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Standardization of intravenous insulin therapy improves the efficiency and safety of blood glucose control in critically ill adults

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Abstract Objective: Aggressive glycemic control improves mortality and morbidity in critically ill adults, however implementation of such a strategy can be logistically difficult. This study evaluates the efficiency and safety of a nurse-managed insulin protocol in critically ill adults.

Design: Combined retrospective-prospective before-after cohort study. **Setting:** Twenty-one bed, medical/surgical ICU in a tertiary care hospital. **Patients:** Two cohorts of 50 consecutive ICU patients requiring insulin infusions. **Intervention:** Patients in the control cohort received insulin infusions titrated according to target blood glucose ranges and sliding scales at the physician's discretion. Patients in the interventional cohort received an insulin infusion adjusted using a standardized protocol targeting a blood glucose of 4.5–6.1 mmol/l (81–110 mg/dl).

Measurements and main results: Efficiency was measured by comparing the time to reach, and the time spent within, the target range between co-

horts. Safety was assessed by comparing the incidence of severe hypoglycemia, the frequency of rescue dextrose administration and the cumulative time that the infusion was held for hypoglycemia between cohorts. Patients in the interventional cohort reached their target more rapidly (11.3 ± 7.9 vs 16.4 ± 12.6 h; $p=0.028$) and maintained their blood glucose within the target range longer (11.5 ± 3.7 vs 7.1 ± 5.0 h/day; $p<0.001$) than controls. The standardized protocol yielded a four-fold reduction in the incidence of severe hypoglycemia (4 vs 16%; $p=0.046$) and reduced the median frequency of dextrose rescue therapy (0 [0–0.91] vs 0.17 [0–1.2] episodes/patient per day; $p=0.01$) as compared to controls. **Conclusion:** Standardization of intensive insulin therapy improves the efficiency and safety of glycemic control in critically ill adults.

Keywords Insulin · Critical illness · Protocol · Hyperglycemia · Safety · Intensive care unit

Introduction

Hyperglycemia in critically ill patients has been associated with an increased susceptibility to infection and impaired immune response. Previously, hyperglycemia was considered to be an appropriate response to stress, however it is now being recognized as a predictor of negative outcomes including mortality [1, 2, 3, 4]. Hyperglycemia in critically ill patients may be due to

increases in catecholamine production, hepatic gluconeogenesis, relative insulin resistance and iatrogenic factors such as corticosteroid therapy and total parenteral nutrition (TPN) [5, 6, 7].

Only within the last decade has it been suggested that the hyperglycemia observed during stress may contribute to the morbidity and mortality in the ICU [8]. Recently Van den Berghe and colleagues reported the effect of intensive insulin therapy in 1,548 surgical ICU patients

requiring mechanical ventilation [9, 10]. They found a 42% relative reduction in ICU mortality ($p=0.04$) and a 20% relative reduction in the number of patients requiring prolonged stays in the ICU ($p=0.003$). Supportive therapies for organ failure as well as the risk of infectious and neuromuscular complications were also reduced. Although this was a single center study of primarily surgical patients, the mortality and morbidity benefit observed warrant the consideration of aggressive glucose control for all ICU patients who experience hyperglycemia [1].

There are several obstacles to overcome before such a therapy can be implemented outside the clinical trial setting where specially trained study nurses and physicians monitor it on a continuous basis. At our institution, considerable heterogeneity in the prescribing patterns of continuous insulin infusions exist with respect to both the target blood glucose range and the insulin dose titration scale. Following the publication of the Van den Berghe study, attempts at more intensive insulin infusions resulted in frequent episodes of hypoglycemia requiring rescue with intravenous dextrose infusions. Finally, physician and nursing staff felt that the titration scales did not adequately maintain serum glucose within the target range. Since the role of tight glycemic control in the ICU is increasingly recognized as an important and potentially life-saving intervention, we developed and evaluated a nurse-managed intensive insulin therapy protocol in a prospective, pre-post intervention cohort study with respect to efficiency, safety and nursing workload.

