Sliding Scale Regular Human Insulin for Identifying Critically Ill Patients Who Require Intensive Insulin Therapy and for Glycemic Control in those with Mild to Moderate Hyperglycemia

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Abstract: Two sliding scale regular human insulin (RHI) algorithms (SSI) were retrospectively evaluated to identify those who develop severe hyperglycemia (blood glucose (BG) $\geq$ 180 mg/dL) and for glycemic management of continuously-fed, critically ill trauma patients with mild to moderate hyperglycemia (BG 126 to 179 mg/dL). Assignment of low or high SSI was based upon anticipated severity of difficulty in glycemic control. BG was obtained every 3 to 6 hours. Target BG range was 70 to 149 mg/dL. Patients who were unable to achieve a BG < 150 mg/dL with SSI and who required a continuous intravenous RHI infusion were identified. Twenty-five of 121 patients (21%) failed SSI necessitating more intensive insulin therapy. The low and high intensity SSI groups exhibited a baseline BG of 123 $\pm$ 33 mg/dL and 164 $\pm$ 20 mg/dL (P = 0.001). Average BG for each group was 129 ± 14 mg/dL and 145 ± 21 mg/dL (P = 0.001). Each group spent 20 ± 4 and 16 ± 5 hours/day within the target BG range (P = 0.001), respectively. Mild hypoglycemia (BG 40 - 60 mg/dL) occurred in 11% and 7% of patients from each group (P = N.S.). Severe hypoglycemia (BG < 40 mg/dL) occurred in zero and two (5%) patients, respectively (P = N.S). SSI served as a useful technique to identify those requiring more intensive insulin therapy and was safe and efficacious for continuously-fed, critically ill trauma patients with mild to moderate hyperglycemia.

Keywords: Hyperglycemia, hypoglycemia, insulin, critical care, trauma, enteral nutrition, parenteral nutrition.

INTRODUCTION

Trauma patients frequently experience stress-induced hyperglycemia following injury [1]. Hyperglycemia in critically ill patients with traumatic injuries has been associated with increased morbidity and mortality [2-4]. Much research regarding achievement of glycemic control with continuous intravenous (IV) regular human insulin (RHI) infusion algorithms has been done since the landmark van den Berghe trial [5]. However, increased risk of severe hypoglycemia and worsened outcomes have been demonstrated with use of continuous IV RHI infusions when targeting low blood glucose concentrations (BG) of 80 to 110 mg/dL [6]. As a result, most guidelines recommend a target blood glucose (BG) range of 140 to 180 mg/dL for critically ill patients [7-9] although certain critically ill surgical subpopulations including our population with traumatic injuries have been shown to benefit from tighter BG control < 140 to 150 mg/dL [3,4,10,11].

Although continuous IV RHI infusions are effective in achieving glycemic control, they impart a substantial workload burden on nursing personnel, necessitating frequent BG determinations and infusion titrations usually on an hourly basis. In addition, continuous IV RHI infusions are associated with an increased risk for causing life-threatening hypoglycemia [12] and should be employed only when other viable techniques for glycemic control have failed or are not feasible. Therefore, it is impractical and potentially unsafe to prescribe a continuous IV RHI infusion for all patients in the intensive care unit (ICU) and it becomes necessary to triage which ICU patients will require a continuous infusion. Our approach has been to administer a continuous IV RHI infusion for patients with severe hyperglycemia (BGs $\geq$ 180 mg/dL) [13-15]. It is necessary to also have a surveillance technique to identify patients who develop severe hyperglycemia during incremental increases in carbohydrate intake from advancement of parenteral nutrition (PN) or enteral nutrition (EN) that were not experiencing hyperglycemia prior to nutrition therapy.

We have employed sliding scale RHI therapy (SSI) for identifying continuously-fed, critically ill patients who ultimately require aggressive insulin therapy and for treatment of mild to moderate hyperglycemia [16]. SSI is a method of prescribing a fixed amount of either subcutaneous or IV RHI based on the patient's BG at

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that sampled time. The procedure is typically repeated every 3 to 6 hours depending on the anticipated difficulty in achieving glycemic control. The sliding scale technique has been criticized by others and it has been suggested to completely abandon this methodology for hospitalized patients [17-19]. The recommendation for avoidance of SSI stems from studies where diabetic patients with severe hyperglycemia could not be effectively controlled [17-19]. Unfortunately, inattention was paid with respect to severity of the hyperglycemia, etiology (diabetes, stress-induced, or both), nutritional intervention, or the sliding scale dosing regimen itself. As a result, we suggest that lack of attention to these details for many of these studies was a potential cause of these poor results.

