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Study on the relationship of acute ketosis intoxication and type 2 diabetes mellitus

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ABSTRACT

Objective: To study the change of serum C-reactive protein (CRP) levels and its correlation with ketosis in type 2 diabetes mellitus patients with acute ketosis intoxication. **Methods:** A retrospective analysis was conducted for the patients with type 2 diabetes mellitus from August 2015 to January 2016. The patients combined with ketosis were included into diabetic ketosis group and the patients without ketosis were included into negative control group. The clinical data were collected from two groups including general data, blood pressure, liver function and the levels of blood fat, glycosylated hemoglobin, blood ketone, β-hydroxybutyric acid and CRP. The discrepancy of clinical data between two groups was analyzed. **Results:** The levels of glycosylated hemoglobin [(11.6 ± 2.1)% *vs.* (8.3 ± 1.9)%], blood ketone [0.65 (0.3, 1.75) *vs.* 0.1 (0.1, 0.2) mmol/L], β-hydroxybutyric acid [0.595 (0.303, 1.775) *vs.* 0.08 (0.06, 0.15) mmol/L] and CRP [0.595 (0.303, 1.775) *vs.* 0.08 (0.06, 0.15) mmol/L] were significant higher than those of negative control group, while the levels of blood pressure, blood fat and aminopherase had no significant difference. The serum CRP levels showed positive correlation with blood ketone and β-hydroxybutyric acid ($r = 0.490$ and $r = 0.478$, respectively). **Conclusions:** Poor blood glucose control for a long time and strengthening inflammatory response are correlated with the status of acute ketosis in type 2 diabetes mellitus patients. The CRP levels in ketosis patients were significantly elevated and could be used to evaluate the degree of ketosis.

1. Introduction

Diabetic ketosis (DK) is one of the common acute complications in diabetes mellitus patients and this disease caused by ketosis has always been considered as the important feature of type 1 diabetes mellitus [1,2]. Nevertheless, in recent years, more and more foreign scholars found that type 2 diabetes mellitus is also quite common in diabetes mellitus patients caused by ketosis and ketoacidosis. Umpierrez research showed that the ratio of

type 2 diabetes mellitus is taking up more than half in Afro-American diabetes mellitus patients caused by ketoacidosis[3]. Kim study revealed that the ratio of type 2 diabetes mellitus is up to 40% in Korean diabetes mellitus patients caused by ketoacidosis[4]. Therefore, clinical scholars pay more attention to these type 2 diabetes mellitus patients combined with ketosis.

All DK patients are in an acute and inflammatory condition. Acute phase reactive protein CRP, proinflammatory cytokine IL-6 and suppression of inflammatory cytokine IL-10 have a large number of synthesis and secretion in an acute condition[5–7]. A number of studies have confirmed that CRP levels are significant higher and related with the degree of severity of ketosis in the serum of type 1 diabetes mellitus patients combined with ketosis[8–10]. However, the synthetic condition of CRP has not been reported clearly in the body of type 2 diabetes mellitus patients combined with ketosis so far. CRP is a kind of acute phase reactive protein, which is compounded and secreted from hepatic cell under inducing of proinflammatory cytokine such as IL-6 and so on and can participate in inflammatory response by activating inflammatory factors secreted from macrophage and promoting inflammatory

cell sticking to inflammatory site. In the following study, we analyze the change of serum C-reactive protein (CRP) levels and its correlation with ketosis in type 2 diabetes mellitus patients with acute ketosis intoxication.

2. Materials and methods

2.1. Study object

A total of 100 type 2 diabetes mellitus patients were collected randomly from Department of Endocrinology, the 117th Hospital of Chinese People's Liberation Army from August 2015 to January 2016 and were retrospectively analyzed. Inclusion and exclusion criteria of cases were as follows: (1) met the diagnostic criteria for type 2 diabetes mellitus established by World Health Organization (1999); (2) all the serum glutamic acid decarboxylase antibody (GAD-Ab), islet cell cytoplasmic antibody (ICA) and insulin autoantibody were negative; (3) type 1 diabetes mellitus, gestational diabetes mellitus and other specific types of diabetes mellitus were excluded and (4) the patients with a state of infection and fever after operation were excluded. In 100 patients, 67 cases were male and 33 cases were female. A total of 52 cases were received the treatment of oral hypoglycemic drugs, 11 cases were received insulin treatment and 37 cases were received the treatment of oral hypoglycemic drugs combined with insulin. According to the following criteria to judge ketosis: blood glucose levels were more than 13.9 mmol/L and ketonuria was more than 1+. A total of 39 cases diagnosed with ketosis were collected into DK group and 61 cases not combined with ketosis diagnosis were collected into NC group.

