



Original article

Correlation between the glucose level and the development of acute pancreatitis

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ABSTRACT

Objective: To investigate the correlation between the level of glucose in serum and the development of acute pancreatitis (AP).**Methods:** Data of 153 AP cases were collected, in which there were 130 patients with mild AP (MAP), 4 with moderate-severe AP (MSAP) and 19 with severe AP (SAP). At the time of admission, following indexes of patients were recorded: glucose, APACHE II score, TNF- α and C-reaction protein (CRP).**Results:** At the time of admission, the levels of glucose in serum and APACHE II scores in the MSAP and SAP groups were significantly higher than those in the MAP group, but after treatment, the level of glucose in serum was recovered in 95.8% of the patients in the MAP group, while this digit in the SAP group remained to be 68.4%; in the SAP group, the levels of TNF- α and CRP in patients with sustained hypertension were significantly higher than those with non-persistent hypertension; in terms of the length of stay in hospital, the SAP group was shorter than that in the non-treatment group, and the difference had statistical significance ($p < 0.05$). Moreover, we found that the level of glucose in serum was positively correlated with the APACHE II scores, TNF- α and CRP.**Conclusion:** Glucose level in serum can be used as one of the indicators for evaluating the severity and development of AP in clinical practice.© 2018 Production and hosting by Elsevier B.V. on behalf of King Saud University. This is an open access article under the CC BY-NC-ND license (<http://creativecommons.org/licenses/by-nc-nd/4.0/>).

1. Introduction

Acute pancreatitis (AP) is an inflammatory injuries, including edema, hemorrhage and necrosis in pancreas caused by tissue autodigestion in relation to various pathogens (Mizock, 2001). Generally, AP is categorized into the mild AP (MAP), moderate severe AP (MSAP) and severe AP (SAP) (Carroll et al., 2007). Among AP patients, almost 20% of them can evolve into the SAP, manifesting dysfunction in multiple organs or focal complications, which contributes to the fact that the mortality rate has exceeded 20% despite of the rapid progress in diagnosis and treatment (Cely et al, 2004; Bank et al., 2002). Research has shown that during

the progression of AP, glucose at a high level can promote the release of inflammatory cytokines (Dauphine et al, 2004), thus affecting the progression of disease. Hence, in this paper, we observed the correlated indexes of AP patients in different categories, including the glucose level, so as to investigate the correlation between the glucose at a high level and progression of AP.

2. Material and methods

2.1. General data

Enrollment criteria were stipulated according to the relevant guidelines of AP of Committee of Pancreatic Diseases of Chinese Society Of Gastroenterology, Chinese Medical Association revised in 2013 Carroll et al. (2007), while the guidelines revised in 2013 were also adopted for the gradation criteria of AP: (a) typical history of acute abdominal pains; (b) significant elevations in the activities of amylase in blood and urine; (c) pancreatic edema, effusion or necrosis according to CT or ultrasonic B examination. In this study, a total of 175 patients were enrolled from this hospital, including 106 males and 69 females; patients aged between 19

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and 82 years old with an average of (53 ± 17) years old. Patients with basic diabetes mellitus or clinical history of diabetes mellitus were excluded, and all enrolled patients were matched against the age, gender and other history of diseases.

2.2. Collection of data and grouping

At admission, we collected the fasting glucose level, APACHE II score and variations in level of glucose within 3 days in all patients, as well as the levels of TNF- α and CRP in serum of SAP patients. Besides, 3 days later, all SAP high-glucose patients were divided into two groups randomly (n = 6 for each group). For intervention group, patients took up insulin to control the glucose, in which for those with glucose level higher than 15 mmol/L, additional normal saline was given, while for those with glucose level lower than 15 mmol/L, additional sugar was given. For control group, patients only received the regular treatment. The length of stay in hospital of all patients was recorded. According to the changes in glucose level with the lapse of time in hospital, patients were divided into two groups, i.e. the persistent hyperglycemia group [Dauphine et al., 2004](#) and the non-persistent hyperglycemia group. In all subjects, 2 SAP patients died of the multi-organ failure at the second day after admission.

2.3. Indicators and methods of detection

2.3.1. Measurement of glucose level

In this experiment, hexokinase method was used with a normal range between 3.8 and 6.1 mmol/L. At 6 a.m. on the second and third days after admission, patients were required to measure the fasting glucose. Persistent hyperglycemia is defined as follows: Fasting glucose levels at admission and 6 a.m. on second and third days after admission were higher than the normal level, and two of these results were not lower than 11.1 mmol/L.

