

Two different glyceic control ways applied to treat severe acute pancreatitis.

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Abstract

Objective: To determine the optimum blood glucose target values between two classic glyceic control goals and compare their efficacy and safety in patients with Severe Acute Pancreatitis (SAP).

Methods: 112 SAP patients included in the study were randomly divided into two groups: group A for a blood sugar control target value of 7.8-10 mmol/L and group B for a blood glucose control target value of 6.1-8.3 mmol/L. The glyceic control parameters, prognostic parameters and adverse events during glyceic control were compared.

Results: Group A achieved glyceic control goals more quickly than group B, and had significantly less severe hypoglycemic events and glucose treatment events ($p < 0.05$). No significant differences in moderate/severe malnutrition rates, the incidence of infection, MODS incidence, the average ICU stay, 28 day mortality, and hyperglycemic parameters were observed ($p > 0.05$) between the two groups.

Conclusion: Glyceic control target of 7.8-10 mmol/L can reduce the risk of hypoglycemia in patients with SAP and is achieved faster and more safely than a glyceic control target of 6.1-8.3 mmol/L.

Keywords: Glyceic control goal, SAP, Hypoglycemia, Prognosis.

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Introduction

Severe Acute Pancreatitis (SAP) patients are prone to hyperglycemia with an incidence ranging from 40% to 90% due to pancreatic endocrine dysfunction [1,2]. Elevated blood glucose level and its prolonged duration have a direct impact on the outcome and prognosis of SAP [3]. Strict blood glucose control can effectively improve the prognosis, but the optimal target glucose level for glyceic control has not been established and is still an area of focus in recent studies. Leuven et al. showed that when Intensive Insulin Therapy (IIT) was used to maintain blood glucose within the normal range of 4.4-6.1 mmol/L, an increase in the incidence of severe hypoglycemia was observed [4], which could have a strong negative impact on the prognosis of patients. It is commonly thought that a target glucose level of < 8.3 mmol/L can significantly reduce the incidence of hypoglycemia in critically ill patients [5]. A target glucose level of 6.1-8.3 mmol/L is widely accepted as a safe and effective range for glyceic control in patients with SAP (6). Inzucchi et al. [7] demonstrated that lowering blood glucose from 12.8 mmol/L to 10.0 mmol/L could reduce mortality, but lowering blood glucose any further may confer no additional benefits. The international guideline recommended a blood glucose target of

7.8-10.0 mmol/L for patients with severe medical conditions [8]. Currently, there is no study comparing blood sugar control targets of 6.1-8.3 mmol/L and 7.8-10.0 mmol/L. In this study, a prospective, randomized, controlled clinical method was used to examine the efficacy and safety of two different glyceic control targets and their effects on the prognoses of patients with SAP.

Subjects and Methods

General information

112 patients with SAP were recruited at the ICU of Hunan Provincial People's Hospital from January 2012 to June 2013. The inclusion criteria were as follows: 1) patients ≥ 18 years of age; 2) patients with an APACHE II score ≥ 10 points on first admission to the ICU; and 3) patients with a fasting glucose level ≥ 6.9 mmol/L or random blood glucose level > 11.1 mmol/L and glycosylated haemoglobin $\leq 6\%$. The exclusion criteria included: 1) patients with diabetes; 2) patients receiving more than 2/3 of their total caloric intake through enteral nutrition; 3) pregnant and lactating patients; 4) patients with chronic liver and/or renal insufficiency; 5) patients with insulin allergy; and 6) patients with a history of

long-term hormone use. This study was approved by the Hunan Provincial People's Hospital Medical Ethics Committee.

Method of glycemetic control

The effects of two blood sugar control targets, the blood glucose concentration of 7.8-10 mmol/L and 6.1-8.3 mmol/L) were investigated in two groups of SAP patients: group A with the blood glucose concentration being controlled at 7.8-10 mmol/L and group B at 6.1-8.3 mmol/L. Patients who had blood glucose concentration within 7.8-8.3 mmol/L were randomly assigned to the two groups. All patients received standardized SAP treatment from the same group of doctors and team of nurses. Continuous intravenous infusion of insulin was given from 30 min to 4 h (50 U regular insulin in 48.75 ml of 0.9% sodium chloride). Peripheral blood glucose was dynamically monitored. The Portland standard [9] and the optimization of glycemetic control [10] were used to detect the concentration of blood glucose regulated by insulin.