Methods

Study design and participants

This study was conducted in a 21-bed, mixed medical/surgical ICU of a tertiary care teaching hospital where the nurse to patient ratio is 1:1 during most of a patient's care. Approval for this study was obtained from the Ottawa Hospital Research Ethics Board. Two cohorts of 50 consecutive patients each requiring insulin infusions for hyperglycemia were compared. Patients in the first cohort (the control cohort) were prescribed "ad hoc" insulin infusions at the discretion of the physician caring for the patient. As a result, the target ranges for serum glucose and titration scales were not standardized. Data in the control cohort were collected both retrospectively and prospectively from June through November, 2002, and served as the control to which the interventional cohort would be compared. Patients in the second cohort (the interventional cohort) were prescribed insulin infusions using a standardized protocol (Fig. 1).

Development of an intensive insulin therapy protocol


The protocol was developed with input from a variety of clinicians including ICU nurses, clinical pharmacists, ICU physicians and endocrinologists. The intent was that this protocol would replace all "ad hoc" insulin infusions prescribed in the ICU unless it was intended for the management of diabetic ketoacidosis or hyperosmolar non-ketotic coma. The protocol was standardized with respect to the target blood glucose (4.5–6.0 mmol/l [81–110 mg/dl])

and the patient's nurse was responsible for interpreting trends in blood glucose and titrating the insulin infusion according to the titration scale in the protocol. All blood glucose measurements were performed from capillary blood samples using the Accu-Check Inform (Roche Diagnostics, Mannheim, Germany). The frequency of glucose measurements decreased over time, in accordance with the protocol, as insulin requirements stabilized and large fluctuations in blood glucose became infrequent. Patients in the interventional cohort who were not being fed upon initiation of the insulin infusion received 200 g of dextrose per day by intravenous infusion until enteral or parenteral nutrition was initiated. The insulin infusion was held when blood glucose dropped below 4.0 mmol/l (72 mg/dl) and the threshold for dextrose "rescue" was set at a blood glucose of 2.5 mmol/l (45 mg/dl). In comparison, the insulin infusions prescribed in the control cohort were not standardized. The target range, frequency of blood glucose measurement, threshold for hypoglycemic rescue with dextrose and insulin infusion titration scale were prescribed at the discretion of the primary physician. In both cohorts, the patient's primary physician determined the duration of therapy and no patient was discharged from the ICU on an insulin infusion.

The two cohorts were separated temporally by a 1-month period during which the ICU nursing staff, team physicians and clinical pharmacists were trained in the use of a standardized intensive insulin infusion protocol and educated on the goals of glycemic control. Training was accomplished by a series of group in-services and one-to-one discussions conducted by an ICU pharmacist outlining the goals of both the trial and the intervention. One of the study investigators was available to answer questions pertaining to the protocol at least 5 days a week. After the training period, the standardized protocol was implemented and all subsequent patients admitted to the ICU who required a therapeutic intervention for the management of hyperglycemia received intensive insulin therapy in accordance with the protocol.

Data collection

The data collected for each patient were grouped into demographics and end points related to glucose control, safety and nursing workload. Demographic data consisted of reasons for admission, therapeutic modalities (inotrope and mechanical ventilation requirements, corticosteroid administration and need for TPN), illness severity (APACHE II score) and the prevalence of comorbidities. Data with respect to glucose control, safety and nursing workload were collected on a daily basis for the entire duration of the insulin infusion. Glucose control was evaluated using baseline blood glucose values obtained prior to initiating the insulin infusion, the time taken to reach the target blood sugar, the lowest and highest blood glucose each day and the time spent within the target range. Patient safety was measured by recording the cumulative time that the insulin infusion was held for hypoglycemia and the number of times that the patient required an intravenous "rescue" dose of dextrose for a blood glucose of less than 2.5 mmol/l (45 mg/dl). Severe hypoglycemia was recorded as blood glucose readings of less than 2.2 mmol/l (40 mg/dl) or if any patient experienced any clinical symptoms of hypoglycemia (i.e. tachycardia, diaphoresis, seizures, etc.) regardless of the blood glucose concentration. Nursing compliance was measured by recording the number of protocol violations observed, defined as the number of times that the nurse intervened (i.e., adjusted the insulin infusion) not in accordance with the protocol or the prescribed titration scale. Nursing workload was indirectly measured by the frequency of blood glucose measurements performed.

