Intensive Care Med (2001) 27: 1931–1936
DOI 10.1007/s00134-001-1138-9

EXPERIMENTAL

Arnaldo Dubin
Elisa Estenssoro
Gastón Murias
Héctor Canales
Pablo Sottile
Julio Badie
Marcelo Barán
Fernando Pálizas
Mercedes Laporte
Mariana Rivas Díaz

Effects of hemorrhage on gastrointestinal oxygenation

Received: 7 July 2000
Final revision received: 27 December 2000
Accepted: 20 September 2001
Published online: 10 November 2001

A. Dubin (✉) · E. Estenssoro · G. Murias · H. Canales · P. Sottile · J. Badie · M. Barán · F. Pálizas · M. Laporte · M. Rivas Díaz
Cátedra de Farmacología,
Facultad de Ciencias Médicas,
Universidad Nacional de La Plata,
calle 42 No 577, (1900) La Plata, Argentina
E-mail: adee@infovia.com.ar
Phone: +54-221-4220507
Fax: +54-11-48230283

Abstract *Objectives*: (1) To demonstrate that metabolic parameters are better indicators of tissue hypoxia than regional and whole oxygen consumption (VO_2). (2) To compare intramucosal pH (pHi) in different gastrointestinal segments.
Design: Prospective, interventional study.
Setting: Research laboratory at a university center.
Subjects: Fourteen anesthetized, mechanically ventilated dogs.
Interventions: Twenty milliliters per kilogram bleeding.
Measurements and main results: We placed pulmonary, aortic and mesenteric venous catheters, and an electromagnetic flow probe in the superior mesenteric artery, and gastric, jejunal and ileal tonometers to measure flows, arterial and venous blood gases and lactate, and intramucosal PCO_2. We calculated systemic and intestinal oxygen transport (DO_2) and consumption (VO_2), pHi and arterial minus intramucosal PCO_2 (ΔPCO_2). Then, we bled the dogs and repeated the measurements after 30 min. Systemic and intestinal DO_2 fell (26.0 ± 7.3 versus 8.9 ± 2.6 and 71.9 ± 17.3 versus 24.6 ± 9.6 ml/min per kg, respectively, $p < 0.0001$). Systemic and intestinal VO_2 remained unchanged (5.5 ± 1.3 versus 5.4 ± 1.3 and 15.7 ± 5.0 versus 14.9 ± 5.3 ml/min per kg, respectively). Gastric, jejunal and ileal pHi (7.13 ± 0.11 versus 6.96 ± 0.17, 7.18 ± 0.06 versus 6.97 ± 0.15, 7.12 ± 0.11 versus 6.94 ± 0.14, $p < 0.05$) and ΔPCO_2 (21 ± 13 versus 35 ± 23, 15 ± 5 versus 33 ± 16, 23 ± 17 versus 38 ± 20, $p < 0.05$) changed accordingly. Arterial and mesenteric venous lactate and their difference, rose significantly (1.7 ± 0.9 versus 3.7 ± 1.4 and 1.8 ± 0.8 versus 4.3 ± 1.5 mmol/l, 0.1 ± 0.6 versus 0.6 ± 0.7 mmol/l, $p < 0.05$).
Conclusions: During hemorrhage, systemic and intestinal VO_2 remained stable. However, hyperlactatemia and intramucosal acidosis evidenced anaerobic metabolism. pHi changes paralleled in the three intestinal segments.

Keywords Intramucosal pH · Tonometry · Shock · Oxygen consumption · Oxygen delivery · Lactate

Introduction

Many studies have analyzed the effects of different types of injury on intestinal oxygenation. Nelson et al. showed that, during progressive bleeding, intestinal oxygen uptake (VO_2i) is compromised early, even without changes in systemic VO_2 [1]. This limited ability for oxygen extraction makes the intestine suitable to track oxygen metabolism. Tissue oxygenation monitoring with tonometry, which measures gastrointestinal intramuco-

sal pH (pHi), has been reasonably established in recent years [2]. Grum et al. showed that intestinal pHi reductions correlated with gut VO_2 decreases [3]. Other investigators have demonstrated the prognostic significance of gastric intramucosal acidosis. [2, 4]. However, there is no definite evidence that gastric intramucosal acidosis resembles the intramucosal acidosis of other gut sections. Some studies have analyzed pHi behavior in different segments of the gastrointestinal tract [5, 6], but their results have been inconclusive.

