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Effect of insulin pump and continuous intravenous insulin on ketone body metabolism, blood gas indexes and stress state in patients with diabetic ketoacidosis

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ABSTRACT

Objective: To study the effect of insulin pump and continuous intravenous insulin on ketone body metabolism, blood gas indexes and stress state in patients with diabetic ketoacidosis. **Methods:** Patients with diabetic ketoacidosis who were treated in Meizhou Maternal and Child Heath Hospital between May 2014 and March 2017 were selected as the research subjects and randomly divided into the group A who received subcutaneous insulin infusion by insulin pump and the group B who received intravenous small-dose insulin injection by micropump. The indexes of ketone body, blood gas and stress were measured before and after treatment. **Results:** 12 h and 24 h after treatment, serum β-hydroxybutyrate, MDA, NE, ACTH and Cor contents of both groups of patients were significantly lower than those before treatment while pH, HCO_3^- and base excess levels as well as serum SOD, GSH-Px, CAT and TAC contents were significantly higher than those before treatment, and serum β-hydroxybutyrate, MDA, NE, ACTH and Cor contents of group A were significantly lower than those of group B while pH, HCO_3^- and base excess levels as well as serum SOD, GSH-Px, CAT and TAC contents were significantly higher than those of group B. **Conclusion:** Subcutaneous insulin infusion by insulin pump can improve ketone body metabolism, acidosis status and stress state in patients with diabetic ketoacidosis.

1. Introduction

Type 2 diabetes mellitus is the most common endocrine metabolism disease in China, and there are many acute and chronic complications in the course of disease. Diabetic ketoacidosis (DKA) is a common acute complication in diabetic patients. It develops rapidly and can threaten life safety if not treated promptly[1,2]. Exogenous supplementation of insulin is the key to treat DKA and it is very important to select a reasonable route of insulin infusion. Intravenous infusion of insulin and subcutaneous multiple injection of insulin are the most common insulin-infusion methods. The effect of reducing blood glucose is accurate, but the controllability is poor. Continuous subcutaneous insulin infusion by insulin pump is the insulin-infusion method developed in recent years, which can simulate human insulin secretion mode and adjust the dose of insulin according to the changes of blood sugar, and has strong controllability[3,4]. In the following studies, we specifically analyzed the effect of insulin pump and continuous intravenous insulin on ketone body metabolism, blood gas indexes and stress state in patients with diabetic ketoacidosis.

2. Case information and research methods

2.1 General case information

Patients with diabetic ketoacidosis who were treated in Meizhou Maternal and Child Heath Hospital between May 2014 and March 2017 were selected as the research subjects, all the patients were clearly diagnosed with type 2 diabetes mellitus, admitted into hospital for abdominal pain, nausea, dehydration and other symptoms, and with blood glucose 16.7-33.3 mmol/L, arterial blood pH＜7.35 and positive blood ketone body on admission. The patients with starvation ketoacidosis and diabetic hyperosmotic state were excluded, and a total of 42 patients were enrolled in the study.

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The patients with diabetic ketoacidosis were divided into group A and group B by random number table. Group A included 13 men and 8 women, they were 42-63 years old, and the course of diabetes was 3-8 years; group B included 12 men and 9 women, they were 45-65 years old, and the course of diabetes was 3-9 years. There was no statistically significant difference in general information between the two groups (P>0.05).

2.2 Therapy

Both groups of patients received massive fluid infusion, electrolyte disorder correction and other conventional treatment after admission, group A received subcutaneous insulin infusion by insulin pump on the basis, and the method was as follows: 0.5 U/kg was referred to calculate the total daily insulin dose, 50% of the total dose was the base quantity, and the other 50% was additional quantity before meals. Group B received intravenous small-dose insulin injection by micropump on the basis, and the method was as follows: 0.1 U/kg/h dose was referred at first for intravenous insulin injection by micropump, the blood glucose was monitored every h, intravenous micropump was stopped when blood glucose was below 13.9 mmol/L, and the proportion of 1 U insulin: 4-6 g glucose was referred to add the insulin to 5% glucose injection, which was by intravenous drip.

2.3 Laboratory index test

Before treatment as well as 12 h and 24 h after treatment, cubital venous blood was collected from two groups of patients and centrifuged to separate serum, automatic biochemical analyzer was used to determine β-hydroxybutyrate, NE, ACTH and Cor contents, and radioimmunoprecipitation kits were used to detect SOD, GSH-Px, CAT and TAC contents; arterial blood was collected to detect pH, HCO3- and base excess levels by the blood gas analyzer.

2.4 Statistical methods

SPSS 20.0 software was used to input data, differences between groups were analyzed by t test and $P<0.05$ indicated statistical significance in differences in test results.