We propose that SSI therapy serves a useful technique in clinical practice when used appropriately. Specifically, the aims of this study were to ascertain the frequency of critically ill patients with traumatic injuries would require a continuous IV RHI infusion upon implementation of continuous EN or PN [14] that were not identified prior to initiation of nutrition therapy by use of BG monitoring with the SSI methodology; determine if SSI therapy could effectively manage those who exhibit mild to moderate hyperglycemia (BG 126 to 179 mg/dL); and finally, to evaluate if SSI therapy is safe (avoidance of severe hypoglycemia).

METHODS

Adult patients (> 17 years of age), who were admitted to the Presley Trauma Center of Regional One Health in Memphis, TN from January 2014 until April 2015 and referred to the NSS for continuous enteral nutrition (EN) or parenteral nutrition (PN) were evaluated for potential study inclusion. Patients without severe hyperglycemia (BG $\geq$ 180 mg/dL) receiving EN or PN were prescribed SSI coverage as part of their routine clinical care. Upon initiation of PN or EN, dextrose was eliminated from large volume parenteral solutions and IV medications whenever possible. Patients were excluded from this study if they: experienced severe hyperglycemia prior to initiation of EN or PN therapy and were given a continuous IV RHI infusion [13,14], received a non-NSS sanctioned SSI regimen prescribed by the primary service, required < 3 days of the NSS-directed SSI algorithm, received oral anti-diabetic agents or subcutaneous intermediate-acting Neutral Protamine Hagedorn (NPH) or long-acting (insulin glargine) insulin therapy, or had an ad-libitum oral intake during the observation period. Patients were classified as diabetic based on past medical history with receipt of anti-diabetic medications or a plasma hemoglobin A_{1c} concentration of > 6.5%.

Patients were preferentially given EN via a small-bore nasogastric/nasoenteric feeding tube. PN was given to patients unable to tolerate EN or when EN was contraindicated. Prior to initiation of EN or PN, elimination of dextrose from large volume IV solutions (e.g., D5 0.45% NaCl, D5 Ringer's lactate and small volume parenteral medications) was done whenever possible [16]. Patients fed enterally were given a reduced carbohydrate EN formula or a high protein/low calorie EN formula whenever a specialized EN formula (e.g., glutamine/fish oil-containing, fluid restricted, renal failure) was not indicated [20]. Dextrose intake from the PN formulation was restricted to < 4 to 5 mg/kg/min [21]. If EN or PN was temporarily or abruptly discontinued, a 5% dextrose containing IV fluid was administered at least at the same infusion rate as the EN or PN until nutrition therapy could be resumed in order to prevent hypoglycemia [14].

Patients were assigned by members of the NSS to receive one of two different SSI algorithms based on the perceived need for intensity of the insulin therapy. Patients without a history of diabetes mellitus (DM) and whose baseline BG prior to nutrition therapy was < 150 mg/dL initially received lower intensity SSI (Table **1**). Patients at higher risk of developing hyperglycemia (those with a history of DM or with stress-induced hyperglycemia and without severe hyperglycemia prior to initiation of nutrition therapy) were assigned to initially receive the higher intensity SSI (Table **1**). Patients receiving the low intensity SSI were given 2 units of IV RHI for every 25 mg/dL in BG above 125 mg/dL with a ceiling dose of 16 units for a BG > 300 mg/dL. Patients prescribed higher intensity SSI were given 3 units of IV RHI for every 25 mg/dL in BG above 125 mg/dl with a ceiling dose of 24 units for a BG > 300 mg/dL. Timing of initial BG determinations was done every 3, 4, or 6 hours and was empirically chosen by members of the NSS but could be adjusted and discontinued depending on patient response. Patients who were given the lower intensity SSI regimen had BG monitoring typically every 6 hours whereas those assigned the higher intensity regimen were prescribed BG monitoring every 3 to 4 hours. Point-of-care BG concentrations were determined by the glucose dehydrogenase method using the Accu-Chek® Inform II System (Roche Diagnostics Corporation, Indianapolis, IN, USA).