Our goal was to describe the effects of hemorrhage on intestinal oxygenation. We tried to answer the following questions: (1) Are there traces of tissue hypoxia, evidenced as intramucosal acidosis, before the beginning of VO_2 dependence on DO_2? (2) What is the relationship between pHi and other parameters of intestinal and systemic oxygenation? (3) Are pHi reductions in stomach, jejunum and ileum equivalent?

Materials and methods

Animal preparation

This study was approved by the local animal care committee. Fourteen mongrel dogs, weighing 22.1 ± 3.1 kg (mean ± SD), were anesthetized with 30 mg/kg of sodium pentobarbital, with supplementary doses of 1 mg/kg given each hour or as necessary. They were intubated and ventilated with a volumetric respirator (Harvard Apparatus Dual Phase Control Respirator Pump Ventilator, model 613 A, Harvard Apparatus, Southnatick, Mass., USA), with a tidal volume of 15 ml/kg, FIO_2 of 0.21 and respiratory rate of 15/min. Neuromuscular blockade was provided by intravenous 0.06 mg/kg of pancuronium bromide. Ranitidine, 50 mg, was infused intravenously.

We advanced a Swan-Ganz catheter (flow-directed thermodilution fiberoptic pulmonary artery catheter model P 7110, Abbott Critical Care Systems, Mountain View, Calif., USA) into the pulmonary artery through the right external jugular vein to measure pressures and to sample blood. Catheters were placed in the left femoral artery and vein to measure mean arterial pressure (MAP), to administer drugs and fluids, and to perform bleeding. A gastric tonometer was placed in the stomach to measure pHi and its position was checked manually through palpation.

After a midline laparotomy had been performed, a splenectomy was carried out to prevent autotransfusion. The superior mesenteric artery was dissected and an electromagnetic flow probe was placed around it. A catheter was advanced through a small mesenteric proximal vein to the intestine into the superior mesenteric vein to sample blood. Two small enterotomies were performed to place jejunal and ileal tonometers. After careful hemostasis, the abdominal contents were returned to the cavity and the abdomen was closed.

Measurements and calculations

Mean arterial pressure (MAP) was measured (Statham P23 AA, Statham, Hato Rey, Puerto Rico) and registered (Gould RS 3400, Gould, Cleveland, Ohio, USA) through the whole experiment. Cardiac output (CO) was measured in triplicate by thermodilution using 5 ml of saline at 0 °C (Oximetrix SO_2/CO Computer, Abbott Laboratories, North Chicago, Ill. USA). CO was indexed to body weight. Superior mesenteric artery blood flow (SMAF) was measured with an electromagnetic probe (Spectramed Blood Flowmeter model SP 2202 B, Spectramed, Oxnard, Calif., USA) and is related to gut weight.

Arterial, mixed venous and mesenteric venous PO_2, PCO_2 and pH were measured with a blood gas analyzer (ABL 30, Radiometer, Copenhagen, Denmark). Hemoglobin and oxygen blood saturations (% HbO_2) were measured by using a co-oximeter calibrated for canine blood (OSM 3, Radiometer, Copenhagen, Denmark). Arterial, mixed venous and mesenteric venous contents (CaO_2, CvO_2 and $CmvO_2$) were calculated as $Hb \times 1.34 \times \%HbO_2 + PaO_2 \times 0.0031$. Systemic and intestinal oxygen transport and uptake (DO_2, VO_2, DO_2i and VO_2i, respectively) were estimated as $DO_2 = CO \times CaO_2$; $VO_2 = CO \times (CaO_2 - CvO_2)$; $DO_2i = SMAF \times CaO_2$ and $VO_2i = SMAF \times (CaO_2 - CmvO_2)$. Systemic and intestinal oxygen extraction ratios (O_2ER and O_2ERi) were calculated as $(CaO_2 - CvO_2)/CaO_2$ and $(CaO_2 - CmvO_2)/CaO_2$, respectively.

