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Effects of nutritional support combined with insulin therapy on serum proteins, inflammatory factors, pentraxin-3, and serum amylase levels in patients with diabetic ketoacidosis complicated with acute pancreatitis

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Abstract

To explore the effects of nutritional support combined with insulin therapy on serum protein, procalcitonin (PCT), C-reactive protein (CRP), tumor necrosis factor-α (TNF-α), pentraxin-3 (PTX-3), and serum amylase (AMS) levels in patients with diabetic ketoacidosis complicated with acute pancreatitis.

A total of 64 patients with diabetic ketoacidosis complicated with acute pancreatitis admitted to our hospital from January 2018 to February 2019 were enrolled in this prospective study. They were divided into the study group and the control group according to the random number table method, with 32 patients in each group. Patients in the study group were given nutritional support combined with insulin therapy, and patients in the control group were given insulin therapy.

There were no significant differences in general data including age, gender, body mass index, course and type of diabetes, acute physiology and chronic health evaluation II, RANSON, CT grades between the 2 groups before treatment (all $P > .05$). After 7 days of treatment, the clinical efficacy of the study group was significantly higher than that of the control group (study group vs control group, 94.44% vs 75.00%, $P < .05$). After 7 days of treatment, the levels of prealbumin and albumin in the study group were significantly higher than those in the control group ($P < .05$). After 7 days of treatment, the levels of PCT, CRP, TNF-α, PTX-3, and AMS in the 2 groups were significantly lower than those before treatment ($P < .05$), and the levels of PCT, CRP, TNF-α, PTX-3, and AMS in the study group were significantly lower than those in the control group. After 7 days of treatment, the levels of IgG, IgM, and IgA in the 2 groups were significantly higher than those before treatment, and the levels of IgG, IgM, and IgA in the study group were significantly higher than those in the control group ($P < .05$).

Nutritional support combined with insulin is obviously effective in the treatment of diabetic ketoacidosis complicated with acute pancreatitis, which can improve serum protein levels, reduce inflammatory response, improve immune function, and is worthy of clinical application.

Abbreviations: ALB = albumin, AMS = serum amylase, CRP = C-reactive protein, HGB = hemoglobin, PA = prealbumin, PCT = procalcitonin, PTX-3 = pentraxin-3, TNF-α = tumor necrosis factor-α, TP = total protein.

Keywords: acute pancreatitis, C-reactive protein, diabetic ketoacidosis, insulin, nutritional support, pentraxin-3, serum amylase, serum protein level, serum protein procalcitonin, tumor necrosis factor-α

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The study protocol was approved by the Ethics Committee of Tangshan Worker Hospital. Informed consent was obtained from all the study subjects before enrollment.

Consent for publication is not applicable.

The authors have no conflicts of interest to disclose.

The datasets generated during and/or analyzed during the current study are available from the corresponding author on reasonable request.

