



Sequential nutrition support with the combination of parenteral and enteral nutrition in the management of severe acute pancreatitis

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Background: Severe acute pancreatitis (SAP) patients are in a highly catabolic state, and reasonable nutritional support is important in improving prognosis. This retrospective study was designed to assess the efficacy of combined sequential therapy of total parenteral nutrition with enteral nutrition (TPN-EN) in the management of SAP patients.

Methods: The clinical data (including recovery time, APACHE II score, and hematological indicators) of 39 SAP patients who had received TPN-EN in our center in the past 6 years were retrospectively analyzed. Furthermore, the results were compared with those in 39 patients treated with total parenteral nutrition (TPN) alone (control group).

Results: One week after the nutritional therapy (week 1), the APACHE II score, serum calcium, and arterial blood lactate and albumin levels were not significantly different between the TPN-EN group and the control group, and the control group had better blood glucose control. However, the APACHE II score, serum calcium, and arterial blood lactate and albumin levels in the TPN-EN group were significantly improved compared with the control group at weeks 2 and 3, and blood glucose control showed no significant difference between these two groups. Serum creatinine levels were not significantly different between these two groups throughout the treatment.

Conclusions: TPN-EN can improve the prognosis of SAP patients and shorten hospital stay without increasing the visceral burdens.

Keywords: Severe acute pancreatitis (SAP); combined sequential nutrition support therapy; total parenteral nutrition (TPN)

Received: 27 February 2019; Accepted: 10 June 2019; published: 28 June 2019.

doi: 10.21037/dmr.2019.06.02

View this article at: <http://dx.doi.org/10.21037/dmr.2019.06.02>

Introduction

Severe acute pancreatitis (SAP) is a common clinical critical disease with a high mortality rate. SAP patients are in a highly catabolic state, and reasonable nutritional support is important in improving the prognosis (1). A total of 35 SAP patients received combined sequential therapy of total parenteral nutrition with enteral nutrition (TPN-EN) in our hospital from December 2012 to December 2018, and the outcomes were satisfactory.

Methods

General data

A total of 74 SAP patients received nutrition support therapy in our center from December 2012 to December 2018, among whom 35 patients [23 males and 12 females aged 26–62 years (41.7 years), including 26 non-surgical cases and 9 surgical cases] received TPN-EN, and 39 patients [25 males and 14 females aged 28–59 years (40.2 years), including 22 non-surgical cases and 17 surgical cases] received TPN alone (control group). The diagnosis was confirmed based on clinical manifestations, laboratory tests, intraoperative findings, and/or contrast-enhanced computed tomography. The Ranson score was >3 in all cases. According to the classification of the Chinese Society of Pancreatology, organ dysfunction can be divided into three degrees (2). In our current series, dysfunction of one organ was found in 14 patients, dysfunction of two organs in 38 patients, and multiple organ dysfunction in 22 patients. The general data showed no significant difference between the TPN-EN group and control group ($P>0.05$) (Table 1).

Nutrition support therapy

Hemodynamics was stable immediately after admission or surgery. The respiratory status was improved. Antibiotics and somatostatin were routinely used. Fluid, electrolyte, and acid-base imbalances were corrected. Organ function support therapy was applied by infusing 50–100 mL of 20% albumin daily or every other day to maintain plasma albumin level and colloid osmotic pressure. Meanwhile, abdominal signs and blood urease amylase level were monitored. Nutritional support was initiated within 48 to 72 hours of admission or after surgery. The TPN-EN group received combined and sequential TPN and EN. TPN was applied firstly via a central venous catheter. Kabiven™ PI (1,440 mL) (Fresenius Kabi, Wuxi, China) was used

Table 1 General data of the two groups

Group	n	Organ dysfunction			Average age (years)
		1	2	>2	
TPN-EN group	35	6	18	11	41.7
Control group	39	8	20	11	40.2

TPN-EN, total parenteral nutrition with enteral nutrition.

to provide energy. The supply of energy by glucose was increased according to patients' body weight: initially 84–105 kJ/(kg·d); after the blood glucose was maintained between 5.6 and 11.1 mmol/L, it was gradually increased to 126–147 kJ/(kg·d), with a ratio of energy to nitrogen (E/N) of 418.4–627.6 kJ:1g. During this period, if the abdominal distension was relieved, the bowel sounds were heard, the anal exhaust or defecation recovered, and the blood/urine amylase levels became normal, isotonic saline was instilled through a nasointestinal tube at a rate of 500 mL/d (25–50 mL/h) for 1 day.