As the nutrition therapy was progressed towards goal intake, glycemic control was re-evaluated daily by

Table 1: Intravenous Sliding Scale RHI Algorithms*

BG mg/dL	Lower Intensity SSI	Higher Intensity SSI
< 40	Give 25 g D50W IV; call MD	Give 25 g D50W IV; call MD
40 - 69	Give 12.5 g D50W IV; call MD	Give 12.5 g D50W IV; call MD
70 - 125	0 units RHI	0 units RHI
126 - 150	2 units RHI	3 units RHI
151 - 175	4 units RHI	6 units RHI
176 - 200	6 units RHI	9 units RHI
201 - 225	8 units RHI	12 units RHI
226 - 250	10 units RHI	15 units RHI
251 - 275	12 units RHI	18 units RHI
276 - 300	14 units RHI	21 units RHI
> 300	16 units RHI; call MD	24 units RHI; call MD

*BG, blood glucose concentration; D50W, 50% dextrose in water; IV, intravenously; MD, on call resident physician; RHI, regular human insulin; SSI, sliding scale regular human insulin therapy; BG sampling frequency ranges from every 3 h to 6 h. BG (mmol/L) = BG (mg/dL) *0.0555.

the interdisciplinary members of the NSS as part of standard care [16] to ascertain if more intensive insulin therapy was needed. SSI failure was evidenced by escalation to either the higher intensity SSI (for the lower intensity SSI regimen), or initiation of NPH insulin with concurrent SSI, or a continuous IV RHI infusion with discontinuation of the SSI. If patients initially failed lower intensity SSI and were escalated to higher intensity SSI, data were collected for both groups, with each occurrence reported as a separate patient case. SSI was discontinued if BG was maintained in the target BG range (70 mg/dL to 149 mg/dL) at goal nutrition intake with minimal RHI intake (e.g., $\leq$ ~ 6 units/d).

The patients' electronic medical record and nutrition support service records were retrospectively reviewed for data retrieval. Data were recorded for a maximum of 8 days following initiation of SSI therapy. Day 0 was a partial day when the SSI and concurrent nutrition therapy was initiated. Serum laboratories were obtained from each patient at approximately 0100 daily and performed by the hospital laboratory as part of routine clinical care. The Injury Severity Score (ISS) [22] was scored by trained nurses according to the American Association for the Surgery of Trauma scales for anatomic injury severity and recorded within the data repository of the Tennessee trauma registry at Regional One Health.

Efficacy of the SSI algorithms was evaluated by mean BG and the number of hours per day spent within the target BG range. Time within or outside the target BG range was calculated based on an assumption that the BG concentration was reflective of the observed time period before the next BG determination. The SSI algorithm was considered successful if BGs were generally maintained within 70 to 149 mg/dL with no effort by NSS personnel to escalate the current SSI therapy to more aggressive RHI therapy. The SSI algorithm was considered a failure if therapy was escalated to the higher intensity SSI (from the lower intensity SSI regimen) or addition of subcutaneous intermediate-acting Neutral Protamine Hagedorn (NPH) insulin was added [23] or if the SSI was discontinued and a continuous IV RHI infusion [13,14] was initiated. The standard deviation of each patient's mean daily BG concentrations was used as a reflection of the patients' glycemic variability as described by others.[24,25] Safety was assessed by ascertaining the number of patients who experienced at least one episode of mild to moderate hypoglycemia (BG 40 to 69 mg/dL) or severe hypoglycemia (BG < 40 mg/dL). Any patient who experienced an episode of hypoglycemia was counted once regardless of the number of hypoglycemic episodes for determination of proportion of patients who experienced hypoglycemia.

Data were analyzed using SigmaPlot for Windows version 11.2 (Systat Software Inc., Point Richmond, VA). Data were evaluated for normality of distribution by using the Shapiro-Wilk test. Independent variables were compared by applying the Student's t test for unpaired variables if the data were normally distributed or the Mann-Whitney U test. Differences between groups for categorical data were analyzed by chi-square analysis. Continuous data were expressed as mean ± standard deviation. A p-value ≤ 0.05 indicated

statistical significance. The study was approved by and conducted in accordance with the guidelines set forth by the Institutional Review Board at the University of Tennessee Health Science Center and Research Office of Regional One Health (study reference number 14-03437-XM). Since all measurements were performed as part of the routine clinical care, non-interventional, and confidentiality procedures were maintained, the requirement for informed consent was waived.

