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# Effect of early enteral nutrition (EN) on endotoxin in serum and intestinal permeability in patients with severe acute pancreatitis

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**Abstract. – OBJECTIVE: This work aimed at studying the effect of early enteral nutrition (EN) on serum endotoxin and intestinal permeability in patients with severe acute pancreatitis.**

**PATIENTS AND METHODS: 70 cases of patients with severe acute pancreatitis were cured in our hospital from April 2015 to January 2016. Patients selected were randomly divided into two groups including a group of patients having parenteral nutrition (group PN) and that had enteral nutrition (group EN). The results were assessed by: 1) the differences of serum endotoxin level; 2) the differences of the lactulose/mannitol ratio of urine, before intervention and one and two weeks after the intervention.**

**RESULTS: Before the intervention, both groups had similar levels of serum endotoxin and the same lactulose/mannitol excretion rate of urine ($p>0.05$). One and two weeks after the intervention, the serum endotoxin level and the lactulose/mannitol excretion rate of urine of the group PN were significantly higher than the group EN ($p<0.05$).**

**CONCLUSIONS: Compared with PN, EN has a bigger effect on serum endotoxin and intestinal permeability in patients with severe acute pancreatitis. EN can better promote the elimination of serum endotoxin and reduce intestinal permeability. Therefore, EN deserves clinical expansion.**

Key Words
EN, Patients with severe acute pancreatitis, Serum endotoxin, Intestinal permeability, Effect.

## Introduction

Acute pancreatitis is a kind of common acute abdomen in surgical practice[1,2]. Nowadays, along with the improvement of medical technology, the cure rate of acute pancreatitis has gradually increased, but the mortality rate is still high[3]. In recent years, clinical studies have shown that, among all, the bacterial translocation is a relevant factor posing a threat to the lives of patients with acute pancreatitis[4,5]. Herein, we have analyzed the effect of EN on serum endotoxin and intestinal permeability in patients with severe acute pancreatitis.

## Patients and Methods

### Patients

70 cases of patients with severe acute pancreatitis were cured in our hospital from April 2015 to January 2016. Patients selected were randomly divided into the group PN and group EN by random number table.

Among 35 cases of patients in the EN group, there were 27 male cases and 8 female cases of the age from 21 to 65-year-old, averaging (44.89±5.13) years old. The APACHE-II score of patients was (11.82±3.28) points. As well, among the 35 cases of patients in the PN group: there were 25 male cases and 10 female cases, at the age from 22 to 65-year-old, averaging (44.13±5.29) years old. The APACHE-II score of patients was (11.52±3.13) points.

The baseline data, such as patients' ages, APACHE-II score, and gender as defined above showed no statistical difference, and thus comparable.

This study was approved by the Ethics Committee of Zhumadian Central Hospital. Signed written informed consents were obtained from all participants before the study.

### Methods

All patients were given routine interventions such as the correction of electrolyte acid-base disturbance and supplement of blood capacity


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after admission to the hospital. The PN group was given PN intervention and nourished through central venous catheterization. The intervention was implemented 24 to 72 hours after admission to the hospital. The fat was 500 ml of 20% medium-long chain lipid emulsion. Meanwhile, 1000-1500 ml of 11.4% compound amino acid was given to patients. The exogenous insulin supplemented according to the monitoring result of blood sugar and blood sugar was controlled within 6.1-8.1 mmol/L. The various microelements and vitamins were supplemented at the same time.

The EN group was given EN intervention. After placement of jejunum nutrient canal, if patients suffer no severe enteral paralysis, gastrointestinal hemorrhage, shock, intestinal fistula or intestinal obstruction. 24-48 hours after admission, 500 ml of 37°C isotonic saline nasal feeding was given at the speed of 40-60 ml/h on the first day. 100 ml of isotonic saline and 5% glucose saline were given at the same speed on the second day, and the 500 ml of nutrition fiber isotonic saline was given on the third day. If the patients remained tolerant without any signs of adverse reactions, the nutrition fiber isotonic saline can be gradually adjusted to 1000-1500 ml/d.