2.3.2. Measurement of TNF- α

In this experiment, enzyme-linked immunosorbent assay (ELISA) was adopted in normal range of <10 ng/mL. In the morning of the second day after admission, TNF- α level in serum was determined in peripheral venous blood.

2.3.3. Measurement of CRP

In this experiment, immunoturbidimetry was adopted in normal range of <8 mg/mL. In the morning of the second day after admission, CRP level in serum was determined in peripheral venous blood.

2.4. Statistical methods

All data were processed using SPSS 17.0 for Windows. Measurement data were presented as mean ± standard deviation ($\bar{x} \pm s$), and as for the comparisons, *t* test was adopted for comparison between two samples, while analysis of variance for the intergroup comparison among different samples. For data not conforming to the normal distribution, non-parameter test was adopted. For enumeration data, chi-square test was adopted for comparison. Consecutive correction was carried out for samples with theoretical frequency < 5. Linear correlation analysis was carried out for bivariate data. *p* < 0.05 suggested that the difference had statistical significance.

3. Results

3.1. Glucose level at admission as well as the APACHE II score and changes in glucose level in patients with varying degrees of AP

In MSAP and SAP groups, the levels of glucose in serum and APACHE II scores at admission were significantly higher than those in MAP group, and the analysis of variance revealed that the difference had statistical significance (*p* < 0.01). However, comparison between MSAP and SAP groups showed that the difference had statistical significance (*p* > 0.05; [Table 1](#)). Consecutive measurements of fasting glucose in the morning within 3 days after admission indicated that after active fluid therapy, MAP patients recovered, but in the SAP group, 3 days after admission, patients with hyperglycemia occupied as high as 68.4% ([Table 2](#)).

3.2. Correlations of glucose level of SAP patients with the levels of TNF- α and CRP as well as the APACHE II scores

In the SAP group, TNF- α and CRP levels in serum of patients with persistent hyperglycemia were significantly higher than those in non-persistent hyperglycemia, and the difference had statistical significance (*p* < 0.01; [Table 3](#)).

3.3. Analysis of the correlation between glucose level and all indicators of AP patients in different groups

Glucose level in serum was correlated with the APACHE II score and levels of TNF- α and CRP in serum, and the difference had statistical significance (*p* < 0.05; [Table 4](#)).

Table 1

Glucose level and APACHE II score of patients with varying degrees of AP at admission ($\bar{x} \pm s$).

	MAP (n = 120)	MSAP (n = 36)	SAP (n = 19)
Glucose level (mmol/L)	8.10 ± 3.20	12.14 ± 3.55*	14.32 ± 3.15*
APACHE II scores	9.41 ± 3.09	10.05 ± 3.39*	12.48 ± 3.33*

Note: **p* < 0.01 vs. MAP group

Table 2

Changes in the number of hyperglycemia patients after treatment (n).

	Number of hyperglycemia patients		
	First day	Second day	Third day
MAP (n = 120)	34	10	5
MSAP (n = 36)	36	27	9
SAP (n = 9)	19	14	13

Table 3

Comparison of the levels of TNF- α and CRP in serum of SAP patients (n, $\bar{x} \pm s$).

	N	TNF- α (ng/mL)	CRP (ng/mL)	APACHE II score
Persistent hyperglycemia group	13	26.40 ± 11.05	143.28 ± 61.11	15.32 ± 3.99
Non-persistent hyperglycemia group	4	15.37 ± 9.20	87.51 ± 45.39	11.25 ± 2.13
<i>t</i>		4.72	4.41	2.32
<i>p</i>		0.001	0.001	0.039

Table 4Correlations between the glucose level and indicators ($\bar{x} \pm s$).

	Glucose level (mmol/L)			p
	3.8–6.1	6.1–11.1	11.1–17.5	
APACHE II score	8.22 ± 3.15	10.33 ± 3.24	13.40 ± 5.03	0.628
TNF- α (ng/mL)	17.82 ± 11.33	22.25 ± 9.06	26.43 ± 13.23	0.802
CRP (ng/mL)	119.61 ± 49.17	137.57 ± 54.21	151.73 ± 72.29	0.773

Table 5Comparison of the length of stay in hospital of SAP patients after glucose control (n, $\bar{x} \pm s$).

	N	Length of stay (d)	t	p
Intervention group	6	24 ± 12	2.31	0.042
Non-intervention group	6	38 ± 10		

3.4. Correlation between the glucose level and length of stay in hospital of SAP patients

In SAP patients, glucose level was controlled through saline/glucose + insulin therapy, and we found that the length of stay in hospital was significantly shorter than that in the non-intervention group with statistically significant difference ($p < 0.05$; Table 5).