RESULTS

Patient Characteristics

Four hundred and forty-six patients admitted to Regional One Health between January 2014 to April 2015 who were referred to the NSS for EN or PN were evaluated for potential inclusion with a total of 121 cases enrolled in the study (Figure **1**). Patients were most commonly excluded from the study if they were treated in non-trauma intensive care units, received non-NSS directed SSI therapy, given < 3 days SSI therapy, required NPH insulin or a continuous IV RHI infusion (Figure **1**). Thirty-two of the 446 screened patients (7%) required a continuous IV RHI infusion at the time of or prior to starting continuous nutrition therapy due to the presence of a BG $\geq$ 180 mg/dL. Patient age ranged from 18 to 85 years. Few patients were diabetic (12%), received corticosteroids (0.4%), or received vasopressors (0.6%). A significantly greater proportion of patients who received the higher intensity SSI were concurrently infected (48% vs. 18%; P = 0.001), had diabetes mellitus (24% vs. 6%; P = 0.013), and were older (54 years vs. 45 years; P = 0.016). Specialized nutrition support was initiated 3 ± 2 days following admission to the ICU. Other patient characteristics are given in Table **2**.

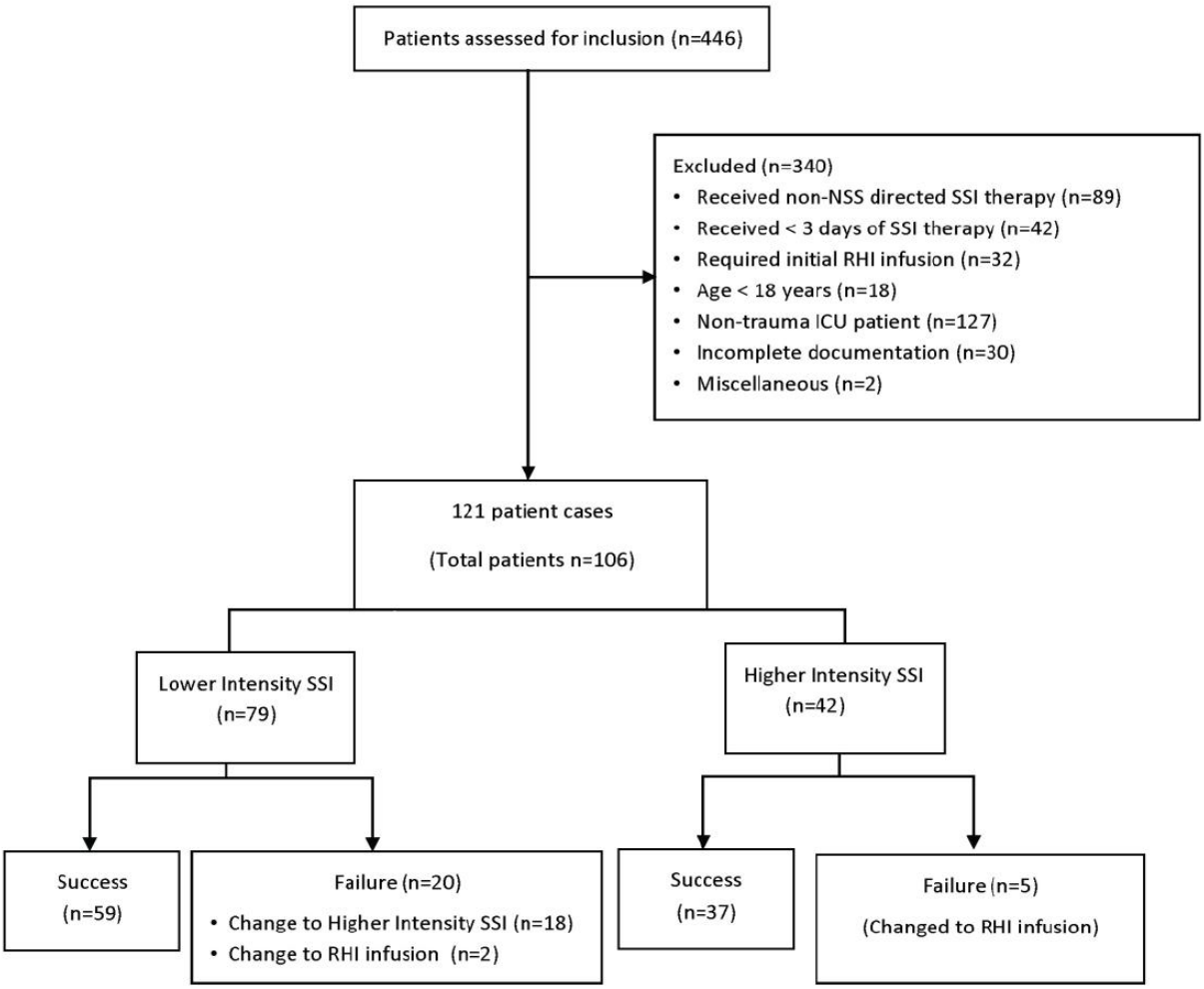

Figure 1: Patient selection and treatment.*

*ICU, intensive care unit; NSS, nutrition support service; RHI, regular human insulin; SSI, sliding scale insulin therapy. Two patients that received SSI classified as miscellaneous were due to have never received EN or PN (n=1) or readmission to the trauma intensive care unit and previously evaluated (n=1).

Efficacy and Safety of SSI Therapy

A total of 25 of 121 patients (21%) failed initial SSI therapy necessitating a more intensive insulin regimen. When stratified by SSI intensity, 20 of 79 patient cases (25%) failed lower intensity SSI and 5 of 42 patient cases (12%) failed higher intensity SSI. Seven of the 121 patients (6%) who initially received SSI therapy required a continuous intravenous insulin infusion. Four patients (5%) in the lower intensity group were assigned more frequent BG observations than every 6 hours (e.g., every 3 or 4 hours) as