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1. Introduction

Diabetes is a common chronic disease of the endocrine system, which is a serious threat to the population health, and its incidence is increasing year by year.[1] With the rapid economic development and the improvement of people's living standards, the proportion of diabetic patients in China is increasing rapidly. The prevalence of diabetes in China has soared from 0.67% in 1980 to 11.2% in 2017.[1] Without timely and effective control of blood glucose, patient with diabetes is prone to multiple complications, in which ketoacidosis is the most common. Acute pancreatitis is a common complication of diabetic ketoacidosis, with an incidence of 10% to 15%.[2] Insufficient insulin or insulin resistance in patients with diabetic ketoacidosis will increase stress hormones and trigger metabolic disorders, which may lead to death of patients in severe cases.[3,4] In clinical practice, if the patient has diabetic ketoacidosis complicated with acute pancreatitis, the condition is critical and the mortality rate is extremely high. Diabetic ketoacidosis and pancreatitis can be induced and promoted by each other, so how to treat them and improve the prognosis of patients is a difficult problem that clinical medical workers need to face. Nutritional support combined with drug therapy is an important way to treat patients with diabetic ketoacidosis and pancreatitis. Diabetic patients are showed abnormal glucose, lipid, and protein metabolism, and some patients often have serious complications. This state will directly affect the entire treatment process, which is not conducive to the treatment of the primary disease, reduce the patient's quality of life, and even affects the prognosis. Therefore, reasonable and effective nutritional support is of positive significance to most malnourished diabetic patients. Nutritional support not only maintains a good metabolic status, but also avoids the occurrence of complications such as abnormal blood glucose levels, water metabolism disorders, ketosis or hyperosmolar coma, infections and nerve damage. Meanwhile, it can improve the patient's nutritional status and maintain the balance of various nutrients required by the human body. Acute gastrointestinal dysfunction and gastrointestinal mechanical obstruction can occur in the early stage of acute pancreatitis, accompanied by intestinal barrier dysfunction and reduced nutritional status and immune function, which is not conducive to the prognosis of patients.[5,6] Therefore, nutritional support combined with drug therapy may be an important way to treat diabetic ketoacidosis complicated with acute pancreatitis. There have been some clinical studies on the effect of insulin in the treatment of diabetic ketoacidosis, but there are few studies on nutrition support combined with insulin in the treatment of diabetic ketoacidosis complicated with pancreatitis at present. Herein, our study aimed to explore the therapeutic effects of nutritional support combined with insulin therapy in patients with diabetic ketoacidosis complicated with acute pancreatitis, and to observe its effects on the nutritional condition, inflammatory response, immune function of patients.

2. Materials and methods

2.1. Clinical data

Sixty-four patients with diabetic ketoacidosis complicated with acute pancreatitis who were admitted to Tangshan Worker Hospital from January 2018 to February 2019 were included in this prospective study. They were divided into the study group and the control group according to the random number table method, with 32 patients in each group. Patients in the study group were given nutritional support combined with insulin therapy, and patients in the control group were given insulin therapy. This study was approved by the Ethics Committee of Tangshan Worker Hospital, and all patients signed informed consent. This study was conducted in accordance with the Helsinki Declaration of the World Medical Association.

Sample size calculation: according to the formula,[7] the sample size was estimated by mean value comparison, $n_c=(\mu_{1-\alpha/2}+\mu_{1-\beta})2s2(1+1/k)/(\mu_t-\mu_c)2$, nc was the number of cases of the control group. $\mu_{1-\alpha/2}$ and $\mu_{1-\beta}$ represented the percentage of 1-α/2 and 1-β in the standard normal distribution, t represented the mean of the experimental group, c represented the mean of the control group, s was the combined standard deviation of the 2 groups, and k was the ratio of the number of cases in the 2 groups. $\alpha = 0.05$, $\beta = 0.01$, $s=\sqrt{\frac{(n_1-1)s_12+(n_2-1)s_22}{n_1+n_2-2}}$ (n_1 and n_2 were the number of cases in the 2 groups, s_1 and s_2 were the standard deviations of the 2 groups). According to the regulations of the State Food and Drug Administration, 15% was the withdrawal rate, so the grouping sample size of this study was $n=11\times1/(1\sim0.15)=31.43\approx32$. Therefore, 64 patients with diabetic ketoacidosis and pancreatitis who were admitted to our hospital from January 2018 to February 2019 were selected as the research subjects. The method of randomized controlled study was adopted, and the ratio of the 2 groups was 1:1.

