

The effect of insulin pump combined with ulinastatin on the levels of PCT, TG, PTX-3, and CX3CL1 in patients with diabetic ketoacidosis and pancreatitis

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Abstract

The aim of this research is to observe the effect of insulin pump combined with Ulinastatin on the levels of procalcitonin (PCT), triglycerides (TG), pentraxin-3 (PTX-3), and C-X3-C motif chemokine ligand 1 (CX3CL1) in patients with diabetic ketoacidosis and pancreatitis.

A total of 72 patients with diabetic ketoacidosis and pancreatitis who were admitted to our hospital from February 2016 to February 2020 were selected as the research subjects. They were divided into study groups (36 cases, given insulin pump combined Ulinastatin treatment) and control group (36 cases, given insulin pump treatment). Statistics of changes in blood amylase (AMS), blood glucose, blood ketones, glycosylated hemoglobin (HbA1c), PCT, TG, PTX-3, and chemokine CX3CL in pancreatic tissue before and after treatment.

After treatment, the clinical efficacy of the study group was significantly higher than that of the control group (94.44% vs 75.00%), the difference was significant ($P < .05$). After treatment, the clinical symptoms (abdominal distension, abdominal pain, body temperature, blood sugar, HbA1c and blood amylase) in the study group were significantly less time-to-normal than in the control group, and the difference was significant ($P < .05$). After treatment, the AMS, blood sugar, HbA1c, and blood ketones of the 2 groups were all lower than before treatment, and the study group's AMS, blood sugar, HbA1c, and blood ketones were all lower. In the control group, the difference was significant ($P < .05$). After treatment, the 2 groups of PCT, TG, PTX-3, and CX3CL were all lower than before treatment, among which the study group PCT, TG, PTX-3, and CX3CL1 were lower than the control group, the difference was significant ($P < .05$). After treatment, the total adverse reaction rate of the 2 groups was not significantly different ($P > .05$), but the total adverse reaction rate of the study group was lower than that of the control group.

The combination of insulin pump and ulinastatin in the treatment of patients with diabetic ketoacidosis complicated with acute pancreatitis has a effect, which can shorten the recovery time of clinical symptoms, reduce the levels of PCT, TG, PTX-3, and CX3CL1, and has fewer adverse reactions. It is worthy of clinical application.

Abbreviations: AMS = blood amylase, CX3CL1 = C-X3-C motif chemokine ligand 1, PCT = procalcitonin, PTX-3 = pentraxin-3, TG = triglycerides.

Keywords: C-X3-C motif chemokine ligand 1, diabetic ketoacidosis with pancreatitis, insulin pump, pentraxin-3, procalcitonin, triglycerides, ulinastatin

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DW and CY contributed equally to this article.

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Ethical Approval: The study protocol was approved by the Ethics Committee of Tangshan Worker Hospital and all patients signed the informed consents before the study. The formulation of the study protocol conformed to the relevant requirements of the World Medical Association Declaration of Helsinki.

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1. Introduction

In recent years, the incidence of diabetic ketoacidosis is increasing year by year. In addition to the clinical symptoms of “polydipsia, polyuria, polyphagia, and weight loss,” there are also related symptoms such as metabolic acidosis, metabolic disorders, and increased ketone bodies in the blood. It has the characteristics of rapid onset, rapid change, and serious condition, which seriously endangers the health of patients.^[1,2] Acute pancreatitis is one of the common complications in patients with diabetic ketoacidosis, which mainly refers to the presence of hemorrhage or even necrosis in the pancreas, and its main clinical symptoms are vomiting, fever, and abdominal pain.^[3,4] Pancreatitis can cause pancreatic self-digestion, edema, infection, necrosis, and so on. When severe, it can lead to persistent organ failure. The clinical process of 20% of patients is dangerous, which will have a serious impact on the treatment of diabetic ketoacidosis.^[5] At present, the patients with diabetic ketoacidosis and pancreatitis are often treated with drugs to correct the clinical symptoms such as pancreatic tissue edema and congestion. Insulin pump not only can promote the body to absorb glucose, but also can play a role in the generation of ketone bodies and the decomposition of fat.^[6] Ulinastatin inhibits the secretion and release of inflammatory factors.^[7] However, there are few reports about the use of insulin pumps combined with ulinastatin in the treatment of diabetic ketoacidosis combined with pancreatitis. Acute phase proteins have a role in detecting the presence of inflammatory diseases, and studies by Simsek et al^[8] found that pentraxin-3 (PTX-3) was elevated in the setting of acute pancreatitis and had value in the diagnosis of acute pancreatitis. C-X3-C motif chemokine ligand 1 (CX3CL1) is an important chemokine, and a study by Uchida et al found higher CX3CL1 expression in the setting of acute pancreatitis compared with normal pancreas.^[9] It indicated that CX3CL1 had diagnostic value for acute pancreatitis.

