ORIGINAL ARTICLE

Glycemic profile and effectiveness and safety of insulin therapy in septic patients

Is the blood glucose level sufficient?

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KEY WORDS

intensive insulin therapy, sepsis

ABSTRACT

INTRODUCTION Hyperglycemia in sepsis is managed by intensive insulin therapy, which can cause hypoglycemia.

OBJECTIVES The aim of the study was to evaluate the glycemic profile as well as safety and effectiveness of a nurse-controlled insulin therapy protocol in patients with severe sepsis and septic shock.

PATIENTS AND METHODS The study included 16 septic patients who died (nonsurvivors) and 61 septic patients who survived. Glycemia was measured every 4 h, and the dose of insulin infusion was adjusted to maintain glycemia of 4.4 mmol/l to 8.3 mmol/l. We analyzed glycemia levels and daily variations, insulin dose, episodes of hypo- and hyperglycemia.

RESULTS Nonsurvivors and survivors had similar mean glycemia levels (7.38 vs. 7.08 mmol/l; $p = 0.20$) and insulin requirements (median [Me] = 26.9 vs. 23.9 units/d; $p = 0.22$; Me = 1.7 vs. 1.4 units/h; $p = 0.25$). Daily glycemia variation (Me = 4.81 vs. 3.03 mmol/l; $p < 0.001$), episodes of hypoglycemia (18.8% vs. 3.3%; $p = 0.02$), spontaneous severe hypoglycemia (12.5% vs. 0%; $p = 0.006$) and hyperglycemia (75.0% vs. 45.9%; $p = 0.04$) were higher and more frequent in nonsurvivors. Three of 5393 blood samples (0.05%) met severe insulin-induced hypoglycemia criteria, and 74.4% of samples met the recommended range of 4.4–8.3 mmol/l.

CONCLUSIONS Patients who died experienced more episodes of hyperglycemia, spontaneous hypoglycemia and greater variation in the daily glycemia level. Daily glycemia variation is more reliable than a mean glycemic level in evaluating glucose homeostasis in septic patients. Few episodes of severe insulin-induced hypoglycemia occurred while using the nurse-controlled insulin therapy protocol.

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INTRODUCTION Many critical illnesses including severe sepsis and septic shock result in a condition described as "stress diabetes".[1,2] Peripheral insulin resistance, characterized by hyperinsulinemia, increased gluconeogenesis, and impaired peripheral insulin-mediated glucose uptake, plays a central role in dysregulation of glucose homeostasis, leading to hyperglycemia. Although hyperglycemia has been considered an adaptive and beneficial response to stress, it may have detrimental effects.[3] Recommendations from the 2008 Surviving Sepsis Campaign suggest using a validated protocol for insulin dose adjustment and targeting glucose levels to <8.3 mmol/l.[4] These recommendations are based on the results of a randomized controlled clinical trial which demonstrated that intensive insulin therapy reduced overall in-hospital mortality by 34%, bloodstream infections by 46%, acute renal failure requiring dialysis or hemofiltration, and critical-illness polyneuropathy. The greatest benefits concern patients with multiple-organ failure due to severe sepsis and septic shock.[5] Further studies[6-10] confirmed the beneficial effects of intensive insulin therapy and tight glycemic control; however, results of a meta-analysis of 34 randomized clinical trials did not show significant reduction

TABLE 1 Diagnostic criteria of severe sepsis and septic shock[4,26]

Severe sepsis – presence of sepsis, plus organ hypoperfusion or dysfunction due to sepsis
hypotension due to sepsis
increased blood lactate levels
oliguria (diuresis <0.5 ml/kg/h for >2 h, despite adequate fluid challenge)
ALI with PaO_2/FiO_2 <250, when pneumonia is not the source of infection
ALI with PaO_2/FiO_2 <200, when pneumonia is the source of infection
serum creatinine >176.8 μmol/l
serum bilirubin >34.2 μmol/l
platelet count <100 000 × 10^6/l
coagulation abnormalities (INR >1.5)
Septic shock
presence of sepsis
vasopressor dependency after adequate volume resuscitation
refractory hypotension
• systolic blood pressure <90 mmHg
• mean arterial pressure <65 mmHg, or a 40 mmHg drop in systolic blood pressure compared to baseline
• unresponsive to a fluid challenge of 20–40 ml/kg

Abbreviations: ALI – acute lung injury, FiO_2 – fraction of inspired oxygen, INR – international normalized ratio, PaO_2 – partial pressure of oxygen in arterial blood

in mortality from this treatment.[11] Hypoglycemia associated with intensive insulin therapy occurs 4–7 times more frequently in patients treated with strict glycemic control, and sepsis itself may be a risk factor for severe hypoglycemia <2.2 mmol/l.[12,13] The aim of the study was to evaluate the glycemic profile, as well as safety and effectiveness of a nurse-controlled intensive insulin therapy protocol in patients with severe sepsis and septic shock.