2.2. Inclusion and exclusion criteria

Inclusion criteria: in line with the diagnostic criteria for diabetic ketoacidosis complicated with acute pancreatitis[8]: blood glucose ≥ 16 mmol/L, blood pH < 7.35, blood ketone body ≥ 5.5 mmol/L, blood amylase > 125 U/L, elevated blood amylase and/or lipase ≥3 times the upper limit of normal; symptoms suggestive of abdominal pain consistent with a diagnosis of acute pancreatitis (acute, sudden, persistent, severe epigastric pain often radiating to the back); CT or magnetic resonance imaging (MRI) or abdominal B-ultrasound findings consistent with the imaging features of acute pancreatitis, and breath of rotten apple smell; patients with high compliance and normal mentality; and all patients or their families signed informed consent. Exclusion criteria: patients allergic to the drugs used in this study; severe infectious diseases; lactating or pregnant women; severe heart, liver, and kidney diseases; malignant tumors; hematological system diseases; and cognitive dysfunction.

2.3. Treatment measures

All patients were fasted and water was forbidden after admission, and they were given routine management such as continuous gastrointestinal decompression, acid suppression, and anti-inflammation. At least 4 L of intravenous fluid was replenished to the patients daily. The metabolic acidosis of the patients was corrected, and a small amount of sodium bicarbonate was used if necessary. Intake of any diet was prohibited during the treatment of all patients, and energy was given as intravenous infusion. All patients were given anti-infective treatment. For patients in the control group, blood amylase levels, blood electrolyte levels, blood routine, urine routine, arterial blood gas, blood lipid, and blood biochemical indexes were detected after admission. After the diagnosis was confirmed, routine clinical treatment was given. Insulin 0.1 U/(kg h) was added to 0.9% sodium chloride injection for continuous intravenous drip, once every 4 to

6 hours, and blood sugar and ketone bodies were monitored regularly. One the ketones bodies were turned negative, the drug was administered at a basic dose of 0.02 U/(kg h). Low molecular weight heparin 100 IU/kg was injected subcutaneously every time, once every 12 hours. According to the patient's clinical symptoms, symptomatic treatment was performed, including correction of acid–base imbalance, correction of electrolyte disorders, potassium supplement, multiple organ function maintenance and so on. If the patient suffered from respiratory failure, oxygen was given by mask or nasal catheter to maintain oxygen saturation above 95%, and arterial blood gas was detected dynamically. Liver protection therapy should be given if abnormal liver function occurred; and volume resuscitation and other supportive treatment should be given to stabilize hemodynamics if the patient developed acute renal failure. At the same time, treatment measures such as fasting, antibiotics, gastrointestinal decompression, somatostatin, and routine nutritional support were taken.

On the basis of the treatment measures of the control group, patients in the study group were given with a personalized nutritional support scheme that met the special nutritional needs and total calories throughout the day according to the general conditions of patients, such as height and weight, history of food allergy, nutritional risk index, previous nutritional status, dietary habits, etc. A trans-nasal placement of jejunal nutrition tube was conducted. When intubating the patient, the integrity of the medical device should be checked first, and the advantages and operations of enteral nutrition support were explained to the patient and the patient's family, so as to relieve the patient's tension emotion during the intubation process, which will lead to muscle stiffness and damage to local blood vessels. Nutritional support needs to follow the guidelines of "from less to more", "from thin to thick", and "from slow to fast". Forty-eight hours after the patient was admitted to the hospital, nutritional support was given, and 250 mL of sugar saline was injected at a rate of 25 mL/h, and gradually increased to 60 mL/h after adaptation. The next day, the 200 mL of Ruineng was used, and the target calorie was gradually increased to 25 kcal/kg/d in the later period. In the course of treatment, it was necessary to pay attention to supplementing electrolytes and trace elements, and insisted on eating small and frequent meals. If the patient was intolerant, the nutritional support program can be adjusted according to the patient's specific situation and the severity of the disease. All of the above treatments were continuously given for 5 days after 48 hours of admission in the 2 groups of patients, for a total of 7 days.