3. Results

3.1 Serum ketone body metabolism index contents

Before treatment as well as 12 h and 24 h after treatment, serum ketone body metabolism index β-hydroxybutyrate contents of group A were (1.64±0.11) mmol/L, (0.58±0.06) mmol/L, (0.34±0.05) mmol/L respectively and serum ketone body metabolism index β-hydroxybutyrate contents of group B were (1.67±0.19) mmol/L, (0.91±0.12) mmol/L, (0.76±0.08) mmol/L respectively. Before treatment as well as 12 h and 24 h after treatment, analysis of serum ketone body metabolism index β-hydroxybutyrate contents between two groups of patients was as follows: serum β-hydroxybutyrate contents were not significantly different between two groups of patients before treatment (P>0.05); 12 h and 24 h after treatment, serum β-hydroxybutyrate contents of both groups of patients were significantly lower than those before treatment (P<0.05), and serum β-hydroxybutyrate contents of group A were significantly lower than those of group B (P<0.05).

3.2 Arterial blood gas analysis index levels

Before treatment as well as 12 h and 24 h after treatment, analysis of arterial blood gas analysis indexes pH, HCO_3^- and base excess between two groups of patients was as follows: pH, HCO_3^- and base excess levels were not significantly different between two groups of patients before treatment (P>0.05); 12 h and 24 h after treatment, pH, HCO_3^- and base excess levels of both groups of patients were significantly higher than those before treatment (P<0.05), and pH, HCO_3^- and base excess levels of group A were significantly higher than those of group B (P<0.05).

3.3 Serum oxidative stress index contents

Before treatment as well as 12 h and 24 h after treatment, analysis of serum oxidative stress indexes SOD (U/L), GSH-Px (U/L), CAT (U/L), TAC (kU/L) and MDA (μmol/L) between two groups of patients was as follows: serum SOD, GSH-Px, CAT, TAC and MDA

Table 1.
Changes in arterial blood gas analysis indexes before and after treatment.

Groups	n	Time	pH	HCO_3^-	Base excess
Group A	21	Before treatment	7.26±0.84	12.82±1.62	-7.63±0.89
		12 h after treatment	7.37±0.91*#	16.71±2.18*#	-5.42±0.78*#
		24 h after treatment	7.42±0.88*#	19.41±2.35*#	-4.24±0.56*#
Group B	21	Before treatment	7.25±0.79	12.79±1.47	-7.71±0.94
		12 h after treatment	7.30±0.85*	14.21±1.87*	-6.55±0.89*
		24 h after treatment	7.34±0.92*	15.87±2.05*	-5.73±0.67*

*: comparison of indexes between before and after treatment, $P<0.05$; #: comparison of indexes between group A and group B, $P<0.05$.

Table 2.

Changes in serum oxidative stress indexes before and after treatment.

Groups	*n*	Time	SOD	GSH-Px	CAT	TAC	MDA
Group A	21	Before treatment	75.2±9.3	64.7±8.9	16.4±2.0	5.11±0.78	14.2±1.9
		12 h after treatment	98.4±11.8*#	89.4±11.2*#	21.5±3.3*#	8.41±0.94*#	10.1±1.5*#
		24 h after treatment	110.3±14.6*#	97.6±10.4*#	25.6±3.8*#	9.94±1.07*#	8.3±1.0*#
Group B	21	Before treatment	75.6±8.8	65.2±8.6	16.6±2.1	5.04±0.72	14.5±1.7
		12 h after treatment	85.2±10.9*	77.4±8.4*	18.3±2.4*	6.84±0.87*	12.7±1.6*
		24 h after treatment	98.3±11.4*	82.1±9.5*	20.7±2.9*	7.62±0.91*	10.6±1.4*

*: comparison of indexes between before and after treatment, $P<0.05$; #: comparison of indexes between group A and group B, $P<0.05$.

Table 3.

Changes in serum stress hormones before and after treatment.

Groups	*n*	Time	NE	Cor	ACTH
Group A	21	Before treatment	116.2±14.7	328.5±52.5	9.32±1.05
		12 h after treatment	78.5±9.5	245.2±31.9	6.52±0.88
		24 h after treatment	70.2±8.8	214.5±25.6	5.03±0.78
Group B	21	Before treatment	116.7±15.2	331.1±49.5	9.41±0.98
		12 h after treatment	97.5±11.4	285.2±36.2	7.84±0.94
		24 h after treatment	84.2±10.7	240.1±32.8	6.51±0.82

*: comparison of indexes between before and after treatment, $P<0.05$; #: comparison of indexes between group A and group B, $P<0.05$.

contents were not significantly different between two groups of patients before treatment ($P>0.05$); 12 h and 24 h after treatment, serum SOD, GSH-Px, CAT and TAC contents of both groups of patients were significantly higher than those before treatment while MDA contents were significantly lower than those before treatment ($P<0.05$), and serum SOD, GSH-Px, CAT and TAC contents of group A were significantly higher than those of group B while MDA contents were significantly lower than those of group B ($P<0.05$).

3.4 Serum stress hormone contents

Before treatmentas well as 12 h and 24 h after treatment, analysis of serum stress hormones NE (ng/mL), ACTH (pmol/L) and Cor (nmol/L) between two groups of patients was as follows: serum NE, ACTH and Cor contents were not significantly different between two groups of patients before treatment ($P>0.05$); 12 h and 24 h after treatment, serum NE, ACTH and Cor contents of both groups of patients were significantly lower than those before treatment ($P<0.05$), and serum NE, ACTH and Cor contents of group A were significantly lower than those of group B ($P<0.05$).

