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Effect of enteral nutrition and ecoimmunonutrition on bacterial translocation and cytokine production in patients with severe acute pancreatitis

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ABSTRACT

Background: Severe acute pancreatitis (SAP) with severe complications such as multiple organ failure, necrosis, abscess, and formation of pancreatic pseudocysts often gives rise to a high mortality despite intensive treatment. Parenteral nutrition (PN), elemental enteral nutrition, and ecoimmunonutrition (EIN) hastened the recovery of SAP patients, stimulated gastrointestinal motility, and alleviated the degree of systemic inflammatory response syndrome. This study aimed to examine the effects of enteral nutrition (EN) and EIN on bacterial translocation and cytokine production in patients with SAP.

Methods: One hundred eighty-three SAP patients were randomly divided into three groups receiving PN, EN, or EN + EIN. Acute Physiology and Chronic Health Evaluation II scores, complications (systemic inflammatory response syndrome, multiorgan failure, and infections), intestinal bacterial strains of stool, and plasma concentrations of endotoxin, tumor necrosis factor α (TNF-α), and interleukin (IL) 6 and IL-10 were evaluated.

Results: The percentage of pancreatic sepsis, multiple organ dysfunction syndrome, and mortality was significantly lower in the EN group and was further lower in the EN + EIN group than that in the PN group. The plasma concentrations of TNF-α and IL-6 and APACHE II scores were significantly decreased in the EN group and were further lowered in the EN + EIN group than those in the PN group. The plasma concentration of IL-10 was higher in the EN group and was further increased in the EN + EIN group than that in the PN group.

Conclusions: EN plays effective roles in the treatment of SAP by decreasing the expression of endotoxin, TNF-α, and IL-6 and the bacterial translocation, enhancing the expression of IL-10, and the combination of EIN with EN results in more therapeutic benefits than EN alone.

1. Introduction

Severe acute pancreatitis (SAP) with severe complications such as multiple organ failure, necrosis, abscess, and formation of pancreatic pseudocysts often gives rise to a high mortality (30%–40%) despite intensive treatment [1]. Alcohol consumption is a leading cause for both acute and chronic pancreatitis, followed by gallstones and autoimmune diseases, and so

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forth [2]. It is generally believed that pancreatitis is caused by the self-digestion of pancreatic acinar cells after the conversion of the inactive trypsinogen to the active trypsin. SAP is a hypermetabolic and hyperdynamic process that creates a state of catabolic stress with acute inflammatory responses and consequent nutritive damage. Most complications and deaths that occur in SAP are because of inflammatory immune responses to pancreatic necrosis and/or infection. An increasing body of evidence suggests that the gut plays an important role in the immune and inflammatory responses to SAP. Experimental data suggest that the endogenous cytokines involved in this response are stimulated by endotoxin and other bacterial products absorbed by a metabolically altered intestine. Experimental studies indicated that pancreatic infection in SAP appeared to be due to the translocation of bacteria from the gut to mesenteric lymph nodes, peritoneal fluid, and blood and then from these sites to the pancreas itself. The main mechanisms that governed the processes of bacterial translocation in SAP are probably related to the overgrowth of enteric flora because of intestinal dysfunction, damage to intestinal permeability, and impairment of host immunity. Endothelial and epithelial barrier functions are important to protect against potential invasion of enteric microorganisms, and their function may also be essential to prevent the development of multiple organ dysfunction. Several studies in patients with severe trauma and burns have shown that total enteral nutrition (TEN) significantly diminishes the acute inflammatory response phase and the incidence of septic complications compared with total parenteral nutrition (TPN) [3,4]. The possible mechanism of this differential response is that feeding through the gut would maintain the intestinal barrier function, thus precluding bacterial and toxin translocation from the intestinal lumen.

