Implementation of a Safe and Effective Insulin Infusion Protocol in a Medical Intensive Care Unit

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OBJECTIVE — In a recent randomized controlled trial, lowering blood glucose levels to 80–110 mg/dl improved clinical outcomes in critically ill patients. In that study, the insulin infusion protocol (IIP) used to normalize blood glucose levels provided valuable guidelines for adjusting insulin therapy. In our hands, however, ongoing expert supervision was required to effectively manage the insulin infusions. This work describes our early experience with a safe, effective, nurse-implemented IIP that provides detailed insulin dosing instructions and requires minimal physician input.

RESEARCH DESIGN AND METHODS — We collected data from 52 medical intensive care unit (MICU) patients who were placed on the IIP. Blood glucose levels were the primary outcome measurement. Relevant clinical variables and insulin requirements were also recorded. MICU nurses were surveyed regarding their experience with the IIP.

RESULTS — To date, our IIP has been employed 69 times in 52 patients admitted to an MICU. Using the IIP, the median time to reach target blood glucose levels (100–139 mg/dl) was 9 h. Once blood glucose levels fell below 140 mg/dl, 52% of 5,808 subsequent hourly blood glucose values fell within our narrow target range; 66% within a "clinically desirable" range of 80–139 mg/dl; and 93% within a "clinically acceptable" range of 80–199 mg/dl. Only 20 (0.3%) blood glucose values were <60 mg/dl, none of which resulted in clinically significant adverse events. In general, the IIP was readily accepted by our MICU nursing staff, most of whom rated the protocol as both clinically effective and easy to use.

CONCLUSIONS — Our nurse-implemented IIP is safe and effective in improving glycemic control in critically ill patients.

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In 2001, a large randomized controlled trial from Leuven, Belgium, demonstrated that normalization of blood glucose levels using an intensive insulin infusion protocol (IIP) improved clinical outcomes in patients admitted to a surgical intensive care unit (ICU) (1). In the Leuven study, intensive insulin therapy (to maintain blood glucose levels between 80 and 110 mg/dl) reduced ICU mortality by 42% and also reduced the incidence of bloodstream infections, the incidence of acute renal failure, the need for prolonged ventilatory support, and the duration of ICU stay. Strict glycemic control appears to be beneficial in other intensive care settings as well. In the DIGAMI (Diabetes Mellitus, Insulin Glucose Infusion in Acute Myocardial Infarction) study (2,3), an intravenous insulin-glucose infusion (followed by an outpatient multidose subcutaneous insulin regimen) improved long-term prognosis in diabetic patients following acute myocardial infarction. In patients undergoing open heart surgery, the use of a perioperative IIP dramatically reduced the incidence of deep sternal wound infections (4).

Based on this emerging clinical evidence, there are increasing efforts worldwide to maintain strict glycemic control in critically ill patients. However, achieving this goal requires extensive nursing efforts, including frequent bedside capillary glucose monitoring ("fingersticks") and the implementation of complex IIPs, and such increased work demands may not be readily accepted by a busy ICU nursing staff. Moreover, a prevalent fear of hypoglycemia among hospital staff further hinders the widespread acceptance of intensive IIPs. Worldwide, critical care physicians and endocrinologists are in search of safe, standardized methods of achieving tight glycemic control in critically ill patients.

A detailed review of the literature failed to produce a comprehensive, validated IIP that was both complex enough to achieve strict blood glucose control and practical enough to be easily implemented by ICU nurses without the need for expert supervision or frequent deviation from protocol. This work describes our institution's early clinical experience with a safe, effective IIP that was both easily implemented and readily accepted by our MICU nursing staff.

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Abbreviations: APACHE II, Acute Physiology And Chronic Health Evaluation II; ICU, intensive care unit; IIP, insulin infusion protocol; MICU, medical ICU.

A table elsewhere in this issue shows conventional and Système International (SI) units and conversion factors for many substances.

RESEARCH DESIGN AND METHODS

— Our MICU is a 14-bed unit of the Yale New Haven Hospital, a 944-bed tertiary care referral center located in New Haven, Connecticut. Nearly 40% of MICU patients are admitted for primary respiratory failure. Other common diagnoses (together accounting for another one-third of admissions) include gastrointestinal hemorrhage, sepsis/hypotension, acute renal failure, and primary cardiovascular events. MICU patients are cared for by the internal medicine house staff of the Yale New Haven Hospital, under the direct supervision of clinical ICU fellows and board-certified critical care physicians. In the MICU, the patient-to-nurse ratio is either 1:1 or 2:1. The annual in-MICU mortality rate is 14%.

