Effect of Early Enteral Nutrition on Serum Inflammatory Factors and Intestinal Mucosal Permeability in Patients with Severe Acute Pancreatitis

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ABSTRACT

Background: *To analyze the effect of early enteral nutrition on serum inflammatory factors and intestinal mucosal permeability in patients with severe acute pancreatitis.*

Methods: *A total of 55 patients with severe acute pancreatitis were divided into 2 groups: the control group (n = 27), who received routine treatment and the observation group (n = 28), who received early enteral nutrition. The expression of serum inflammatory factors and the permeability of the intestinal mucosa were compared between the 2 groups before and after treatment, and rates of infection and mortality within 30 days were statistically analyzed.*

Results: *The recovery duration of serum and urine amylase and the length of hospital stay in the observation group were shorter than those in the control group. The white blood cell counts, levels of procalcitonin, and the expression of interleukin-6 (IL-6) in the observation group were lower than those in the control group 7 days after the treatment was commenced, and the differences were statistically significant (P < .05). The concentration of diamine oxidase in the serum and the urinary lactulose to mannitol (L/M) ratio in the observation group were lower than those in the control group 7 days after treatment was commenced. The infection rate in the observation group (21.43%) was lower than that in the control group (51.85%) (P < .05). There was no difference in the 30-day mortality between the 2 groups (P > .05).*

Conclusion: *Early enteral nutrition may reduce the expression of serum inflammatory factors, decrease the permeability of the intestinal mucosa, and improve the prognosis of patients with severe acute pancreatitis.*

Keywords: *Early enteral nutrition, severe acute pancreatitis, serum inflammatory factors, intestinal permeability*

INTRODUCTION

Pancreatitis is one of the most common acute abdominal conditions. Severe acute pancreatitis is a critical illness with complex clinical and biological manifestations; it is often accompanied by infection and persistent organ failure and has a mortality rate of 36-50%.[1] Currently, nonsurgical treatment is favored in the treatment of severe acute pancreatitis and individualized early comprehensive treatment should be adopted to improve prognosis and survival rates. Nutritional support is an important component of the treatment of severe acute pancreatitis, and its 2 main forms are enteral nutrition and parenteral nutrition. Some studies[2] have demonstrated that parenteral nutrition does not stimulate pancreatic secretions, but will lead to the translocation of intestinal bacteria and increase the risk of infection in the long term. Enteral nutrition can help to maintain the balance and stability of the intestinal flora, protect the integrity of the intestinal tract, and promote the recovery of the intestinal barrier function. Previous studies have suggested that early enteral nutrition can affect food digestion and aggravate intestinal injury.[3,4] After analysis and verification of a large volume of research data, it is considered that early enteral nutrition should be defined as that commencing 48 h after the onset of the disease and that this has a high degree of safety.[5,6] In the present study, early enteral nutrition was employed in patients with severe acute pancreatitis to assess its influence on serum inflammatory factors and intestinal mucosal permeability.

MATERIALS AND METHODS

Clinical Data

The inclusion criteria were as follows: (1) Patients who met the diagnostic criteria for severe acute pancreatitis specified

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in the Chinese guidelines for the diagnosis and treatment of acute pancreatitis (Shenyang, 2019).[7] (2) Patients who were admitted within 24 h of the onset of the disease. (3) Patients with clear cognition and good mental states. (4) Patients who were able to be informed about the research and who had signed their consent. The exclusion criteria were as follows: (1) Patients with autoimmune diseases or previous chronic pancreatitis. (2) Patients with malignant tumors or intestinal dysfunction. (3) Pregnant or lactating females. (4) Patients who could not cooperate with the follow-up procedure. Fifty-five patients admitted to our hospital with severe acute pancreatitis from January 2019 to January 2020 were enrolled. The patients were divided into 2 groups according to the therapeutic method assigned: the observation group (28 cases) and the control group (27 cases). There was no significant difference between the 2 groups in their baseline data ($P > .05$), and their baseline characteristics were comparable. The details are shown in Table 1.