2.4. Observation indexes

In both groups, the serum protein levels (prealbumin [PA], albumin [ALB], total protein [TP] and hemoglobin [HGB]), levels of procalcitonin (PCT), C-reactive protein (CRP), tumor necrosis factor-α (TNF-α), pentraxin-3 (PTX-3), blood amylase (AMS), and immune protein IgG, IgM, IgA levels were measured before treatment and after 7 days of treatment. Besides, the clinical efficacy and occurrence rate of related complications of the 2 groups after 7 days of treatment were calculated.

The evaluation criteria of clinical efficacy were as follows.[9,10] Markedly effective: all clinical symptoms disappeared, fasting blood glucose <11.1 mmol/L, pH was 7.35 to 7.45, serum bicarbonate was 22 to 28 mmol/L, urine ketone body was negative, and blood ketone body <0.3 mmol/L. Effective: Partial clinical symptoms improved, fasting blood glucose <16.7 mmol/L, pH was 7.35 to 7.45, serum bicarbonate was 22 to 28 mmol/L, urine ketone body was negative, and blood ketone body <0.3 mmol/L. Ineffective: all clinical symptoms did not disappear or alleviate, fasting blood glucose ≥16.7 mmol/L, serum bicarbonate <18 mmol/L, pH < 7.3, blood ketone body did not reach the normal level, and serum amylase did not drop to less than 3 times the normal value. Effective rate = (number of markedly effective cases + number of effective cases) × 100%. The occurrence of fever, hypoglycemia, infection and related complications (dizziness, vomiting, abdominal distension, etc) during the treatment of the 2 groups were counted.

For each patient in both groups, 3 to 5 mL fasting elbow vein blood was extracted before treatment and 7 days after treatment and was stored in the refrigerator at −50°C after centrifugation. The serum protein levels (PA, ALB, TP, HGB levels), PCT, CRP, TNF-α, PTX-3, AMS levels and immune protein IgG, IgM, IgA levels were detected. The electrochemiluminescence was used to detect PCT levels. The levels of CRP, PTX-3, and TNF-α were detected by enzyme linked immunosorbent assay using fully automatic biochemical analyzer produced by Hitachi, Japan, and microplate reader produced by Shanghai JingGong Industrial Co., Ltd. The kits were all purchased from Shanghai HengYuan Biotechnology Co., Ltd. Glucose oxidase method was used to detect the levels of AMS. Sysmex XE-2100 hematology analyzer was used to detect the levels of PA, ALB, TP, and HGB. Immunoturbidimetry was used to detect the levels of IgG, IgM, and IgA.

2.5. Statistical methods

All the data collected in this study were analyzed using SPSS 21.0 software. Normally distributed measurement data were expressed as mean ± standard deviation. Paired t test was used to assess the significance of difference between pre- and after-treatment, and 2 independent sample T tests were used for comparison between 2 groups. Non-normally distributed measurement data were expressed as median (interquartile range) and rank-sum test was used for comparison between 2 groups. The categorical data was expressed as rate (%), and the chi-square test was used for comparison between 2 groups. $P < .05$ was considered statistically significant.

3. Results

3.1. Baseline data between the two groups

The patients in the study group were 22~68 years old, with an average age of 51.03 ± 5.21 years old, and there were 18 male patients and 14 female patients. The evaluation results of the severity of illness in the study group were as follows, acute physiology and chronic health evaluation II score[11]: 19 patients with score > 8 points, 13 patients with score < 8 points; RANSON score[12]: 17 patients with score > 3 points, 15 patients with score < 3 points; CT grade[13]: 12 patients with grade B, 19 patients with grade C, 1 patient with grade D. The patients in the control group were 22~69 years old, with an average age of 50.98 ± 5.19 years old, and there were 17 male patients and 15 female patients. The evaluation results of the severity of illness in the control group were as follows, acute physiology and chronic health evaluation II score: 17 patients with score > 8 points, 15 patients with score < 8 points; RANSON score: 16 patients with

Table 1

Comparison of general data between the 2 groups.