 The Ottawa Hospital <input type="checkbox"/> Civic <input type="checkbox"/> General	L'Hôpital d'Ottawa PHYSICIAN'S ORDERS ORDONNANCES MÉDICALES Intensive Care Unit-Unité des soins intensifs Intravenous Insulin Infusion Protocol Protocole d'infusion d'insuline par voie intraveineuse																															
	Medication Allergies/Reactions	Substances or Food Allergies/Reactions																														
<p>NOTE: Not for patients with diabetic ketoacidosis (DKA) or hyperosmolar, nonketotic coma</p> <p>1. 50 units Humulin R insulin in 50 mL normal saline (concentration 1 unit/mL).</p> <p>2. If patient is not being fed (i.e. no enteral feeding or TPN)</p> <p style="padding-left: 20px;"><input type="checkbox"/> Infuse D50W at 16mL/hr <i>centrally</i> (i.e. approximately 200g dextrose/day)</p> <p>OR <input type="checkbox"/> If no central IV access, infuse D10W <i>peripherally</i> at 80 mL/hr</p> <p style="padding-left: 20px;">Once feeding is started, titrate the dextrose down by 4 mL/hr (for D50W) or by 20 mL/hr (for D10W) every hour until off</p> <p>3. INITIAL INFUSION RATE: Measure blood glucose stat, "<i>by glucose meter only</i>"; when glucose > 6.1 mmol/L, start initial insulin infusion as follows:</p> <table border="1" style="margin-left: 40px;"> <tr> <td>Blood glucose (mmol/L)</td> <td>< 6.1</td> <td>6.1-8</td> <td>8.1-12</td> <td>> 12</td> </tr> <tr> <td>Insulin infusion rate (units/hr)</td> <td>Hold</td> <td>1</td> <td>2</td> <td>3</td> </tr> </table> <p style="padding-left: 20px;">OR Start insulin infusion rate at ____ units/hr</p> <p>4. INSULIN SLIDING SCALE: Measure blood glucose from finger-sticks <i>by glucose meter only</i> q1-2 h and adjust insulin dose as follows: *</p> <p style="padding-left: 20px;">NOTE: If feeds are temporarily stopped (i.e. prior to surgery) the insulin infusion should also be stopped until feeds are restarted.</p> <table border="1" style="margin-left: 40px;"> <thead> <tr> <th>Blood Glucose (mmol/L)</th> <th>Insulin Infusion Adjustment</th> </tr> </thead> <tbody> <tr> <td>0 - 2.5</td> <td>Call MD. Stop insulin infusion. Give 25 mL of D50W and recheck blood glucose in 30 min. When blood glucose is > 6.1, restart insulin at 50% of the previous rate**</td> </tr> <tr> <td>2.6 - 3.9</td> <td>Stop insulin infusion. Check blood glucose in 30 minutes*** When blood glucose is > 6.1, restart insulin at 50% of the previous rate**</td> </tr> <tr> <td>4 - 4.4</td> <td>If current rate > 5 units/hr: decrease rate by 2 units/hr If current rate ≤ 5 units/hr: decrease rate by 0.5 units/hr.</td> </tr> <tr> <td>4.5 - 6</td> <td>Target range (no change)</td> </tr> <tr> <td>6.1 - 8</td> <td>If the blood glucose is lower than the last test: no change. If the blood glucose is the same or higher than the last test: increase rate by 0.5 units/hr</td> </tr> <tr> <td>8.1 - 10</td> <td>If the blood glucose is lower than the last test: no change. If the blood glucose is the same or higher than the last test: increase rate by 1 units/hr</td> </tr> <tr> <td>10.1 - 14</td> <td>If the blood glucose is lower than the last test: no change. If the blood glucose is the same or higher than the last test: increase rate by 1.5 units/hr</td> </tr> <tr> <td>14.1 - 22</td> <td>Increase rate by 2 units/hr. If the blood glucose is > 14.1 for 3 consecutive tests, increase the insulin rate by 50% (e.g. from 8 units/hr to 12 units/hr) and call Physician. Check blood glucose in 30 min.</td> </tr> <tr> <td>> 22</td> <td>Call MD</td> </tr> </tbody> </table> <p>5. If at any time the blood glucose decreases by > 50%, decrease the insulin rate by 50% (e.g. from 8 units/hr to 4 units/hr) and recheck blood glucose in 1 hour.</p> <p>6. If blood glucose has not decreased to less than 10 mmol/L 8 hours after initiation of the protocol, contact a physician for a bolus insulin order</p> <p>7. When patient is no longer being continuously fed (i.e. trying diet as tolerated), contact MD for subcutaneous insulin sliding scale order.</p> <p>* if blood glucose has been stable for 12 hours (i.e. insulin drip changing by only +/- 0.5 units/hr) can decrease frequency of glucoscans to q3-4h. If subsequent readings require changes in insulin drip of > +/-0.5 units/hr resume q1-2h glucoscan frequency.</p> <p>** true type 1 insulin dependant diabetics should not have the insulin infusion shut off completely. For these patients, decrease the infusion rate to 0.5 units/hr, rather than stopping the infusion.</p> <p>*** if blood glucose is the same or lower than the previous reading after holding the insulin infusion for 30 minutes, give 25 ml of D50W and recheck in 30 minutes.</p>			Blood glucose (mmol/L)	< 6.1	6.1-8	8.1-12	> 12	Insulin infusion rate (units/hr)	Hold	1	2	3	Blood Glucose (mmol/L)	Insulin Infusion Adjustment	0 - 2.5	Call MD. Stop insulin infusion. Give 25 mL of D50W and recheck blood glucose in 30 min. When blood glucose is > 6.1, restart insulin at 50% of the previous rate**	2.6 - 3.9	Stop insulin infusion. 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> 22	Call MD																															
Signature (Physician-Médecin)		Name printed-Nom imprimé	Date	Time-Heure																												
Signature (Nurse-Infirmière)		Date	Time-Heure	Signature (ACC-CCA)	Date	Time-Heure																										