Intramucosal PCO_2 and pHi were measured with tonometers (TRIP NGS II Catheter, Tonometrics Division, Instrumentarium, Helsinki, Finland) [7]. We calculated differences between intramucosal PCO_2 (gastric, jejunal and ileal) and arterial PCO_2 (gastric ΔPCO_2, jejunal ΔPCO_2 and ileal ΔPCO_2, respectively). To determine whether mucosal anaerobic metabolism developed after hemorrhage, we used the Dill nomogram to predict mesenteric venous % HbO_2 (% HbO_{2v}^{Dill}) from intramucosal PCO_2 [8].

An enzymatic electrode (Stat profile 9 plus, Nova Biomedical, Waltham, Mass., USA) was used to measure arterial and venous lactate. Intestinal efflux of lactate was calculated as SMAF times arterial minus mesenteric venous lactate difference.

Experimental procedure

Basal measurements were performed after a stabilization period, which was defined by steady CO, SMAF and mixed venous % HbO_2. Then, 20 ml/kg of blood was extracted through the femoral artery at a rate of 5 ml/kg per min. The measurements were repeated after 30 min (ischemia). Dogs' temperatures were maintained at 37 ° C, with a heating lamp, throughout the experiment.

Statistical analysis

Measurements are reported as means ± SD. The data of the basal period were compared with ischemia with paired *t*-test. Multiple comparisons were analyzed with ANOVA and Student-Newman-Keuls test. Differences with a p value of less than 0.05 were considered significant.

Results

Hemorrhage caused marked effects on hemodynamic and oxygen transport variables (Fig. 1). MAP, CO, SMAF, DO_2 and DO_2i fell significantly, but both systemic and intestinal VO_2 remained stable due to increases in systemic and intestinal oxygen extractions (Table 1). Notwithstanding this, signs of tissue hypoxia were quite evident, like decreases of systemic pH, bicarbonate and arterial, mixed venous and mesenteric venous base excesses (Table 2) and arterial and mesenteric

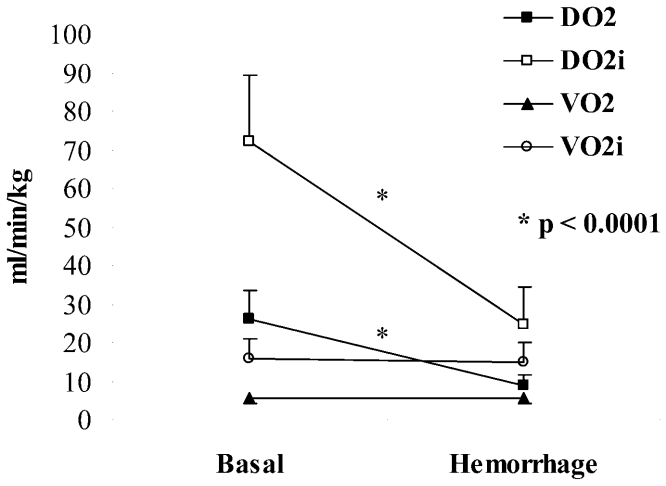

Fig. 1 Systemic and intestinal oxygen transport and consumption (DO_2, DO_2i, VO_2 and VO_2i, respectively) in basal and ischemic conditions

venous hyperlactatemia. Gastric, jejunal and ileal ΔPCO_2 and pHi changed accordingly (Fig. 2). pHi variation coefficients were 1.6, 0.8 and 1.6%, respectively, in the basal period, and 2.4, 2.2 and 2.1% during ischemia. However, the decreases of gastric, jejunal and ileal pHi were greater than that of arterial pH (0.16 ± 0.09, 0.21 ± 0.14 and 0.18 ± 0.13 versus 0.07 ± 0.03, respectively; $p < 0.05$). Arterial and mesenteric venous lactate levels rose significantly (1.7 ± 0.9 versus 3.7 ± 1.4, $p < 0.001$, and 1.8 ± 0.8 versus 4.3 ± 1.5 mmol/l, $p < 0.0001$)as did the lactate veno-arterial difference ($0.1 \pm .6$ to 0.6 ± 0.7 mmol/l, $p < 0.05$). Intestinal efflux of lactate increased more than 100% (0.037 ± 0.064 versus 0.082 ± 0.114 mmol/min per kg), but it did not reach statistical significance due to a large SD.