4. Discussion

AP refers to mild or severe inflammatory responses, which can activate the pancreatic enzymes, so as to digest the pancreatic tissues (Bollen et al., 2008; Brunkhorst et al., 2008). MAP in almost 80% or 90% of patients is categorized into self-limited diseases with little possibilities to progress into generalized reactions. However, there are 20% to 30% of AP patients with rapid progression in disease condition, which usually evolves into the generalized inflammatory responses, leading to severe injuries to pancreas, multiple-organ failure, or even death.

In the early stage of SAP, a variety of inflammatory cytokines are activated to release the cytokines and inflammatory mediators, giving rise to the systemic responsive syndrome (Meyfroidt et al., 2010), in which a great many of factors are involved through positive feedback; this can gradually magnify the inflammation. However, once the system can hardly tolerate the inflammation, it will diffuse systemically, resulting in multi-organ inflammatory injuries and dysfunctions. Bank S et al (Bank et al., 2002) found that a high level of glucose can activate the release of inflammatory cytokines, thereby triggering a series of inflammatory reactions, and in some instances, rapid progression may lead to injuries to multiple organs. Van den Berghe et al. (2001) also confirmed that progression can be blocked or alleviated through anti-inflammation and -oxidation therapies. Literatures also compared the glucose level with the single-organ failure rate, multi-organ failure rate, ICU-transfer rate, and mortality rate, and the results indicated that a high level of glucose can serve as a key indicator of multi-organ failure and poor prognosis (Schaffler et al., 2007). Thus, glucose level is closely correlated with the inflammatory responses in AP, which can affect the progression of disease through activating the inflammatory responses. High-level glucose can be used as one of the reference indicators for evaluating the severity of AP in clinical practice.

In this paper, among AP patients, we found that the incidence rates of hyperglycemia in MSAP and SAP groups were significantly higher than those in the MAP group, and through the active fluid therapy after admission, glucose levels of MAP patients recovered

within 3 days; as for MSAP patients, somewhat amelioration was observed; however, nearly half of the SAP patients remained to be tortured by hyperglycemia. Indicators obtained at admission also showed different condition of patients, levels of glucose and APACHE II scores. Thus, a high level of glucose can indicate the severity of AP, affect the therapeutic effect and impair the recovery. A study Bollen et al., 2008 also confirmed that a high level of glucose can alter the effect of non-surgery treatment for AP patients at an early stage, thereby influencing the disease course. From Table 3, we could find that in SAP patients, significant increases were identified in the levels of TNF- α and CRP in serum of patients with persistent hyperglycemia, suggestive of the close correlation between the high-level glucose and the inflammation as well as its severity in disease progression. Thus, it is very necessary to control the glucose level rationally, but enormous studies are required to figure out the rational range that is conducive to the recovery of disease.

Dungan et al. (2011) conducted a study on autoimmune pancreatitis (AIP), and believed that a series of autonomous antigens can initiate the AIP through acting on the regulatory T cells, T-helper 1 (Th1) cells, releasing the interferon, interleukin and TNFs, which can further act upon the inflammatory cells and facilitate the progression of AIP. Besides, a study (Oh et al., 2006) also revealed that obesity and glucose levels can also be used as key indexes to evaluate the severity of AP. Also, some studies also pointed out that a good living style, scientific diet and appropriate exercise can reduce the recurrence of AP with effective control of the glucose level and body weight (Kosiborod et al., 2008) In addition, a literature reported that infection is associated with the progression of SAP strongly, which is also thought to be the key to success of therapy (Cely et al., 2004).

Moreover, in this paper, the levels of TNF- α and CRP in serum were augmented in the patients with persistent hyperthermia, provoking the question whether there is a certain correlation between the hyperglycemia and the inflammation in disease course. Furthermore, studies are also required to explore the relevant mechanism. For patients at an early stage of AP, the severity and importance of organs involved in the injuries are more than the pancreas itself (Liu et al., 2006; Dos Santos et al., 2018; Alsharidah et al., 2018; Yildiz et al., 2017; Pati et al., 2017; Tatar et al., 2017), while multi-organ injuries are strongly associated with the inflammatory responses caused by hyperglycemia. Thus, in clinical treatment of AP, great attention should be paid to the glucose level, and rational control of glucose might be critical to the development and treatment of AP through affecting the inflammatory responses.

5. Conclusion

In this study, we preliminarily investigated the correlation between the state of hyperglycemia in AP patients and the severity of disease, and found that appropriate intervention on the glucose level of patients can affect the disease progression. However, this study is limited by the small sample size, and how hyperglycemia affects the development and prognosis of disease still required enormous large-sample, multi-center and long-term clinical and laboratory studies.

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