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The Effect of Enteral Nutrition on Intra-Abdominal Pressure in Severe Acute Pancreatitis Patients

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Severe acute pancreatitis (SAP) is a serious surgical disease with a mortality of 25% to 40%.[1,2] Patients with SAP tend to have elevated intra-abdominal pressure (IAP), which eventually leads to intra-abdominal hypertension (IAH). IAH causes organ dysfunctions such as respiratory, circulatory, and renal failure, known as abdominal compartment syndrome (ACS).[3,4] About 11% of SAP patients suffer from complications of ACS. SAP patients complicated with ACS, a special type of pancreatitis, tend to have a mortality of 66.7%.[5,6] Nutritional support is emerging as a vital component of the management of SAP, and enteral nutrition (EN) is reported to be the best nutritional support in SAP.[7] EN avoids total parenteral nutrition (TPN) complications, maintains intestinal health, and may prevent the progression of multiple organ failure.[8] In this prospective randomized study, we focused on the effect of EN on IAP in SAP patients. Through comparison with the control group, we demonstrate whether the EN support can decrease the IAP in SAP patients and show the therapeutic effect.

Materials and Methods

Patients

A total of 80 consecutive SAP patients who were treated in the Surgery Department of the Central Hospital of Huzhou from August 2010 to April 2015 were included in the study. The age of the patients ranged from 24 to 77 years (mean: 55.3 years; median: 47 years). There were 37 males (46.2%) and 43 females (53.8%), the male-to-female ratio was 0.86:1. When they were hospitalized, the severity of SAP was evaluated according to CT serious index (CTSI)[9]; acute physiology and chronic health evaluation II (APACHE II) score[10]; and the diagnostic criteria and severity grade for AP proposed by the Japanese Ministry of Health, Labor, and Welfare.[11] The diagnosis of ACS was made as previously described.[12] Demographic

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Table 1 Demographic data, CTSI score, APACHE II score, ICP data, ACS occurrence rate, and severity grade ratio of the two groups when hospitalized (mean ± SD)

	Control group ($n = 40$)	Study group ($n = 40$)
Age, y	56.2 ± 6.7	54.7 ± 9.2*
Sex, male/female	18/22	19/21*
ICP, cmH_2O	18.7 ± 3.6	19.5 ± 3.4*
CTSI score	7.9 ± 1.6	8.2 ± 1.5*
APACHE II score	18.2 ± 3.9	17.5 ± 4.5*
ACS rate, %	20.0	17.5*
Severity grade, II/III	33/7	32/8*

*$P > 0.05$ *vs* control group

data, CTSI, APACHE II scores, severity grade for SAP, and ACS occurrence rate were not statistically different between the study and control groups (Table 1).

Methods

We randomly divided 80 SAP patients admitted for routine nonoperative conservative treatment into a study group and a control group (40 patients in each group). Two groups all received Da Cheng Qi Decoction enema (one dose, 100 mL) for 2 hours once a day during hospitalization to accelerate the gastrointestinal function recovery. One dose of Da Cheng Qi Decoction consists of 10 g *Rheum officinale* Baill, 10 g sodium sulfate, 10 g *Magnolia obavata*, 10 g *Fructus aurantii*, 10 g *Radix paeoniae rubra*, and 10 g *Raphanus sativus*.[13] In the study group, an enteral tube was placed. When the subjects were hospitalized, they were shifted to an endoscopic suite and a 16-Fr. single lumen 125-cm long red rubber feeding tube was placed over a 400-cm long stainless steel guidewire (Wilson Cook, Winston-Salem, North Carolina) beyond the ligament of Treitz using fluoroscopic control. When the patient's gastrointestinal function recovered, a test feed with 500 mL of normal saline was administered over a period of 4 to 5 hours and nutrition feed (Nutrison, 500 mL: 500 kcal, protein 20 g, fat 19.5 g, carbohydrate 61.5 g, fiber 7.5 g, minerals 2.5 g, vitamins 150 mg, Nutricia Co., Rockville, Maryland) was started subsequently for 7 days. Minor complications such as diarrhea and distension were managed by altering the infusion rate and adding an antimotility agent. The control group received TPN for 7 days. The targeted caloric and protein requirements in two groups were 29.8∼34.7 $kcal \cdot kg^{-1} \cdot d^{-1}$, and 1.75∼2.25 $g \cdot kg^{-1} \cdot d^{-1}$ of protein. EN feeding was started at low flow rates—an initial rate of 20 mL/h until achievement of the full regime of EN. Routine nonoperative conservative treatment modalities included gastrointestinal decompression, life support, continuous peripancreatic vascular pharmaceutical infusion,[14,15] and drug therapy. Nitrogen balance (NB) data and Intracystic pressure (ICP) data that could reflect the IAP conditions were tested on hospitalization day and on days 1 through 7 of treatment. ICP data were defined using the methods by Fusco *et al*.[16] NB data were defined using the test methods by Hesgsted *et al*.[17] Outcomes of the treatment including abdominalgia relief time, ACS occurrence rate and operation rate of pancreas debridement. APACHE II scores, defined using a commercial computing program (Microsoft APACHE II, version 5.1, Microsoft Corp, Redmond, Washington) were applied for analysis.

