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Higher glucose variability in type 1 than in type 2 diabetes patients admitted to the intensive care unit: A retrospective cohort study

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ABSTRACT

Purpose: Although the course of disease of type 1 and type 2 diabetes differs, the distinction is rarely made when patients are admitted to the intensive care unit (ICU). Here, we report patient- and admission-related characteristics in relation to glycemic measures of patients with type 1 and type 2 diabetes admitted to the ICU.
Materials and methods: A retrospective chart review was performed of 1574 patients with diabetes admitted between 2004 and 2011 to our ICU. Glycemic measures included mean glucose, the incidence of hypoglycemia and hyperglycemia, percentage of glucose values in/below/above target, and glucose variability. The ICU and hospital mortality were secondary outcomes.
Results: We classified 2% (n = 27) of patients as having type 1 diabetes and 98% (n = 1547) as having type 2 diabetes. Patients with type 1 diabetes were significantly younger, had a lower body mass index, and were more frequently admitted to the ICU for medical diagnoses. No differences in glycemic measures were found, apart from a 20% higher glucose variability in the type 1 diabetes group.
Conclusions: Patients with type 1 diabetes showed a higher glucose variability, but overall glycemic control was not different between patients with type 1 and type 2 diabetes. Very few diabetes patients admitted to the ICU have type 1 diabetes.

1. Introduction

The optimal blood glucose management of critically ill patients remains highly debated among critical care physicians. Increasing evidence shows that perhaps not 1 single glycemic target "fits" for all patients admitted to the intensive care unit (ICU) [1]. Recently, 2 large observational studies have shown that the presence of diabetes affects the association between several measures of glycemic control and mortality [2,3]. Specifically, in nondiabetic critically ill patients, mean glucose, hypoglycemia, and glucose variability are associated with increased mortality; whereas, among critically ill patients with diabetes, hypoglycemia and glycemic variability are associated with increased mortality [2-4]. As a result, it has been suggested that targets in patients with diabetes should be set higher, as avoidance of hypoglycemia is even more important than in nondiabetic patients [1-3].

Remarkably, the distinction between the specific type of diabetes (type 1 or type 2 diabetes) has not been made in the major investigations with regard to glycemic control and mortality and is often mentioned as a study limitation [2,3,5]. If at all, diabetic patients are classified according to treatment (oral, insulin therapy or diet only, or insulin-treated and non-insulin–treated diabetes mellitus). Using these classifications, patients with type 1 diabetes will still be "mixed" with patients with type 2 diabetes. This may lead to inaccurate interpretations with regard to glycemic control in the ICU. In this report, we classified patients with diabetes as type 1 or type 2 and we describe patient- and admission-related characteristics in relation to glycemic measures of patients with type 1 and type 2 diabetes admitted to the ICU. We hypothesized that type 1 patients would in general be younger, with less comorbidity, and different diagnoses at admission as compared with patients with type 2 diabetes. As a consequence of the nature of disease, we expected type 1 patients to have worse glycemic control during their ICU stay.

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2. Materials and methods

A retrospective chart review was performed on the existing cohort of patients with diabetes (n = 1638) admitted to the 24-bed medical/surgical ICU at the Onze Lieve Vrouwe Gasthuis, Amsterdam between 2004 and 2011 [3]. According to national guidelines, this research is exempted from ethical approval because of its retrospective character. Therefore, no consent from patients was needed.

2.1. Glucose regulation protocol

All patients were treated according to a standard blood glucose regulation protocol, which was targeted to achieve glucose values of 4.0 to 7.0 mmol/L from 2004 to 2009 and 5.0 to 9.0 mmol/L from April 2009 until 2011. Insulin adjustments were advised using a fully computerized sliding scale algorithm, which is connected to the clinical information system [6]. Glucose was measured from blood samples obtained from an arterial catheter using the Accu-chek glucose meter (Roche/Hitachi, Basel, Switzerland).

2.2. Data collection

Baseline demographic variables, admission diagnoses, and severity of disease score (Acute Physiology and Chronic Health Evaluation [APACHE] II) were collected for all patients at ICU admission. Glucose values, insulin doses, medication and nutrition data, and mortality rates were extracted from patient records. Available glycosylated hemoglobin levels (within 3 months before ICU admission) were collected retrospectively from patient medical records. Patients with diabetes were selected based on the use of glucose lowering medication at admission. To make a distinction between type 1 and type 2 diabetes, all available medical outpatient records and admission history were reviewed. Type 1 diabetes was defined on the basis of epidemiological data; treatment with insulin and a diagnosis at 30 years or younger [7]. In addition, no oral glucose-lowering therapy was allowed to be classified as type 1 diabetes. The diagnosis type 1 diabetes was verified by a telephone call to the patient's general practitioner. Type 2 diabetes was assumed in all other cases.

2.3. Study end points

The primary end point of this analysis was glycemic control during ICU admission. Glycemic measures were as follows: mean blood glucose, admission blood glucose, amount of glucose values, percentage of blood glucose measurements in, above, and below target range, hypoglycemia (<2.2 mmol/L) and hyperglycemia (>15.0 mmol/L), glucose variability (expressed as mean absolute glucose [MAG] change and SD), and insulin data. Secondary end points included ICU and hospital mortality, length of stay at the ICU, and ventilator days.

