Utilization of a Computerized Intravenous Insulin Infusion Program to Control Blood Glucose in the Intensive Care Unit


ABSTRACT

Background: This proof of concept study was designed to evaluate the safety and effectiveness of an intravenous insulin dosing calculator, the Clarian GlucoStabilizer™ program, and to determine the feasibility of its use as part of a glycemic control program. This paper discusses the impact of the GlucoStabilizer program on the glycemic control of intensive care patients with hyperglycemia.

Methods: Patients admitted to the intensive care unit (ICU), requiring intravenous insulin, were treated using the GlucoStabilizer program. This program calculates an insulin drip rate based on the low and high blood glucose (BG) levels of the desired target range, the patient’s current and previous BG levels, and an insulin sensitivity factor, with a goal of safely and expeditiously achieving and maintaining the patient’s BG in the target range.

Results: From October 2004 through March 2006, the GlucoStabilizer program has been used to treat 2,398 patients in the ICUs, with 177,279 BG measurements in its database. In these patients, 61.0% of BGs have been in the target range of 80–110 mg/dL, while 90.9% have been in the wider range of 60–150 mg/dL. The average BG was 106.5 mg/dL (SD 39.1 mg/dL), and the frequency of hypoglycemia (BG < 50 mg/dL) was 0.4%. These results compare favorably with the level of glycemic control in the 3 months before implementation of the GlucoStabilizer program.

Conclusions: Use of the GlucoStabilizer program in the ICU resulted in improved glycemic control compared to the previous manually calculated glycemic control protocols.

INTRODUCTION

Implementing glycemic control programs

In recent years, there has been a steady accumulation of evidence linking glycemic control to reduced morbidity and mortality in critically ill patients.1–6 In recognition of this emerging evidence, the American College of Endocrinology in early 2004 published a position statement on inpatient diabetes and meta-
bolic control, recommending blood glucose (BG) level upper limits of 110 mg/dL for patients in intensive care unit (ICUs) and 180 mg/dL for patients in non-ICUs. These guidelines were recently reaffirmed, but with a cautionary note on the multiple institutional obstacles and personal attitudes standing in the way of the widespread adoption of glycemic control as a standard of care in U.S. hospitals. Among the more significant barriers to adoption are the fear of hypoglycemia, the increase in nursing workload, the need to upgrade computer-based clinical information systems to monitor and assess the safety and effectiveness of the glycemic control program, the lack of clinical and administrative resources, education and training for hospital staff, skepticism regarding the benefits of glycemic control, and a general resistance to change. Though some of these barriers may be more of a perceived than a real problem, overcoming and conquering them are absolutely essential for a successful glycemic control program.

**Insulin dosing calculators**

As part of the implementation of a glycemic control program, it is typically necessary to design and introduce new insulin dosing protocols. These protocols are normally more aggressive than the previous ones and require more frequent BG testing. If not introduced properly, these protocols may be resisted, simply on the basis of clinical inertia and increased nursing workload. In addition, the more aggressive BG targets may arouse fears of increased hypoglycemia, and there may be a concern over the difficulty of manually calculating insulin doses and making clinical decisions based on more complex paper protocols.

Insulin dosing calculators can help to ease these concerns. Because these calculators can reliably calculate insulin doses and alert the nurse when a patient’s BG should be measured, a significant nursing burden can be lifted. Fears of increased hypoglycemia should be relieved with the knowledge that the insulin dosing calculator has been shown to be safe and effective in practice. In recent years, insulin dosing calculators have been introduced and demonstrated to be successful adjuncts to a glycemic control program. One particular insulin dosing program has successfully been used as part of an innovative glycemic control program at two Clarian Health Partners (Clarian) hospitals in Indianapolis, IN. Data to support the safety and effectiveness of this program are provided in this paper.

**The SUGAR™ (Systematic Utilization of Glucose Assessment and Response) program**

Indiana University physicians and residents attend two Clarian hospitals in the greater Indianapolis area: (1) Methodist Hospital (Methodist), a 763-bed semiprivate hospital, where the attending physicians are all Indiana University and private-practice physicians; and (2) University Hospital (University), a 317-bed academic medical center and one of the largest transplant centers in the Midwest, where the attending physicians are all Indiana University faculty and residents. In early 2003, in light of a significant burden of hyperglycemia in these two hospitals and in recognition of the benefits of glycemic control, Indiana University physicians and Clarian Health Partners came together to design a comprehensive approach to managing hyperglycemia at Methodist and University. The result was the SUGAR program, which was initiated in June 2003 and implemented in a number of stages. Though an insulin dosing calculator was not part of the initial SUGAR program, it was realized that such a calculator would become an essential component of the program. In late 2004, the Clarian GlucoStabilizer™ program was introduced in the ICUs of Methodist and University, replacing the tedious insulin dosing calculations that had been part of the previously used paper protocols.