4. Discussion

Diabetic ketoacidosis (DKA) is a common acute complication of diabetes mellitus, and infection and hypoglycemic drug withdrawal are the common causes of DKA. Abnormal elevated blood glucose and blood ketone can produce cytotoxicity, influence the islet β cell secretion and cause insufficient insulin secretion[5,6]. Therefore, exogenous supplementation of insulin is the key to treat DKA. Multiple subcutaneous injection and intravenous injection are the common ways to supplement the insulin, the hypoglycemic effect is exact, but the former way of insulin injection causes great fluctuation of insulin content and is not conducive to the stability of blood glucose, and the latter will increase the risk of hypoglycemia. Continuous subcutaneous insulin infusion by insulin pump is a newly emerging way of insulin injection that can intelligently simulate physiological insulin secretion mode and continuously infuse insulin, which not only avoids the fluctuations of insulin levels caused by daily multiple subcutaneous injections, but can also reduce the risk of hypoglycemia caused by intravenous insulin[7,8]. In recent years, the continuous subcutaneous insulin infusion by insulin pump is increasingly used in the treatment of diabetes, and study has shown that insulin pump for treatment of diabetic ketoacidosis is more effective than conventional intravenous insulin to promote the blood ketone body to turn negative and the blood glucose to reach the standard[9].

In this study, the effects of insulin pump and continuous intravenous insulin treatment on diabetic ketoacidosis were analyzed. The increased ketone body generation, increased base consumption and metabolic acidosis are the characteristics of diabetic ketoacidosis[10,11]. Acetone, β-hydroxybutyrate and acetoacetic acid are the ketone bodies produced by the fatty acid in the liver after β-oxidation, and the increase in the production of β-hydroxybutyrate is most significant in the process of ketosis[12,13]. In the study, the changes in serum β-hydroxybutyrate contents were analyzed to reflect the ketone body metabolism, and the results showed that serum β-hydroxybutyrate contents of both groups of patients significantly decreased after treatment, and serum β-hydroxybutyrate contents of group A were significantly lower than those of group B. This indicates that insulin application by insulin pump can be more effective than continuous intravenous insulin in inhibiting ketogenesis and improving ketone body metabolism. Blood gas indexes were analyzed to further reflect the state of acidosis, and the results showed that pH, HCO_3^- and base excess levels of both groups of patients significantly increased after treatment, and pH, HCO_3^- and base excess levels of group A were significantly higher than those of group B. This indicates that insulin application by insulin pump can be more effective than continuous

intravenous insulin in correcting the acidosis state of patients with diabetic ketoacidosis.

The persistent hyperglycemic environment and acidosis in patients with diabetic ketoacidosis can result in massive generation of oxygen free radicals, which can cause tissue injury by oxidative stress response. The lipid in tissue cells is the most common target of oxygen free radicals, the oxidation reaction between lipid and oxygen free radicals will cause cell structure damage and function damage, and also produce lipid oxidation product MDA[14,15]. In the activation of oxidative stress reaction, antioxidant enzymes such as SOD, GSH-Px and CAT can eliminate oxygen free radicals to a certain extent, but excessive generation of oxygen free radicals can cause excessive consumption of antioxidant enzymes and weaken the antioxidant capacity. In the study, analysis of the changes in serum anti-oxidation indexes and oxidation products before and after treatment showed that serum SOD, GSH-Px, CAT and TAC contents of both groups of patients significantly increased while MDA contents significantly decreased after treatment, and serum SOD, GSH-Px, CAT and TAC contents of group A were significantly higher than those of group B while MDA contents were significantly lower than those of group B. This indicates that insulin application by insulin pump can be more effective than continuous intravenous insulin in inhibiting oxidative stress response and reducing the production of oxygen free radicals and the consumption of antioxidant enzymes in patients with diabetic ketoacidosis.

Ketoacidosis is the acute complication of diabetes, the elevated blood glucose and blood ketone body contents in the short term and the activation of oxidative stress reaction are strong stressors for the body, and they can cause the increased secretion of a variety of endocrine hormones in the body. The adrenal gland is an important gland that participates in the stress response process and mediates stress-related endocrine hormone secretion, and both the NE secreted by adrenal medulla and the Cor secreted by the cortex are related to the stress response[16]. In the stress state, the high level of sympathetic excitability will promote the adrenal medulla to secrete NE, which affects the systemic hemodynamic state; increased ACTH in the pituitary gland will stimulate the adrenal cortex to secrete Cor, which affects energy metabolism and enhances the body's ability to withstand stress and trauma. In the study, analysis of the changes in serum stress hormones before and after the treatment showed that serum NE, ACTH and Cor contents of both groups of patients significantly decreased after treatment, and serum NE, ACTH and Cor contents of group A were significantly lower than those of group B. This indicates that insulin application by insulin pump can be more effective than continuous intravenous insulin in reducing the stress state and reducing the secretion of stress hormones in patients with diabetic ketoacidosis.

Subcutaneous insulin infusion by insulin pump can be more effective than continuous intravenous insulin in improving ketone body metabolism, acidosis state and stress state of diabetic ketoacidosis.

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