PATIENTS AND METHODS This retrospective study was performed in a seven-bed mixed medical-surgical intensive care unit (ICU) at a university hospital. The glycemic profile of patients who survived and died due to severe sepsis and septic shock was evaluated, and the safety and effectiveness of a nurse-controlled intensive insulin therapy protocol was examined. We identified patients who were admitted to the ICU between January 2005 and December 2008 with severe sepsis and septic shock, diagnosed and classified according to the Surviving Sepsis Campaign guidelines (TABLE 1). The scope of the analysis included the first 14 days in the ICU, during which patients required the most intensive treatment. Classification to survivors and nonsurvivors was based on the outcome after ICU stay.

TABLE 2 Intensive insulin therapy protocol

Blood glucose level (mmol/l)	Insulin infusion rate (IU/h)
0–4.4	0
4.5–6.9	1
7.0–10.0	2
10.1–13.0	3
13.1–16.9	4
17.0–21.1	5
>21.1	call an intensivist

Abbreviations: IU – international unit

An intensive insulin therapy protocol in the ICU was managed by the nursing staff. Strict glycemic control was maintained by continuous intravenous infusion of short-acting insulin. The dose of insulin infusion was adjusted by the nursing staff according to the protocol presented in TABLE 2. Arterial blood glycemia levels were measured every 4 h, and the insulin dose was adjusted according to the results. The goal of the therapy was to maintain glycemia of 4.4 mmol/l to 8.3 mmol/l. If the blood glucose level exceeded the recommended range, additional samples were taken every 1 or 2 h. Such increased frequency of testing occurred until glycemia level returned to the desirable range. If the blood glucose level was >21.1 mmol/l an intensivist was called who reduced infusion rate of parenteral nutrition and/or conversed tube feeding diet e.g., with monounsaturated fatty acids as the main energy source. When the blood glucose level was <4.4 mmol/l the intensivist recommended intravenous bolus of 40% glucose. The glycemic profile was compared by dividing patients into two groups. The first group included 16 patients who died of severe sepsis and septic shock (referred to as nonsurvivors), while the second group included 61 patients who survived (referred to as survivors). We analyzed mean blood glucose levels, daily blood glucose variations (calculated as the difference between the highest and the lowest daily glycemia level), mean daily insulin infusion duration, mean dose of insulin (units of insulin/d, units of insulin/h), episodes of severe hypoglycemia (defined as blood glucose level <2.2 mmol/l), episodes of hypoglycemia <3.3 mmol/l (considered as a threshold level for appropriate central nervous system functioning), episodes of spontaneous hypoglycemia <2.2 mmol/l and <3.3 mmol/l (defined as episodes of hypoglycemia after insulin infusion had been discontinued for at least 8 h), episodes of hypoglycemia <4.4 mmol/l, episodes of hyperglycemia >8.3 mmol/l (above the upper range value recommended in the treatment of sepsis), episodes of hyperglycemia >10.0 mmol/l, and hyperglycemia >11.1 mmol/l. The effectiveness of nurse-managed intensive insulin therapy protocol was evaluated by analyzing the percentage of all blood samples and blood glycemia levels within the 4.4–8.3 mmol/l range. The protocol safety was examined by analyzing the percentage of blood glycemia levels <2.2 mmol/l (severe hypoglycemia) and <3.3 mmol/l (hypoglycemia). The blood glucose level measured on admission to the ICU was excluded from the analysis.