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2-PHARMACY-PHARMACIE

3-NURSING-SOINS INFIRMIERS

Fig. 1 Intensive insulin therapy protocol

Statistical analysis

All continuous outcome variables were compared using the two-sided Student's *t*-test or the Mann-Whitney U test and the number of times dextrose rescue was required for hypoglycemia was compared using the chi-square statistic. Daily lowest and highest blood glucose measurements were compared using an analysis of variance for repeated measures. Probability values less than 0.05 were indicative of statistical significance. All statistics were calculated using SPSS version 10.0.5 (SPSS, Chicago, IL).

Results

Data were analyzed from a total of 100 patients: 50 in the control cohort and 50 in the interventional cohort. Seventy-three percent of the 100 patients were admitted to the ICU under a medical service with the most common reasons for admission being septic shock and respiratory failure. (Table 1) Almost all patients were mechanically ventilated and more than half were administered corticosteroids during the time that they received their insulin infusion. Approximately 70% of the patients had a previous history of diabetes, of which more patients in the control group required insulin therapy alone or in combination with other oral antidiabetic agents prior to admission.

There was significant heterogeneity among both the target blood glucose ranges and titration scales prescribed for patients in the control cohort. The targets ranged from lower limits as low as 4.0 mmol/l (72 mg/dl) to upper limits as high as 12 mmol/l (216 mg/dl). The width of these targets also varied in size from 2 mmol/l (36 mg/dl) to 6 mmol/l (108 mg/dl). The dextrose rescue administration threshold was almost universally set at less than 4 mmol/l (72 mg/dl). For comparison, the target range in the interventional cohort was almost always narrower (4.5–6.0 mmol/l [81–110 mg/dl]).

Target glucose concentrations were achieved more rapidly (11.3±7.9 vs 16.4±12.6 h; $p=0.028$) in the interventional cohort than in the control cohort, respectively (Table 2). The mean time spent within the target range was significantly greater among patients in the interventional cohort (11.5±3.7 h per day) than in the control cohort (7.1±5.0 h per day; $p<0.001$) despite the fact that the target range in the interventional cohort was narrower (Fig. 2). The intensive insulin protocol was found to be safe as evidenced by a four-fold reduction in patients experiencing severe hypoglycemia in the interventional cohort (4 vs 16%, $p=0.046$; Table 2). Fewer patients in the interventional cohort required intravenous dextrose "rescue" for hypoglycemia. However, the threshold for dextrose administration was lower in this cohort. The median number of hours that the insulin infusion was held for hypoglycemia was also shorter in the interventional cohort, however this did not reach statistical significance. (Table 2) Regardless, no patient in either group experi-