	Study group (n = 32)	Control group (n = 32)	t/χ^2	*P*
Age (yr)	51.03 ± 5.21	50.98 ± 5.19	0.038	.970
Gender (male/female)	18/14	17/15	0.063	.802
BMI (kg/m^2)	24.32 ± 3.11	24.11 ± 2.88	0.280	.780
Course of diabetes (yr)	5.21 ± 1.03	5.17 ± 0.89	0.166	.869
Type of diabetes			0.591	.442
Type I	21	18		
Type II	11	14		
APACHEII (points)			0.254	.614
>8	19	17		
<8	13	15		
RANSON (points)			0.063	.802
>3	17	16		
<3	15	16		
CT grade			0.265	.875
Grade B	12	14		
Grade C	19	17		
Grade D	1	1		

APACHE = acute physiology and chronic health evaluation.

score > 3 points, 16 patients with score < 3 points; CT grade: 14 patients with grade B, 17 patients with grade C, 1 patient with grade D. There was no statistically significant difference in baseline data between the 2 groups ($P > .05$), and the data were comparable (Table 1).

3.2. Comparison of clinical efficacy between the two groups

After 7 days of treatment, the clinical efficacy of the study group was significantly higher than that of the control group (study group vs control group, 93.75% vs 71.88%, $P < .05$), as shown in Table 2.

3.3. Comparison of serum protein levels between the two groups

Before treatment, there was no significant difference in the levels of PA, ALB, TP, and HGB between the 2 groups ($P > .05$). After 7 days of treatment, the levels of PA and ALB in the 2 groups were significantly higher than those before treatment ($P < .05$); while the levels of HGB and TP showed no significant changes compared with those before treatment ($P > .05$). After 7 days of treatment, the levels of PA and ALB in the study group were significantly higher than those in the control group ($P < .05$); while there was no significant difference in the levels of HGB and TP between the 2 groups ($P > .05$), as shown in Table 3.

Table 2

Comparison of clinical efficacy between 2 groups.

Item	Study group (n = 32)	Control group (n = 32)	*P* value
Markedly effective (n [%])	17 (53.13)	11 (34.38)	
Effective (n [%])	13 (40.63)	12 (3.75)	
Ineffective (n [%])	2 (6.25)	9 (28.13)	
Total effective number (total effective rate) (n [%])	30 (93.75)	23 (71.88)	.020

3.4. Comparison of PCT, CRP, TNF-α, PTX-3, and AMS levels between the two groups

Before treatment, there was no significant difference in the levels of PCT, CRP, TNF-α, PTX-3, AMS between the groups ($P > .05$). After 7 days of treatment, the levels of PCT, CRP, TNF-α, PTX-3, and AMS in the 2 groups were significantly lower than those before treatment ($P < .05$), and the levels of PCT, CRP, TNF-α, PTX-3 and AMS in the study group were significantly lower than those in the control group ($P < .05$), as shown in Table 4.

3.5. Comparison of immune function between the two groups

Before treatment, there was no significant difference in the levels of IgG, IgM, and IgA between the 2 groups ($P > .05$). After 7 days of treatment, the levels of IgG, IgM and IgA in the 2 groups were significantly higher than those before treatment ($P < .05$), and the levels of IgG, IgM, and IgA in the study group were significantly higher than those in the control group ($P < .05$), as shown in Table 5.

3.6. Comparison of the occurrence rate of related complications between the two groups

After 7 days of treatment, the total occurrence rate of related complications in the study group was significantly lower than that in the control group (study group vs control group, 6.25% vs 28.13%, $P < .05$), as shown in Table 6.

4. Discussion

According to epidemiological studies,[14] the number of diabetic patients in China has reached nearly 114.4 million, ranking

Table 3

Comparison of serum protein levels between 2 groups.