In recent years, several prospective randomized studies have proposed early TEN for patients with acute pancreatitis as a therapeutic tool to attenuate systemic inflammatory response syndrome (SIRS) and septic complications [5,6]. How to prevent bacterial translocation and protect the intestinal mucosa from being damaged might be a key to limiting the septic complication in SAP. Many clinical studies pointed out that compared with parenteral nutrition (PN) and elemental enteral nutrition, ecoimmunonutrition (EIN) hastened the recovery of SAP patients, stimulated gastrointestinal motility, and alleviated the degree of SIRS [7]. The potential advantages of this strategy would include a support of the intestinal barrier to prevent the bacterial translocation. The objective of this study was to compare the TPN, TEN, and EIN in the management of patients with SAP, with regard to efficacy, security, morbidity, mortality, bacterial translocation, and changes of endotoxin, tumor necrosis factor α (TNF-α), interleukin (IL) 6, and IL-10 levels.

2. Materials and methods

2.1. Patients

This is a prospective double-blind study, and a total of 183 patients diagnosed with SAP who were admitted to the intensive care unit of our hospital between January 2006 and December 2011 were recruited and randomly divided into three treatment groups: PN, EN, and EN + EIN. SAP was diagnosed using criteria based on the Consensus of the International Symposium on Acute Pancreatitis (Atlanta definition) [5]. General inclusion criteria for the study were defined as follows: (1) age of the patients ranged from 18 to 45 y, (2) the time interval between onset of typical abdominal symptoms and study inclusion was $\leq$48 h, and (3) gastrointestinal ileus or distension was present.

Patients were excluded if they (1) had evidence or a known history of renal dysfunction (creatinine >1.5 mg/dL); (2) were pregnant or lactating; (3) were expected to receive an intervention involving dialysis, plasmapheresis, or other physiological support requiring extracorporeal blood removal; (4) were suffering from inflammatory bowel disease; (5) had infections at the time of admission to the hospital; and (6) received recent nonsteroidal anti-inflammatory drugs. Patients who died within 48 h after admission to intensive care unit were also excluded. This prospective, randomized clinical study protocol was approved by the Ethics Committee of Southern Medical University, Guangzhou, China, and informed consent was obtained from all subjects. Demographic data, serum level of amylase, computed tomography (CT) scan severity index, APACHE II scores, abdominal compartment syndrome rate, and severity grade ratio were not statistically different between the three groups.

The diagnosis was confirmed by elevations in levels of pancreatic enzymes (amylase and lipase), abdominal ultrasound and contrast-enhanced abdominal CT imaging and chronic health evaluation II (APACHE II) score, and the diagnostic criteria and severity grade for acute pancreatitis proposed by the Japanese Ministry of Health, Labor, and Welfare. All patients underwent a rigorous clinical treatment protocol consisting of adequate central venous fluid replacement, hemodynamic monitoring *via* central venous pressure, analgesia, proton pump inhibitors to prevent stress ulcers, prophylaxis with imipenem for pancreatic infection, and respiratory and renal support as needed. No participant in this trial was discharged from hospital or died within the first week after admission.

Patient demographic data are shown in Tables 1 and 2. In all groups, standard formulas without specific immunomodulating nutrients were used. PN patients received a 24-h continuous infusion of TPN through a central venous catheter (subclavian or jugular). Venous infusion was started at a rate of 40 mL/h and increased 20 mL/h every 4 h until the required supports were met. The goal of feeding rates was to administer a rate of 2 g proteins/kg/day and 35 kcal/kg/day. A ratio of 120:1 of nonprotein calories-to-nitrogen was aimed for. The patients in the EN group received TEN (PEPTISORB; Nutricia S.R.L., Madrid, Spain) within 48 h through a single-lumen, 114-cm long nasojejunal 10 F feeding tube whose tip was placed, under fluoroscopic screening, close to Treitz ligament. The initial infusion rate was 25 mL/h with increases of 25 mL/4 h until requirements were reached. The goal of feeding rates was the same as that proposed for PN group (2.0 g proteins/kg/day and 30 kcal/kg/day). In the EIN group, live combined *Bacillus subtilis* and *Enterococcus faecium* enteric-coated capsules (Beijing Han Mei Pharmaceutical Company Limited, Beijing, China) were added (0.5 g po tid) and supported by the same method applied in the EN group.