Statistical analysis

All data were prepared and compiled using a statistical computer program (SPSS for windows, version 13.0, SPSS, Inc, Chicago, Illinois). The data were expressed as mean ± SD. Kolmogorov-Smirnov test was used for the pattern of data distribution. Student's unpaired *t*-test was used to compare data between the 2 groups when they were normally distributed. The Mann-Whitney *U*-test was used when the data were not normally distributed. Chi-square and Fisher's exact tests were used for quantitative data. Logistic analysis was used for multivariate correlation analysis. A value of $P < 0.05$ was considered statistically significant.

Results

ICP, NB, and APACHE II scores

On day 1 of treatment, the ICP data obtained from the study group were higher than those obtained from the control group ($P < 0.05$). On days 4 and 5 of treatment, the ICP data obtained from the study group were lower than those obtained from the control group ($P < 0.05$). The ICP data significantly decreased from the 4th treatment day in the study group ($P < 0.05$), while significantly decreasing from the 6th treatment day in the control group ($P < 0.05$). On days 3 through 5 of treatment, the APACHE II scores of the study group were lower than those of the control group ($P < 0.05$). The cumulative scores of APACHE II were significantly decreased from the 3rd treatment day in the study group ($P < 0.05$), while significantly decreasing from the 6th treatment day in the control group ($P <$

Table 2 ICP data, NB data, and APACHE II score of the 2 groups (mean ± SD)

	ICP			APACHE II scores			NB (g/kg)		
	Control group ($n = 40$)	Study group ($n = 40$)	*P*-value	Control group ($n = 40$)	Study group ($n = 40$)	*P*-value	Control group ($n = 40$)	Study group ($n = 40$)	*P* value
HPd	18.7 ± 3.6	19.5 ± 3.4		18.2 ± 3.9	17.5 ± 4.5		–0.42 ± 0.03	–0.45 ± 0.03	
d1	17.4 ± 3.8	29.5 ± 3.2	<0.05	17.9 ± 4.1	16.4 ± 3.5		–0.43 ± 0.03	–0.44 ± 0.01	
d2	16.2 ± 1.9	15.8 ± 2.5		16.5 ± 3.9	14.2 ± 4.2		–0.41 ± 0.03	–0.32 ± 0.12	
d3	15.9 ± 3.1	15.6 ± 2.7		13.5 ± 1.9	9.7 ± 1.9[a,b]	<0.05	–0.33 ± 0.02	0.12 ± 0.07[a,b]	<0.05
d4	15.2 ± 3.7	8.2 ± 1.5[a,b]	<0.05	12.4 ± 2.2	7.4 ± 1.7[a,b]	<0.05	–0.41 ± 0.04	0.12 ± 0.07[a,b]	<0.05
d5	14.7 ± 2.9	8.7 ± 3.2[a,b]	<0.05	10.8 ± 2.0	4.6 ± 1.5[a,b]	<0.05	0.12 ± 0.22△	0.12 ± 0.12[b]	
d6	7.5 ± 3.5△	7.9 ± 3.9[b]		5.2 ± 2.7△	4.3 ± 2.0[b]		0.13 ± 0.02△	0.13 ± 0.12[b]	
d7	8.1 ± 2.7△	7.4 ± 2.8[b]		4.2 ± 1.6△	3.8 ± 1.5[b]		0.13 ± 0.02△	0.12 ± 0.04[b]	

HPd: Hospitalization day.

[a]Value of $P < 0.05$ means the ICP, NB and APACHE II scores of study group versus that of the control group.

[b]Value of $P < 0.05$ means the ICP, NB and APACHE II scores of the study group versus that of HPd. △$P < 0.05$ means the ICP, NB, and APACHE II scores of the control group versus that of HPd.

0.05). In the study group, the patient's NB data increased significantly on the 3rd treatment day ($P < 0.05$), while increasing significantly on the 5th treatment days in the control group ($P < 0.05$), as shown in Table 2.