2.4. Statistical analysis

Continuous data are expressed as mean ± SD for normally distributed variables and median (interquartile range) for other variables. Categorical data are expressed as the number of subjects. Group comparisons are performed using the *t* test for normally distributed data and Mann-Whitney *U* test for other continuous variables. Fisher exact test was used for categorical variables. A *P* value less than .05 was considered statistically significant. Statistical analyses were performed using IBM SPSS software 20.0 (SPSS Inc, Chicago, IL).

3. Results

Of the 1638 charts reviewed, data from a total of 1574 patients were included in the analysis. Excluded were 55 (3%) readmissions, 4 (0.2%) patients with a diagnosis of type 3 diabetes (due to pancreas-related disorders), and 5 (0.2%) patients who erroneously had a diagnosis of diabetes. The remaining cohort consisted of 27 (2%) patients with type 1 diabetes and 1547 (98%) patients with type 2 diabetes. Table 1 summarizes demographic- and admission-related characteristics of both cohorts. Compared with patients with type 2 diabetes, patients with type 1 diabetes were significantly younger (57 ± 12 vs 68 ± 10 years; $P < .001$) and had a lower body mass index (BMI) (24.6 ± 4 vs 28.7 ± 5 kg/m^2; $P < .001$) at ICU admission. The APACHE II score was similar in both cohorts, also after modification for age [8]. Medical admissions (admission categories sepsis and metabolic) occurred more frequently in patients with type 1 diabetes ($P = .004$), whereas in patients with type 2 diabetes, surgical (cardiovascular) admissions were more common ($P = .03$). Two patients in the type 1 diabetes group were admitted for diabetic ketoacidosis. Furthermore, mechanical ventilation and the use of vasopressor drugs were more frequent in patients with type 2 diabetes ($P = .04$ and .003). Preadmission glycosylated hemoglobin level was significantly higher in patients with type 1 diabetes ($P < .01$), although only a few preadmission values were available for type 1 patients.

3.1. Glycemic control

Table 2 compares the glycemic measures between patients with type 1 and type 2 diabetes. Glucose variability expressed as the MAG change was almost 20% higher in patients with type 1 diabetes

Table 1
Demographic- and admission-related characteristics of the type 1 and type 2 diabetes cohorts

	Patients with type 1 diabetes (n = 27)	Patients with type 2 diabetes (n = 1547)	*P*
Age (y)	57 ± 12	68 ± 10	<.001
Male sex	14 (52)	981 (64)	.23
BMI (kg/m^2)	24.6 ± 4	28.7 ± 5	<.001
APACHE II score on admission	16 (12-18)	16 (13-20)	.28
Age-modified APACHE II score	12 (10-15)	11 (9-15)	.57
Medical admissions	10 (37)	231 (15)	.004
Surgical admissions	17 (63)	1316 (85)	.004
Cardiothoracic surgery patients	16 (59)	1181 (76)	.07
APACHE II admission category			
Cardiovascular	18 (67)	1295 (84)	.03
Sepsis	4 (15)	74 (5)	.04
After cardiac arrest	0 (0)	34 (2)	1.0
Gastrointestinal	0 (0)	37 (2)	1.0
Hematological	0 (0)	1 (0.1)	1.0
Renal	0 (0)	6 (0.4)	1.0
Metabolic	2 (7.4)	10 (0.6)	.02
Neurological	1 (3.7)	10 (0.6)	.17
Respiratory	2 (0.1)	80 (5.2)	.65
Use of vasopressor drugs	23 (85)	1473 (95)	.04
Use of corticosteroids	27 (100)	1544 (100)	1.0
Mechanical ventilation[a]	21 (78)	1466 (95)	.003
Continuous venovenous hemofiltration	3 (11)	99 (6)	.25
Glucose-lowering therapy at admission[b]			
Metformin	–	964 (63)	
Mean daily dose (mg)	–	1515 ± 730	
Insulin	27 (100)	572 (37)	<.001
Mean daily dose (IU)	51 ± 19	64 ± 41	.01
Sulfonylureas	–	602 (39)	
Thiazolidinediones	–	40 (2.6)	
Dipeptidyl peptidase-4 inhibitors	–	5 (0.3)	
Combination tablets	–	11 (0.7)	
Other	–	8 (0.5)	
Unknown	–	53 (3.4)	
No DM medication	–	14 (0.9)	
Glycosylated hemoglobin level (%)[c]	9.7 (8.1-12.8)	7.3 (6.3-8.3)	.01
Total parenteral nutrition	0 (0)	7 (0.5)	1.0
Enteral nutrition	8 (30)	410 (27)	.67

Data presented as mean ± SD, n (%) or median (interquartile range).
[a] In the first 24 hours of ICU admission.
[b] Glucose-lowering medication use at home.
[c] Glycosylated hemoglobin level was collected in 240 patients (type 1 n = 5; type 2 n = 235).