Observation index	Study group (n = 32)		Control group (n = 32)		*P* value‡
	Before treatment	7 days after treatment	Before treatment	7 days after treatment	
PA (U/L)	157.41 ± 7.14	172.51 ± 6.26*	157.21 ± 8.14	150.31 ± 6.03#	<.001
ALB (mmol/L)	31.24 ± 4.17	35.46 ± 3.16*	31.56 ± 4.21	28.42 ± 0.57#	<.001
TP (mmol/L)	58.22 ± 5.69	65.85 ± 0.73	58.24 ± 4.15	61.08 ± 0.98	.895
HGB (g/L)	111.53 ± 7.23	100.41 ± 0.56	111.58 ± 7.56	105.24 ± 3.61	.882

ALB = albumin, HGB = hemoglobin, PA = prealbumin, TP = total protein.

* Compared with that before treatment in the study group, $P < .05$.

Compared with that before treatment in the control group, $P < .05$.

‡ Comparation between the study group and the control group 7 days after treatment, $P < .05$.

Table 4

Comparison of PCT, CRP, TNF-α, PTX-3, AMS levels between 2 groups.

Observation index	Study group (n = 32)		Control group (n = 32)		*P* value‡
	Before treatment	7 days after treatment	Before treatment	7 days after treatment	
PCT (U/L)	1.77 ± 0.13	0.15 ± 0.04*	1.82 ± 0.11	0.51 ± 0.12†	<.001
TNF-α (ng/mL)	6.01 ± 2.23	1.17 ± 0.52*	6.06 ± 2.11	3.33 ± 0.41†	<.001
CRP (mmol/L)	69.24 ± 7.38	10.52 ± 2.11*	69.33 ± 7.11	13.77 ± 3.01†	<.001
PTX-3 (ng/mL)	9.57 ± 0.41	0.23 ± 0.08*	9.54 ± 0.51	0.44 ± 0.06†	<.001
AMS (U/L)	431.77 ± 22.15	63.21 ± 3.89*	432.65 ± 20.04	89.67 ± 5.79†	<.001

AMS = amylase, CRP = C-reactive protein, PCT = procalcitonin, PTX-3 = pentraxin-3, TNF-α = tumor necrosis factor-α.

* Compared with that before treatment in the study group, $P < .05$.

† Compared with that before treatment in the control group, $P < .05$.

‡ Comparation between the study group and the control group 7 days after treatment, $P < .05$.

second in the world and the incidence of young patients is increasing. Patients with diabetic ketoacidosis and acute pancreatitis are often accompanied by fatigue, abdominal pain, nausea, vomiting, nonspecific increase of lipase, blood amylase and urine amylase, temporary increase of blood glucose, acid–base imbalance, and disturbance of water and electrolyte, etc. Moreover, the 2 diseases can influence each other, then increasing the complexity and danger of the disease, and even leading to the death of the patient. In addition, the abnormal activation of pancreatic enzymes in patients with acute pancreatitis leads to edema, digestion, and necrosis of pancreatic tissue, which then leads to the release of a large number of inflammatory mediators and makes the body in a state of immune dysfunction. In the early stage of the disease, the body is in a state of high metabolism and high protein decomposition, with great consumption and increased nutritional requirements. At the same time, most of the patients are accompanied by gastrointestinal dysfunction and will suffer from malnutrition to varying degrees, which will affect the prognosis of the patients. Nutritional status is an important factor affecting blood sugar. Therefore, when treating diabetic ketoacidosis complicated with acute pancreatitis, it is necessary to pay attention to the nutritional status of patients to improve the prognosis and prevent related complications.[15]