The study was conducted in accordance with the Declaration of Helsinki (as was revised in 2013). The study was approved by the Ethics Committee of Shaanxi Provincial People's Hospital and informed consent was taken from all the patients.

METHODS

Both groups of patients received standard comprehensive therapy after admission, including fasting, intravenous fluids, gastrointestinal decompression, anti-infection, inhibition of gastric acid secretion, correction of water–electrolyte imbalances and acid-base disorders, and proton pump inhibitors, somatostatin, and other drugs to inhibit pancreatic enzyme activity. Patients in the control group received parenteral nutritional support, i.e., an infusion of nutrients via a peripheral or central vein. Patients in the observation group received routine treatment, accompanied by enteral nutrition, which was provided 48 h after the onset of the disease in patients with stable vital signs. The total energy intake was calculated according to the Harris–Benedict formula, and the nutritional support provided to each group was equal in terms of calories and amount of nitrogen. The total energy provided was 25-30 kcal/kg/d and the amount of nitrogen was 0.15-0.20 g/kg/d. In the observation group, under monitoring by nasogastric endoscopy, the enteral nutrition tube was placed below the ligament of Treitz. Thirty minutes later, the position of the nasogastric tube was confirmed and the external end was fixed, with the head of the bed raised to 30-45°. On the first day, 500 mL of isotonic saline was infused by slow drip, to confirm that there was no abdominal pain, abdominal distension, or other discomfort. On the second day, a suspension of Peptisorb® Liquid (Netherlands newdighia-Wuxi Co., Ltd.) was infused for 22-24 h, by an enteral nutrition infusion pump. The rate and quantity of the infusion were gradually increased, and the initial suspension of low-concentration amino acids was gradually replaced by a high concentration of whole protein preparation. The initial infusion rate was 20-30 mL/h, and this was gradually increased to 100-140 mL/h. An oral diet was gradually introduced after the abdominal pain had resolved and the routine blood and urine tests had returned to normal.

Observation Indices

(1) The recovery durations of the serum and urine amylase and the length of hospital stay of the 2 groups were compared and these data were recorded and the average values were calculated. (2) The expressions of serum inflammatory factors in the 2 groups were compared before and 7 days after the commencement of treatment. Peripheral venous blood (3 mL) was drawn and the levels of interleukin-6 (IL-6), procalcitonin (PCT), and white blood cells (WBCs) were measured. (3) Intestinal permeability in the 2 groups was compared. The level of D-lactin was determined by improved enzymatic spectrophotometry. The ratio of lactulose to mannitol (L/M) in the urine was determined by high-performance liquid chromatography (HPLC). (4) The infection rate and the 30-day mortality of the 2 groups were compared.

Statistical Methods

SPSS 20.0 software was used for data analysis. The measurement data were expressed as ±s and the *t*-test was

Table 1. Comparison of the Baseline Clinical Data Between the 2 Groups

Groups	Case	Age (Year)	APACHE II Score (points)	Gender	Type of Disease
				Male/Female	Biliary/Hyperlipidemic
Observation group	28	49.05 ± 4.52	22.14 ± 3.69	13/15	18/10
Control group	27	48.79 ± 4.50	21.98 ± 3.65	16/12	15/12
t/χ^2 value		0.214	0.162	0.328	0.437
P		.416	.436	.567	.509

adopted. The count data were expressed as percentages (%) and the χ^2 test was adopted. $P < .05$ was considered statistically significant.

RESULTS

Comparison of the Recovery Duration of the 2 Groups

As shown in Table 2, the recovery duration of the serum and urine amylase and the length of hospital stay in the observation group were shorter than those in the control group, and the differences were statistically significant ($P < .05$).

Comparison of the Expression of Inflammatory Factors of the 2 Groups

There was no significant difference in the levels of WBC, PCT, or IL-6 between the 2 groups before treatment ($P > .05$). The levels of WBC, PCT, and IL-6 decreased significantly 7 days after the start of treatment; the decrease was more pronounced in the observation group, and the difference was statistically significant ($P < .05$). The details are shown in Table 3.