Table 1 Baseline characteristics. The data are reported as either median (range) or mean ± standard deviation

	Control group <i>n</i> =50	Intervention group <i>n</i> =50
Demographics		
Age (years)	63±15	62±13
Gender, male (%)	27 (54)	31 (62)
Weight (kg)	80±18	79±21
Admitting service (%)		
Medical	35 (70)	38 (76)
Surgical	15 (30)	12 (24)
Reason for Admission		
Respiratory failure	6	13
Cardiovascular event	3	3
Cerebrovascular event	8	0
Oncological emergency	1	0
GI bleed	2	2
Septic shock	12	17
Pneumonia	3	5
Other infection	2	3
Trauma	1	0
Cardiothoracic surgery	3	1
Abdominal surgery	5	4
Therapeutic modalities		
Mechanical Ventilation (%)	47 (94)	50 (100)
Vasopressors (%)	19 (38)	24 (48)
Corticosteroids (%)	26 (52)	32 (64)
TPN (%)	19 (38)	12 (24)
Illness severity		
APACHE II on admission	22.4±7.7	23.1±7.6
APACHE II at initiation of insulin	20.4±8.0	20.7±7.1
Comorbidities		
History of diabetes (%)		
Treated with insulin	7 (14)	2 (4)
Treated with oral anti-diabetic agents and/or diet control	29 (58)	32 (64)
No diabetes	14 (28)	16 (32)
ESRD at baseline (%)	6 (12)	2 (4)
Creatinine clearance	49±28	56±30
Liver failure at baseline (%)	2 (4)	5 (10)
Infection (%)	41 (82)	45 (90)
Length of ICU stay (days)	9	10
ICU survival (%)	22 (44)	32 (64)

GI gastrointestinal, TPN total parenteral nutrition, ESRD end stage renal disease

enced any clinically significant adverse events due to hypoglycemia (i.e., seizures, hemodynamic compromise).

The nursing workload was significantly increased, as approximately 35% more glucose measurements were required with the intensive insulin protocol (Table 2). Furthermore, 50 consecutive patients received insulin via the protocol in a 3 month period, whereas it took 6 months to identify the same number of consecutive patients receiving insulin infusions prior to the implementation of the protocol. At the same time, nurses were less likely to deviate from the protocol in the interventional cohort than the prescribed titration scales in the control cohort.

Table 2 Primary and secondary outcomes. The data are reported as either median (range) or mean \pm standard deviation

	Control group <i>n</i> =50	Intervention group <i>n</i> =50	<i>p</i> value
Glucose Control			
Baseline blood glucose (mmol/l)	14.0 \pm 4.4	12.4 \pm 4.2	0.102 ^a
Duration of insulin therapy (days)	7.6 \pm 5.2	7.8 \pm 6.1	0.876 ^a
Time to reach target blood glucose (h)	16.4 \pm 12.6	11.3 \pm 7.9	0.028 ^a
Number of hours per day within the target range	7.1 \pm 5.0	11.5 \pm 3.7	<0.001 ^a
Safety			
Number of hours the infusion was held per patient per day for hypoglycemia, median (range)	1.3 (0–14.1)	0.8 (0–5.6)	0.09 ^b
Number of patients experiencing severe hypoglycemia (<2.2 mmol/l ^c) (%)	8 (16)	2(4)	0.046 ^d
Number of times D50 W rescue given per day, median (range)	0.17 (0–1.2)	0 (0–0.91)	0.01 ^b
Nursing compliance/workload			
Number of protocol violations per day, median (range)	0.5 (0–2.6)	0.1 (0–1.1)	<0.001 ^b
Number of glucose readings per day	8.3 \pm 3.0	11.3 \pm 2.7	<0.001 ^a

