

Evaluation of blood glucose values in critically ill patients before and after implementation of an intensive insulin infusion protocol

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This retrospective study evaluated the effect of an intensive insulin infusion protocol on blood glucose values in five intensive care units at Baylor University Medical Center. The protocol involved an equation in which the hourly blood glucose value and an adjusted multiplier were used to determine the insulin infusion rate. The default target blood glucose range was 90 to 120 mg/dL. Results showed that blood glucose values taken by diabetic fingerstick were significantly better in March 2006, after initiation of the protocol, than in March 2005, before use of the protocol, for the percentage of patients both with a blood glucose value

>150 mg/dL ($P < 0.001$) and with a blood glucose value >120 mg/dL ($P < 0.001$). The percentage of patients with a blood glucose value ≤ 80 mg/dL was not significantly different between the two time periods ($P > 0.10$). The increased number of diabetic fingerstick values within a desired range was achieved without a significantly higher number of blood glucose values ≤ 80 mg/dL. It can be theorized that wide use of the protocol was at least partly responsible for the significant change in blood glucose values.

Hyperglycemia in critically ill patients is caused by a number of factors. Stress-induced hyperglycemia, commonly defined as blood glucose value >200 mg/dL, is an endogenous process resulting from the inflammatory response that occurs in critical illness. Hyperglycemia can also be triggered by exogenous substances, including pharmacologic agents such as corticosteroids, immunosuppressants, sympathomimetics, and dextrose infusions, as well as parenteral and enteral nutrition (1).

The current focus on tight blood glucose control in critically ill patients began with a now landmark trial by Van den Berghe and colleagues published in late 2001 (2). Numerous studies since then, in various populations of intensive care unit (ICU) patients, have sought to prove, or disprove, the idea that tight blood glucose control is beneficial.

In their first study, Van den Berghe and colleagues compared intensive insulin therapy (blood glucose maintained between 80 and 110 mg/dL with insulin infusion) with conventional treatment (insulin infusion initiated only if blood glucose exceeded 215 mg/dL and then maintained between 180 and 200 mg/dL with insulin infusion) in a surgical ICU. Their prospective randomized controlled study included 1548 patients, who were predominantly cardiothoracic surgery patients. In patients who were in the ICU for more than 5 days, intensive insulin therapy resulted in a significantly reduced ICU mortality rate, as well as significant improvement in outcomes such as length of ICU stay, duration of mechanical ventilation, incidence of bloodstream infections, acute renal failure requiring dialysis, critical illness polyneuropathy, and hyperbilirubinemia. The study was not blinded for logistical reasons (2).

In 2003, Krinsley published results of a retrospective review of 1826 consecutive ICU patients (heterogeneous population), which further reinforced the idea that elevated blood glucose values during critical illness were associated with increased morbidity and mortality. Upon review of blood glucose values, the mean and maximum values were significantly higher in nonsurvivors than in survivors. The lowest mortality rate occurred in the group with mean glucose values between 80 and 99 mg/dL. Hospital mortality increased progressively with each 20-mg/dL increase in glucose range, leading to the conclusion that even modestly elevated blood glucose in the ICU leads to increased hospital mortality in a heterogeneous patient population (3).

The following year, Krinsley published results of a study of 800 consecutive ICU admissions (heterogeneous population) after institution of an intensive glucose management protocol; comparators were 800 historical control patients admitted the year immediately preceding the study period. The intensive intravenous insulin protocol was initiated if two successive glucose values exceeded 200 mg/dL; the protocol maintained glucose values <140 mg/dL. The patients in the intensive glucose management group had significantly decreased hospital mortality rates, length of ICU stay, and incidence of new-onset renal insufficiency and blood transfusion (4).