### Observation Indexes and Standards

The research results were assessed by[6]: (1) the differences of serum endotoxin level (2) the differences of the lactulose/mannitol ratio before the intervention, one and two weeks after intervention.

### Statistical Analysis

SPSS21.0 (SPSS, Inc., Chicago, IL, USA) software was adopted to count relevant data of patients with severe acute pancreatitis. (x±s) was used to express the serum endotoxin level and the lactulose/mannitol excretion rate of urine. The *t*-test was applied to measurement data. $p<0.05$ was considered to be statistically significant.

## Results

### Comparisons of the Serum Endotoxin Levels before and after Intervention

Before the intervention, the two groups had similar levels of serum endotoxin and the same lactulose/mannitol excretion rate of urine ($p>0.05$). However, one and two weeks after intervention, the serum endotoxin level and the lactulose/mannitol ratio of urine of the group PN were significantly higher than the group EN ($p<0.05$) (Table I).

### Comparison of Inflammatory Factor Levels

Before the treatment, comparison of inflammatory factor levels between the group EN and the group PN revealed no statistical significance ($p>0.05$). After treatment, the levels of inflammatory factors in the group EN including the levels of TNF-α (989±148) pg/mL, IL-1β (415±97) pg/mL, IL-6 (402±105) pg/mL and IL-8 (373±95) pg/mL were all significantly lower than those of the group PN ($p<0.05$) (Table II).

### Comparison of the Lactulose/mannitol Excretion Rate of Urine before and after Intervention

Before the intervention, the two groups had similar levels of serum endotoxin and the same lactulose/mannitol excretion rate of urine and *t*-test showed no significant difference ($p>0.05$); one and two weeks after intervention, the serum endotoxin level and the lactulose/mannitol excretion rate of urine of the group PN were significantly higher than the group EN (Table III).

## Discussion

Acute pancreatitis in terms of body fluid volume can be divided into low-volume acute pancreatitis, normal-volume acute pancreatitis and high-volume acute pancreatitis[7]. Low-volume acute pancreatitis should be actively rehydrated

**Table I.** The comparisons of the serum endotoxin level before and after intervention (x±s, EU/ml).

| Group | Before | Intervention for one week | Intervention for two weeks |
|---|---|---|---|
| Group EN | 0.12±0.06 | 0.11±0.03 | 0.06±0.03 |
| Group PN | 0.11±0.06 | 0.21±0.12 | 0.25±0.13 |
| *t* | 0.274 | 9.024 | 10.761 |
| *p* | 0.452 | 0.000 | 0.000 |

**Table II.** Comparison of inflammatory factors levels.

| Group | Cases | | TNF-α (pg/mL) | IL-1β (pg/mL) | IL-6 (pg/mL) | IL-8 (pg/mL) |
|---|---|---|---|---|---|---|
| Group EN | 35 | Before | 1349±184 | 634±127 | 591±117 | 563±114 |
| | | After | 989±148[ab] | 415±97[ab] | 402±105[ab] | 373±95[ab] |
| Group PN | 35 | Before | 1338±180 | 650±129 | 597±121 | 560±112 |
| | | After | 1203±152[a] | 572±108[a] | 536±107[a] | 483±102[a] |

**Table III.** Comparison of the lactulose/mannitol excretion rate of urine before and after intervention ($\bar{x}$±s, L/M).

| Group | Before intervention | Intervention for one week | Intervention for two weeks |
|---|---|---|---|
| Group EN | 0.0924±0.0215 | 0.0632±0.0134 | 0.0312±0.0045 |
| Group PN | 0.0932±0.0242 | 0.0822±0.0252 | 0.0726±0.0146 |
| *t* | 0.035 | 6.935 | 8.358 |
| *p* | 0.885 | 0.000 | 0.000 |