Continuous data were presented as mean with standard deviation or median (Me) with lower (Q1) and upper quartile (Q3), and ordinal data

TABLE 3 Demographic and laboratory parameters of the patients

Variable	Nonsurvivors (n=16)	Survivors (n=61)	p
age, years (Me; Q1–Q3)	59.0; 46.5–65.5	53.0; 35–60	0.46
men, n (%)	7 (43.7%)	40 (65.6%)	0.11
CRP (mg/dl) (Me; Q1–Q3)	153.2; 106.0–217.4	126.7; 98.3–166.8	0.29
leukocytes ($\times 10^9$/l) (Me; Q1–Q3)	13.7; 7.5–24.8	14.8; 12.1–19.8	0.78
serum bilirubin (mg/dl) (Me; Q1–Q3)	2.02; 1.05–2.79	0.84; 0.52–1.12	0.002
serum creatinine (mg/dl) (Me; Q1–Q3)	1.32; 0.59–3.47	0.67; 0.49–1.22	0.04
positive blood culture, n (%)	10 (62.5%)	35 (57.4%)	0.71

Abbreviations: CRP – C-reactive protein, Me – median, Q1 – lower quartile, Q3 – upper quartile

TABLE 4 Clinical parameters of the patients

Variable	Nonsurvivors (n=16)	Survivors (n=61)	p
weight, kg (Me; Q1–Q3)	67.5; 60–87.5	70.0; 60–84	0.80
days in the ICU (Me; Q1–Q3)	6; 3–17	14; 7–30	0.03
APACHE II (Me; Q1–Q3)	26; 22.5–30.5	13; 9.5–20	<0.001
mechanical ventilation, n (%)	16 (100%)	60 (98%)	0.57
steroids, n (%) standard regimen 200 mg/d in continuous infusion during 7 days in decreasing doses	8 (50%)	37 (60.1%)	0.44
vasopressors, n (%)	16 (100%)	59 (96.7%)	0.67
vasopressors (μg/kg/min); (Me; Q1–Q3)	0.20; 0.12–0.39	0.12; 0.08–0.17	0.051
preexisting kidney disease, n (%)	4 (25%)	8 (13.1%)	0.25
hypertension, n (%)	4 (25%)	14 (22.95%)	0.86
coronary artery disease, n (%)	4 (25%)	7 (11.5%)	0.17
acute or chronic pancreatitis, n (%)	3 (18.8%)	12 (19.6%)	0.93

Abbreviations: APACHE II – Acute Physiology and Chronic Health Evaluation, a scale evaluating and providing objective information on the severity of illness on admission to ICU (the more points the patient receives, the more severe the patient's condition is), ICU – intensive care unit, others – see TABLE 3

were presented as a number with percentage. Results were analyzed statistically with the t-test, Mann-Whitney test (most data did not pass the Shapiro-Wilk normality test), χ^2 test, and Fisher exact test. A p <0.05 was considered statistically significant.

RESULTS Demographic, laboratory and clinical characteristics of the two groups are presented in TABLE 3 and TABLE 4. All patients received mixed parenteral-enteral nutrition. Coexisting illnesses occurred in a comparable proportion of patients in both groups, with a history of cancer present in 5 of 16 (31.2%) nonsurvivors and in 20 of 61 (32.8%) survivors, and diabetes in 3 (18.7%) nonsurvivors and in 10 (16.4%) survivors. Patients who died had higher mean bilirubin and creatinine levels. The proportion of patients who received corticosteroids and vasopressors did not differ. Mean blood glucose level (nonsurvivors: 7.38 ±0.98 mmol/l vs. survivors 7.08 ±0.83 mmol/l; p = 0.20), insulin requirements per day (nonsurvivors: Me = 26.9 units/d; Q1–Q3 = 17.0–46.8 units/d vs. survivors: Me = 23.9 units/d; Q1–Q3 = 10.6–35.3 units/d; p = 0.22), and insulin requirements per hour (nonsurvivors: Me = 1.7 units/h, Q1–Q3 = 1.3–2.2 units/h vs. survivors: Me = 1.4 units/h, Q1–Q3 = 1.0–1.9 units/h; p = 0.25) were similar in both groups. Daily blood glucose level variation differed significantly between the groups (nonsurvivors: Me = 4.81 mmol/l; Q1–Q3 = 3.89–6.47 mmol/l vs. survivors: Me = 3.03 mmol/l; Q1–Q3 = 2.15–4.08 mmol/l); p <0.001). Of the 16 nonsurvivors, 3 (18.8%) patients experienced at least one episode of severe hypoglycemia, compared with 2 of 61 (3.3%) patients who survived (p = 0.02). None of the 61 survivors experienced an episode of spontaneous severe hypoglycemia, compared with 2 of 16 nonsurvivors (12.5%, p = 0.006). This association was not observed for insulin-induced severe hypoglycemia (TABLE 5). A tendency for more frequent episodes of hypoglycemia <3 mmol/l was observed in the nonsurvivor group (7 [43.8%] patients) compared with survivors (13 [21.3%] patients; p = 0.07; statistically nonsignificant). Spontaneous hypoglycemia <3.3 mmol/l occurred more frequently in nonsurvivors (5 [31.3%] patients) than in survivors (3 [4.9] patients]; p = 0.003). Again, this relation was not observed for insulin-induced hypoglycemia <3.3 mmol/l (TABLE 5). The groups did not differ in the frequency of hypoglycemia <4.4 mmol/l (TABLE 5). No hemodynamic deterioration, convulsions, or neurological complications were noted in association with any hypoglycemic event.