Comparison of Intestinal Mucosal Permeability of the 2 Groups

There was no significant difference in the intestinal mucosal permeability of the 2 groups before treatment ($P > .05$). The concentration of DAO and the urinary L/M ratio were lower in the observation group than in the control group 7 days after the start of treatment, and the differences were statistically significant ($P < .05$) (Table 4).

Comparison of the Infection Rates and 30-day Mortality of the 2 Groups

The new-onset infection rate in the observation group was lower than that in the control group, and the difference

Table 2. Comparison of the Recovery Duration of the Serum amylase and Urine Amylase and the Length of Hospital stay Between the 2 Groups ($\bar{x} \pm s$, d)

Groups	Case	Recovery Duration of the Serum Amylase	Recovery Duration of the Urine Amylase	Length of Hospital Stays
Observation group	28	5.14 ± 1.28	12.49 ± 3.52	14.86 ± 2.85
Control group	27	7.84 ± 1.32	17.85 ± 4.17	25.78 ± 3.19
t		7.701	5.158	13.399
P		.008	.010	.001

Table 3. Comparison of the Serum Inflammatory Cytokines Before the Treatment and 7 Days after the Treatment Between the 2 Groups ($\bar{x} \pm s$)

	WBC ($\times 10^9$/L)		PCT (ug/L)		IL-6 (ng/L)	
Groups	Before Treatment	7 Days After Treatment	Before Treatment	7 Days After Treatment	Before Treatment	7 Days After Treatment
Observation group	16.05 ± 1.84	9.18 ± 1.57	6.07 ± 1.14	1.51 ± 0.36	96.51 ± 24.58	35.65 ± 11.75
Control group	15.97 ± 1.85	12.87 ± 1.61	5.96 ± 1.15	2.95 ± 0.41	94.78 ± 25.01	48.46 ± 13.49
t	0.161	8.606	0.356	13.855	0.259	3.759
P	.436	.002	.362	.001	.398	.012

Table 4. Comparison of the Permeability of Intestinal Mucosa Between the 2 Groups ($\bar{x} \pm s$)

	DAO (U/L)		L/M	
Groups	Before Treatment	7 Days After Treatment	Before Treatment	7 Days After Treatment
Observation group	1.60 ± 0.32	1.15 ± 0.34	0.030 ± 0.004	0.062 ± 0.007
Control group	1.58 ± 0.31	2.48 ± 0.53	0.029 ± 0.005	0.084 ± 0.007
t	0.235	5.077	0.821	11.652
P	.407	.010	.208	.001

Table 5. Comparison of the Infection Rate and the 30-day Mortality Between the 2 Groups [n (%)]

Groups	Case	Infection Rate	30-day Case Fatality Rate
Observation group	28	6 (21.43%)	1 (3.57%)
Control group	27	14 (51.85%)	1 (3.70%)
χ^2 value		5.498	0.482
P		.019	.488

was statistically significant ($P < .05$). There was no difference in the 30-day mortality between the 2 groups ($P > .05$). The details are shown in Table 5.

DISCUSSION

Acute pancreatitis is the occurrence of acute pancreatic edema, necrosis, and hemorrhage due to increased enzyme activity in the pancreas in response to a range of factors. Patients with severe acute pancreatitis are critically unwell, experiencing severe oxidative stress, inflammation, gastrointestinal paralysis, and edema in the early stage of the disease; gastrointestinal function is seriously impaired, and there is a serious risk of abdominal compartment syndrome.[8] At the same time, the intestinal barrier is damaged, and this is prone to cause intestinal bacterial translocation. As the result of endotoxins entering the bloodstream, intestinal infection, an inflammatory cascade reaction and multiple organ failure may occur and may lead to death.[9,10]