Observational parameters

Glycemetic control values: The amount of time required to achieve the target blood sugar level, hyperglycemic index, and average blood sugar were measured.

Prognostic indicators: Prevalence of moderate/severe malnutrition, incidence of nosocomial infection, MODS incidence, the average monitoring hours, and 28 day mortality. Serum protein <28 g/L was judged as the occurrence moderate/severe malnutrition. Diagnosis of nosocomial infectious was performed in reference to the Hospital Infection Diagnostic Criteria issued by the Ministry of Health of China [11].

Glycemetic control adverse events: severe hypoglycemic events, 50% glucose treatment events, and hyperosmolar coma

events. Blood glucose <2.2 mmol/L was considered severe hypoglycemia. 50% glucose treatment event is defined as intravenously injecting 20-40 ml 50% glucose when blood sugar <3.9 mmol/L. 12 The diagnostic criteria for hyperosmolar coma followed five indicators: 1) blood glucose >33.3 mmol/L; 2) blood sodium is low, normal, or >145mmol/L; 3) normal or high levels of ketones in the blood; 4) plasma osmolality >350 mmol/L; and 5) urine tests strongly positive for sugar.

Statistical analysis

Data were analysed using SPSS17.0 statistical package. Measurement data was presented as mean ± SEM and using t-test. Counting data were analysed using χ² test. P<0.05 was considered statistically significant. Sigmaplot software was used to calculate high glycemetic index.

Results

Comparison of general information between the two groups of patients

Of the 112 patients, 3 patients (1 patient in group A and 2 patients in group B) left the hospital during ICU treatment without permission. 109 patients completed the glycemetic control investigation. The conditions of 104 patients improved, and these patients were returned to the general ward after ICU treatment. 5 patients died within 28 days of admission to the ICU. No significant differences were found in age, gender, etiology, APACHEII score, ICU admission glucose, ICU albumin, and glycated haemoglobin were observed between two groups (p>0.05) (Table 1).

Table 1. The comparison of general conditions between the two groups of patients ($\bar{x} \pm S$).

Group	n	Sex (case) M/F	Age (years)	Cause (case)			APACHE II score	Blood sugar (mmol/L)	Glycated haemoglobin (%)	Albumin (g/L)
				Biliary	lipid	other				
A	55	29/26	49.1 ± 17.1	24	17	14	17.0 ± 5.9	14.6 ± 4.5	4.9 ± 0.4	31.9 ± 4.5
B	54	28/26	47.9 ± 18.2	15	18	13	16.7 ± 6.5	13.9 ± 5.2	5.0 ± 0.3	32.6 ± 4.0
χ ²		0.008	0.3548	1.351			0.2524	0.7519	1.4745	0.8578
P		0.927	0.7234	0.509			0.8012	0.4537	0.1433	0.3929

Glycemetic control efficacy in two groups of patients

The amount of time required to achieve the target glycemetic goals in group B was significantly longer than that in group A

(p<0.05). Hyperglycemic index in group A was significantly greater than that in group B (p>0.05). The mean blood glucose values in the two groups were in the target range (Table 2).

Table 2. The comparison of glycemetic control indicators between the two groups.

Group	n	Amount of time required to achieve glycemetic control goal (h)	Hyperglycemic index (mol/L)	Mean blood sugar (mol/L)
A	55	4.31 ± 1.52	0.87 ± 0.26	9.0 ± 0.9

B	54	6.53 ± 2.17*	0.75 ± 0.21#	7.3 ± 1.1
t		6.1956	2.6479	8.838
P		0	0.0093	0

Prognostic indicators and adverse events for two groups of patients

No significant difference in the incidence of moderate/severe malnutrition, incidence of infection, MODS incidence, the average care hours, and 28 day mortality were observed

between the two groups (p>0.05). Severe hypoglycemia and 50% glucose treatment events were significantly lower in group A than in group B (p<0.05). No hyperosmolar coma occurred in the two groups of patients (Table 3).

Table 3. Adverse events and prognostic indicator for two groups of patients (case (%)) h).