Basal and ischemic $\%HbO_{2v}{}^{Dill}$ values, derived from gastric, jejunal and ileal tonometer PCO_2 values, were $19 \pm 62\%$ and $-17 \pm 66\%$ ($p < 0.02$). Ischemic values were not only different from basal ones but became negative (Fig. 3).

Discussion

In recent years, tonometry has emerged as a useful tool with which to evaluate gut mucosal oxygen metabolism, as blood flow to the stomach and intestine is early and disproportionately reduced in shock and low-flow states. Intramucosal acidosis can rise from several mechanisms. First, it might appear because of tissue hypoxia. At the onset of anaerobic metabolism, CO_2 rises because of the bicarbonate buffering of protons generated by strong acids and ATP hydrolysis [9]. Tonometry might certainly identify this CO_2 excess. Besides, in hypoperfusion states, aerobically generated CO_2 could also accumulate as a result of lack of removal [10]. Moreover, in experimental endotoxemia, intramucosal acidosis could develop as a signal of real, deep metabolic disorders of sepsis, in the absence of tissue hypoxia and hypoperfusion [11].

In the present study, though DO_2 fell, systemic and intestinal VO_2 were maintained through increases in systemic and intestinal O_2ER. This was to be expected, as we did not reach the critical DO_2 level needed to jeopardize VO_2, stated by Nelson et al. as 7.9 ± 1.9 and 9.7 ± 2.7 ml/min per kg for systemic and intestinal VO_2, respectively [1]. However, and as a key finding of this study, there was multiple evidence of anaerobic metabolism, such as metabolic acidosis, hyperlactatemia and intramucosal acidosis. We reason that, in this model, tissue hypoxia might have been the main mechanism responsible for intramucosal acidosis. During the experiment, intestinal VO_2 remained stable but the veno-arterial lactate difference rose significantly, which can be ascribed to the onset of intestinal anaerobic metabolism.

Schlichtig and Bowles, in a low-flow experimental model and with the aid of the nomogram of Dill, concluded that, below critical DO_2, the appearance of CO_2 in the gut lumen was due to anaerobic production and not to the accumulation of aerobic source [8]. Briefly, Dill's nomogram rests upon the almost perfect linear relationship between venous PCO_2 and venous $\%HbO_2$ in aerobic conditions, with stable CO_2 to O_2 exchange ratio. It follows that, if the venous PCO_2 is known, venous $\%HbO_2$ is predictable ($\%HbO_{2v}{}^{Dill}$) and, if it agrees with the measured venous $\%HbO_2$ value, the appear-

Table 1 Systemic and intestinal hemodynamic and oxygen transport parameters in basal conditions and after hemorrhage

	Basal	Ischemia	*p*
Mean arterial blood pressure (mmHg)	145 ± 21	88 ± 24	< 0.00001
Cardiac output (ml/min per kg)	121 ± 29	48 ± 14	< 0.00001
Superior mesenteric artery blood flow (ml/min per kg)	338 ± 91	135 ± 55	< 0.00001
Systemic oxygen transport (ml/min per kg)	26.0 ± 7.3	8.9 ± 2.6	< 0.00001
Systemic oxygen consumption (ml/min per kg)	5.5 ± 1.3	5.4 ± 1.3	NS
Intestinal oxygen transport (ml/min per kg)	71.9 ± 17.3	24.6 ± 9.6	< 0.00001
Intestinal oxygen consumption (ml/min per kg)	15.7 ± 5.0	14.9 ± 5.3	NS
Systemic oxygen extraction ratio	0.22 ± 0.06	0.62 ± 0.11	< 0.00001
Intestinal oxygen extraction ratio	0.23 ± 0.07	0.60 ± 0.10	< 0.00001

Table 2 Arterial, mixed venous and mesenteric venous blood gases in basal conditions and after hemorrhage