2.2. Clinical data collection

After admitting to hospital, all patients received a physical examination and measurement to record the height and weight and calculate body weight index (BMI). Riva-rocci sphygmomanometer was used to measure systolic pressure (SBP) and diastolic pressure (DBP). Peripheral vein blood was collected under the fasting state. Beckman fully automatic biochemical analyser was used to detect triglyceride (TG), total cholesterol (TC), alanine aminotransferase (ALT), aspartate aminotransferase (AST) and β-hydroxybutyric acid levels. Clean catch midstream urine was collected and urine acetone bodies levels were disposed with semi-quantitative analysis by chemical method. After collecting terminal blood, blood ketone levels were detected by Optium Xceed blood ketone instrument manufactured from Abbott Company. Full-automatic Afinion AS100 Analyzer (Afinion Company) was used to measure glycosylated hemoglobin levels.

2.3. Statistical methods

SPSS 20.0 software was used to input data. Measurement data were examined using homogeneity of variance of which the data accorded to homogeneity of variance were expressed as mean ± SD and were analyzed by *t*-test, while the data not accorded to homogeneity of variance were expressed as median (P25, P75) and were analyzed by nonparametric rank and inspection. Enumeration data were expressed as frequency and were analyzed by *Chi*-square test. The correlativity between two

variables was analyzed by Pearson correlation. Difference was statistically significant ($P < 0.05$).

3. Results

3.1. General clinical data of two group patients

DK group included 28 male cases and 11 female cases [(47.8 ± 12.4) years, (23.9 ± 3.1) kg/m^2 BMI, (127.2 ± 13.2) mmHg SBP, (83.8 ± 8.6) mmHg DBP, (5.5 ± 1.8) mmol/L TG, (2.0 ± 0.76) mmol/L cholesterol, (24.1 ± 12.7) IU/mL ALT, (19.7 ± 11.9) IU/mL AST and 11.6% ± 2.1% glycosylated hemoglobin]. NC group included 39 male cases and 22 female cases [(55.5 ± 10.8) years, (24.7 ± 2.9) kg/m^2 BMI, (130.7 ± 19.8) mmHg SBP, (84.7 ± 12.3) mmHg DBP, (5.2 ± 1.3) mmol/L triglyceride, (2.1 ± 1.5) mmol/L cholesterol, (27.8 ± 14.5) IU/mL ALT, (21.8 ± 14.5) IU/mL AST and 8.3% ± 1.9% glycosylated hemoglobin]. According to statistic analysis, the gender, BMI, blood pressure and triglyceride, cholesterol, AST and ALT levels of DK group had no significant difference with NC group. The age in DK group was significant lower than NC group, while glycated hemoglobin levels were significant higher than those in NC group (Table 1).

3.2. Blood ketone and β-hydroxybutyric acid levels of patients in two groups

After homogeneity of variance test, blood ketone and β-hydroxybutyric acid levels of two groups were not accordant with homogeneity of variance and were expressed as median (P25, P75). In DK group, blood ketone level was [0.65 (0.3, 1.75)] mmol/L and β-hydroxybutyric acid level was [0.595 (0.303, 1.775)] mmol/L. In NC group, blood ketone level was [0.1 (0.1, 0.2)] mmol/L and β-hydroxybutyric acid level was [0.08 (0.06, 0.15)] mmol/L. After nonparametric rank sum test, blood ketone and β-hydroxybutyric acid levels of patients in DK group were significant higher than NC group (Figure 1).

3.3. Serum CRP contents of patients in two groups

According to homogeneity of variance test, serum CRP contents of patients in two groups were not accordant with homogeneity of variance and were expressed as median (P25, P75). Serum CRP contents of patients in DK group {[4.78 (2.85, 7.63)] mg/L} were significant higher than serum CRP contents in NC group {[2.45 (2.10, 3.07)] mg/L} (Figure 2).

Table 1

General clinical data of two group patients.

Parameter	DK (*n* = 39)	NC group (*n* = 61)	*P*
Gender (male/female)	28/11	39/22	> 0.05
Age (years)	47.8 ± 12.4	55.5 ± 10.8	< 0.01
BMI (kg/m^2)	23.9 ± 3.1	24.7 ± 2.9	> 0.05
SBP (mmHg)	127.2 ± 13.2	130.7 ± 19.8	> 0.05
DBP (mmHg)	83.8 ± 8.6	84.7 ± 12.3	> 0.05
TG (mmol/L)	5.5 ± 1.8	5.2 ± 1.3	> 0.05
TC (mmol/L)	2.0 ± 0.76	2.1 ± 1.5	> 0.05
ALT (IU/L)	24.1 ± 12.7	27.8 ± 14.5	> 0.05
AST (IU/L)	19.7 ± 11.9	21.8 ± 14.5	> 0.05
HbA1c (%)	11.6 ± 2.1	8.3 ± 1.9	< 0.01

HbA1c: Glycosylated hemoglobin.