opposed to 30 (71%) patients in the higher intensity group (P = 0.001). Time spent in the target BG range was 16 ± 5 hours per day for the higher intensity SSI group and 20 ± 4 hours per day for the lower intensity SSI group (P = 0.001; Table **3**). The higher intensity group required 16 ± 10 units of RHI per day, while the lower intensity group required 4 ± 4 units of RHI per day (P = 0.001; Figure **2** and Table **3**). Twenty one of 106 non-diabetic

Table 2: Patient Characteristics*

Variable	Lower Intensity SSI	Higher Intensity SSI	P
N	79	42	
Age, y	45 ± 18	54 ± 18	0.016
Sex, Male/Female, n/n	63/16	30/12	0.420
Race			0.584
African American, n	27	10	
Caucasian, n	39	26	
Hispanic/Other, n	13	6	
Admit Diagnosis			0.532
Assault/fall	13	5	
GSW/KSW	12	4	
MVA	50	32	
Other	4	1	
Injury Severity Score	30 ± 14	26 ± 10	0.231
Traumatic brain injury, n	43 (54%)	31 (74%)	0.059
Concurrent infection, n	14 (18%)	20 (48%)	0.001
BMI, kg/m^2	28.5 ± 6.9	29.1 ± 5.6	0.611
Weight, kg	87 ± 23	89 ± 19	0.559
Diabetes mellitus, n	5 (6%)	10 (24%)	0.013
WBC, $cells/mm^3$	13.5 ± 14.5	13.5 ± 7.0	0.998
C-reactive protein, mg/L	25.4 ± 11.4	25.5 ± 10.0	0.984
Initial Tmax (°C)	38.6 ± 0.7	38.6 ± 0.6	0.658
Initial SUN, mg/dL	21 ± 14	15 ± 9.1	0.006
Initial serum creatinine, mg/dL	0.9 ± 0.4	1.0 ± 0.9	0.632
Prealbumin, mg/dL	8.7 ± 4.7	8.9 ± 3.8	0.859
Albumin, g/dL	2.5 ± 0.5	2.5 ± 0.3	0.684
EN/PN, n/n	68/11	35/7	0.346
Day NS started, d	3 ± 2	3 ± 2	0.560
Mortality, n	12 (15%)	9 (21%)	0.522
Hospital length of stay, d	30 ± 17	33 ± 20	0.410
ICU length of stay, d	18 ± 10	21 ± 15	0.307
Ventilator days, d	14 ± 10	19 ± 19	0.069

*BG, blood glucose concentration; BMI, body mass index; EN, enteral nutrition; GSW, gunshot wound; KSW, knife stab wound; ICU, intensive care unit; MVA, motor vehicle accident; N, number; NS, nutrition support; PN, parenteral nutrition, SSI, sliding scale regular human insulin therapy; SUN, serum urea nitrogen; Tmax, maximum temperature; WBC, white blood cell count. Serum C-reactive protein (nmol/L) = serum C-reactive protein (mg/L) * 9.524; serum creatinine (umol/L) = serum creatinine (mg/dL) * 88.4; serum urea nitrogen (mmol/L) = serum urea nitrogen (mg/dL)* 0.357.