Hyperglycemia occurred more frequently than hypoglycemia in all patients. Only episodes of hyperglycemia >8.3 mmol/l occurred at statistically similar levels in the two groups (TABLE 5). Hyperglycemia >10.0 mmol/l occurred in 14 (87.5%) nonsurvivors and 35 survivors (57.4%; p = 0.03), and hyperglycemia >11.1 mmol/l was observed in 12 (75.0%) nonsurvivors and 28 survivors (45.9%; p = 0.04).

Regarding safety and effectiveness of intensive insulin therapy a total of 5393 blood samples and blood glucose levels were examined. Only 3 of 77 (3.9%) patients experienced one insulin-induced episode of severe hypoglycemia, and 3 of 5393 (0.05%) blood glycemia samples matched the criteria for severe insulin-induced hypoglycemia. A mean glucose level maintained by intensive insulin therapy was 7.14 ±0.87 mmol/l, and 4013 (74.4%) samples were in the recommended range of 4.4–8.3 mmol/l (TABLE 6). When a higher upper limit of blood glucose concentration of

TABLE 5 Glycemic profile – results

	Nonsurvivors (n=16)	Survivors (n=61)	p
mean daily insulin infusion duration (h/day) (Me; Q1–Q3)	16.8; 5.5–21.3	10.9; 5.9–18.9	0.23
glycemia <4.4 mmol/l, n (%)	13 (81.3%)	44 (72.1%)	0.46
insulin-induced hypoglycemia <2.2 mmol/l, n (%)	1 (6.2%)	2 (3.3%)	0,58
insulin-induced hypoglycemia <3.3 mmol/l, n (%)	2 (12.5%)	11 (18.0%)	0.60
hyperglycemia >8.3 mmol/l, n (%)	16 (100%)	55 (90.1%)	0.19

Abbreviations: see TABLE 3

TABLE 6 Efficacy and safety of intensive insulin therapy protocol

Blood glucose level	Number of samples	Percentage of samples
<2.2 mmol/l	3	0.05
2.2–3.3 mmol/l	27	0.5
3.4–4.3 mmol/l	114	2.1
4.4–8.3 mmol/l	4013	74.4
8.4–10.0 mmol/l	816	15.1
10.1–11.1 mmol/l	182	3.4
>11.1 mmol/l	238	4.4
total	5393	100

10.0 mmol/l was allowed, over 90% of analyzed blood samples matched the desired range.