Insulin infusion protocol: history and implementation

Following publication of the Leuven study in November 2001, our critical care physicians attempted to implement strict glycemic control in the MICU. This effort was generally unsuccessful, largely because our MICU nurses were uncomfortable with "low-normal" blood glucose levels and lacked the experience to effectively manage intensive insulin infusions. As a result of erratic glycemic control and some episodes of hypoglycemia, our MICU director (M.D.S.) contacted the clinical director of our Endocrine section (S.E.I.) to design and implement an effective IIP. This work resulted directly from this clinical communication. It was not designed as a research study; however, detailed clinical follow-up was required to safeguard and improve patient care in the MICU.

Our IIP is shown in Fig. 1. The protocol was designed based on our empirical observations regarding blood glucose control in critically ill patients. In designing the IIP, we focused on the three main data elements used by experienced clinicians to adjust insulin infusions: *1*) the current blood glucose value, *2*) the previous blood glucose value, and *3*) the current insulin infusion rate. In other words, our IIP is based primarily on the velocity of glycemic change rather than on absolute blood glucose levels. The protocol was specifically designed to be implemented by the MICU nursing staff without the need for ongoing physician input. To facilitate early acceptance by critical care physicians and MICU nurses, the IIP was aimed at a conservative blood glucose target of 100–139 mg/dl. Following a series of brief (30-min) inservice training sessions, the protocol was made available to our clinical providers, who were ultimately responsible for the clinical decision to utilize it in their MICU patients.

Employing the IIP involves a simple three-step process, as shown in Fig. 1. First, the nurse must determine the current blood glucose value; this value then guides him or her to one of the four columns in the IIP table. Second, the nurse must determine the hourly rate of blood glucose change by subtracting the current blood glucose level from the prior value; this rate then drops one down to a specific cell within the column. Finally, specific nursing instructions are found to the far right of the identified cell. Actual changes in the insulin infusion rate (in units per hour) are determined using the second table below, which corrects for the current insulin infusion rate. The clinical use of the IIP can be easily explained and demonstrated during a brief training session.

Clinical experience with the IIP began in October 2002. In general, the IIP was recommended for all MICU patients whose blood glucose levels exceeded 200 mg/dl. This recommendation was not strictly enforced.

Data collection methods

All clinical variables were collected prospectively. Baseline (admission) clinical variables included age, sex, race, height, weight, history of diabetes, principal reason for ICU admission, and Acute Physiology And Chronic Health Evaluation II (APACHE II) score (5). APACHE II is a validated severity-of-illness scale that uses clinical and biochemical data (pulse, blood pressure, sodium, hematocrit, etc.) to stratify acutely ill patients by risk for death; higher APACHE II scores indicate increased severity of illness.

Blood glucose levels, insulin doses, and relevant clinical interventions were collected from the active hospital chart and MICU nursing records. We focused on four clinical interventions—corticosteroids, vasopressors, enteral nutrition, and parenteral nutrition, which our group has previously shown to be risk factors for poor glycemic control in the MICU (6). Each day, relevant medical records were reviewed for possible adverse events related to the IIP. All patients were followed until MICU discharge. Two months after implementation of the IIP, 29 MICU nurses completed an anonymous written survey regarding their clinical impressions.

Blood glucose levels were measured using a standard hospital glucose meter (Surestep Flexx; Lifescan, Johnson & Johnson, New Brunswick, NJ). The frequency of blood glucose measurements was guided by the IIP. When blood glucose values were not obtained every hour, hourly blood glucose values were calculated by averaging known blood glucose levels from the hours before and after missing values.

Statistical analysis

Except where noted, all clinical data are expressed as means ± SD or as a percentage. Baseline variables were compared using the Student's *t* test or χ^2 test. Blood glucose values between patient groups were compared using the Student's *t* test. Insulin requirements, which were not normally distributed, were compared using the Wilcoxon rank-sum test. All tests of significance were two tailed. *P* values <0.05 were considered statistically significant.

