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Moderate glycemic control safe in critically ill adult burn patients: A 15 year cohort study

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ABSTRACT

Introduction: Hyperglycemia is a metabolic alteration in major burn patients associated with complications. The study aimed at evaluating the safety of general ICU glucose control protocols applied in major burns receiving prolonged ICU treatment.

Methods: 15year retrospective analysis of consecutive, adult burn patients admitted to a single specialized centre. Exclusion criteria: death or length of stay <10 days, age <16years. Variables: demographic variables, burned surface (TBSA), severity scores, infections, ICU stay, outcome. Metabolic variables: total energy, carbohydrate and insulin delivery/24 h, arterial blood glucose and CRP values. Analysis of 4 periods: 1, before protocol; 2, tight doctor driven; 3, tight nurse driven; 4, moderate nurse driven.

Results: 229 patients, aged 45 ± 20 years (mean ± SD), burned 32 ± 20% TBSA were analyzed. SAPSII was 35 ± 13. TBSA, Ryan and ABSI remained stable. Inhalation injury increased. A total of 28,690 blood glucose samples were analyzed: the median value remained unchanged with a narrower distribution over time. After the protocol initiation, the normoglycemic values increased from 34.7% to 65.9%, with a reduction of hypoglycaemic events (no extreme hypoglycemia in period 4). Severe hyperglycemia persisted throughout with a decrease in period 4 (9.25% in period 4). Energy and glucose deliveries decreased in periods 3 and 4 ($p < 0.0001$). Infectious complications increased during the last 2 periods ($p = 0.01$).

Conclusion: A standardized ICU glucose control protocol improved the glycemic control in adult burn patients, reducing glucose variability. Moderate glycemic control in burns was safe specifically related to hypoglycemia, reducing the incidence of hypoglycaemic events compared to the period before. Hyperglycemia persisted at a lower level.

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Abbreviations: ITT, intensive insulin therapy (4.5–6.0 mmol/l); Extreme, extreme hypoglycemia (<2.3 mmol/l); Hypo, moderate hypoglycemia (<4.0 mmol/l); hyper, moderate hyperglycemia (>8.1–10.0 mmol/l); Severe, severe hyperglycemia (>10.0 mmol/l); TBSA, total burns surface area; ABSI, abbreviated burn severity index; SAPS II, simplified acute physiology score.

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1. Introduction

Hyperglycemia is a common metabolic alteration in critical ill patients [1], while hypoglycemia is a threatening complication [2]. Abnormal blood glucose values are associated with an increased morbidity and mortality in critical ill (ICU) patients, including in major burns casualties [3,4].

A large randomized study published in 2001 changed our views on the optimal glycemic management [5]. A tight glycemic control by means of ''intensive insulin therapy'' (IIT 4.1–6.0 mmol/l) was shown to reduce mortality in ICU surgical patients [6]. The concept was thereafter extended to all critical ill patients [7,8]. Unfortunately several subsequent contradictory studies raised doubts about the external validity of the Leuven study [4]. In 2009 the international, multicenter ''NICE-SUGAR'' study including 6104 patients [9] confirmed that this tight glucose control resulted in higher mortality rates than the more moderate target (i.e. <8 or <10 mmol/l) in a mixed medico-surgical population fed mainly by the enteral route.

Stress-induced hyperglycemia is a multifactorial and complex process. Before 2001, hyperglycemia up to 15 mmol/l was tolerated without treatment in major burns, and considered to be an adaptive response. Thereafter, hyperglycemia became a source of concern. Major burn casualties represent a very special subset of critically ill patients. Despite important improvements in resuscitation and surgical management, metabolic alterations remain particularly intense and prolonged compared to general ICU patients [10]. Holm et al showed that glycemia >8 mmol/l and especially >11.1 mmol/l were associated with a poor clinical evolution [11,12], with an increased risk of infectious complications as wound infection, pneumonia, ventilator associated pneumonia (VAP), urinary tract infection and bacteremia. Pidcoke et al. showed that high glucose variability was associated with increased mortality in patients with burns >20% TBSA [13]: in that study hyperglycemia was the most important contributor to variability and to infectious complications. These studies suggested that blood glucose values closer to normal might decrease the number of infections and possibly mortality, sepsis being the main cause of death in burns [14,15].

Although the trials investigating IIT included a few burn patients the numbers were insufficient to draw conclusions regarding the optimal glucose levels [14,16–18]: burn cohort studies remain few. To our knowledge, there is only one study addressing the risk of hypoglycemia in adult burn patients, leading to the absence of strong recommendation about a specific target in this patient category [19,20].

Glycemic control was introduced in our multidisciplinary ICU in 2002 [21]: the initial glucose target was the tight 4–6 mmol/l range, with progressive widening to a moderate control of 6–8 mmol/l [9]. As the patients with severe thermal injury are treated within the multidisciplinary ICU, the same glycemic target was applied to them, without knowing if this practice was optimal for the critically ill burn patient. The aims of the present quality control study were to investigate if the internal recommendations had been applied in the burn cohort over a 15 year period, and to evaluate the safety of glycemic control in major burns receiving prolonged ICU treatment.

2. Methods

The study was conducted after approval by the Cantonal Ethics Committee. The requirement for consent was waived due to the absence of intervention and low risk nature of the project.

2.1. Study design

The study is a retrospective analysis of consecutive patients admitted to the computerized burn ICU of the university hospital of Lausanne (CHUV) in Switzerland between 2000 and June 2014. Inclusion criteria were: age ≥16 years, burns receiving ICU treatment whatever their size, and an ICU stay ≥10 days. The exclusion criteria were death or early discharge from the ICU within 10 days after admission. The investigation included the first 21 days after admission. The inclusion cut-off of 10 days aimed at enrolling only the severely burned patients, who needed a prolonged ICU stay. Then observation was limited to 21days, to minimize the influence of additional complications appearing after 3 weeks of ICU stay.

Patient variables were age, admission weight and height, burn size (total body surface area = TBSA), full thickness burn, inhalation injury, severity indices (abbreviated burn severity index = ABSI) score [22], Ryan score [23] and SAPSII [24]), number of infections, length of mechanical ventilation, length of ICU stay and outcome.

2.2. Glucose control

Four periods were considered according to the evolution of the ICU's blood glucose management protocol. Period 1 (2000–2001): before introduction of any systematic glucose control. Period 2 (2002-2006): introduction of a doctor driven tight glycemic control with target values between 4.0 and 6.0 mmol/l. The nurse in charge of the patient had to inform the physician if the values were not achieved and change in insulin treatment were done according to the doctors prescription. Period 3 (2007–2010): evolution of the protocol with introduction of an autonomous nurse driven tight glycemic control with target values between 4.0 and 6.0 mmol/l. The target values were prescribed by a physician. The nurse in charge of the patient could adapt the Insulin therapy independently to meet the target values. In case of hypoglycemia or persistent hyperglycaemic values the physician had to be informed systematically by the nurse. Period 4 (2011–2014): the autonomic nurse driven glycemic control was pursued as in period 3, indeed with change of the target values to a moderate glycemic control between 6.0 and 8.0 mmol/l which was prescribed by a physician after the NICE-sugar study. The Insulin administration was done by a continuous intravenous perfusion during all 4 periods.

2.3. Blood glucose determination

Blood gases, including blood glucose, were determined on a point of care machine (Radiometer, ABL800 FLEX, Copenhagen, Denmark). The frequency of the sampling was highly