The American Journal of Surgery (2010) 200, 111–117

The American Journal of Surgery®

Scientific (Exp)/Research

Bacterial translocation and infected pancreatic necrosis in acute necrotizing pancreatitis derives from small bowel rather than from colon

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KEYWORDS:
Acute pancreatitis;
Bacterial translocation;
Colon;
Small bowel;
Sepsis

Abstract

BACKGROUND: The clinical course of acute necrotizing pancreatitis (ANP) is determined by the superinfection of pancreatic necrosis. To date, the pathophysiology of the underlying bacterial translocation is poorly understood. The present study investigated the bacterial source of translocation.

METHODS: A terminal loop ileostomy was applied in rats. Selective digestive decontamination (SDD) of either the small bowel or the colon was performed. After 3 days of SDD, severe ANP was induced. At 24 hours, bacterial translocation was assessed by cultures of bowel mucosa, mesenteric lymph nodes, and pancreas using a scoring system (0–4).

RESULTS: Without SDD, pancreatic infection was present in all cases with an average score of 2.67. Colon SDD reduced pancreatic superinfection to 1.67 (not significant). SDD of the small bowel significantly reduced superinfection to 1.0 ($P < .005$).

CONCLUSIONS: Bacterial translocation from the colon is less frequent than translocation from the small bowel. Thus, the small bowel seems to be the major source of enteral bacteria in infected pancreatic necrosis.

Clinical courses of acute pancreatitis are variable. Most episodes are mild and self-limiting within 3 days to 5 days.[1] However, in approximately 15% to 20% of cases, severe pancreatitis associated with organ failure and/or local complications such as pancreatic necrosis develops.[2–6] The mortality rate of severe acute pancreatitis is as high as 20% to 30%[7–9] with 2 peaks during the course of the disease.[8] The first peak of mortality occurs within the first week after the onset of symptoms and is characterized by systemic inflammatory response syndrome associated with pulmonary, cardiovascular, and renal insufficiency. The second peak is often observed 3 weeks to 4 weeks after admission.[10] The main cause for this late deterioration with systemic organ failure is bacterial superinfection of necrotic pancreatic tissue and the subsequent development of septic complications.[11–14] Thus, patients with infected pancreatic necrosis represent a high-risk group for the development of sepsis associated with fatal outcome.[3,15]

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Manuscript received April 7, 2009; revised manuscript August 2, 2009

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doi:10.1016/j.amjsurg.2009.08.019

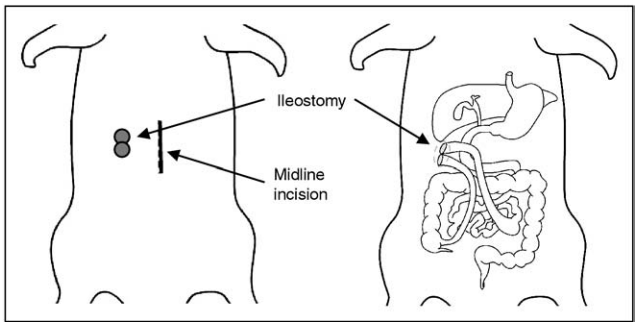

Figure 1 Surgical procedure of the ileostomy (simplified illustration of the gastrointestinal tract) After midline incision, the ileum was mobilized 2 to 3 cm before the ileocecal valve. An ileostomy was pulled through a second paramedian abdominal incision. Half of the circumference of the loop was opened, and the enterostomy was fixed by single sutures.

Bacterial translocation is considered the main cause for superinfection of pancreatic necrosis.[16] Pancreatic necrosis usually develops within the first 4 days after the onset of symptoms to its full extent.[10] Subsequently, changes in intestinal motility and flora, mucosal barrier function, and immune response lead to bacterial translocation with subsequent superinfection of pancreatic necrosis.[17,18] The pathomechanism and particularly the route of bacterial translocation in severe acute necrotizing pancreatitis is not completely understood.[17] Hematogenous dissemination of bacteria[19] or lymphatic spread have been advocated.[20] It is generally agreed on that bacterial translocation from the gut displays the main origin of secondary pancreatic infection.[18] However, because there is no evidence whether the bacteria predominantly derive from the small bowel[18,21] or the colon,[22,23] to date the exact source of bacterial translocation remains unknown.[17,24]

In the present study, we selectively decontaminated different parts of the gut to evaluate whether the origin of bacterial translocation is the small bowel or the colon.

Methods

Animals

The present study was approved by the Committee of Animal Care of the Regierungspräsidium Karlsruhe, Germany. Inbred male Wistar rats (300–340 g) were used for experiments. Care was provided in accordance with the German law for the use of laboratory animals outlined in the "Tierschutzgesetz in der Fassung der Bekanntmachung vom 18 August 1986 (BGB1.I S. 1319)." Animals were allowed free access to food and water during the whole experiment.

Performance of the ileostomy

Surgical anesthesia was induced by a short carbon dioxide narcosis followed by intramuscular ketamine (Ketanest® S, 50, 40 mg/kg BM; Parke Davis, Berlin, Germany) and xylazine (Rompun® 2%, 6 mg/kg; Bayer, Leverkusen, Germany). After shaving the abdomen and careful disinfection with antiseptic solution, a short midline laparotomy was performed. The ileum was mobilized approximately 2 cm to 3 cm before the ileocecal valve. An ileostomy was pulled through a second paramedian abdominal incision. After closure of the abdomen, half of the circumference of the mobilized loop of ileum was opened, and the enterostomy was fixed by single sutures (Fig. 1).

Selective digestive decontamination

To selectively decontaminate the colon, 5 mL selective digestive decontamination (SDD) solution (.5 mg/mL gentamycin and polymyxin B) was applied into the aboral portion of the enterostomal once a day over 3 days, which corresponds to an anterograde decontamination of the colon. For decontamination of the small bowel, SDD solution was given orally together with drinking water at the same concentration (.5 mg/mL). Rats that drank less than 8 mL/d were excluded from the study. To achieve decontamination of both the small bowel and the colon, SDD solution was administered into the ileostomy at the same time orally as described earlier.

Experimental design

In the pancreatitis control group (control, n = 6), ileostomy was performed without bowel decontamination (Fig. 2). After 3 days, acute necrotizing pancreatitis was induced as described later. In the first experimental group (SDD colon, n = 6), colon decontamination was performed by an application of SDD solution anterograde into the descending branch of the ileostomy daily over 3 days. In the second experimental set (SDD small bowel, n = 6), small bowel decontamination was performed by the administration of SDD solution orally, and in a third experimental group (SDD small bowel and colon, n = 6), the small bowel and

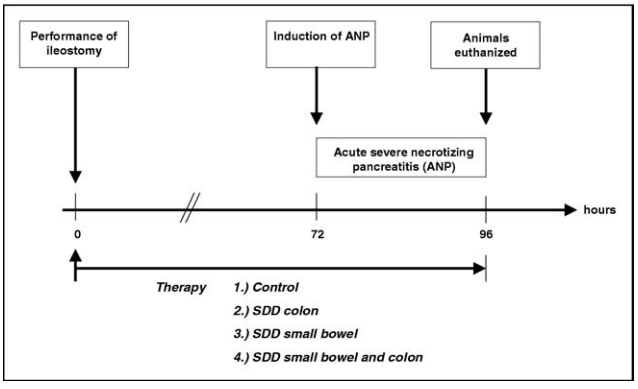

Figure 2 Experimental design. A terminal loop ileostomy was applied followed by SDD of either the colon, the small bowel, or both over the course of 3 days. Subsequently, ANP was induced, and animals were harvested after 24 hours.