This study will investigate the effect of insulin pump combined with ulinastatin on procalcitonin (PCT), triglycerides (TG), PTX-3, and CX3CL1 levels in diabetic ketoacidosis patients with pancreatitis, to provide guidance for clinical treatment.

2. Patients and methods

2.1. Patients

From February 2016 to February 2020, 72 patients with diabetic ketoacidosis and pancreatitis were treated in our hospital. These patients were divided into the study group and the control group by random number table method, 36 cases each. The age of the study group was 41 to 72 years, the average age was (51.83 + 5.43) years, 15 male patients and 21 female patients, the course of diabetes was 5 to 17 years, the average course of diabetes was (11.21 + 2.31) years, and the type of diabetes was: 23 cases of type I, 13 cases of type II. According to the results of arterial blood gas analysis, the grade of diabetic ketoacidosis was severe (pH < 7.0) in 5 cases, moderate (pH 7.24–7.0) in 14 cases, and mild (pH > 7.25) in 17 cases. The age of patients in the control group ranged from 40 to 73 years, with an average age of (51.79 + 5.56) years. There were 16 male patients and 20 female patients. The duration of diabetes was 5 to 18 years. The average duration of diabetes was 11.34 + 2.45 years. There were 24 cases of type I and 12 cases of type II diabetes. According to the results of arterial blood gas analysis, the grade of diabetic ketoacidosis was severe (pH < 7.0) in 4 cases, moderate (pH 7.24–7.0) in 15 cases, and mild (pH > 7.25) in 17 cases. There was no significant difference in general

data between the 2 groups, which was comparable ($P > .05$). The study protocol was approved by the Ethics Committee of Tangshan Worker Hospital and all patients signed the informed consents before the study. The formulation of the study protocol conformed to the relevant requirements of the World Medical Association Declaration of Helsinki. This study was approved by the ethics committee, and all patients gave written informed consent.

2.2. Inclusion and exclusion criteria

Inclusion criteria were: meeting the diagnostic criteria for diabetic ketoacidosis: China Guidelines for the Prevention and Treatment of Type 2 Diabetes (2017)^[10]; meeting the diagnostic criteria for acute pancreatitis: Chinese Medical Association Surgical Society Guidelines for the Diagnosis and Treatment of Acute Pancreatitis (2014)^[11]; complete clinical data; patients and their families with informed consent and signing informed consent; the patients were mentally normal and had good compliance.

Exclusion criteria were: allergy to drugs used in this study; pregnancy and lactation; acute complications such as lactic acidosis and hyperglycemic hyperosmolar coma; patients with malignant tumors, severe heart, liver and kidney diseases, and hematological diseases; patients with severe infectious diseases.

2.3. Methods

All patients underwent electrocardiogram examination after admission, and the changes in blood pressure, oxygen saturation, and respiration were closely monitored. At the same time, the proton pump inhibitor omeprazole (manufacturer: Changzhou Siyao Pharmaceutical Co., Ltd; approval number: GYZZ H10950086) was given for acid suppression treatment, and somatostatin (manufacturer: Nanjing Changao Pharmaceutical Co., Ltd; approval number: GYZZ H20043583) was injected into the infusion pump to inhibit pancreatic enzyme secretion, combined with the conventional treatment of acute pancreatitis, including rehydration, gastrointestinal decompression, fasting water, and amino acids. On the basis of the above treatment, the control group was given a continuous subcutaneous injection of an insulin pump. The dose of insulin (manufacturer: Xuzhou Wanbang Jinqiao Pharmaceutical Co., Ltd; approval number: GYZZ H32024567) was 0.1 U (kg.h). At the same time, the ketone body and blood glucose of the patients were regularly tested. If the ketone body turned negative, the patients were treated with 0.02U (kg.h) based dose for 15 days.