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Table. Blood glucose group comparisons by period and intensive care unit

Intensive care unit	Blood glucose >120 mg/dL Number (%)		Blood glucose >150 mg/dL Number (%)		Blood glucose ≤80 mg/dL Number (%)	
	March 2005	March 2006	March 2005	March 2006	March 2005	March 2006
2 South	1363 (80.9)*	1697 (59.9)	1060 (62.7)*	1109 (38.9)	84 (5.0)	149 (5.2)
4 North	844 (55.5)*	477 (26.4)	448 (29.5)*	199 (11.0)	111 (7.3)	125 (6.9)
4 Truett	1070 (64.5)*	1080 (40.7)	666 (40.1)*	589 (22.2)	131 (7.9)	235 (8.9)
4 West	1048 (62.1)*	750 (42.1)	638 (37.5)*	415 (23.4)	111 (6.5)	110 (6.2)
CCU	749 (72.9)*	773 (53.3)	501 (48.8)*	433 (29.9)	82 (8.0)	134 (9.2)
Total	5074 (66.9)*	4777 (45.4)	3313 (43.6)*	2745 (26.1)	519 (6.8)	753 (7.2)

* $P < 0.001$ for comparing the differences between 2005 and 2006.

CCU indicates coronary care unit.

In 2006, Van den Berghe and colleagues published results of a study of intensive insulin therapy in 1200 medical ICU patients. This study had the same design as their surgical ICU study. The mortality rate was significantly reduced in patients who received intensive insulin therapy who were in the ICU for more than 3 days; however, in patients whose ICU stay was <3 days, the mortality rate in the intensive insulin group was increased. According to the post hoc analysis, the intensive insulin therapy likely did not cause harm. The authors hypothesized that patients staying in the ICU <3 days may have had higher mortality due to withdrawal of treatment for medical futility. Morbidity was significantly decreased in all patients in the intensive insulin therapy group, resulting in a decreased incidence of acute kidney injury, duration of mechanical ventilation, length of ICU stay, and length of hospital stay. As in the previous study, treatment groups were not blinded (5).

In recognition of a need for intensive insulin therapy at Baylor University Medical Center (BUMC), a multidisciplinary group was formed in late 2004 to address the issue. After review of numerous insulin infusion protocols, one was selected for pilot study in the ICUs. The protocol chosen involves an equation in which the hourly blood glucose value and an adjusted multiplier are used to determine the insulin infusion rate. The target blood glucose range can be determined by the prescriber on an individual basis. After a pilot study, minor changes were made to enhance the safety of the protocol, including changing the default target blood glucose range from 80–120 mg/dL to 90–120 mg/dL, thereby potentially avoiding blood glucose values below the desirable range. In addition, the treatment threshold for low blood glucose values was changed from 70 mg/dL, which had been the institutional standard value to trigger treatment for hypoglycemia, to 60 mg/dL. After research and discussion, it was decided that if tight glucose control was the ultimate goal, treating a blood glucose value of 70 mg/dL with dextrose in an asymptomatic patient would not be clinically useful. Following the changes, a second phase of the pilot study was done, which showed the protocol to be efficacious at maintaining blood glucose values within a desirable range (80–120 mg/dL), with an acceptable rate of hypoglycemia. Based on the pilot study results, the protocol was adopted as the standard insulin infusion in all ICUs at BUMC.

MATERIALS AND METHODS

Data were collected from the five ICUs at BUMC. Blood glucose readings by diabetic fingerstick (DFS) were classified according to the following three schemes: <90 mg/dL, 90–120 mg/dL, and >120 mg/dL; <80 mg/dL, 80–150 mg/dL, and >150 mg/dL; and ≤200 mg/dL and >200 mg/dL. Blood glucose readings were evaluated for the following three periods: March 2005, prior to initiation of the new protocol, and October 2005 and March 2006, both following the initiation of the new protocol. Data for October 2005 were not complete and thus were not included in the analysis.

Statistical analysis utilized a chi-square test to evaluate the association between the blood glucose classifications and the time periods and between the blood glucose classifications and the ICUs. A log-linear model was used to evaluate the association between the blood glucose classifications and the time periods and the ICUs. A P value <0.05 was considered significant.

RESULTS

After initiation of the protocol, significantly fewer patients had blood glucose values >120 mg/dL or >150 mg/dL. There were no significant differences between the two periods for the rate of blood glucose ≤80 mg/dL for all ICU units (*Table, Figure*).