DISCUSSION The study confirmed the clinical importance of blood glucose level variation, episodes of spontaneous hypoglycemia, safety of higher than recommended target blood glucose values, and safety and effectiveness of nurse-controlled intensive insulin therapy protocols in the treatment of septic patients. The two groups had almost identical mean blood glucose levels, so it might have appeared as if their glucose homeostasis was comparable. However, patients who died of severe sepsis and septic shock experienced episodes of hyperglycemia and hypoglycemia more often, which was reflected by higher daily blood glucose variation compared with survivors. In most studies on glycemic homeostasis in critically ill patients, septic patients are only a subgroup in populations analyzed as a whole. There are no data from clinical trials focusing only on patients with sepsis. Widely cited results of randomized clinical trials performed by Van den Berghe et al. in 2001 and 2006 proved a beneficial effect of strict glycemic control on mortality.[5,6] Reduction in mortality was highest in the subgroup of patients with multiple organ failure due to sepsis.[5] Similarly, implementation of tight blood glucose control accounted for a 30% reduction in death rate in a subgroup of 75 patients with septic shock in a nonrandomized trial performed by Krinsley in 2004.[7] In our study, we focused only on patients with severe sepsis and septic shock, and we found no difference in mean blood glucose levels between patients who survived and those who died. A retrospective analysis by Krinsley in 2003, which included 1826 critically ill patients, compared mean blood glucose levels between patients who died and survived. Mean glucose values were significantly higher in nonsurvivors than in survivors for the entire group and for each subgroup except for that of 92 patients with septic shock.[14] In the discussion on tight glucose control, the issue of blood glucose variation has been raised. Results from a large observational study of 7049 patients cited in the Surviving Sepsis Campaign suggested that decreasing the variability of blood glucose concentration might be an important aspect of glucose control. The standard deviation of glucose concentration was a significant independent predictor of ICU and hospital mortality.[15] A recent study published in June 2009 proves that blood glucose variability is responsible for increased risk of death in critically ill patients. The study mentions also sepsis among factors which increase the risk of blood glucose variability.[13] In our study, patients who died had greater daily blood glucose variation. A mean glucose concentration is not a reliable marker of the glycemic profile in patients with sepsis, and the analysis of blood glucose variation should be included in the evaluation of glucose homeostasis. Tight glucose control and lower blood glucose levels reduce mortality.[5-7] In our study, more nonsurvivors experienced episodes of hyperglycemia >10.0 mmol/l and >11.1 mmol/l, but not of hyperglycemia >8.3 mmol/l. The NICE-SUGAR trial (Normoglycaemia in Intensive Care Evaluation and Survival Using Glucose Algorithm Regulation) that compared target blood glucose concentrations of 4.5–6.0 mmol/l vs. 8.0–10.0 mmol/l, proved that a blood glucose target of <10 mmol/l resulted in lower mortality than a target of 4.5–6.0 mmol/l did.[16] It seems that even higher glucose levels than those suggested in the Surviving Sepsis Campaign guidelines are safe. Higher acceptable blood glucose concentrations may allow less intensive insulin therapy and may reduce episodes of hypoglycemia (6.8% of patients in the intensive-control group and 0.5% in the conventional-control group ($p < 0.001$) in the NICE-SUGAR study) and variation in blood glucose levels, as they are both related to intensive insulin therapy and tight blood glucose control management. The implementation of intensive insulin therapy has raised the problem of hypoglycemia. Hypoglycemia occurs 4–7-fold more frequently in patients treated with strict glycemic control, while sepsis itself is among the risk factors responsible for hypoglycemia.[12,13,16-18] Two multicenter randomized controlled trials of intensive insulin therapy, one involving patients with severe sepsis (Efficacy of Volume Substitution and Insulin Therapy in Severe Sepsis or VISEP trial)[19], and the second performed in medical and surgical ICU patients (Glucontrol Study: Comparing the Effects of Two Glucose Control Regimens by Insulin in

Intensive Care Unit Patients)[20], were discontinued due to a high frequency of hypoglycemia. The detrimental effect of hypoglycemia on the central nervous system has been demonstrated, but it remains unclear whether hypoglycemia is related to an increased risk of death in patients with sepsis.[3] In our study, episodes of severe hypoglycemia and hypoglycemia <3.3 mmol/l were more frequent in patients who died of severe sepsis and septic shock. A correlation between hypoglycemia and increased mortality was observed in the analysis performed by Van den Berghe et al.[5,6] Patients who died experienced more episodes of spontaneous severe hypoglycemia and hypoglycemia <3.3 mmol/l, despite the fact that they received higher doses of vasopressors (TABLE 4). The main factors responsible for episodes of spontaneous hypoglycemia might be liver dysfunction (nonsurvivors had higher bilirubin levels [TABLE 3]) and a condition called critical illness-related corticosteroid insufficiency. This syndrome is characterized by peripheral tissue resistance to corticosteroids, which leads to an excessive proinflammatory response, hypoglycemia, and hypotension not responsive to fluid resuscitation and requiring vasopressors.[21] According to our results, spontaneous hypoglycemia seems to be a more important factor contributing to the death of septic patients than insulin-induced hypoglycemia. The Surviving Sepsis Campaign guidelines emphasize that further studies of protocols are needed to establish safety and effectiveness in controlling blood glucose concentrations and blood glucose variation in patients with severe sepsis.[4] Implementation of standardized protocols of intensive insulin therapy is a safe and effective method of maintaining normoglycemia.[22] Selection of an appropriate protocol of strict glycemic control is a complicated and individual matter, which should be adjusted to the profile of ICU patients, because many factors affect blood glucose concentration. The lack of consensus on optimal insulin dosage, clinical variability of patients, and increased concern about risk of severe hypoglycemia related to tight glycemic control are just a few of the factors that make intensive insulin therapy a medical challenge. In our study, 3.9% of patients experienced one insulin-induced episode of severe hypoglycemia. Previous studies have reported more frequent episodes of hypoglycemia <2.2 mmol/l in the subgroup of patients with sepsis, from 12.1% in the VISEP population[19] to 19.6% in the study performed by Van den Berghe et al.[17,18] In our study, severe hypoglycemia and hypoglycemia <3.3 mmol/l associated with intensive insulin therapy occurred in a comparable percentage of patients who survived and who died of severe sepsis and septic shock. As for the effectiveness of a nurse-controlled intensive insulin therapy protocol, 74.4% of blood glucose levels met the reference range of 4.4–8.3 mmol/l. When we allowed a higher upper range of blood glucose concentration, i.e., of 10.0 mmol/l (as in the NICE-SUGAR trial), over 90% of the analyzed blood samples were within the desired range.