On the basis of the above treatment, the research group was given an intravenous infusion of ulinastatin (manufacturer: Guangdong Tianpu Biochemical Pharmaceutical Co., Ltd; approval number: GYZZ H19990134), and 100,000 U of ulinastatin was dissolved in 250 mL of glucose (5.0%) by intravenous infusion, once a day, 30 minutes after the end of the drip, continuous drip for 15 days.

2.4. Outcomes

The changes of AMS, blood glucose, HbA1c, a blood ketone body, PCT, TG, PTX-3, and CX3CL1 before and after treatment were counted, and the recovery time, clinical efficacy and adverse reactions of clinical symptoms (abdominal distension, abdominal pain, body temperature, blood glucose, and blood amylase) after treatment were observed.

Table 1**Comparison of clinical efficacy between 2 groups, n (%).**

Groups	Markedly effective	effective	Ineffective	Total effective number (total effective rate)
Study group (n=36)	19 (52.78%)	15 (41.67%)	2 (5.56%)	34 (94.44%)
Control group (n=36)	13 (36.11%)	14 (38.89%)	9 (25.00%)	27 (75.00%)
χ^2				5.258
P				.022

Clinical efficacy: markedly effective: blood glucose <11.1 mmol/L, serum bicarbonate, blood gas analysis, and blood ketone body reached the normal level, and all clinical symptoms disappeared; effective: blood glucose index was <16.7 mmol/L, serum bicarbonate, blood gas analysis, and blood ketone body reached the normal level, all clinical symptoms were significantly improved; ineffective: fasting blood glucose <16.7 mmol/L, serum bicarbonate <18 mmol/L, blood gas analysis pH <7.3, and blood ketone body reached the normal level, serum amylase did not fall below 3 times the normal value, abdominal pain and other clinical symptoms did not disappear or alleviate. Effective rate = marked efficiency + effective rate.

Laboratory examination: 3 to 5 mL of fasting venous blood was collected from all patients after admission and treatment, centrifuged and stored in a -30 °C refrigerator for future use, and AMS, blood glucose, HbA1c, blood ketone body, PCT, TG, PTX-3, and CX3CL levels were detected. CX3CL and PTX-3 in patient serum were quantified using the enzyme linked immunosorbent assay (CX3CL1, RayBiotech, Norcross, GA; PTX-3, Fcmacs, Nanjing, China). AMS, blood glucose, HbA1c, and blood ketone body were detected by automatic biochemical analyzer manufactured by GE company in the United States; TG was detected by Hitachi 7600-20 automatic biochemical analyzer, the kit was purchased from Landau, UK; PCT was detected by electrochemiluminescence method; Hitachi automatic biochemical analyzer manufactured by Hitachi company in Japan was used. DG5031 microplate reader produced by Shanghai Jinggong Industrial Co., Ltd. PTX-3 was detected by enzyme-linked immunosorbent assay, and the kits were purchased from Shanghai Hengyuan Biotechnology Co., Ltd. AMS level was detected by glucose oxidase method.

The occurrence of adverse reactions: detailed statistics of vomiting, dizziness, dysdefecation, and other adverse reactions during the treatment.

2.5. Statistics

SPSS 21.0 software was used for statistical analysis (SPSS Inc, Chicago, IL). Measuring data were expressed as mean \pm standard deviation, and repeated measures analysis of variance was used to analyze the data of each group, and *t* test was used to compare the data between groups and within groups; if it did not conform to

the normal distribution, the median was used and the rank-sum test was used. Count data were expressed as a rate (%) and compared using the χ^2 test. $P < .05$ was a significant difference.

3. Results

3.1. Comparison of clinical efficacy between 2 groups

After treatment, the clinical efficacy of the study group was significantly higher than that of the control group (94.44% >75.00%), the difference was significant ($P < .05$, Table 1).

3.2. Comparison of clinical symptoms recovery time between 2 groups

After treatment, the clinical symptoms (abdominal distension, abdominal pain, body temperature, blood glucose, HbA1c, and blood amylase) remission time in the study group was significantly less than that in the control group, and the difference was significant ($P < .05$, Table 2).