If there was no change in abdominal signs and the blood/urine amylase did not increase, the second step (i.e., combination of TPN and EN) was performed, and the EN preparation used was Nutrison Liquid (Nutricia, Wuxi, China). EN support followed the principle of gradual progress from small amount to large amount, and the infusion speed, concentration, and temperature of the nutrient solution were adjusted in a timely fashion according to the changes in abdominal signs and the amount and nature of stools.

The third step (i.e., total enteral nutrition, TEN) was then initiated, and the preparation used was Ensure (Abbott, Shanghai, China), which was gradually replaced by oral diets. In the control group, TPN was used until the symptoms and signs disappeared and the blood cells and blood/urine amylase returned to normal; finally, TPN was gradually replaced by oral or nasointestinal feeding.

All patients signed informed consent. The study was approved by the Ethics Committee of the Sixth Hospital Affiliated to Sun Yat-sen University, and the ethical approval number is L2012ZSLYEC-090.

Statistical analysis

Statistical analysis was performed using SPSS 17.0 software package. Measurement data were compared using *t*-test and rates were compared using Chi square test. A *P* value of $P<0.05$ was considered statistically significant.

Table 2 Surgery, deaths, and recovery in two groups

Group	Surgery	Death	Intestinal function recovery time (d)	Ascites absorption time (d)	Hospital stay (d)	Average hospital cost (10,000 RMB yuan)
TPN-EN group	9*	2*	2.3±1.1*	7.5 ±2.4*	20.6±9.8*	5.3±2.1
Control group	17*	5*	5.4±2.2*	10.3±3.6*	34.5±10.4*	5.5±1.7

*, P<0.05. TPN-EN, total parenteral nutrition with enteral nutrition.

Table 3 Changes in APACHE II score and hematological indicators in the two groups

Parameters	On the first day of admission (day 1)		Day 7		Day 14		Day 21	
	TPN-EN group	Control group	TPN-EN group	Control group	TPN-EN group	Control group	TPN-EN group	Control group
APACHE II	12.9±1.6	13.1±1.4	11.5±1.1	12.4±1.2	7.3±1.5*	10.8±1.5*	4.1±2.1*	8.2±1.9*
Glucose (mmol/L)	8.9±2.5	8.3±1.9	7.6±1.1*	6.9±1.4*	5.4±1.3	5.6±2.1	5.2±1.5	5.5±2.3
Calcium (mmol/L)	1.53±0.14	1.59±0.18	1.69±0.15	1.70±0.20	1.90±0.11*	1.85±0.15*	1.99±0.09	2.01±0.13
Albumin (g/L)	25.1±2.5	24.9±3.4	28.3±3.3	28.2±2.9	32.5±2.7*	29.5±1.9*	33.9±1.4*	32.0±2.8*
Lactate (mmol/L)	4.4±1.1	4.3±1.4	3.1±0.8	3.2±1.2	1.9±0.6*	2.3±1.4*	1.0±0.5	1.1±1.5
Blood creatinine (mmol/L)	205±98	199±101	159±68	166±57	101±70	99±64	89±54	85±66

*, P<0.05. TPN-EN, total parenteral nutrition with enteral nutrition.

Results

The recovery and various scores and hematological parameters of patients in the TPN-EN group and control group after different treatments are summarized in *Tables 2* and *3*.