**SUBJECTS AND METHODS**

**Clarian GlucoStabilizer program**

The GlucoStabilizer program, for which a patent is currently pending, supports systematic and standardized titration of intravenous insulin drip rates for control of BG within a selected target range. It is menu-driven, and includes options for starting a new insulin drip,
stopping/holding a drip, resuming a prior drip, entering a BG value, specifying the initial target range, specifying the initial insulin sensitivity factor (ISF), and exiting the program. At the initiation of a drip run, the current BG level is entered, and, if the user-specified defaults for the target range and the initial ISF are not acceptable, a target range (e.g., 80–110 mg/dL in the ICU) and an initial ISF can be entered. The ISF, whose initial value is typically 0.02, is a key component of the insulin dose calculation, as it models the individual patient’s glycemic response to insulin. With an ISF of 0.02, for example, the recommended insulin dose is in-

![Graph of Blood Glucose Measurements](image1)

**FIG. 1.** Percentage of BG measurements in selected ranges for the 177,279 BG measurements in the GlucoStabilizer database for Methodist and University ICU patients with a target range of 80–110 mg/dL from October 2004 to March 2006.

![Graph of Mean Blood Glucose Measurements](image2)

**FIG. 2.** Means and SDs of BG measurements (mg/dL) during the first 24 h of GlucoStabilizer drip runs with a starting BG >110 mg/dL at Methodist and University ICUs from October 2004 to March 2006.
creased by 0.02 units/h for each mg/dL increase in the current BG. This multiplier is implicit in the tables for closed-loop insulin delivery published in 1982 by White et al.15 These tables were also the inspiration for the first insulin dose calculator announced in 1986.16 Upon entry of the initial values, the program calculates the initial insulin infusion rate in units/h. The program also determines the amount of time before the next BG level is measured. This interval is initially set for every 60 min. It is adjusted whenever a new BG is entered, based on the current and previous BG values. At the scheduled time for the next measurement, the program sounds an alarm, alerting the nurse, for example, to perform a BG test. When the new BG is entered, the program determines a new value for ISF, calculates a new insulin infusion rate, and schedules the time for the next measurement. The ISF is typically modified in increments of 0.01, adjusted up if the patient response is above target range or down if below target range. After 4 h of a stable drip, the program lengthens the testing interval to 120 min. The program is especially vigilant for signs of hypoglycemia. If BG ≤70 mg/dL, the insulin drip is stopped, a dextrose 50% (D50) bolus is administered, based on the formula $(100 - \text{BG}) \times 0.4 \text{ g}$, and the next test is scheduled for 15 min later. The insulin drip recommences after a BG measurement greater than 70 mg/dL is recorded. For patients who are eating, intravenous insulin boluses are calculated and administered with a default insulin-to-carbohydrate ratio of 1 unit/10 g of carbohydrates. Individual carbohydrate ratios may also be selected. The value and timestamp of the BG tests, the calculated ISF, the calculated infusion rate, the calculated testing interval, and any D50 recommendations are saved to a computer server for subsequent review and analysis. The program has the capability of allowing treating physicians to monitor glucose levels and insulin infusion rates from networked hospital computers at remote locations to assist with prompt consultation and inter-

![Time to Target](image)

**FIG. 3.** Kaplan-Meier estimated time to target (80–110 mg/dL) curve for GlucoStabilizer drip runs at Methodist and University ICUs from October 2004 to March 2006.
vention. The program also allows customization of default values and BG monitoring intervals. Customization can be done for an individual patient, a particular location, or a group of locations. At Methodist and University, for example, the default target range in the ICU is 80–110 mg/dL, while in the Medical/Surgical and Progressive Care units, the default target range is 100–150 mg/dL.

**Statistical analysis**

Independent samples *t* tests were used for all statistical comparisons. Survival analysis curves were constructed using Kaplan-Meier methodology. All analyses were performed using SPSS version 14.0 (SPSS Inc., Chicago, IL).

**RESULTS**

The GlucoStabilizer program has been used in ICUs, progressive care units, and Medical/Surgical units, with a number of different target ranges. In the ICU, the target range is typically 80–110 mg/dL, while in Medical/Surgical units, the target range is typically 100–150 mg/dL. Because the GlucoStabilizer program has seen its greatest application by far in the ICU with a target range of 80–110 mg/dL, results are presented for this setting only. For ICU patients, the single criterion for using the GlucoStabilizer program was physician request for intravenous insulin to control hyperglycemia. Use of the GlucoStabilizer program is becoming standard whenever the patient has two BG values ≥110 mg/dL.