3.3. Comparison of AMS, blood glucose, and blood ketone bodies between 2 groups

Before treatment, AMS, blood glucose, HbA1c, and blood ketone bodies were compared between the 2 groups ($P > .05$). After treatment, AMS, blood glucose, and blood ketone body in both groups decreased compared with before treatment, and AMS, blood glucose and blood ketone body in the study group were lower than those in the control group, with significant differences ($P < .05$, Table 3)

3.4. Comparison of PCT, TG, PTX-3, and CX3CL1 between 2 groups

Before treatment, there were no significant differences in PCT, TG, PTX-3 and CX3CL1 between the two groups ($P > .05$); after treatment, PCT, TG, PTX-3, and CX3CL1 in the 2 groups decreased compared with before treatment, and PCT, TG, PTX-3, and CX3CL1 in the study group were lower than those in the control group, with significant differences ($P < .05$, Table 4).

Table 2**Comparison of clinical symptoms recovery time between 2 groups.**

Groups	Abdominal distention	Abdominal pain	Body temperature	Blood glucose	Blood amylase	HbA1c
Study group (n=36)	5.39 \pm 0.32	5.27 \pm 0.31	3.16 \pm 0.21	7.83 \pm 0.93	3.89 \pm 0.32	8.24 \pm 0.24
Control group (n=36)	8.81 \pm 0.45	8.97 \pm 0.42	5.23 \pm 0.45	11.83 \pm 1.02	6.22 \pm 0.37	12.31 \pm 1.14
<i>t</i>	-37.162	-42.527	-25.011	-17.387	-28.578	-20.962
P	<.001	<.001	<.001	<.001	<.001	<.001

Table 3
Comparison of AMS, blood glucose, and blood ketone bodies between 2 groups.

Groups	Time	AMS, U/L	Blood glucose, mmol/L	blood ketone bodies, mmol/L	HbA1c (%)
Study group (n=36)	Before treatment	437.92±23.87	27.02±2.38	7.45±0.36	17.16±3.45
	After treatment	68.29±4.21	10.17±2.01	2.04±0.07	9.13±1.11
Control group (n=36)	Before treatment	438.03±21.82	26.87±1.65	7.41±0.23	16.87±2.57
	After treatment	90.73±6.63	13.21±1.62	4.62±0.12	10.42±0.51
T		0.020	0.275	0.562	0.404
P		.984	.784	.576	.687
t*		91.499	29.126	88.509	13.294
P*		<.001	<.001	<.001	<.001
t [#]		91.375	35.445	64.528	14.770
P [#]		<.001	<.001	<.001	<.001
t ^{##}		-17.143	-7.065	-111.427	-6.336
P ^{##}		<.001	<.001	<.001	<.001

AMS = blood amylase. T and P were compared before treatment between the 2 groups; t* and P* were compared before and after treatment in the study group; t[#] and P[#] were compared before and after treatment in the control group; t^{##} and P^{##} were compared after treatment between the 2 groups.

3.5. Comparison of adverse reactions between the 2 groups

After treatment, there was no significant difference in the incidence of total adverse reactions between the 2 groups ($P > .05$, Table 5).

4. Discussion

According to relevant clinical studies,^[12] blood glucose should be controlled in patients with diabetes, and ketoacidosis can be easily induced if blood glucose is not well controlled. In addition, Diabetic ketoacidosis is the main cause of death in patients with type I diabetes, and it seriously threatens the health of patients with type II diabetes.^[13] Patients with early diabetic ketoacidosis are asymptomatic and difficult to identify. If not promptly treated effectively, the patient's condition progresses rapidly and will seriously affect the patient's life and health. When diabetic patients have polydipsia, polyuria, weight loss, dehydration, disturbance of consciousness, deep breathing, and other symptoms, the patient should be considered to be diabetic ketoacidosis. Diabetic ketoacidosis can be associated with a variety of complications, the most serious complication is acute pancreatitis, in which 15% of diabetic ketoacidosis can be complicated with acute pancreatitis. The pathogenesis of diabetic

ketoacidosis complicated with acute pancreatitis may be the disorder of glucose metabolism, protein metabolism and lipid metabolism in the body of diabetic ketoacidosis patients, which will lead to the dysfunction of the autonomic nervous system, reduce the contractile capacity of the gallbladder, and easily lead to infection when the infectious substance enters the gallbladder. In addition, patients with secondary infection of the gallbladder and pancreas can develop acute pancreatitis due to low immunity in patients with diabetic ketoacidosis.^[14]