Log-linear analysis confirmed a significant association between the blood glucose classifications (using the 80-mg/dL cut point) and the periods (protocol effect, before and after) and the ICUs ($P < 0.05$).

DISCUSSION

The DFS results demonstrate an improvement in overall blood glucose values after implementation of the intensive insulin infusion protocol in the critically ill patient population at BUMC. Furthermore, the increased number of DFS values within a desired range was achieved without a significantly higher number of blood glucose values ≤80 mg/dL.

Several limitations to the data must be considered. First, the data include DFS values for all ICU patients in the designated 1-month time periods, even those patients who had no intervention for blood glucose control. Because the data could not be separated by individual patient, many outlier values are likely

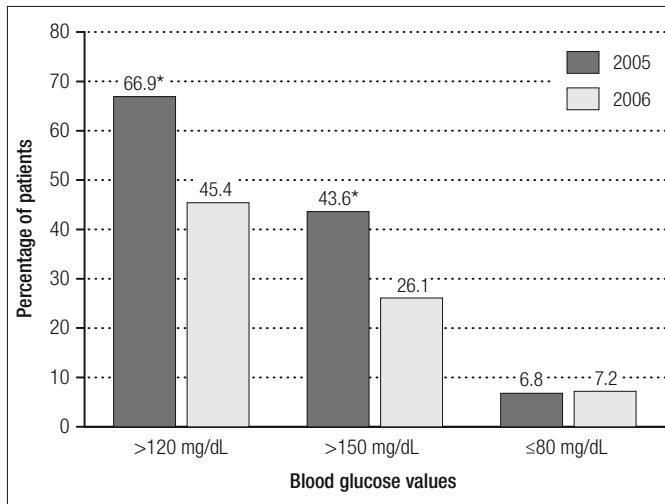


Figure. Distribution of blood glucose values from all intensive care units according to time period. Asterisk indicates significant difference between time periods ($P < 0.001$).

included. Also, serum blood glucose values are not included in the data analysis.

The March 2005 data for the 4 North and 3 North ICUs were not a completely accurate reflection of the blood glucose values prior to implementation of the intensive insulin infusion protocol, as the pilot study began in February 2005 in these units. However, data in the presented format were not available before March 2005.

Another limitation is that the data do not offer a true estimate of the incidence of hypoglycemia. The reporting of blood glucose values ≤ 80 mg/dL cannot be equated with hypoglycemia, since hypoglycemia is typically defined as blood glucose values of 60 to 70 mg/dL or even lower in some practice settings. Nevertheless, the data are consistent between time periods.

Finally, as is typical in retrospective analyses, it is possible that other changes in practice may have contributed to the change in blood glucose values in the ICU patient population at BUMC. Especially possible is the likelihood that overall awareness among prescribers about the benefits of tight blood glucose control in critically ill patients led to more aggressive treatment of hyperglycemia.

Due to limitations in the data, it cannot be conclusively stated that any observed improvement in blood glucose values in ICU patients at BUMC was a direct result of implementation of the intensive insulin infusion protocol. However, it can be theorized that wide use of the protocol was at least partly responsible for the significant change in blood glucose values.

Additional tools to help improve glycemic control have been implemented at BUMC since March 2006, including a progressive sliding scale insulin protocol as well as a standing delegated medical order to check DFS on all ICU patients for the first 24 hours of admission if no other glycemic control interventions are ordered. More recent DFS data from the ICU patients at BUMC will likely be analyzed to see if the combined efforts to improve blood glucose control have been valuable.

Many studies published in recent years have validated various insulin infusion protocols and demonstrated improvement in morbidity and mortality in ICU patients when blood glucose is tightly controlled. Further studies are needed to determine the optimal range of blood glucose values and which populations of ICU patients will benefit most from efforts to achieve tight blood glucose control.

Acknowledgments

The authors would like to thank Yahya A. Daoud, biostatistician, as well as the numerous health care team members who have contributed to the success of this protocol.

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