Nutritional support is an essential component of the treatment of severe acute pancreatitis. The main forms of nutritional support in this context are complete parenteral nutrition and enteral nutrition. Complete parenteral nutrition can provide the nutrition that patients require and improve their prognosis, but it cannot promote normal gastrointestinal function. Long-term complete parenteral nutrition is likely to cause changes in the intestinal flora and atrophy of the intestinal mucosa, which may impair the barrier function of the intestinal mucosa and lead to enterogenous infection.[11,12] In contrast, enteral nutritional support cannot only provide energy and nutrition, but also enhance gastrointestinal function, maintain the balance and stability of intestinal flora, and prevent intestinal mucosal damage.[13] It can also reduce intestinal inflammation and the dysfunction of various organs. In addition, enteral nutrition may enhance the ability of the portal system to absorb nutrients and transport them to the liver, which can regulate the release of visceral protein, helping to maintain the normal structure of the intestinal mucosa and reducing the occurrence of intestinal flora translocation.[14]

However, the optimal timing of enteral nutrition support remains uncertain. It is generally believed that enteral nutrition commenced too early will increase the burden on the pancreas and cause abdominal distension.[15] Based on the results of a large number of studies, the earliest appropriate time for initiation of enteral nutritional support has been defined as 48 h after the onset of the disease, and this would be regarded as early enteral nutrition. In other words, enteral nutritional support may be employed after stabilization of hemodynamics and the internal environment.[16,17] In the present study, the recovery durations of serum and urine amylase in the observation group were shorter than those in the control group, and the infection rate was lower in the observation group (21.43%) than in the control group (51.85%) ($P < .05$). There was no difference between the 2 groups in their 30-day mortality ($P > .05$). The present study suggests that early enteral nutrition may promote clinical recovery, reduce the length of hospital stays, and reduce the incidence of infection; this is consistent with the findings reported by Chen Yu.[18]

Infection is the main cause of death in patients with severe acute pancreatitis, and more than 90% of the secondary infections are caused by intestinal flora translocation. Increased permeability of the intestinal mucosa is the underlying cause of bacterial translocation. Lactulose and mannitol are important indices for the evaluation of intestinal mucosal integrity because they are not easily metabolized by the human body and have high urinary recovery rates. An increased urinary L/M ratio indicates an increased permeability of the intestinal mucosa.[19] DAO is produced by bacterial metabolism in the intestine. In acute pancreatitis, acute intestinal bleeding occurs and the epithelium on the top of the intestinal mucosal villi is shed, increasing the permeability of the intestinal mucosa and making the proliferating bacteria in the intestine release a large amount of DAO. In the present study, the concentration of DAO and the urinary L/M ratio in the observation group were lower than those in the control group 7 days after the commencement of treatment ($P < .05$). These results suggest that early enteral nutrition could significantly improve the integrity of the intestinal mucosa and assist patients' recovery. Early enteral nutrition may help to maintain the stability of the intestinal flora and internal environment, and thereby reduce the incidence of infection.

An inflammatory reaction is an early response in patients with severe acute pancreatitis. In the early stage of the disease, under the stimulation of pancreatic enzymes, inflammatory cells such as monocytes and macrophages become activated, releasing a large number of WBCs as well as IL-6 and other inflammatory cytokines.[20] PCT, an acute response protein, is highly expressed in severe bacterial and/or fungal infections and sepsis. In the present study, after 7 days of treatment, the levels of WBCs, IL-6, and PCT in the observation group were significantly lower than those in the control group, and the differences were statistically significant ($P < .05$). These results suggest that early enteral nutrition may reduce the inflammatory reaction, possibly by enhancing immune function and inhibiting the release of endotoxins. However, there are limitations to this study. Firstly, The low number of patients was not enough to support the conclusions solidly. Secondly, we did not check for pancreatitis complications in addition to mortality on the 30th day. Thirdly, the absence of changes in the patient's clinic with enteral feeding in addition to laboratory data during follow-up was also regrettable. We will try our best to design more strictly and make up these problems in the following research.

CONCLUSION

In conclusion, early enteral nutrition in patients with severe acute pancreatitis can reduce the expression of serum inflammatory factors and the permeability of intestinal mucosa, and improve prognosis; these findings are worthy of attention.

Ethics Committee Approval: The study was conducted in accordance with the Declaration of Helsinki (as was revised in 2013). The study was approved by the Ethics Committee of the Shaanxi Provincial People's Hospital.

Informed Consent: Written informed consent was obtained from all participants.

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