Limitations of our study included a small number of patients, and the design of a retrospective, uncontrolled, one-center study. However, the number of patients is limited even in randomized controlled trials investigating tight glycemic control in sepsis.[23-25]

In conclusion, more patients who died due to severe sepsis and septic shock had episodes of spontaneous hypoglycemia (<2.2 mmol/l and <3.3 mmol/l), episodes of hyperglycemia >10.0 mmol/l and >11.1 mmol/l, and had higher daily blood glucose level variation compared with patients who survived. It cannot be judged whether hypoglycemia, hyperglycemia, and mean daily blood glucose variation were the factors that increased mortality in patients with severe sepsis and septic shock or whether they were only markers of an increased risk of death. A mean blood glucose level is not a reliable parameter to evaluate glucose homeostasis in patients with sepsis, and daily blood glucose variation should be included in the analysis of the glycemic profile. A very low (0.05%) percentage of episodes of severe hypoglycemia induced by insulin infusion confirmed the safety of nurse-controlled intensive insulin therapy protocol.

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Profil glikemiczny oraz skuteczność i bezpieczeństwo intensywnej insulinoterapii u pacjentów z sepsą

Czy poziom glukozy jest wystarczający?

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intensywna insulinoterapia, sepsa

STRESZCZENIE

WPROWADZENIE Hiperglikemia u pacjentów z sepsą jest kontrolowana przez intensywną insulinoterapię, co może prowadzić do epizodów hipoglikemii.

CELE Celem pracy była ocena profilu glikemii oraz bezpieczeństwa i skuteczności protokołu intensywnej insulinoterapii nadzorowanej przez zespół pielęgniarski i stosowanej u chorych z ciężką sepsą i wstrząsem septycznym.

PACJENCI I METODY Badanie objęło 16 septycznych pacjentów, którzy zmarli i 61 septycznych pacjentów, którzy przeżyli. Poziom glikemii był mierzony co 4 godziny, a dawka insuliny była dostosowywana tak, aby utrzymać glikemię w przedziale 4,4–8,3 mmol/l. Analizie poddano średnie poziomy glikemii, dobowe wahania glikemii, zapotrzebowanie na insulinę, epizody hipo- i hiperglikemii.

WYNIKI Pacjenci, którzy zmarli i ci, którzy przeżyli mieli porównywalne średnie dobowe poziomy glikemii (7,38 *vs* 7,08 mmol/l; p = 0,20) oraz zapotrzebowanie na insulinę (mediana = 26,9 *vs* 23,9 jednostek międzynarodowych (IU) na dobę; p = 0,22; mediana = 1,7 *vs* 1,4 IU/h; p = 0,25). Dobowe wahania poziomu glikemii (mediana = 4,81 *vs* 3,03 mmol/l; p <0,001), epizody hipoglikemii (18,8% *vs* 3,3%; p = 0,02), spontanicznej ciężkiej hipoglikemii (12,5% *vs* 0%; p = 0,006) oraz hiperglikemii (75,0% *vs* 45,9%; p = 0,04) były większe i wystąpiły częściej w grupie pacjentów, którzy zmarli. Trzy z 5393 analizowanych próbek krwi (0,05%) spełniły kryteria ciężkiej indukowanej insuliną hipoglikemii, a 74,4% próbek mieściło się w zalecanym zakresie glikemii 4,4–8,3 mmol/l.

WNIOSKI Pacjenci, którzy zmarli, doświadczyli więcej epizodów hiperglikemii, spontanicznej ciężkiej hipoglikemii i mieli większe dobowe wahania poziomu glikemii. Dobowe wahania glikemii są bardziej wiarygodnym parametrem niż średni poziom glikemii, w ocenie homeostazy glukozy u pacjentów z sepsą. Schemat intensywnej insulinoterapii nadzorowanej przez zespół pielęgniarski skutkował niewielką liczbą indukowanych insuliną epizodów ciężkiej hipoglikemii.

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