RESULTS

Patients

At the time of data analysis, our IIP had been used 69 times in 52 MICU patients. Thirty-eight patients were placed on the IIP on just one occasion. In 14 patients, the IIP was formally discontinued for ≥12 h, but was resumed after the recurrence of hyperglycemia. Three of these 14 patients were placed on the IIP on three separate occasions. Baseline characteristics of the 52 IIP patients are shown in Table 1, including ICU admission diagnoses and the frequency of relevant clinical interventions. None of the 52 patients had surgery while admitted to the MICU. The median blood glucose level upon ICU admission was 212 mg/dl (interquartile range 156–254 mg/dl).

Glycemic control

For the 69 insulin infusions employed, the median duration was 61 h (range 7–521 h), with 33 (48%) infusions still running at 72 h. The mean blood glucose level at IIP initiation was 299 ± 96 mg/dl (median 272 mg/dl), and the mean time

YALE INSULIN INFUSION PROTOCOL

The following insulin infusion protocol is intended for use in hyperglycemic adult patients in an ICU setting, but is not specifically tailored for those individuals with diabetic emergencies, such as diabetic ketoacidosis (DKA) or hyperglycemic hyperosmolar states (HHS). When these diagnoses are being considered, or if BG≥ 500 mg/dL, an MD should be consulted for specific orders. Also, please notify an MD if the response to the insulin infusion is unusual or unexpected, or if any situation arises that is not adequately addressed by these guidelines.

Initiating an Insulin Infusion

1.) INSULIN INFUSION: Mix 1 U Regular Human Insulin per 1 cc 0.9 % NaCl. Administer via infusion pump (in increments of 0.5 U/hr).
2.) PRIMING: Flush 50 cc of infusion through all IV tubing before infusion begins (to saturate the insulin binding sites in the tubing).
3.) TARGET BLOOD GLUCOSE (BG) LEVELS: **100-139 mg/dL**
4.) BOLUS & INITIAL INSULIN INFUSION RATE: Divide initial BG level by 100, then round to nearest 0.5 U for bolus AND initial infusion rate.
Examples: 1.) Initial BG = 325 mg/dL: 325 ÷ 100 = 3.25, round ↑ to 3.5: IV bolus 3.5 U + start infusion @ 3.5 U/hr.
2.) Initial BG = 174 mg/dL: 174 ÷ 100 = 1.74, round ↓ to 1.5: IV bolus 1.5 U + start infusion @ 1.5 U/hr.

Blood Glucose (BG) Monitoring

1.) Check BG hourly until stable (3 consecutive values within target range). In hypotensive patients, capillary blood glucose (i.e., fingersticks) may be inaccurate and obtaining the blood sample from an indwelling vascular catheter is acceptable.
2.) Then check BG q 2 hours; once stable x 12-24 hours. BG checks can then be spaced to q 4 hours IF:
a.) no significant change in clinical condition AND b.) no significant change in nutritional intake.
3.) If any of the following occur, consider the temporary resumption of hourly BG monitoring, until BG is again stable (2-3 consecutive BG values within target range):
a.) any change in insulin infusion rate (i.e., BG out of target range)
b.) significant changes in clinical condition
c.) initiation or cessation of pressor or steroid therapy
d.) initiation or cessation of renal replacement therapy (hemodialysis, CVVH, etc.)
e.) initiation, cessation, or rate change of nutritional support (TPN, PPN, tube feedings, etc.)

Changing the Insulin Infusion Rate

If BG < 50 mg/dL:
D/C INSULIN INFUSION Give 1 amp (25 g) D50 IV; recheck BG q 15 minutes.
⇒ When BG ≥ 100 mg/dL, wait 1 hour, then restart insulin infusion at 50% of original rate.

If BG 50-74 mg/dL:
D/C INSULIN INFUSION If symptomatic (or unable to assess), give 1 amp (25 g) D50 IV; recheck BG q 15 minutes.
If asymptomatic, give 1/2 Amp (12.5 g) D50 IV or 8 ounces juice; recheck BG q 15-30 minutes.
⇒ When BG ≥ 100 mg/dL, wait 1 hour, then restart infusion at 75% of original rate.