Discussion

SAP patients already have a negative nitrogen balance characterized by high decomposition and high metabolism, which underpins the important role of nutritional support in SAP treatment. Many studies have shown that TPN support treatment can induce rest in the digestive glands, reduce the secretion of digestive juices (e.g., pancreatic juice), and thus dramatically improve the prognosis (3,4). However, TPN has numerous limitations as it may cause intestinal mucosal atrophy, prolong the recovery time, and even cause bacterial translocation from the intestines, thus aggravating the disease condition. Recent research has shown that EN support in the early and middle

stages of the disease allows the absorption of nutrients via intestinal mucosa, thus achieving faster improvement in the prognosis of SAP patients than TPN nutrition support (5). However, multiple early nutrition support approaches have been proposed with varying efficacy. (6) As shown in our current study, indicators suggestive of SAP including serum calcium, arterial blood lactate, and APACHE II scores were significantly improved in the second and third week compared with the control group. The improvements were not obvious in the first week, which might be because the EN had not yet exerted its efficacy within a short period of time. The long and mid-term operation rates and the hospital stay duration were also improved.

Etiologically, pancreatitis is mainly caused by trypsin self-digestion. Therefore, increased secretion of pancreatic enzymes should be avoided during EN support, so as to prevent disease progression. The secretion of pancreatic juices can be divided into three phases: head, stomach, and intestine. Nutrients can stimulate the massive secretion of pancreatic juices through the gastroduodenum (7). If

nutrients, especially proteins and fat emulsions, are directly administered through the upper jejunum, their stimulation on pancreatic juice secretion is minimal (8). Thus, we administered the EN nutrients by placing the nasointestinal tube in the upper part of the jejunum. Elemental diet was applied in the early stage and then gradually replaced by normal diets.

During the natural history of SAP, pancreatic islet cells will be damaged to varying degrees, and some patients may even develop pancreatitis-related diabetes in the later stages of the disease (9). Paradoxically, glucose is needed to supply energy during the nutritional support therapy. In our current study, we also found EN and intravenous nutrition performed during the first week after admission made it difficult to control blood sugar. Our solutions included increasing the insulin dose and using an elemental diet (which has smaller impact on blood glucose) for early EN. The blood glucose control became similar between the TPN-EN group and control group after weeks 2 and 3, which may be related to the early recovery of islet cell function and the reduction of stress after EN support. In addition, SAP patients often have dysfunctions in other organs, especially the kidneys and lungs. Nutritional support should avoid increasing visceral burdens in these patients. Our results showed that, compared with TPN alone, TPN-EN did not increase kidney burden. On the contrary, after the early recovery of intestinal function in SAP patients, the abdominal distension is alleviated and the intra-abdominal pressure is reduced, which decreases the influence on renal blood flow and thus is more conducive to the recovery of renal function (10).

Notably, the disease condition and duration differ among SAP patients. Therefore, the volume and timing of nutritional support should be strictly tailored. EN should be immediately terminated if SAP recurs or worsens (11), and a sequential nutrition support therapy may be re-initiated after the disease is relieved again.

Acknowledgments

Funding: Funded by the Science and Technology Program of Guangdong Province (2017A020215036) and the Science and Technology Program of Guangzhou City (201806020036).

Footnote

Provenance and Peer Review: This article was commissioned

by the Guest Editors (Changhua Zhang and Liang Li) for the series “Nutritional Support for Digestive Surgery” published in *Digestive Medicine Research*. The article has undergone external peer review.

Conflicts of Interest: All authors have completed the ICMJE uniform disclosure form (available at <http://dx.doi.org/10.21037/dmr.2019.06.02>). The series “Nutritional Support for Digestive Surgery” was commissioned by the editorial office without any funding or sponsorship. The authors have no other conflicts of interest to declare.

Ethical statement: The authors are accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved. The patients in this study were fully informed and signed the informed consent statement. The study was conducted in accordance with the Declaration of Helsinki (as revised in 2013). This study was approved by the Ethics Committee of the Sixth Hospital Affiliated to Sun Yat-Sen University (Ethical Approval No. L2012ZSLYEC-090).

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doi: 10.21037/dmr.2019.06.02

Cite this article as: Zhou T, Yu H, Ma N, Yu Z, Chen J, Tang F, Jiang Z, Li Y, Hou Z, Gan W, Chen S. Sequential nutrition support with the combination of parenteral and enteral nutrition in the management of severe acute pancreatitis. *Dig Med Res* 2019;2:12.