From October 2004 through March 2006, the GlucoStabilizer program was used to treat 2,398 ICU patients with a target range of 80–110 mg/dL. There were a total of 4,302 drip runs (i.e., program executions) for these patients. There could be multiple drip runs for the same patient. There are 177,279 BGs in the database for these patients, 61.0% of which have been in the target range of 80–110 mg/dL, while 90.9%
have been in the wider range of 60–150 mg/dL. The frequency of hypoglycemia (BG < 50 mg/dL) was 0.4%. Recovery from hypoglycemia was rapid. The average interval until the next measurement after a BG ≤ 50 mg/dL was 26.1 min, and the next BG measurement after hypoglycemia averaged 106.4 mg/dL. Figure 1 shows the percentage of BG measurements in various clinically relevant ranges. Note the relatively low percentage of measurements in the hypoglycemic and hyperglycemic ranges. The average BG was 106.5 mg/dL (median 98.0 mg/dL, SD 39.1 mg/dL). In Figure 2, the hourly average BG during the course of drip runs with a starting BG greater than 110 mg/dL is shown.

Restricting our attention to the 2,889 drip runs with a starting BG greater than 110 mg/dL and at least 10 BG measurements, the starting BG averaged 205.5 mg/dL, and 99.2% of the drip runs achieved the target. The average of all BGs after the target was achieved was 98.1 mg/dL, and 68.7% of these BGs remained in the target range. The time to achieve the target range is presented in Figure 3 as a Kaplan-Meier curve. The average time to target was 6.9 h (95% confidence interval, 6.75–7.09 h), and the median time to target was 6.0 h (95% confidence interval, 5.84–6.25 h).

Impact on glycemic control

To assess the impact of the GlucoStabilizer program on glycemic control, the levels of glycemic control before and after the introduction of the GlucoStabilizer program were compared. Prior to the introduction of the GlucoStabilizer program, a paper protocol was in use in the ICUs. This paper protocol had two algorithms for insulin infusion. For both algorithms, the target BG range was 90–130 mg/dL, hourly testing was supported, and a 25-mL intravenous D50 bolus was given when BG ≤ 70 mg/dL. Intravenous drip rates were found in a decision table based on the current BG. Because there was no way to remind the nurse of
the time for the next BG measurement and because the use of the decision tables was cumbersome, the paper protocol was difficult to use. Some of the significant improvements introduced by the GlucoStabilizer program were the alarms prompting the nurse to measure BG, automatically calculated drip rates based on the patient’s previous BG responses to insulin doses, variable D50 doses when BG ≤70 mg/dL, and a narrower target range.

Figures 4 and 5 present a monthly record of the percentage of BGs <110 mg/dL and the average BG, respectively, in the ICUs at Methodist and University. In both Figures 4 and 5, there was improvement in glycemic control during the staged introduction of the GlucoStabilizer program in the ICUs from October 2004 through February 2005. These analyses included all ICU patients, whether or not they were treated using the GlucoStabilizer program. The percentage of measurements <110 mg/dL in the ICUs in the 3 months before introduction of the GlucoStabilizer program was 31.5%, compared to 51.5% in the following 3 months (P < 0.001, Fig. 6). Improvements in glycemic control were not accompanied by an increase in hypoglycemia. The frequency of hypoglycemia (BG <50 mg/dL) when using the GlucoStabilizer program was 0.4%, compared to a baseline level of 0.5% in the ICUs during the 3 months before introduction of the GlucoStabilizer program.

**DISCUSSION AND CONCLUSIONS**

Initial experience with the GlucoStabilizer program in the ICU setting has been encouraging. The GlucoStabilizer program appears to be effective, with an average time to target of 6.9 h, and safe, with a low hypoglycemia (BG <50 mg/dL) rate of 0.4%. None of the hypoglycemic events was felt to be clinically significant, and all were reversible. This hypoglycemia rate compares favorably with a different intravenous insulin dosing calculator, the Glucommander, with a reported hypoglycemia rate (BG <50 mg/dL) of 0.6%.11

![FIG. 6. Percentage of BG measurements <110 mg/dL in the 3 months before and 3 months after introduction of the GlucoStabilizer in Methodist ICUs (ICU Groups 1–3) and University ICUs (ICU Groups 4 and 5). The columns contain the total number of BG measurements. (ICUs with the same GlucoStabilizer introduction date are grouped together.)](image-url)
The number of BG tests performed in the ICUs increased from 54,500 in the 3 months prior to introduction of the GlucoStabilizer program to 71,762 in the following 3 months, a 31.7% increase. This increase is felt to reflect a tight control regarding retest intervals. The alarm reminder mechanism and the automatic drip rate calculation greatly simplified what had been a complex and burdensome paper protocol.

Though this study focused on the use of the GlucoStabilizer program in the ICU setting, the GlucoStabilizer program has also been used in Medical/Surgical units and Progressive Care units. Depending on the clinical environment and particular patient needs, the defaults for the lower and upper BG targets and the initial ISF can be changed at the beginning of the drip run. The GlucoStabilizer program is easily installed and operates on any networked computer in the hospital or physician’s office for remote access and monitoring. The GlucoStabilizer program also stores BG values and dosing recommendations in a database for review of algorithm efficacy and quality control purposes.

The results of this study indicate that the GlucoStabilizer computerized intravenous insulin dosing program can be safely and effectively used in the ICU and could be one way to achieve glycemic control in hospitalized inpatients.

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