If BG ≥ 75 mg/dL:
STEP 1: Determine the CURRENT BG LEVEL - identifies a COLUMN in the table:

BG 75-99 mg/dL	BG 100-139 mg/dL	BG 140-199 mg/dL	BG ≥ 200 mg/dL

STEP 2: Determine the RATE OF CHANGE from the prior BG level - identifies a CELL in the table - Then move right for **INSTRUCTIONS:**
[Note: If the last BG was measured 2-4 hrs before the current BG, calculate the hourly rate of change. Example: If the BG at 2PM was 150 mg/dL and the BG at 4PM is now 120 mg/dL, the total change over 2 hours is -30 mg/dL; however, the hourly change is –30 mg/dL ÷ 2 hours = -15 mg/dL/hr.]

BG 75-99 mg/dL	BG 100-139 mg/dL	BG 140-199 mg/dL	BG ≥ 200 mg/dL	INSTRUCTIONS*
		BG ↑ by > 50 mg/dL/hr	BG ↑	↑ INFUSION by "2Δ"
	BG ↑ by > 25 mg/dL/hr	BG ↑ by 1-50 mg/dL/hr *OR* BG UNCHANGED	BG UNCHANGED *OR* BG ↓ by 1-25 mg/dL/hr	↑ INFUSION by "Δ"
BG ↑	BG ↑ by 1-25 mg/dL/hr, BG UNCHANGED, *OR* BG ↓ by 1-25 mg/dL/hr	BG ↓ by 1-50 mg/dL/hr	BG ↓ by 26-75 mg/dL/hr	NO INFUSION CHANGE
BG UNCHANGED *OR* BG ↓ by 1-25 mg/dL/hr	BG ↓ by 26-50 mg/dL/hr	BG ↓ by 51-75 mg/dL/hr	BG ↓ by 76-100 mg/dL/hr	↓ INFUSION by "Δ"
BG ↓ by > 25 mg/dL/hr *see below*†	BG ↓ by > 50 mg/dL/hr	BG ↓ by > 75 mg/dL/hr	BG ↓ by > 100 mg/dL/hr	HOLD x 30 min, then ↓ INFUSION by "2Δ"

†D/C INSULIN INFUSION; √BG q 30 min; when BG ≥ 100 mg/dL, restart infusion @75% of most recent rate.

***CHANGES IN INFUSION RATE** ("Δ") are determined by the current rate:

Current Rate (U/hr)	Δ = Rate Change (U/hr)	2Δ = 2X Rate Change (U/hr)
< 3.0	0.5	1
3.0 - 6.0	1	2
6.5 - 9.5	1.5	3
10 - 14.5	2	4
15 - 19.5	3	6
20 - 24.5	4	8
≥ 25	≥ 5	10 *(consult MD)*

Figure 1—*Yale Insulin Infusion Protocol.*

Table 1—*Baseline characteristics, admission diagnoses, and relevant clinical interventions employed for 52 MICU patients who were placed on the Yale IIP*

Characteristic	IIP Patients
n	52
Age (years)	59 ± 18
Male sex	62
Race:	
Caucasian	63
African American	19
Hispanic	13
Other	4
BMI (kg/m^2)	28.5 ± 8.3
APACHE II score	23.9 ± 9.2
Admission blood glucose level (mg/dl)	234 ± 149
History of diabetes	56
Primary diagnosis	
Respiratory failure	36
Gastrointestinal hemorrhage	13
Sepsis/hypotension	4
Renal failure	6
Primary cardiovascular events	17
Other	24
Clinical interventions	
Corticosteroid therapy	52
Vasopressor therapy	25
Enteral nutrition	65
Parenteral nutrition	10

Data are means ± SD or percent.

required to achieve target blood glucose levels (100–139 mg/dl) was 10.1 ± 4.6 h (median 9.0 h). Figure 2 illustrates the performance of the IIP during its first 72 h of use.

The IIP facilitated stable glycemic control after target levels were achieved. Once blood glucose levels fell below 140 mg/dl, 52% of 5,808 subsequent hourly blood glucose values fell within our narrow target range of 100–139 mg/dl, 66% within a "clinically desirable" range of 80–139 mg/dl, and 93% within a "clinically acceptable" range of 80–199 mg/dl. Hypoglycemia was rare. Of the 5,808 hourly blood glucose readings following achievement of target levels, only 20 (0.3%) blood glucose values (from 12 patients) were <60 mg/dl. Just three blood glucose values were <40 mg/dl. In all cases, hypoglycemia was rapidly corrected using intravenous dextrose, per protocol. Daily review of the clinical records revealed no clinically significant adverse events that could be attributed to hypoglycemia.