while high-volume acute pancreatitis highlights the limitation of body fluid. Successful treatment of shock accompanied by severe acute pancreatitis lies in explicit volume status and maintenance of appropriate preload[8]. Central Venous Pressure (CVP) used to be applied to the assessment of volume, but it can be influenced by various factors, including right ventricular pump function, circulating blood volume, vascular tone of systemic circulation venous system and intrathoracic pressure[9-11]. Most of the acute pancreatitis belongs to self-limited disease, but some patients may suffer vascular tone change and diffuse damage of vessels resulted by the serious inflammatory reaction around the pancreas, which tends to lead to systemic inflammatory response syndrome. The severe acute pancreatitis is featured by high mortality rate and high incurrence of complications. It can cause damages to the gut barrier function of patients and invasion of bacteria and serum motilin to the human body, which both can result in severe systemic inflammatory response syndrome and pose a great threat to the patient lives[12,13]. Prompt diagnosis and implementation of comprehensive treatment contribute to improving the cure rate and reducing fatality rate[14,15].

Among the nutritional supportive means of severe acute pancreatitis, PN is the main method. The clinical research has shown that PN can meet the hypermetabolism demands of patients with severe acute pancreatitis and have obvious no stimulant effect on pancreatic secretion[16]. Long-term implementation of PN can cause a deficiency of glutamine, a kind of special intestinal nutrient, leading guts to lose mechanical stimulation function of food. As a result, patients may suffer atrophy of gut mucous and damage to intestinal barrier function, which translocate the heterogeneous bacteria or endotoxin, worsen the situation, cause secondary infection of the pancreas and peripancreatic tissue and even cause the death of patients[17-20].

Early enteral nutrition can not only provide all nutrients, but also improve the intestinal barrier function of patients. L/M ratio was a significant indicator to reflect intestinal permeability. Some studies[21] suggested that different levels of L/M ratio increase can be found in AP patients, while the L/M ratio declined significantly after the EN treatment, suggesting the improvement of the intestinal permeability. Another view held that, although EN treatment can improve intestinal permeability in patients, some patients suffer stomachache, diarrhea and poor tolerability at an early phase. The digestive function of patients was weak at the same time. The decomposition of AP was bad at an early phase, and long-term hypoglycemia may cause irreversible nerve damage[22]. In our research, the group PN was given PN intervention and the group EN was given EN intervention. The results showed that, the levels of inflammatory factors in the group EN including TNF-α (989±148) pg/mL, IL-1β (415±97) pg/mL, IL-6 (402±105) pg/mL and IL-8 (373±95) pg/mL were all lower than the group PN after treatment, with differences of statistically significance ($p<0.05$). Before the intervention, the two groups had similar levels of serum endotoxin, and the same lactulose/mannitol excretion rate of urine and *t*-test showed no significant difference ($p>0.05$). One and two weeks after intervention, the serum endotoxin level and the lactulose/mannitol excretion rate of urine of the group PN were significantly higher than the group EN ($p<0.05$). This result indicated that early enteral nutrition

treatment could effectively eliminate endotoxin in serum. The main reason is that EN can better fit people's physiological metabolism, but cause no increase in pancreatic secretion and can promote recovery of intestinal function. Moreover, it is favorable for maintenance of the immune barrier function of the intestinal tract, mechanical and biology, and reduce the incidence of heterogeneous infections[14,15]. Also, we found that the serum endotoxin level of group EN was obviously reduced after one week and two weeks of intervention. Compared with the group PN, EN can greatly reduce the translocation of toxin and heterogeneous bacteria, which can prevent inflammatory cells from releasing continually and excessively. After the intervention, the lactulose/mannitol excretion rate of urine in the group EN was all-lower than the group PN. We believe that maybe it is because glutamine, a special nutrient substance that in EN can effectively maintain mucosa metabolism, reduce the intestinal permeability and decrease bacteria translocation[16,17].

There were some limitations in this research: the cases of patients enrolled in groups were limited, and some severe acute pancreatitis may be treated with hemodialysis because of the over serious condition. Therefore, this work needs further confirmation via a large work sample size.

## Conclusions

Compared with PN, EN has a bigger effect on serum endotoxin and intestinal permeability in patients with severe acute pancreatitis, because can better promote the elimination of serum endotoxin and reduce intestinal permeability. Therefore, EN deserves clinical expansion.

### Conflict of interest

The Authors declare that they have no conflict of interests.

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