Both disorders are further aggravated when diabetic ketoacidosis is complicated by acute pancreatitis. In the clinic, we often use body fluid supplements to reduce blood glucose, and control acid secretion and glucagon in the body at the same time. It can be distributed in the secretory glands inside and outside the tissue cells, constrict the pancreatic enzyme gall bladder, control the secretion of insulin, and promote the secretion of trypsin. It can reduce the infiltration of pancreatic juice into various tissues and organs, improve the microcirculation in the body, and reduce the inflammatory reaction.^[15] Insulin can promote cell uptake of glucose; promote glycogen synthesis, reduce glycogen decomposition; promote glucose oxidation and decomposition, accelerate the utilization of sugar; promote the synthesis and storage of triglycerides; prevent gluconeogenesis.^[16] However, the treatment of pancreatitis needs to inhibit pancreatic secretion and

Table 4
Comparison of PCT, TG, PTX-3, and CX3CL between 2 groups.

Groups	Time	PCT, mg/L	TG, U/L	PTX-3, ng/mL	CX3CL1, ng/mL
Study group (n=36)	Before treatment	1.82±0.21	10.73±2.31	10.93±0.53	2.81±0.37
	After treatment	0.22±0.08	1.36±0.12	0.29±0.09	1.37±0.17
Control group (n=36)	Before treatment	1.79±0.16	10.69±1.94	10.91±0.48	2.79±0.28
	After treatment	0.49±0.03	3.31±0.36	0.51±0.07	2.18±0.16
T		0.682	0.080	0.168	0.259
P		.497	.936	.867	.796
t*		42.719	24.305	118.753	21.219
P*		<.001	<.001	<.001	<.001
t [#]		47.915	22.442	128.639	11.349
P [#]		<.001	<.001	<.001	<.001
t ^{##}		-18.961	-30.832	-11.577	-20.818
P ^{##}		<.001	<.001	<.001	<.001

CX3CL1 = C-X3-C motif chemokine ligand 1, PCT = procalcitonin, PTX-3 = pentraxin-3, TG = triglycerides. T and P were compared before treatment between the 2 groups; t* and P* were compared before and after treatment in the study group; t[#] and P[#] were compared before and after treatment in the control group; t^{##} and P^{##} were compared after treatment between the 2 groups.

Table 5**Comparison of adverse reactions between the 2 groups, n (%).**

Groups	Vomiting	dizziness	Dyschezia	Total incidence of adverse reactions
Study group (n=36)	0	1 (2.78)	1 (2.78)	2 (5.56)
Control group (n=36)	1 (2.78)	1 (2.78)	2 (5.56)	4 (11.11)
χ^2				0.727
<i>P</i>				.394

pancreatic activity and to prevent enterogenous infectious diseases and promote gastrointestinal peristalsis. Yuan et al^[17] and Chen et al^[18] have confirmed that there is a cascade reaction of inflammatory cells in the body of patients with pancreatitis, and it is necessary to give central nervous system analgesia on the basis of a conventional anti-infection treatment to relieve abdominal pain symptoms. Ulinastatin, also known as urinary trypsin inhibitor, is a special glycoprotein hydrolase inhibitor extracted from the fresh urine of healthy adult men. It is commonly used in the treatment of chronic recurrent pancreatitis and acute pancreatitis and can assist in the treatment of acute circulatory failure.^[19] Therefore, ulinastatin was added to the basic treatment of the insulin pump. The results showed that after treatment, the clinical efficacy of the study group was significantly higher than that of the control group ($P < .05$), suggesting that insulin pump combined with ulinastatin has a significant effect on diabetic ketoacidosis complicated with acute pancreatitis.