Research by Shen et al[16] suggested that nutritional support can effectively improve the metabolic state of patients with acute pancreatitis and promote rapid improvement of various biochemical indicators. Jejunal nutritional support can not only improve nutritional status, but also protect intestinal barrier function, and significantly reduce the incidence of complications, without increasing gastrointestinal burden. Studies by Li et al[17] and Xu[18] suggested that nutritional support was of great significance for disease rehabilitation, which can restore intestinal function, reduce the release of inflammatory mediators, and maintain the stability of the intestinal mucosal barrier. Appropriate nutritional support is the basis of all types of diabetes treatment, and is an indispensable prevention and control measure in the course of diabetes at any stage. Insulin therapy is a common treatment of diabetic ketoacidosis. Continuous insulin treatment can promote the maintenance of a high level of insulin in the body, which facilitates the uptake of glucose, and prevents hypokalemia.[19,20] Therefore, this study adopted nutritional support on the basis of insulin treatment for patients with diabetic ketoacidosis complicated with acute pancreatitis. The results showed that after 7 days of treatment, the clinical effective rate of the study group was significantly higher than that of the control group, suggesting that nutritional support combined with insulin treatment was significantly effective in the treatment of patients with diabetic ketoacidosis complicated with acute pancreatitis. At the same time, symptomatic treatments such as fluid therapy, hypoglycemic treatment, and acidosis correction were given to restore plasma osmotic pressure, improve capillary permeability and renal symptoms, which indirectly improved the clinical efficacy.

PA, ALB, TP, and HGB are all markers of nutritional status, in which PA reflects the function of liver synthesis and secretion of proteins, and can be used as an early indicator of liver function damage and reflect the change of the illness and prognosis of disease. ALB is the main protein component of serum TP, it is synthesized by the liver and plays an important role in maintaining blood colloid osmotic pressure, transportation of metabolites, nutrition and so on. TP consists of ALB and globulin. HGB is composed of globin and heme, it is a pigment-containing binding protein and is the main component of red blood cells, which can bind with oxygen to transport oxygen and

Table 5

Comparison of IgG, IgM, IgA levels between 2 groups.

Observation index	Study group (n = 32)		Control group (n = 32)		*P* value‡
	Before treatment	7 days after treatment	Before treatment	7 days after treatment	
IgG (g/L)	7.15 ± 1.01	10.25 ± 2.34*	7.11 ± 1.12	8.16 ± 0.73†	<.001
IgM (g/L)	0.54 ± 0.23	1.55 ± 0.31*	0.55 ± 0.18	0.99 ± 0.06†	<.001
IgA (g/L)	2.08 ± 0.11	3.53 ± 1.31*	2.11 ± 0.09	2.51 ± 1.04†	<.001

* Compared with that before treatment in the study group, $P < .05$.

† Compared with that before treatment in the control group, $P < .05$.

‡ Comparation between the study group and the control group 7 days after treatment, $P < .05$.

Table 6

Comparison of the occurrence rate of related complications between 2 groups.

Item	Study group (n = 32)	Control group (n = 32)	*P* value
Fever (n [%])	0 (0)	2 (6.25)	
Hypoglycemia (n [%])	1 (3.13)	3 (9.38)	
Infection (n [%])	1 (3.13)	2 (6.25)	
Others (n [%])	0 (0)	2 (6.25)	
Total (n [%])	2 (6.25)	9 (28.13)	.010

carbon dioxide.[21] The results of this study showed that after 7 days of treatment, the levels of PA and ALB in the study group were significantly higher than those in the control group, suggesting that nutritional support combined with insulin therapy can effectively help patients with diabetic ketoacidosis complicated with acute pancreatitis recover their nutritional status. PCT is a protein that can be used clinically to evaluate the severity of acute pancreatitis.[20–23] CRP is a nonspecific marker of systemic inflammation. When the body is infected or injured, the content of CRP will increase and reach a peak at 22 to 28 hours, which can be used as an important reaction factor to evaluate the inflammatory response in the body.[24] TNF-α is a common inflammatory cytokine with multiple functions and plays an important role in the body's inflammatory response and immune responses.[25] PTX-3 can be used for the early diagnosis of acute pancreatitis, and has important clinical value for the development and prognosis of the disease.[26] AMS is an important indicator for the assessment of acute pancreatitis. In some patients with diabetic ketoacidosis, it may be accompanied by elevated AMS.[27] Wang and Ye[28] proposed that the combined monitoring of serum PCT, CRP and TNF-α levels has important clinical value and significance for the diagnosis of acute pancreatitis. Research by Gao et al[29] suggested that AMS can be used to evaluate the severity of diabetic ketoacidosis. Research by Tian et al[30] suggested that CRP and AMS can be used to evaluate the severity of acute pancreatitis. The results of this study showed that after 7 days of treatment, the levels of PCT, CRP, TNF-α, PTX-3, and AMS in the study group were significantly lower than those in the control group, suggesting that nutritional support combined with insulin therapy can effectively help reduce the serum inflammatory response in patients with diabetic ketoacidosis complicated with acute pancreatitis and avoid the occurrence of severe hyperamylasemia.