Predictably, when the IIP was halted (usually due to clinical improvement, initiation of oral feeding, and/or the anticipation of ICU discharge), blood glucose levels rapidly rebounded to hyperglycemic levels. For the 12-h time period following cessation of the IIP, mean blood glucose levels climbed to 178 ± 57 mg/dl; by the second 12-h period (i.e., 12–23 h after cessation of the IIP), mean blood glucose levels rose to 200 ± 70 mg/dl.

Effects of relevant clinical variables on the IIP

The effectiveness of the IIP was assessed with regards to the presence or absence of relevant clinical variables. Importantly, the IIP was equally effective in the presence or absence of diabetes. Target blood glucose levels were obtained in a similar time frame in diabetic and nondiabetic patients (9.4 ± 3.0 vs. 10.6 ± 5.6 h, $P = 0.25$). Following the achievement of target values, mean blood glucose levels were similar in diabetic and nondiabetic patients (125 ± 12 vs. 121 ± 18 mg/dl, $P = 0.22$). Blood glucose levels on the IIP were also not significantly affected by age, sex, severity of illness, or the use of corticosteroids, vasopressors, or enteral/parenteral nutrition (data not shown).

Insulin requirements

Overall, the median insulin infusion rate required to maintain normoglycemia was 4.0 units/h (range 1.0–19.0). Interestingly, there were no significant differences between median insulin infusion rates for diabetic (median 4.0 units/h, interquartile range 3.0–6.0) and nondiabetic (median 3.5 units/h, interquartile range 2.0–5.5, $P = 0.23$) patients. Insulin requirements were also not significantly affected by age, sex, severity of illness, or the clinical use of corticosteroids, vasopressors, or enteral/parenteral nutrition (data not shown).

Historical control patients

To assess the general effectiveness of the IIP compared with our previous practice standards, we compared blood glucose levels from the IIP patients to a previously collected cohort of 117 patients consecutively admitted to our MICU in March through April 2002 (6). From this cohort, patients with any blood glucose ≥200 mg/dl were used for comparison because this was the blood glucose cut point recommended for subsequent IIP implementation. Time 0 in this group was defined by the first recorded blood glucose level >200 mg/dl. Using this method, 47 hyperglycemic control patients were identified; of note, 14 of these 47 patients had received nonstandardized intravenous insulin therapy, with most of the remaining patients ordered for a subcutaneous regular insulin sliding scale. Importantly, there were similar proportions of diabetic patients in the IIP and historical patient groups (56 vs. 57%, $P = 0.87$).

Despite a greater severity of illness (APACHE II score 23.9 ± 9.2 vs. 19.0 ± 6.9, $P < 0.01$) and a trend toward higher admission blood glucose levels (234 ± 149 vs. 188 ± 91 mg/dl, $P = 0.08$), our

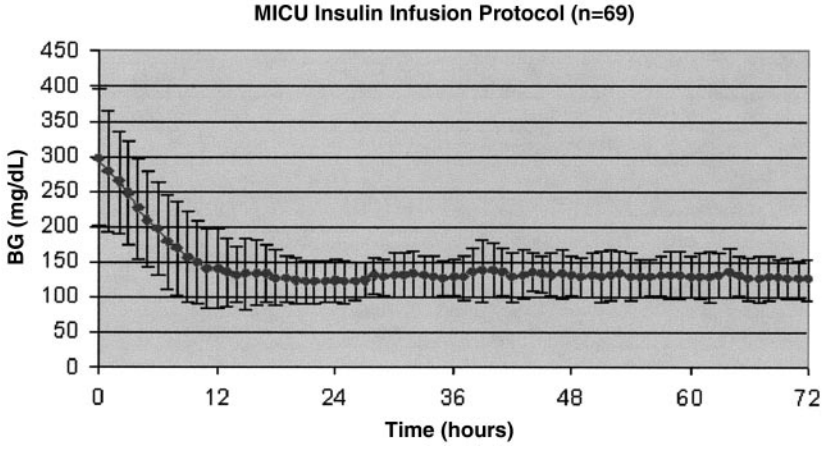

Figure 2—*Performance of the IIP (data points represent the first 72 h of insulin infusion). All blood glucose (BG) levels shown as means ± SD.*

