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The Effect of Hyperglycemia on the Prognosis of Critically Ill Patients Does Not Differ Diabetics from Nondiabetics

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Background: Hyperglycemia is common in critically ill patients, even in those without diabetes, and it is known to increase mortality in patients with or without diabetes in the settings of acute myocardial infarction or acute stroke. However, the clinical effects of admission hyperglycemia are uncertain, and no data is available that compares the prognosis in a heterogenous group of critically ill patients. The aim of this study was to evaluate the effect of hyperglycemia on prognosis in a heterogenous group of critically ill patients with or without diabetes.

Methods: The medical records of 858 consecutive adult patients admitted to a general intensive care unit (ICU) at a University Hospital over 21 months were reviewed. Patients with no records of blood glucose measurements and patients with normoglycemia during the first 3 days were excluded. The remaining 349 patients with hyperglycemia were divided into two groups according to a previous history of diabetes. Hyperglycemia was defined as a fasting blood glucose level of 140 mg/dl or more, or a random blood glucose level of 200 mg/dl or more on 2 or more determinations. The primary end-point of the study was ICU and in-hospital mortality, and its secondary end-point included length of stay in the ICU and hospital.

Results: There were no significant differences in ICU mortality (17.6/19.0%), in-hospital mortality (24.5/24.3%), ICU length of stay (6.6 ± 11.9/6.6 ± 10.4 days), and hospital length of stay (11.4 ± 29.0/12.8 ± 24.3 days) between diabetics and nondiabetics.

Conclusions: Our results indicate that the effects of hyperglycemia on the prognosis of critically ill patients do not differ diabetics from nondiabetics. **(Korean J Anesthesiol 2004; 47: S 10～S 13)**

Key Words: critical care, diabetes, glucose, hyperglycemia, mortality, prognosis.

INTRODUCTION

Hyperglycemia is common in critically ill patients, even in those without diabetes. In fact, hyperglycemia has been known to increase mortality in patients with and without diabetes in the settings of acute critical illness.[1,2)]

It has been known that relative risks of mortality and morbidity in hyperglycemic and normoglycemic patients among diabetes or nondiabetes are different. In a systematic overview, hyperglycemia after acute myocardial infarction increased the risk of in-hospital mortality in patients with and without diabetes, but the relative risks of hyperglycemia in patients with diabetes were smaller than that in patients without diabetes. And the risk of congestive heart failure or cardiogenic shock was increased in patients without diabetes, not in those with diabetes.[1)] The other systematic overview show that hyperglycemia in patients without diabetes compared to those with diabetes was associated with a higher risk in-hospital mortality after acute stroke.[2)] Most studies evaluated the prognosis of the patients with vascular diseases such as myocardial infarction[1,3-7)] or acute stroke.[2,8-10)]

Aim of this study was to evaluate the effect of hyperglycemia on the prognosis in a heterogenous group of critically ill patients with or without diabetes.

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MATERIALS AND METHODS

Medical records of 858 consecutive adult patients admitted to general intensive care unit (ICU) at a University Hospital, from July 1, 2000, to March 31, 2002 were reviewed. Of the 858 patients, 46 patients (5.4%) who had no records of blood glucose measurements and 463 patients with normoglycemia during the first 3 days were excluded. The remaining patients with hyperglycemia were divided into two groups according to previous history of diabetes.

Hyperglycemia was defined as a fasting blood glucose level of 140 mg/dl or more, or random blood glucose level of 200 mg/dl or more on two or more determinations during the first 3 days in ICU. Informations regarding types of intravenous fluid, level of glycated hemoglobin, antidiabetic therapy were not recorded in this study. Data included demographic characteristics, the APACHE II score, ICU mortality, in-hospital mortality, length of ICU stay, and length of hospital stay.

The primary end-point of the study was ICU and in-hospital mortality. Secondary end-point included length of stay in ICU and hospital.

Demographic and outcome variables were compared with the use of Student's t-test, the chi-square test, and the Mann-Whitney U test. All statistical analyses were performed using the statistical package for the SPSS 10.5 with 5% significance level ($P < 0.05$).

RESULTS

Of the 812 patients, 349 patients (43%) showed hyperglycemia at the time of ICU admission. The diabetic group consisted of 102 patients (29%) with a history of diabetes diagnosed before ICU admission. The nondiabetic group consisted of 247 patients with hyperglycemia who had no previous history of diabetes.

The patients characteristics are shown in Table 1. There were no significant differences in the mean age, gender, or the APACHE II score at the time of ICU admission between the two groups.

There were no significant differences in ICU and in-hospital mortality. In addition, there were no significant differences in length of stay in ICU and hospital between the two groups (Table 2).