Wang et al^[20] suggested that the AMS level has become a routine examination for patients with diabetic ketoacidosis, which can determine whether there is acute pancreatitis. The AMS level of patients with diabetic ketoacidosis complicated with acute pancreatitis is higher and lasts longer. The results showed that after treatment, the recovery time of clinical symptoms (abdominal distension, abdominal pain, body temperature, blood glucose, HbA1c, and blood amylase) in the study group was significantly shorter than that in the control group, and the AMS, blood glucose, HbA1c, and blood ketone body in the study group were lower than those in the control group ($P < .05$). The combination therapy can reduce the levels of AMS, blood glucose, HbA1c, and blood ketone bodies, which may be due to the fact that Ulinastatin can produce a variety of enzymes such as plasmin, elastase, and trypsin, which can stabilize the lysosomal membrane, and has inhibitory effects on lysosomal enzyme release, myocardial inhibitory factor secretion, and inflammatory mediator release. At the same time, it can regulate the decline of immune function caused by surgical stimulant trauma, improve renal dysfunction and abnormal protein metabolism, and then play a role in the treatment of diabetic ketoacidosis combined with pancreatitis.

PCT is a new inflammatory marker of infection, which has been widely used in the clinical diagnosis of bacterial infection, sepsis, and other diagnoses, for treatment detection and prognosis evaluation. PTX-3 is a nonspecific inflammatory factor, which can be used in the early diagnosis of acute pancreatitis, and has important clinical value for the development of the disease and prognosis. CX3CL1 is expressed at the top of the extracellular mucin structure and has the functions of chemokines and adhesion factors. Studies by Li et al^[21] suggest that all chemokines need a G-protein-dependent mechanism with leukocyte-specific receptors to induce leukocyte migration and adhesion. CX3CL1 in inflammatory areas can promote NK cell

activation and endothelial cell lysis, which is conducive to the transfer of captured CX3CL1-positive cells in the blood into tissues to fully play the role of adhesion and migration. The disorder of lipid metabolism in diabetic patients mainly manifested by elevated TG, especially in diabetic patients complicated with ketoacidosis, due to insufficient insulin, lipolysis will be further accelerated, leading to abnormal elevation of TG. Therefore, in this study, PCT, TG, PTX-3, and CX3CL1 were used as evaluation indicators after the treatment of diabetic ketoacidosis combined with pancreatitis. The results of this study showed that PCT, TG, PTX-3, and CX3CL1 in the study group were lower than those in the control group after treatment ($P < .05$), suggesting that insulin pump combined with ulinastatin treatment for patients with diabetic ketoacidosis complicated with acute pancreatitis can reduce the inflammatory response, reduce the level of TG, and play a role in chemotaxis and metastasis of related factors to improve the clinical symptoms of patients. This may be due to the fact that the insulin pump can strictly control the amount and time of insulin input, which is more accurate than human control, making the input of insulin closer to the physiological secretion of the human body. Insulin can be quickly absorbed by the subcutaneous fat of patients and give full play to its role. It can effectively control blood glucose in a short time, reduce the toxicity of hyperglycemia, and produce ketone bodies in the body. It is conducive to the recovery of the insulin-antagonistic hormone to the normal level and plays a role in correcting the metabolic disorder of protein and glycosyl fat in the body. It is the best way of insulin infusion.^[22] In addition, this study on adverse reactions found that the use of ulinastatin on the basis of insulin pump treatment will not increase adverse reactions. However, due to the limited number of patients included in this study and the short duration of the study, if there is a need in the later period, the sample size should be expanded to conduct multicenter randomized controlled trials, and the study time should be extended, and its mechanism should be explored.

5. Conclusion

Insulin pump combined with ulinastatin in the treatment of diabetic ketoacidosis complicated with acute pancreatitis has an effect, can shorten the recovery time of clinical symptoms, reduce the levels of PCT, TG, PTX-3, and CX3CL1, and has less adverse reactions, which is worthy of clinical application.