	Basal	Ischemia	*p*
Hemoglobin (g/dl)	16.3 ± 2.1	14.6 ± 2.2	0.04400
Arterial oxygen saturation	0.99 ± 0.02	0.96 ± 0.03	0.00270
Arterial pH	7.33 ± 0.04	7.26 ± 0.06	0.00200
Arterial PO_2 (torr)	101 ± 16	84 ± 13	0.00510
Arterial PCO_2 (torr)	34 ± 4	33 ± 3	NS
Arterial HCO_3 (mmol/l)	17 ± 1	14 ± 2	0.00010
Arterial BE (mmol/l)	–7 ± 2	–12 ± 3	0.00025
Mixed venous oxygen saturation	0.70 ± 0.06	0.36 ± 0.10	< 0.00001
Mixed venous pH	7.31 ± 0.04	7.22 ± 0.07	0.00048
Mixed venous PO_2 (torr)	52 ± 6	33 ± 5	< 0.00001
Mixed venous PCO_2 (torr)	38 ± 8	46 ± 6	0.00710
Mixed venous HCO_3 (mmol/l)	18 ± 3	18 ± 2	NS
Mixed venous BE (mmol/l)	–7 ± 3	–10 ± 3	0.02000
Mesenteric venous oxygen saturation	0.76 ± 0.07	0.38 ± 0.09	< 0.00001
Mesenteric venous pH	7.30 ± 0.04	7.17 ± 0.07	0.00003
Mesenteric venous PO_2 (torr)	51 ± 7	35 ± 5	< 0.00001
Mesenteric venous PCO_2 (torr)	41 ± 4	50 ± 7	0.00035
Mesenteric venous HCO_3 (mmol/l)	20 ± 1	18 ± 3	0.03700
Mesenteric venous BE (mmol/l)	–6.3 ± 1.8	–11.3 ± 4.4	0.00076

To convert torr to kPa, multiply the value by 0.1333

ance of dissolved CO_2 absolutely indicates aerobic metabolism. On the other hand, $\%HbO_{2v}^{Dill}$ less than measured $\%HbO_2$ or less than zero, would indicate the production of metabolic acids like lactate, and then conversion of CO_3H^- to CO_2 in anaerobiosis. During the ischemic period, our $\%HbO_{2v}^{Dill}$ values obtained from gastric, jejunal and ileal mucosal PCO_2 became remarkably negative, which would further imply the presence of anaerobic processes.

The gut is especially sensitive to systemic hypoperfusion. As was pointed out before, the beginning of oxygen supply dependence occurs earlier in the gut than in the whole body [1]. Besides, measurements of regional oxygen transport and uptake parameters have been