DISCUSSION

We found that hyperglycemia was present in 43% of patients admitted to the ICU. Twenty nine percent of these patients had a history of diabetes before ICU admission. Main results of our study show that there were no differences in the effects of hyperglycemia on the prognosis between diabetes and nondiabetes in critically ill patients.

Even though there are no data about the effect of hyperglycemia on the prognosis between diabetes and nondiabetes in a heterogenous group of critically ill patients, some studies show that relative risks of hyperglycemia after acute phase of vascular diseases such as myocardial infarction or stroke were greater in nondiabetic patients than in diabetic patients.[2,7] Hyperglycemia has been demonstrated to increase vascular resistances[12] and impairs vascular endothelium dependent relaxation.[13] It modifies vascular reactivity[14] and may affect the prognosis of acute phase in patients with vascular

Table 1. Patients Characteristics

	Diabetic group (n = 102)	Nondiabetic group (n = 247)
Age (yr)	64.1 ± 12.1	54.2 ± 21.2
Gender (F/M)	54/48	147/100
APACHE II score	16.4 ± 9.0	15.3 ± 8.4

Age and the APACHE II score are expressed as mean ± SD. n: number of patients, Diabetic group: patients with a history of diabetes diagnosed before ICU admission, nondiabetic group: patients with no previous history of diabetes. There were no significant differences between the groups for any parameters ($P < 0.05$).

Table 2. Mortality and Length of Stay

	Diabetic group (n = 102)	Nondiabetic group (n = 247)
ICU mortality (%)	17.6	19.0
In-hospital mortality (%)	24.5	24.3
ICU length of stay (d)	6.6 ± 11.9	6.6 ± 10.4
Hospital length of stay (d)	11.4 ± 29.0	12.8 ± 24.3

ICU and hospital length of stay are expressed as mean ± SD. n: number of patients, Diabetic group: patients with a history of diabetes diagnosed before ICU admission, nondiabetic group: patients with no previous history of diabetes. There were no significant differences between the groups for any parameters ($P < 0.05$).

diseases. Futhermore, hyperglycemia may be directly toxic to the ischemic brain. Indeed, in an animal model of stroke, hyperglycemia facilitated the development of cellular acidosis in the ischemic penumbra and resulted in a greater infarction volume compared with insulin treated hypoglycemic animals.[15] Thus, hyperglycemia may promote the recruitment of potentially salvageable neuron into infarction. Also, hyperglycemic patients are relatively insulin-deficient. Insulin deficiency leads to reduced peripheral uptake of glucose and increased circulating free fatty acids. Free fatty acid may impair endothelium-dependent vasodilation in hyperglycemic patients with acute myocardial infarction.[16]

However, our results show that there were no differences in the effects of hyperglycemia on the prognosis between diabetes and nondiabetes. The possible explanations are: First, this study was undergone in a heterogeneous group of critically ill patients. Other studies showed that hyperglycemia in patients with vascular diseases was associated with poor prognosis.[1,2] It resulted from poor microcirculations. Therefore, the effect of hyperglycemia might be different in critically ill patients other than vascular diseases. Second, It has been suggested that patients with newly diagnosed hyperglycemia had increase in mortality rate compared with known diabetic group.[11] Umpierrez et al[11] suggested that patients with newly diagnosed hyperglycemia were more severely ill than patients with known diabetes. We assessed the severity of disease by using the APACHE II score and the severity between two groups as not different. Third, the patients without diabetes could be dysglycemic (blood glucose level above the normal range but below the threshold for diabetes). In the absence of measurements of glycohemoglobin, the possibility of underlying but undiagnosed diabetes rather than newly developed hyperglycemia must be considered. Dysglycemic patients could be sustained more ischemic damage at the time of infarction as a result of more extensive underlying cerebral vasculopathy.[17] Furthermore, even nondiabetic-range hyperglycemia is associated with endothelial dysfunction.[18] Fourth, the use of glucose lowering therapy in patients with stress hyperglycemia could not be assessed in the study. It is generally known that prognosis of patients with diabetes was poor than without diabetes. Admission hyperglycemia with diabetic patients might be more likely to receive therapy for hyperglycemia while the hyperglycemia without diabetes might be considered as a transient finding in response to the acute illness not requiring medical intervention. Insulin suppresses the secretion and antagonize the harmful effects of tumor necrosis factor, macrophage migration-inhibitory factor, and superoxide anion.[19] Therefore, insulin might be beneficial in acute myocardial infarction and useful in the management of patients with sepsis, and other inflammatory diseases[19] and might lessen the mortality and morbidity in patients with hyperglycemia.[20-22]

This study has a limitation. It does not take account of administration of medications and types of intravenous fluid. Thus, it is possible that some patients may have received steroid or fluid containing glucose at the time of hyperglycemia.

Despite the limitation, this study show that the effects of hyperglycemia on the prognosis of critically ill patients do not differ from diabetes with nondiabetes.

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