Outcomes of treatment

As shown in Table 3, abdominalgia relief time of the study group was shorter than that of the control group ($P < 0.05$), operation rate of pancreas debridement in the study group was significantly lower than that of the control group ($P < 0.05$). ACS occurrence rate of the study group was lower than that of the control group, but there was no significant difference between the 2 groups ($P > 0.05$).

Correlation between ICP data and NB, APACHE II scores, outcome of treatment

The ICP data and APACHE II scores, abdominalgia relief time, and the operation rate of pancreas debridement show positive correlation ($r = 0.749 \sim 0.874$, $P < 0.05$). The ICP data and NB data show negative correlation ($r = –0.826$, $P < 0.05$). The ICP data and ACS occurrence rate show positive correlation, but there was no statistical significance ($r = 0.242$, $P > 0.05$).

Table 3 Relief time of abdominalgia, operation rate of pancreas debridement, and ACS occurrence rate in the 2 groups (mean ± SD)

	Control group ($n = 40$)	Study group ($n = 40$)	*P* value
Relief time of abdominalgia, d	9.9 ± 1.2	4.3 ± 0.9[a]	0.035
ACS occurrence rate, %	20.0 (8/40)	7.5 (3/40)	0.194
Operation rate of pancreas debridement, %	32.5 (13/40)	10.0 (4/40)[a]	0.029

[a]$P < 0.05$ versus control group.

Discussion

It is generally accepted that EN is the best nutritional support in SAP. EN modifies the malnutrition of SAP patients, avoids TPN complications, maintains intestinal health, and prevents enterogenic infection and the progression of multiple organ failure, which could improve the prognosis of SAP patients.[18,19] In our study, the NB data of the group receiving EN increased more rapidly than the group receiving TPN ($P < 0.05$). The APACHE II scores in the study group decreased more rapidly than those of the control group ($P < 0.05$). Abdominalgia relief time and operation rate of pancreas debridement in the study group was significantly lower than those of the control group ($P < 0.05$). These results also proved that EN support can have a therapeutic effect on SAP.

In our study, another important observation is that the ICP data in the study group decreased more rapidly than that of the control group ($P < 0.05$), which demonstrates that administering EN to SAP patients could reduce the IAP more rapidly than administering TPN. It was generally accepted that SAP can result in IAH and ACS.[20,21] The probable mechanisms are:

1. Systemic inflammatory response syndrome (SIRS) triggered by local inflammation in the

pancreas.[22] The fundamental pathophysiology of SIRS is hypercytokinemia, a pathologic condition in which inflammatory cytokines are excessively released from immunocompetent cells.[23] During SIRS, activated inflammatory mediators result in the development of systemic capillary leakage syndrome (SCLS).[24] In SCLS, vascular permeability is increased by the pathologic effects of humoral mediators, leading to interstitial edema and reduction of circulating blood volume.[25] Progressive edema of the peritoneum and gut contents could rapidly increase IAP.

2. Massive pancreatic liquid and pancreatic necrotic tissue collection in the abdominal and retroperitoneal cavity, combined with infection would lead to the formation of abscess, causing intestinal obstruction and erosion of the surrounding organs, which further result in perforation and massive bleeding and recurrence of SIRS and SCLS. Edema caused by the septic retroperitoneal necrosis pushes the peritonitis, thus rapidly increasing IAP.[26]
3. In the treatment of SAP, early resuscitation with a large volume of fluid is essential to maintain organ perfusion. However, aggressive fluid resuscitation may aggravate intestinal edema, further increasing IAP.[27] Abrupt elevation of IAP eventually causes IAH, which leads organ dysfunction such as respiratory, circulatory and renal failure, known as ACS.[28] While the EN support can consolidate the protective screen of gastrointestinal mucosa to prevent damage to them, EN can also reduce enterogenic infection to ameliorate the inflammatory response and SIRS.[7,29] Moreover, EN can prevent the need for aggressive fluid resuscitation with a great quantity of injecting liquid, thus relieving edema in organ tissue. Perhaps through this means, EN shows a more efficient effect on IAP than TPN. In the study of correlation between ICP data and NB, APACHE II scores, and outcome of treatment, we found the ICP data and APACHE II scores, abdominalgia relief time, and the operation rate of pancreas debridement show positive correlation ($P < 0.05$). The ICP and NB data show negative correlation ($P < 0.05$), and demonstrate IAP is an indicator to a poor prognosis of SAP patients. The trend of rapid decrease of IAP would show a positive prognosis of SAP. Thus, we can conclude that the preventive and therapeutic effects of EN on SAP may be a means of decreasing the IAP of SAP.

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