Table 3: Glycemic Response to Sliding Scale RHI therapy*

Variable	Lower Intensity SSI	Higher Intensity SSI	P
N	79	42	
Carbohydrate intake, g/d	144 ± 145	137 ± 73	0.792
RHI intake, units/d	4 ± 4	16 ± 10	0.001
Baseline BG, mg/dL	123 ± 33	164 ± 20	0.001
BG during SSI, mg/dL	129 ± 14	145 ± 21	0.001
BG variability[a], mg/dL	13.2 ± 9.6	14.7 ± 11.3	0.124
#BGs/day	3.4 ± 1.6	5.2 ± 1.4	0.001
BG 70-149 mg/dL, h/d	20 ± 4	16 ± 5	0.001
BG ≥ 150 mg/dL, h/d	4 ± 4	8 ± 5	0.001
BG 40-69 mg/dL, h/d	0.1 ± 0.3	0.1 ± 0.5	0.735
BG < 40 mg/dL, h/d	0 ± 0	0.0 ± 0.2	0.109
Patients with BG 40-69 mg/dL, n	9 (11%)	3 (7%)	0.540
Patients with BG < 40 mg/dL, n	0 (0%)	2 (5%)	0.119

*BG, blood glucose concentration; h, hours; N, number; RHI, regular human insulin; SSI, sliding scale regular human insulin therapy. BG (mmol/L) = BG (mg/dL) *0.0555.
[a]Average standard deviation of the daily mean blood glucose concentration (mean SD ± SD).

patients (20%) compared to 4 out of 15 patients with diabetes (27%) failed initial SSI therapy (P = NS). Figure **2** illustrates mean BGs for both SSI groups remain close to the target range and appear to converge by day 4 of therapy. With an increase in carbohydrate intake as the EN or PN was progressed towards goal intake, RHI dosage also escalated which resulted in an overall decrease in BG for the higher intensity regimen. BGs for the lower intensity regimen appeared to be stable on a daily basis throughout the observation period with concurrent escalation of carbohydrate and RHI intake (Figure **2**).

Target BG concentrations were achieved for most patients in both SSI intensity groups without a significant amount of hypoglycemia. Three patients (7%) experienced at least one episode of mild hypoglycemia and two patients (5%) experienced an episode of severe hypoglycemia (BG < 40 mg/dL) in the higher intensity group. Nine patients (11%) from the lower intensity group experienced at least one episode of mild hypoglycemia and none experienced severe hypoglycemia. No patients had documented hypoglycemic symptoms.

DISCUSSION

Hyperglycemia is a common occurrence when providing specialized nutrition support to critically ill patients[26,27] and if left untreated, can lead to significant detrimental clinical outcomes [2,3,5,10]. In recent years, there has been much discussion regarding the optimal BG target range for critically ill patients, although keeping BG < 140 to 150 mg/dL has been associated with improved clinical outcomes in critically ill patients with severe traumatic injuries [3,5,6,10]. Continuous IV RHI infusions have historically been recommended to achieve glycemic control for critically ill patients [7]; however, they impart a significant demand upon nursing workload, require frequent monitoring and titration, and if not titrated correctly can cause profound hypoglycemia [6,15,28]. As a result, some institutions including ours [16], have routinely implemented the use of SSI therapy in patients without severe hyperglycemia whom require EN or PN. The intention for use of this mode of BG monitoring and insulin therapy has two primary purposes. First, it can be used to identify those patients who may experience severe hyperglycemia during advancement of carbohydrate-containing EN or PN. Secondly, SSI may also serve as a means to manage patients who exhibit mild to moderate hyperglycemia during continuous nutrition therapy.

