Effects of hemorrhage on gastrointestinal oxygenation

Abstract  Objectives: (1) To demonstrate that metabolic parameters are better indicators of tissue hypoxia than regional and whole oxygen consumption ($\text{VO}_2$). (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$_2$ ($\Delta$PCO$_2$). 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 $\Delta$PCO$_2$ (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. pH 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 ($\text{VO}_2$) 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 intramucosal...
sal pH (pHi), has been reasonably established in recent years [2]. Grim et al. showed that intestinal pH reductions correlated with gut VO₂ 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 by decreased furosemide clearance in rat mesentery at the beginning of VO₂ dependence on DO₂? (2) What is the relationship between pH 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, Southnachtack, Mass., USA), with a tidal volume of 15 ml/kg, FIO₂ 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 into the inferior 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 SO2/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 PO₂, PCO₂ and pH were measured with a blood gas analyzer (ABL 30, Radiometer, Copenhagen, Denmark). Hemoglobin and oxygen blood saturations (%HbO₂) were measured by using a co-oximeter calibrated for canine blood (OSM 3, Radiometer, Copenhagen, Denmark). Arterial, mixed venous and mesenteric venous contents (CaO₂, CvO₂ and Cmvo₂) were calculated as Hb × 1.34 × %HbO₂ × PaO₂/0.0031. Systemic and intestinal oxygen transport and uptake (DO₂, VO₂, DO₂i and VO₂i, respectively) were estimated as DO₂ = CO × CaO₂; VO₂ = CO × (CaO₂ – CvO₂); DO₂i = SMAF × CaO₂ and VO₂i = SMAF × (CaO₂ – Cmvo₂). Systemic and intestinal oxygen extraction ratios (O₂ER and O₂ERI) were calculated as (CaO₂ – CvO₂)/CaO₂ and (CaO₂ – Cmvo₂)/CaO₂, respectively.

Intramucosal PCO₂ and pH were measured with tonometers (TRIP NGS II Catheter, Tonometrics Division, Instrumentarium, Helsinki, Finland) [7]. We calculated differences between intramucosal PCO₂ (gastric, jejunal and ileal) and arterial PCO₂ (gastric ΔPCO₂, jejunal ΔPCO₂ and ileal ΔPCO₂, respectively). To determine whether mucosal anoxic metabolism developed after hemorrhage, we used the Dill nomogram to predict mesenteric venous %HbO₂ (%HbO₂ authorized) from intramucosal PCO₂ [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 %HbO₂. 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, DO₂ and DO₂i fell significantly, but both systemic and intestinal VO₂ 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