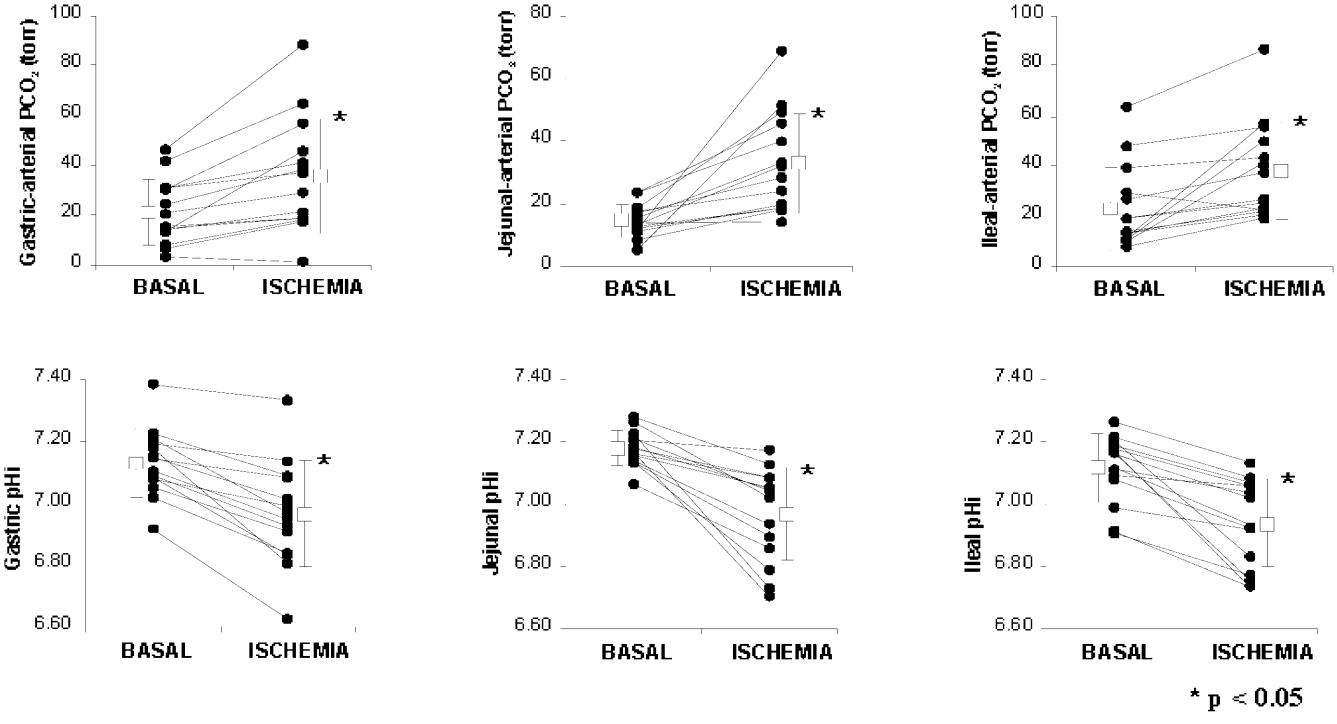

Fig. 2 Gastric, jejunal and ileal intramucosal arterial PCO_2 gradients and intramucosal pH (pHi) behaviors in basal and ischemic conditions. *Black dots* are each individual experiment. *Open squares* are mean values ± SD

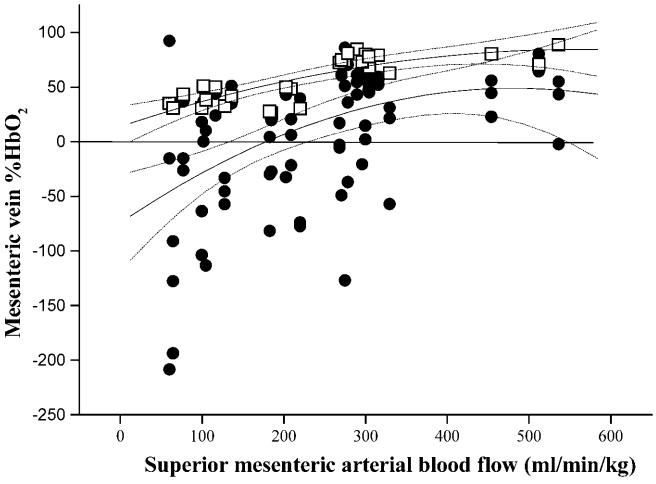

Fig. 3 Relationship between superior mesenteric arterial blood flow and measured mesenteric venous oxyhemoglobin saturation *(squares)* and mesenteric venous oxyhemoglobin saturation derived from intramucosal PCO_2 ($\%HbO_{2v}^{Dill}$)*(black dots)*. *Solid lines* are regression lines. *Dashed lines* are the 95% confidence bands. $\%HbO_{2v}^{Dill}$ were calculated from Dill's nomogram, that states that under aerobic metabolism and steady conditions, the relationship between venous PCO_2 and venous $\%HbO_2$ is linear [8]

claimed as a way to assess oxygen metabolism. However, in our study, intestinal VO_2 remained stable in the face of altered metabolic parameters. Similarly, Fink et al. found ileal intramucosal acidosis in the presence of normal mesenteric VO_2 [12] and Gutierrez et al. have demonstrated that increases in DO_2 with dobutamine in septic patients can reverse hyperlactatemia and gastric intramucosal acidosis, in spite of unmodified VO_2 [13]. Other investigators have reported different results. Grum et al. described a consistent correlation between pHi and intestinal VO_2 during DO_2 decreases induced by ischemia and hypoxia. Initially, both pHi and intestinal VO_2 remained stable and fell when critical DO_2 was achieved [3]. Rozenfeld et al. found that metabolic markers of intestinal hypoxia appeared with the onset of critical DO_2 [14]. These contrary results could be ascribed to different experimental models of hypoperfusion. In the aforementioned studies there was selective reduction in superior mesenteric blood flow, while our model consisted in hemorrhagic shock.