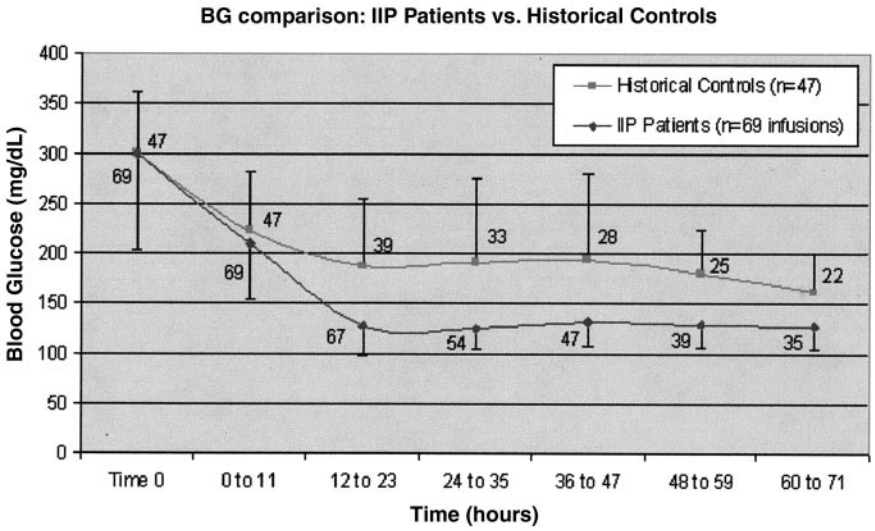

Figure 3—*Comparison of glycemic control between 69 IIP-guided insulin infusion patients (◆) and 47 hyperglycemic (≥200 mg/dl) historical control patients (■). The figure plots mean blood glucose (BG) levels (±SD) by 12-h time intervals. The numbers on the graph represent the number of remaining patients during each 12-h time interval. For all but time 0 and the first 12-h time period,* $P < 0.001$ *for all comparisons between IIP patients and historical control patients.*

IIP patients had better glycemic control than their historical counterparts. Figure 3 compares mean blood glucose values between the two patient groups, assessed by 12-h intervals (for this analysis, hourly comparisons were not possible due to the differing frequency of data collection in the two patient groups). Significant blood glucose differences were evident within 12 h of initial hyperglycemia.

MICU nursing reaction

In general, the IIP was readily accepted by our MICU nursing staff. In anonymous written surveys completed by 29 MICU nurses who employed the IIP, 73% rated the IIP as either "very easy" or "somewhat easy" to use; 86% rated the IIP as either "very effective" or "somewhat effective"; and 75% felt that the IIP was "an overall improvement" compared with previously available nonstandardized insulin infusion orders in the MICU. Though a majority of nurses felt that their workload was increased by the IIP, they generally were enthusiastic about employing the protocol after understanding its rationale and potential benefits. Nine months after its initial implementation, the IIP is still being actively utilized in our MICU.

CONCLUSIONS

— Hyperglycemia occurs in the majority of critically ill patients, even in those without a clinical history of diabetes (1,7). The stress of critical illness induces glucose counterregulatory hormones and a number of alterations in carbohydrate metabolism, including increased peripheral glucose demands, enhanced hepatic glucose production, insulin resistance, and relative insulin deficiency (7). In addition, several commonly employed clinical interventions, such as corticosteroids, vasopressors, and enteral (or parenteral) nutrition, further predispose these patients to elevated blood glucose levels (6). In a variety of clinical settings, stress hyperglycemia has been associated with adverse clinical outcomes. Following myocardial infarction, for example, hyperglycemia predicts increased rates of congestive heart failure, cardiogenic shock, and death (8–10). In patients with acute stroke, elevated blood glucose levels have been associated with increased mortality and with diminished neurologic recovery (11–14). In the general hospital setting, patients with hyperglycemia have higher mortality rates. Importantly, patients with new hyperglycemia have a worse prognosis than that of patients with a known history of diabetes (15). This observation becomes especially significant in the ICU, where the mortality rate for newly hyperglycemic patients approaches one in three (15).

A number of mechanisms have been proposed to explain the relationship between stress hyperglycemia and adverse clinical outcomes. These include attenuated host defense mechanisms, endothelial dysfunction, increased inflammatory cytokines, and changes in myocardial metabolism due to altered substrate availability. This complex topic has been reviewed elsewhere (16–19). However, in the absence of randomized controlled trials, it remained unclear whether hyperglycemia by itself is a causal factor in poor clinical outcomes or merely a reflection of illness severity. In 2001, the Leuven study (1) was the first randomized controlled trial to definitively demonstrate the benefits of intensive glycemic control in surgical ICU patients. Building clinical evidence suggests that the benefits of strict blood glucose control may not be limited to postsurgical patients. Ongoing randomized controlled trials are designed to address this issue.

