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Glucose Metabolism

Failure to achieve euglycemia despite aggressive insulin control signals abnormal physiologic response to trauma☆,☆☆

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Abstract

Purpose: We hypothesize that a failure to normalize a patient's glucose on an automated euglycemia protocol signals an adverse response after trauma and that this response can identify patients with an increased mortality.

Materials and Methods: There were 1246 ventilated, critically ill trauma patients who were placed on an automated euglycemia. All glucose values collected both by laboratory serum measurements and by bedside arterial samples were included in the analysis.

Results: Forty six thousand two hundred eighteen data entries for glucose (mg/dL) were analyzed. *Time to normalization*, defined as the first value in the goal range of 80 to 110 mg/dL, was different between the 2 groups, survivors correcting significantly faster (396 vs 487 minutes; $P = .003$). Mortality in patients who normalized (80-110 mg/dL) in the first 6 hours of admission was 13.6% vs 18.3% in patients requiring greater than 6 hours ($P = .02$). Patients who never normalized also required significantly greater insulin doses despite there being no significant difference in demographic data between the 2 groups.

Conclusions: A posttraumatic patient's response to tight glycemic control revealed important prognostic information about the patients' physiologic status. Patients who failed to reach euglycemia in the first 6 hours of admission had an increased hospital mortality. The time to normalization is significantly longer in those patients who died. Patients who did not correct rapidly required significantly higher insulin doses, suggesting insulin resistance.

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1. Introduction

Hyperglycemia at the time of admission has been used as a marker of mortality in the trauma population over the last several years [1,2]. Authors have shown that untreated hyperglycemia that persists through the patient's admission leads to adverse outcomes [3]. Even before the most recent publications questioning the appropriate goal range [4-6], widespread institution of tight glycemic control (goal 80-110 mg/dL) has not been the standard of care in the trauma population because of concerns and fears of hypoglycemia. When instituted, protocols used more liberal goals (80-150 mg/dL), with mixed results of tight glycemic control's effect on outcome in the trauma population [7,8]. Recent publications in nontrauma populations aimed at addressing the uncertainty of the best goal range have made appropriate goal selection even more challenging [4-6].

Although the question of whether hyperglycemia after trauma is an adaptive mechanism or a pathologic response to stress remains, there is evidence that aiming for euglycemia leads to improved outcomes in other populations [9-13]. Trauma practitioners have questioned the applicability of euglycemia protocols because their patients often represent a young, heterogeneous, critically ill population, which contrasts with the population seen in other studies.

As hyperglycemia protocols become more widespread and effective, traditional means of differentiating patients based on summary measures such as median blood glucose and the percentage of values within goal range become more difficult. The aggressive management of both hypoglycemia and hyperglycemia makes them poor predictors of differentiating survivors from nonsurvivors. Individuals' responses to the initiation of tight glucose control and their responses to insulin as a drug are methods of differentiating these patients. Basic science as well as clinical research supports that hyperglycemia is due to peripheral insulin resistance (IR) as well as increased hepatic glucose production [14-20]. This IR has been shown to be a predictor of poor outcomes in a more diverse critically ill surgical population [21].

Against the backdrop of this IR and hyperglycemia, we sought to further describe the prognostic ability of persistent hyperglycemia while attempting tight glucose control. We developed a computer-based order entry system to assist in the maintenance of euglycemia in critically ill patients that captures all glucose values, insulin doses, and a mathematical multiplier (M) used to determine the insulin dose for each patient. We hypothesize that a failure to normalize a patient's glucose on an automated euglycemia protocol signals an adverse response after trauma and that this response can identify patients with an increased mortality.

2. Materials and methods

2.1. Study population

One thousand eight hundred eighty six patients were admitted to the Vanderbilt University trauma intensive care unit (ICU) from March 1, 2006, to April 26, 2008. There were 1709 patients treated with the tight glucose control protocol using the computer-based order entry system at Vanderbilt University Medical Center who met study criteria. Inclusion criteria for being placed on the protocol were all mechanically ventilated patients found to have blood glucose value greater than 110 mg/dL. Those with lower than 3 glucose values or not surviving the initial 24 hours of admission were excluded from the study as it was felt that they did not have sufficient time to reach a steady state (Fig. 1).

2.2. Insulin protocol

Vanderbilt University developed a computerized care provider order entry system that facilitates the maintenance of euglycemia (blood glucose 80-110 mg/dL) using an intravenous insulin infusion. The adjusted insulin dose is determined by a linear equation that uses an adaptable multiplier based on the glucose response from the previous dosing period. This protocol is based on a system initially described by White et al [22] and further elaborated on by Davidson et al [23]. The adaptability of M to varying physiologic demands (ie, throughout a patient's hospitalization) is a key characteristic of the protocol. Insulin dose is calculated by using the formula:

$$\text{Insulin dose (U/h)} = (M)^{*}[\text{blood glucose (mg/dL)} - 60]$$

M is initially set at 0.03 and can never fall below zero. The insulin dose is then altered by the use of an adapting multiplier, which is controlled by an algorithm (Fig. 2). The protocol's titration has previously been described and

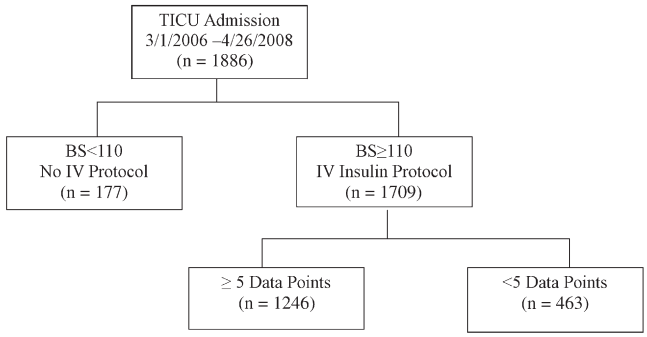

Fig. 1 Study group.