gondim RB de M, Dantas RP & Rola FH (1996). Role of proximal stomach and pylorus on gastric emptying and gastrointestinal transit delays elicited by acute blood volume expansion in awake rats. *Gut*, 39 (Suppl 3): 214 (Abstract).
15. Miolan JP & Roman C (1978). Discharge of efferent vagal fibers supplying gastric antrum: indirect study by nerve suture technique. *American Journal of Physiology*, 235: E366-E373.
16. Fargeas MJ, Fioramonti J & Bueno L (1986). Central α-2 adrenergic control of the pattern of small intestinal motility in rats. *Gastroenterology*, 91: 1470-1475.
17. Ruwart MJ, Klepper MS & Rush BD (1980). Clonidine delays small intestinal transit in the rat. *Journal of Pharmacology and Experimental Therapeutics*, 212: 487-490.
18. Bojo L, Nellgard P & Cassuto J (1992). Effects of selective adrenergic agonists and antagonists on gastric tone in the rat. *Acta Physiologica Scandinavica*, 142: 517-522.
19. Trostel KA, Kata SA & Osborn JW (1991). Does the spinal cord generate functionally significant sympathetic activity in the awake rat? *American Journal of Physiology*, 266: R1102-R1110.
20. Bayens DA, Walters JM & Vesely DL (1988). Atrial natriuretic factor increases the magnitude of duodenal spontaneous phasic contractions. *Biochemical and Biophysical Research Communications*, 155: 1437-1443.
21. Matsushita K, Nishida Y, Hosomi H & Tanaka S (1991). Effects of atrial natriuretic peptide on water and NaCl absorption across the intestine. *American Journal of Physiology*, 260: R6-R12.