Unfortunately, there are many practical barriers to implementing intensive insulin protocols in an ICU. IIPs add significantly to the work of managing ICU patients and thus may not be readily accepted by a busy ICU nursing staff. Every hour, the nursing caregiver must locate a glucose meter, perform a fingerstick, document the results, and make the necessary insulin drip adjustments; this process can take up to 5 min per hour. In addition, the inherent clinical and logistical perturbations of caring for critically ill patients (fluctuating severity of illness, changes in nutritional delivery, off-unit visits to diagnostic imaging, etc.) produce frequent alterations in hourly insulin requirements. Finally, a prevalent fear of hypoglycemia among critical care physicians and nurses further hinders the achievement of strict glycemic control in the ICU.

An effective, validated, nurse-implemented IIP has been elusive in the literature, likely because of the general lack of enthusiasm for strict inpatient glycemic control before publication of the Leuven study in 2001. Existing published IIPs are disadvantaged by excessively conservative blood glucose targets (2,4,20–22) and/or by oversimplified IIP directions, necessitating expert supervision or frequent deviation from protocol (2,4). In addition, detailed blood glucose data using these protocols have not been published. To maximize safety and efficacy, an IIP must take into account not only the current blood glucose level but also the rate of glycemic change and the current insulin infusion rate. By incorpo-

rating all three of these factors, our IIP was successful in maintaining targeted blood glucose control in the majority of MICU patients, with rare (and clinically insignificant) hypoglycemia. In addition, the IIP was easily implemented and well accepted by our MICU nursing staff. Predictably, once the intravenous insulin infusion was discontinued, the recurrence of hyperglycemia was common. Further studies are required to develop subcutaneous insulin protocols designed to minimize this rebound effect.

Though our observational study design was markedly different from that of the randomized, controlled Leuven trial, a few brief comparisons with that study may be useful to best interpret our results. First, the Leuven study was performed in postoperative patients admitted to a surgical ICU. Our study was performed in medical ICU patients, none of whom were postoperative. Second, 56% of our study patients had preexisting diabetes, compared with only 13% of the intensively treated Leuven patients. Expectedly, our patients had higher blood glucose levels on ICU admission (median 212 mg/dl) compared with the Leuven patients, of whom only 11% had admission blood glucose levels >200 mg/dl. Despite these differences, we were able to successfully control blood glucose levels in our patients using somewhat higher insulin infusion rates (4.0 vs. ~3 units/h) than those employed in the Leuven study.

We acknowledge several limitations of this work. First, because this was a clinical quality improvement project intended to benefit our MICU patients, there was no control group established. Recommendations were made regarding blood glucose thresholds for triggering the IIP. However, without solid outcome data in MICU patients, we were hesitant to establish strict inclusion criteria. Second, we recognize that our process of calculating missing hourly blood glucose levels is subject to criticism; however, this procedure was necessary so that all insulin infusions would contribute equally to the statistical analysis. In addition, we verified that this process had little impact on our study results. Third, we acknowledge the inadequacies of using historical control patients. However, these comparisons permitted us to assess the general impact of the IIP within our unit. Because our control patients were in general less ill and had lower admission blood glucose levels than our IIP patients, we felt this to be a valid (and conservative) exercise. Fourth, both nursing adherence to the IIP and nurse ratings of the IIP may have been affected by the daily presence of one or more of the authors. This was unavoidable. Fifth, this work was not designed to address clinical outcomes. To date, the clinical benefits of strict glycemic control in MICU patients have not been formally demonstrated; ongoing studies have been designed to address this issue. Finally, we acknowledge that our conservative blood glucose targets (as compared with the stricter Leuven protocol) may impact the clinical effectiveness and safety of the IIP intervention.

In summary, this work describes in detail the successful implementation of a safe, effective IIP by the nursing staff in a tertiary care MICU. The use of this IIP allows for strict glycemic control in critically ill patients. Future studies should determine whether such control, using insulin infusion protocols like the one described here, will result in improved patient outcomes for patients admitted to an MICU. Optimal target blood glucose levels also need to be more precisely identified.

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