Several underlying mechanisms could explain tissue hypoxia in the face of preserved intestinal VO_2. First, blood flow might have been redistributed to the muscularis mucosae, rendering mucosal layers hypoxic, but with low impact on whole VO_2. However, Lundgren et al. demonstrated that decreases in perfusion pressures redistributed flow towards the mucosa [15]. Second, countercurrent irrigation might induce a functional shunt that could place distal microvilli segments at risk [16]. Rozenfeld et al. suggested that during progressive ischemia, mucosa and serosa might become simultaneously hypoxic with a "patchy" distribution [14]. Our experimental design might have produced hypoxic areas large enough to cause intramucosal acidosis and lactate generation, but not to lower global intestinal VO_2.

Last, we cannot disregard the fact that surgical instrumentation or mucosal barrier ischemic injury could result in bacterial translocation, endotoxemia and subsequent cellular disturbances, which could account for the metabolic derangement observed. In this setting, aerobically generated hyperlactatemia produced by inhibition of pyruvate dehydrogenase, without changes in VO_2, may occur [17]. However, ours is an acute experimental model, whose main feature is hypoperfusion.

The other key finding of this study was that the effects of ischemia were equally reflected in stomach, jejunum and ileum. There was no difference in the behavior of ΔPCO_2 and pHi in the three segments and the variation coefficients were similar under basal and ischemic conditions. However, there has been much controversy about pHi correlations along the gastrointestinal tract. Poole et al. found, in dogs, that reduction of celiac and mesenteric flows to less than 50% of the basal values resulted in intramucosal acidosis in both territories [18] which was greater in the intestine than in the stomach (7.11 versus 7.30). Hartmann et al. [5] and Montgomery et al. [6] studied hemorrhage effects on gastric, small intestine and colonic pHi in pigs. The extent of the hemorrhage was similar to that of our model (16.9 ml/kg), but only intestinal pHi fell. Larger bleedings reduced pHi in the three segments. Walley et al. exposed pigs to progressive hemorrhage and found that gastric ΔPCO_2 at critical gut DO_2 was extremely high and variable (63 ± 40 mmHg) compared to jejunal ΔPCO_2 (17 ± 15 mmHg). They concluded that gastric tonometry is noisy and rather inaccurate [19]. Differences in experimental designs or the species involved could account for the variations observed. For instance, reductions of regional blood flow during cardiopulmonary bypass, evaluated by laser Doppler velocimetry, were equal in rabbit stomach, jejunum and ileum [20]. In addition, despite a larger blood supply, gastric blood flow is more decreased than intestinal blood flow during hemorrhagic shock in dogs [21]. Also, a study of the vascular pattern of the intestinal villi performed in different species showed a more uniform histologic structure in the relatively shorter gastrointestinal tract of the dog [22].

In summary, our data show that, at least in this model of hemorrhagic shock, tissue and metabolic markers of hypoxia such as lactic acidosis and intramucosal acidosis may appear early, even in the absence of dependence of oxygen consumption on oxygen transport. In addition, ΔPCO_2 and pHi showed a similar response to hemorrhage in the three gastrointestinal segments studied. These findings support the value of gastric tonometry as a useful indicator of splanchnic perfusion.