Immune function is an important physiological function of the body, and the largest immune organ of the body is the intestinal tract. Therefore, the intestinal condition directly affects the immune function. Normal intestinal function in the body can prevent the translocation of bacteria and endotoxins, while abnormal intestinal function can lead to body infection and multiple organ failure, leading to increased inflammatory response.[31,32] Patients with diabetic ketoacidosis complicated with acute pancreatitis consume a lot of nutrition. Lack of protein and calories will lead to negative nitrogen balance, resulting in abnormal cell metabolism of the body, and then leads to decreased immune function. Nutritional support can provide enough nutrients for the intestine to repair the damaged tissues and organs, so as to promote the normal metabolic function of cells. IgM appears at the earliest stage of infection and is the most abundant antibody in the body, its level is closely related to the immune function.[33] In addition, long-term fasting and total parenteral nutrition will cause damage to the intestinal mucosal barrier function, which will lead to the translocation of endotoxin and intestinal bacteria, reducing the patient's immune function.[34] The results of this study showed that after 7 days of treatment, the levels of IgG, IgM, and IgA in the study group were significantly higher than those in the control group, suggesting that nutritional support combined with insulin therapy can effectively improve immune function in patients with diabetic ketoacidosis complicated with acute pancreatitis. This may be because nutritional support protects the function of the intestinal mucosal barrier, prevents the translocation of endotoxin and intestinal bacteria, and thus improves the immune function of patients. In addition, the results of this study showed that after 7 days of treatment, the total occurrence rate of related complications in the study group was significantly lower than that in the control group, suggesting that nutritional support combined with insulin therapy can significantly reduce the occurrence rate of related complications in patients with diabetic ketoacidosis complicated with acute pancreatitis. This may be related to the reduction of inflammatory response and the improvement of immunity, but the specific mechanism is still unclear and needs to be confirmed by further studies.

There were some limitations in our study. There were only 64 samples in this study, so multi-center study with a larger sample size will be conducted to further explore specific mechanism of nutritional support combined with insulin therapy in reducing inflammatory response and improving immune function in patients. In this study, only the clinical efficacy and complications after 7 days of treatment were observed, and the effects of nutrition support combined with insulin therapy on long-term blood glucose control and clinical indicators of patients still need to be followed up for a longer time.

In summary, nutritional support combined with insulin therapy can effectively treat patients with diabetic ketoacidosis complicated with acute pancreatitis, improve serum protein levels, reduce the body's inflammatory response, improve immune function, and reduce the occurrence rate of related complications, which is worthy of clinical promotion and application. In the future, the condition of patients with diabetic ketoacidosis complicated with acute pancreatitis should be timely evaluated, and reasonable liquid resuscitations, effective hypoglycemic, lipid-lowering and personalized nutritional support are effective treatment for patients.

Author contributions

CY and DMW contributed to the conception and design of the study; STL, JWX, LSZ, SRY, and RM performed the experiments, collected and analyzed data; CY and DMW wrote the manuscript; all authors reviewed and approved the final version of the manuscript.

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