^a Students *t*-test

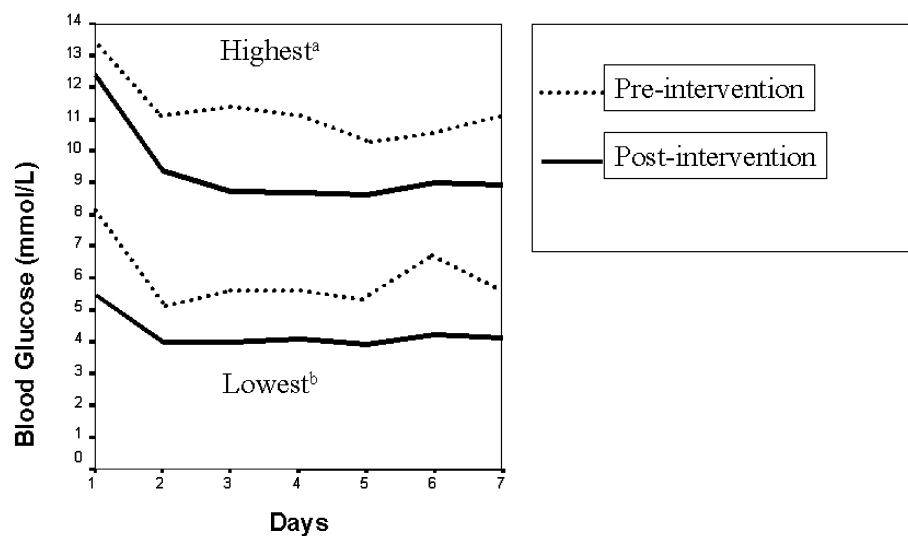
^b Mann-Whitney U test

^c Serum glucose values presented in mmol/l can be converted to mg/dl by dividing by 0.05551

^d Chi-square test

Fig. 2 Highest and lowest daily blood glucose readings.

^a $p=0.003$ (repeated measures analysis of variance), ^b $p<0.001$ (repeated measures analysis of variance)



Discussion

While the need for tighter glycemic control in critically ill patients is increasingly being recognized by ICU clinicians, no universal tool has been identified to facilitate intensive insulin therapy efficiently without compromising patient safety. Due to the nature of the intervention, institutional protocols that standardize prescribing and monitoring are the most appropriate strategy to ensure that the maximum benefit of the therapy is realized while ensuring patient safety [11]. At our institution, the need for a protocol to guide the prescribing and monitoring of insulin infusions was evident due to the significant

heterogeneity and dissatisfaction with the insulin infusions being prescribed. In this study our protocol achieved glycemic control more rapidly and improved the efficiency of intensive insulin therapy by 62% (time [h/day] spent within the target range: 7.1 \pm 5.0 [control] vs 11.5 \pm 3.7 [intervention]) while improving patient safety. This goal was achieved despite the fact that the target range in the interventional cohort was narrower than those used in the control cohort.

While the efficiency of such tools play a large role in dictating their role in clinical practice, the driving force for our institution in undertaking this study was improve the safety of insulin infusions in the ICU. We were unable

to eliminate the incidence of hypoglycemia completely, however this would be an unreasonable expectation of critically ill patients, who have significant fluctuations in metabolic and endocrine demands. Although the frequency of "rescue" doses of dextrose for hypoglycemia was significantly less in the intervention group, it must be recognized that the trigger for rescue therapy was different between the two groups. While the trigger for rescue therapy in the interventional cohort was a blood glucose of less than 2.5 mmol/l (45 mg/dl), the trigger in the control cohort was not standardized but was most frequently 4.0 mmol/l (72 mg/dl). Therefore, in order to have a better safety end point to compare between groups, hypoglycemic events were characterized as being severe using a lower threshold of less than 2.2 mmol/l (40 mg/dl) below which patients can experience neurological manifestations if hypoglycemia is prolonged [12].

Any hypoglycemic event whereby the patient experienced any objective symptoms or signs of hypoglycemia was classified as a severe hypoglycemic episode regardless of the serum glucose concentration. Sixteen percent of patients in the control cohort versus 4.0% in the interventional cohort had severe hypoglycemic events defined as a blood glucose less than 2.2 mmol/l. For comparison, 5.1% of patients in the study by Van den Berghe et al. experienced severe hypoglycemia by the same definition [9].

More diabetic patients in the control cohort required insulin for the management of diabetes prior to admission than those diabetics in the interventional cohort. It is unclear how many, if any, of these patients were true insulin-dependent diabetics. The concern with type I diabetes and insulin infusions is that when the protocol directs the nurse to interrupt the insulin infusion and administer a rescue dose of dextrose for a hypoglycemic reading, the true insulin-dependent diabetic will be unable to utilize the extra glucose and may be at risk for adverse events from intracellular hypoglycemia despite subsequent normoglycemic serum measurements. Although no adverse events were observed as a result of hypoglycemia in this study, our protocol mandates that intensive insulin therapy is inappropriate for patients with diabetic ketoacidosis or hyperosmolar, non-ketotic coma, and that true type I diabetics should not have the insulin infusion completely turned off during hypoglycemic episodes.