Author contributions

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References

- [1] Marzban S, Arbee M, Vorajee N, et al. Non-diabetic ketoacidosis associated with a low carbohydrate, high fat diet in a postpartum lactating female[J]. *Oxf Med Case Rep* 2020;2020:omz026.
- [2] Ahmed T, Ahmed T, Haque R. Rare ST-elevation myocardial infarction mimic: diabetic ketoacidosis with severe hypercalcemia[J]. *Cureus* 2020;12:e9001.
- [3] Mathuram Thiyagarajan U, Ponnuswamy A, Chung A. An enigmatic triad of acute pancreatitis, diabetic ketoacidosis and hypertriglyceridemia: who is the culprit? [J]. *BMJ Case Rep* 2019;12:e217272.
- [4] Timilsina S, Timilsina S, Mandal A, et al. Triad of diabetic ketoacidosis, hypertriglyceridemia, and acute pancreatitis: severity of acute pancreatitis may correlate with the level of hypertriglyceridemia[J]. *Cureus* 2019;11:e4930.
- [5] van Santvoort HC, Besselink MG, Bakker OJ, et al. A step-up approach or open necrosectomy for necrotizing pancreatitis. *N Engl J Med* 2010;362:1491–502.
- [6] Seidinova A, Ishigov I, Peyami C, et al. [Effectiveness of pump insulin therapy in the treatment of type 2 diabetes mellitus (review)][J]. *Georgian Med News* 2018;51–5.
- [7] Li ST, Dai Q, Zhang SX, et al. Ulinastatin attenuates LPS-induced inflammation in mouse macrophage RAW264.7 cells by inhibiting the JNK/NF- κ B signaling pathway and activating the PI3K/Akt/Nrf2 pathway[J]. *Acta Pharmacol Sin* 2018;39:1294–304.
- [8] Simsek O, Kocael A, Kocael P, et al. Inflammatory mediators in the diagnosis and treatment of acute pancreatitis: pentraxin-3, procalcitonin and myeloperoxidase. *Arch Med Sci* 2018;14:288–96.
- [9] Uchida M, Ito T, Nakamura T, et al. Pancreatic stellate cells and CX3CR1: occurrence in normal pancreas and acute and chronic pancreatitis and effect of their activation by a CX3CR1 agonist. *Pancreas* 2014;43:708–19.
- [10] Chinese Diabetes Society. China Guidelines for the Prevention and Treatment of Type 2 Diabetes (2017). *Chin J Diabetes Mellitus* 2018;10:1.
- [11] Pancreatic Surgery Group, Surgery Branch, Chinese Medical Association. Chinese Medical Association Surgical Society Guidelines for the Diagnosis and Treatment of Acute Pancreatitis (2014) [J]. *Chin J Pract Surg* 2015;35:4–7.
- [12] Kuppermann N, Ghetti S, Schunk JE, et al. Clinical trial of fluid infusion rates for pediatric diabetic ketoacidosis. *N Engl J Med* 2018;378:2275–87.
- [13] Doshi P, Potter AJ, De Los Santos D, et al. Prospective randomized trial of insulin glargine in acute management of diabetic ketoacidosis in the emergency department: a pilot study. *Acad Emerg Med* 2015;22:657–62.
- [14] Nair S, Yadav D, Pitchumoni CS. Association of diabetic ketoacidosis and acute pancreatitis: observations in 100 consecutive episodes of DKA [J]. *Am J Gastroenterol* 2000;95:2795–800.
- [15] Wang G, Liu Y, Zhou SF, et al. Effect of somatostatin, ulinastatin and gabexate on the treatment of severe acute pancreatitis [J]. *Am J Med Sci* 2016;351:506–12.
- [16] Mathieu C, Gillard P, Benhalima K. Insulin analogues in type 1 diabetes mellitus: getting better all the time [J]. *Nat Rev Endocrinol* 2017;13:385–99.
- [17] Yuan S, Liao J, Cai R, et al. Acute pancreatitis concomitant with diabetic ketoacidosis: a cohort from South China [J]. *J Int Med Res* 2020;48:300060520912128.
- [18] Chen KL, Zhang HH, Lin L, et al. Clinical observation of xuebijing injection combined with octreotide and ulinastatin in the treatment of acute severe pancreatitis. *China Pharmacy* 2017;28:4540–4.
- [19] Guo Y, Wang Y, Zhang D, et al. [Effect of ulinastatin on isoflurane-induced neuronal apoptosis in the hippocampus of rats][J]. *Nan Fang Yi Ke Da Xue Xue Bao* 2019;39:850–4.
- [20] Wang G, Liu Y, Zhou SF, et al. Effect of somatostatin, ulinastatin and gabexate on the treatment of severe acute pancreatitis. *Am J Med Sci* 2016;351:506–12.
- [21] Li Y, Wang W, Luo C, et al. Electroacupuncture attenuates inflammatory pain by inhibiting the expression of Fractalkine in spinal dorsal horn in rats. *Chin J Neuroanat* 2016;32:169–73.
- [22] Posner BI. Insulin signalling: the inside story [J]. *Can J Diabetes* 2017;41:108–13.