Intramucosal pH and intestinal mucosal damage in ischemia-reperfusion injury

Abstract  Small bowel transplantation (SBT) has become an increasingly promising treatment for short bowel syndrome. The evaluation of graft viability after SBT, however, has not been established, except by mucosal biopsy. We monitored intestinal mucosal acidity in order to detect small intestinal ischemia-reperfusion injury. Mongrel dogs were used in this study. After laparotomy, the small bowel was isolated with a vascular pedicle. A tonometer to measure intramucosal pH (pHi) was then positioned in the terminal ileum. The superior mesenteric artery was occluded with or without concomitant superior mesenteric vein occlusion for 60 or 120 min. The value of pHi was determined from laparotomy (baseline) to 12 h after reperfusion. Whole-thickness specimens of the ileum were taken before ischemia, just before reperfusion, and 1 h afterward. Mucosal injury was graded histopathologically. pHi decreased from baseline in relation to the degree of histopathological mucosal injury. There was a significant correlation between histological findings and the change in pHi. We conclude that monitoring intestinal mucosal acidity is a reliable way of determining graft viability after SBT.

Key words  Intramucosal pH, ischemia-reperfusion injury - Ischemia-reperfusion injury, intramucosal pH - Small bowel preservation

Introduction

Patients with intestinal failure depend upon long-term total parenteral nutrition (TPN) for survival. Small bowel transplantation (SBT) offers these patients a potential alternative to the lifestyle restrictions, complications, and costs associated with long-term TPN [8, 17]. Unfortunately, the results of SBT have often been disappointing because of poor graft function, severe rejection, graft-versus-host disease, infection, and complications of immunosuppressive therapy [11, 15, 30, 34, 35]. Recently, long-term survival after SBT has been enhanced by combined liver and small bowel grafting [6, 18, 20] or treatment with FK506 [11, 34], bringing SBT closer to clinical practice. The assessment of graft viability after SBT and the prevention or early detection of rejection are crucial for successful clinical SBT [30, 34, 35]. The small intestine is particularly susceptible to injury from ischemia and reperfusion. Structural damage to the small intestinal mucosa is observed remarkably soon after the onset of an ischemic period. Some authors have studied the development of morphological changes in the small intestinal mucosa with increasing periods of ischemia with both light [7] and electron microscopy [5]. However, histopathological examination of mucosal punch biopsy specimens is only a partial evaluation. During ischemia and subsequent reperfusion, hypothermia and oxygen deprivation induce endothelial swelling and cause a decline in tissue pH [2]. Boros et al. [4] reported that a 120-min intestinal ischemia time caused a progressive fall in intramucosal pH...
(pHi), and that reperfusion resulted in a slow return to nearly normal pHi values. However, they did not consider the relationship between histological intestinal mucosal damage and pHi. As the tonometric measurement of intestinal mucosa is readily and safely performed [10], we designed this study to clarify the correlation between histological intestinal mucosal change and pHi in intestinal ischemia-reperfusion injury.

### Materials and methods

Twenty-seven healthy mongrel dogs of both sexes weighing 12–20 kg were used. With free access to water, each dog was fasted for 24 h prior to the experiment. After the administration of ketamine hydrochloride (10 mg/kg intramuscular injection), the animals were anesthetized with pentobarbital sodium (10 mg/kg) and pancuronium bromide (0.2 mg/kg), intubated, and connected to a volume-cycled ventilator (MD800, Senko Med. Co. Ltd., Tokyo, Japan) at a tidal volume of 20 ml/kg and a rate of 15 breaths/min. Positive end-expiratory pressure was controlled at 5.0 cm H₂O. Muscular relaxation was obtained with additional pancuronium bromide (0.1 mg/kg). A polyethylene catheter was positioned in the carotid artery and connected to a pressure transducer for recording of arterial pressure. Through a skin incision, a polyethylene catheter for blood sampling was passed via the right femoral vein into the right hepatic vein. The catheter was also used to infuse a lactated Ringer’s solution during the experiment at the rate of 10 ml/kg per hour to compensate for fluid losses due to surgery. Electrocardiograms and esophageal temperature were continuously monitored throughout the study.

Laparotomy was performed after blood pressure and respiratory parameters had stabilized. After laparotomy via a midline incision, the small bowel was isolated with a vascular pedicle from the proximal jejunum to the terminal ileum. Both the superior mesenteric artery and vein were isolated from surrounding lymph nodes, plexuses, and tissues. A small antimesenteric incision was made in the terminal ileum, and a tonometer (Trip, Tonometrics, Helsinki) was placed in the lumen of the gut and secured with a purse-string suture. Animals were randomly placed in one of four groups for different treatments. Group 1 animals (n = 7) received 60-min superior mesenteric artery (SMA) occlusion. Group 2 animals (n = 6) received 120-min SMA occlusion, and group 3 animals (n = 8) received both SMA and SMV occlusion for 120 min. Group 4 animals (n = 6) formed a control in which a sham operation was performed for a comparable time under the same anesthesia.

Mean arterial pressure was measured continuously with transducers. An arterial blood sample was taken via the arterial catheter, and arterial pH was determined at the time of laparotomy, during ischemia, and 1, 3, 6, and 12 h after reperfusion. A hepatic venous blood sample was taken simultaneously and analyzed for oxygen saturation (ShvO₂) using a blood gas analyzer (ABL520; Radiometer, Copenhagen, Denmark). pHi was calculated using the method of Fiddian-Green [13]. The method was based on the principle that PCO₂ in the fluid within a semipermeable balloon attached to a catheter equilibrated with that in the lumen of a hollow