It is important to note that the population in this study was a mixed medical/surgical ICU population, whereas the population evaluated in the Van den Berghe et al. study, from which the intensive insulin therapy protocol was developed, was mainly a cardiac surgery population. Although intensive insulin therapy has not been extensively studied in critically ill medical patients, it has been suggested that this therapy would be most beneficial to surgical patients who have prolonged ICU lengths of stay with septic complications [1]. Arguably, these patients no longer represent the typical post-operative cardiac surgery

patient characterized by a short uncomplicated ICU course. Surgical patients who stay in the ICU for longer than 5 days often do so for the management of medical complications (i.e., infection, ventilatory and fluid management, etc.). Therefore, it is reasonable to assume that after 5 days in the ICU, the difference between a surgical patient and a medical patient may be negligible in terms of benefiting from tight glycemic control [1]. Although studies evaluating the role of intensive insulin therapy in critically ill medical patients are ongoing, it is difficult to disregard the magnitude of benefit shown in the Van den Berghe study with respect to mortality and morbidity.

Evidence-based protocol implementation has considerably influenced the prescribing practices in the ICU from ventilator management to titration of analgesia and sedation [11]. Protocols have been consistently shown to improve patient care, minimize unnecessary prescribing variability and reduce healthcare costs. Although this paper suggests that protocol implementation can improve glycemic control in the ICU, it is important to recognize that implementing a protocol alone can often be unsuccessful. This intervention would have likely been ineffective without an elaborate supportive plan. This is especially true with this protocol, as it significantly increases nursing workload and involves a controversial therapy.

In retrospect, the keys to successful implementation at our institution consisted of several crucial elements. Firstly, it was paramount that we had complete agreement from prescribing physicians that this intervention was worthwhile and would improve patient care, especially since the purpose of this study was to evaluate efficiency and safety, not efficacy. Secondly, and most importantly, nursing acceptance was the greatest challenge since clearly the institution of this protocol increases their workload. Nurses were repeatedly approached for constructive criticism and their ideas for improvement. These comments were evaluated and incorporated by a multidisciplinary team of physicians, nurses and pharmacists who were responsible for the protocol development. Finally, the prescribing physicians and nursing staff were the first ones to be informed of the results of the trial, which reinforced the value of the intervention and their contributions to the protocol development. It is possible that significant differences in the end points of this study may not have been realized had the control group been able to benefit from the same intensive educational and support program as the interventional group. It is, therefore, unlikely that simple protocol implementation alone will reproduce the results described in this study. This process will probably need to be individualized for each institution attempting to institute this or a similar protocol, but the key to successful implementation is the early involvement of all affected parties.

One of the limitations of our study is that the use of historical controls warrants special consideration in the

interpretation of results. Secondly, the before-after cohort design requires that a number of assumptions be made, specifically that the patient populations are similar and that no significant changes in practice other than the intervention are made that would confound the results. We did not identify any differences other than the fact that a pre-printed order form made it much easier to prescribe insulin infusions, leading to more frequent prescribing. There was no significant difference between the two cohorts in terms of severity of illness on admission or therapeutic modalities required. There were significantly more patients in the control cohort admitted for cerebrovascular events (8 vs 0). There were no significant changes in practice or studies that would influence the efficiency or approach to glycemic control. There was an observed difference in survival between the two cohorts in favor of the intervention group (44%

survival in the control group vs 64% in the intervention group), but the potential for statistical error given the small sample size limits the interpretation of this observation. Survival was not one of the outcomes evaluated in this study but this data is included out of interest, despite the fact that no significant generalizations or conclusions can be drawn.

Our results demonstrate that the use of an intensive insulin therapy protocol improves the efficiency and safety of insulin infusions at our hospital when compared to prescriber-dependent sliding scale insulin infusion. However, as with all protocols involving a complicated intervention, the key to successful implementation is the development of an educational and supportive program to ensure that such therapies are used appropriately and that the maximum benefit is realized.

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