Group	n	Moderate/severe malnutrition	Infection	MODS	Average care hours	28-day mortality	Adverse events		
							Severe hypoglycemia	50% glucose treatment	Hyperosmolar coma
A	55	7 (12.7)	13 (23.6)	12 (21.8)	182 ± 46	2 (3.6)	0 (0.0)	3 (5.5)	0
B	54	8 (14.8)	12 (22.2)	11 (20.4)	178 ± 43	2 (3.7)	2 (3.7)	13 (24.1)	0
χ ²		0.1	0.031	0.034	0.4688	0		7.543	
P		0.752	0.861	0.853	0.6402	1	0.243	0.006	1

Discussion

SAP is a common acute disease in the clinic with numerous complications and high mortality. Poor glycemic control not only increases the risk of death in patients, but also increases the incidence of infectious complications. Severe multi-system organ failure can be induced by SAP [12]. Glycemic control is therefore an important part of intensive care of SAP.

Management of blood glucose in critically ill patients is an important topic, but the optimal glycemic control target for SAP patients has yet to be determined. Leuven et al. study [13] showed that the blood sugar control target value of 4.4-6.1 mmol/L can greatly reduce ICU mortality and sepsis, acute renal failure, and incidence of anaemia complications in the patients with IIT compared to a target value of 10.0-11.1 mmol/L. However, following studies were unable to replicate the previous advantages of using a blood sugar control target value of 4.4-6.1 mmol/L [14]. In contrast, IIT leads to increased risk of hypoglycemia [15,16]. Currently, blood sugar management strategies are mainly focused on how to reduce the incidence of hypoglycemia and improve prognosis. The NICE-SUGAR study [17] recommended that a glycemic control target of <8.3 mol/L or 7.8-10.0 mol/L in critically ill patients is helpful in reducing the risk of hypoglycemia [9].

In this study, we compared the advantages between 7.8-10.0 mmol/L and 6.1-8.3 mmol/L blood sugar targets in improving efficacy, safety, and short-term prognosis of patients with SAP. The results showed that the average blood glucose values in two groups of patients reached target levels. The group of patients under the 7.8-10.0 mmol/L target achieved the glycemic control goal more quickly and had less severe hypoglycemic events and glucose treatment events than the

group of patients under the 6.1-8.3 mmol/L target. Low blood glucose is the most common complication of the glycemic control process. A blood glucose level lower than 2.8 mmol/L can cause cognitive impairment or even irreversible neurological damage and death. Due to the pain associated with analgesic sedation or mechanical ventilation reasons, SAP patients cannot verbally communicate with paramedics or medical personnel. Hypoglycemia is therefore difficult to discover. Nurse-driven hypoglycemia treatment protocols [14,18,19] could facilitate early identification and treatment of potentially low blood sugar, while strengthening the monitoring of severe hypoglycemia can prevent and reduce its incidence. However, 50% glucose treatment of severe hypoglycemia also increased the workload of nurses and pain of patients due to blood glucose testing frequency.

This study showed that the hyperglycemic index indicators of two groups of patients were similar without statistically significance, suggesting that the target glycemic control efficacy was the same for two groups. Hyperosmolar coma is another adverse event causing death during glycemic control. Hyperglycemic coma event did not occur in this study because of accurate determination of blood glucose and the glycemic control methods. The prognosis indicators, including moderate/severe malnutrition rates, the incidence of infection, MODS incidence, the average ICU stay, 28 day mortality, were similar without statistical significance between the 2 glucose targets, suggesting that there is no significant difference between these 2 glucose targets in improving early stage prognosis. In this study, multiple organ dysfunction/failure was the leading cause of elevated SAP mortality. No significant difference was observed between the two groups of patients. Infection is the most common complication of SAP. Hyperglycemia is directly

related to systemic inflammatory response syndrome of SAP patients. Blood glucose control can reduce the intra-abdominal infections, lung infections or sepsis. Infection rates in 2 groups of patients were 23.6% and 22.2%, respectively, which is lower than the reported 41.2-62.2% [20] and helps prove that a glycemic control target of 6.1-10.0 mmol/L can reduce infectious complications in patients with SAP.

In conclusion, a blood glucose control target of 7.8-10 mmol/L is better than the 6.1-8.3 mmol/L target in reducing the risk of hypoglycemia in patients with SAP and is more easily and safely achieved.

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