References

1. Nelson DP, King CE, Dodd SL, Schumacker PT, Cain SM (1987) Systemic and intestinal limits of O_2 extraction in the dog. J Appl Physiol 63: 387–394
2. Taylor DE, Gutierrez G (1996) Tonometry. A review of clinical studies. Crit Care Clin 12: 1007–1018
3. Grum CM, Fiddian-Green RG, Pittenger GL, Grant BJB, Rothman ED, Dantzker DR (1984) Adequacy of tissue oxygenation in intact dog intestine. J Appl Physiol 56: 1065–1069
4. Doglio G, Pusajo J, Egurrola M, Bonfigli C, Parra C, Vetere L, Hernandez MS, Fernandez S, Palizas F, Gutierrez G (1991) Gastric mucosal pH as a prognostic index of mortality in critically ill patients. Crit Care Med 19: 1037–1040
5. Hartmann M, Montgomery A, Jönsson K, Haglund U (1991) Tissue oxygenation in hemorrhagic shock measured as transcutaneous oxygen tension, subcutaneous oxygen tension and gastrointestinal intramucosal pH in pigs. Crit Care Med 19: 205–210
6. Montgomery A, Hartmann M, Jönsson K, Haglund U (1989) Intramucosal pH measurement with tonometers for detecting gastrointestinal ischemia in porcine hemorrhagic shock. Circ Shock 29: 319–327
7. Antonsson JB, Boyle CC III, Kruithoff KL, Wang H, Sacristan E, Rothschild HR, Fink MP (1990) Validation of tonometric measurement of gut intramural pH during endotoxemia and mesenteric occlusion in pigs. Am J Physiol 259:G519-G523
8. Schlichtig R, Bowles SA (1994) Distinguishing between aerobic and anaerobic appearance of dissolved CO_2 in intestine during low flow. J Appl Physiol 76: 2443–2451
9. Gutierrez G (1991) Cellular energy metabolism during hypoxia. Crit Care Med 19: 619–626
10. Mathias DW, Clifford P, Klopfenstein HS (1988) Mixed venous blood gases are superior to arterial blood gases in assessing acid-base status and oxygenation during acute cardiac tamponade. J Clin Invest 82: 833–838
11. Vandermeer TJ, Wang H, Fink MP (1995) Endotoxemia causes ileal mucosal acidosis in the absence of mucosal hypoxia in a normodynamic porcine model of septic shock. Crit Care Med 23: 1217–1226
12. Fink MP, Cohn SM, Lee PC, Rothschild HR, Deniz YF, Wang H, Fiddian-Green RG (1989) Effects of lipopolysaccharide on intestinal intramucosal hydrogen ion concentration in pigs: Evidence of gut ischemia in a normodynamic model of septic shock. Crit Care Med 17: 641–646
13. Gutierrez G, Clark C, Brown SD, Price K, Ortiz L, Nelson C (1994) Effect of dobutamine on oxygen consumption and gastric mucosal pH in septic patients. Am J Respir Crit Care Med 150: 324–329
14. Rozenfeld RA, Dishart MK, Tønnessen TI, Schlichtig R (1996) Methods for detecting local intestinal ischemic anaerobic metabolic acidosis by PCO_2. J Appl Physiol 81: 1834–1842
15. Lundgren O, Svanik J (1973) Mucosal hemodynamics in the small intestine of the cat during reduced perfusion pressure. Acta Physiol Scand 88: 551–563
16. Sheperd AP, Kiel JW (1992) A model of countercurrent shunting of oxygen in the intestinal villus. Am J Physiol 262:H1136-H1142
17. Curtis SE, Cain SM (1992) Regional and systemic oxygen delivery/uptake relations and lactate flux in hyperdynamic endotoxin treated dogs. Am Rev Respir Dis 145: 348–354
18. Poole JW, Sammartano RJ, Boley SJ (1987) Hemodynamic basis of the pain of chronic mesenteric ischemia. Am J Surg 153: 171–176
19. Walley KR, Friesen BP, Humer MF, Phang T (1998) Small bowel tonometry is more accurate than gastric tonometry in detecting gut ischemia. J Appl Physiol 85: 1770–1777
20. Bastien O, Piriou V, Aoufi A, Evans R, Lehot JJ (1999) Effects of dopexamine on blood flow in multiple splanchnic sites measured by laser Doppler velocimetry in rabbits undergoing cardiopulmonary bypass. Br J Anaesth 82: 104–109
21. Kaihara S, Rutherford RB, Schwentker EP, Wagner HN (1969) Distribution of cardiac output in experimental hemorrhagic shock in dogs. J Appl Physiol 27: 218–222
22. Jacobson LF, Noer RJ (1952) The vascular pattern of intestinal villi in various laboratory animals and man. Anat Rec 114: 85–101