Our data indicated SSI monitoring was successful in identifying patients who became hyperglycemic during advancement of nutrition therapy that were not severely hyperglycemic prior to initiation of PN or EN. SSI monitoring identified that 21% of patients whom the Nutrition Support Service prescribed SSI therapy needed to be transitioned to intensive insulin therapy. For those critically ill patients with traumatic injuries

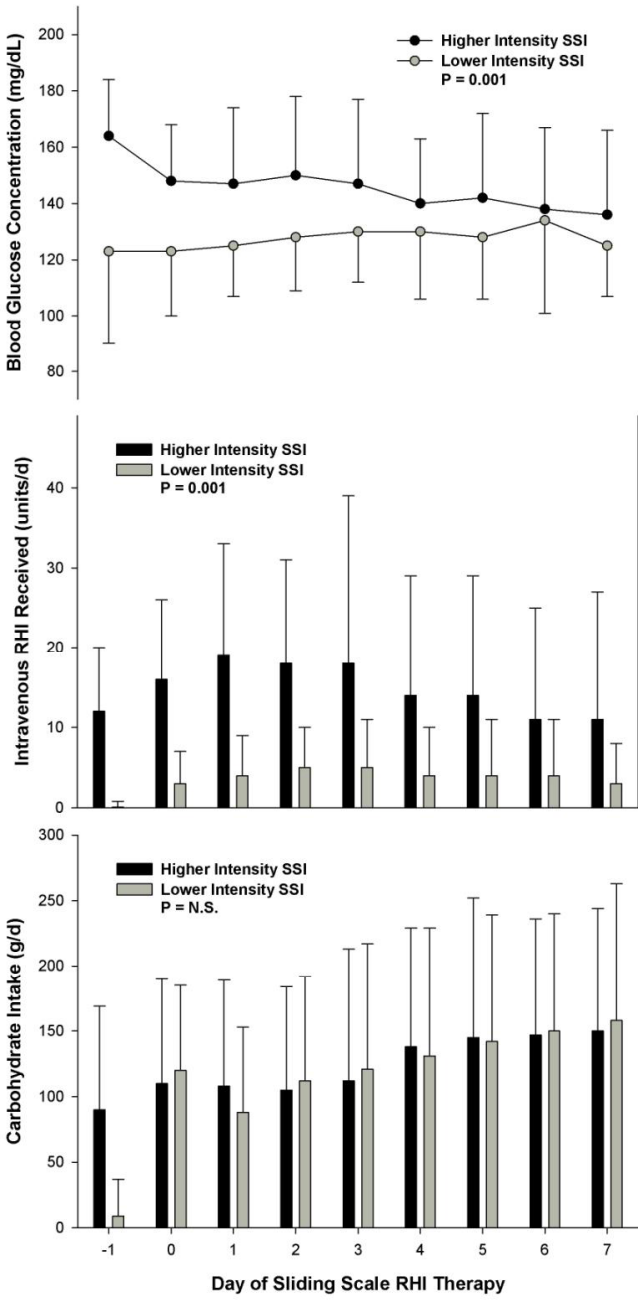

Figure 2: Glycemic response to the higher and lower intensity sliding scale regular human insulin therapy (SSI) during specialized nutrition support.

who only experienced mild to moderate hyperglycemia during continuous nutrition therapy, SSI was effective for the majority of patients. BG concentrations in the target range were achieved for an average duration of 20 and 16 hours daily for the lower and higher intensity SSI regimens, respectively (P = 0.001, Table **3**). However, despite a significantly lower duration of time spent in the BG target range by the higher intensity SSI group, these data should not be misinterpreted to indicate that the lower intensity SSI regimen was more efficacious than the higher intensity SSI algorithm. This disparity was attributed to differences in patient population between groups. Patients who received the higher intensity SSI algorithm had a significantly greater baseline BG (164 versus 123 mg/dL, P = 0.001) prior to initiation of nutrition therapy, a higher prevalence of diabetes mellitus (24% vs. 6%; P = 0.001), and a greater incidence of concurrent infection (48% vs. 18%; P = 0.001) compared to the lower intensity group, respectively (Tables **2** and **3**). Additionally, patients who received the higher intensity SSI regimen were prescribed more frequent BG monitoring, received more insulin, and had a trend towards more BG variability (Table **3**). Thus, the population who received the higher intensity SSI would have been anticipated to have greater difficulty in achieving glycemic control than the lower intensity regimen.

Our results for achieving glycemic control with SSI are divergent from the majority of literature that suggests SSI is ineffective in the management of hyperglycemia for hospitalized patients [17-19]. Our divergent data that favors utility in use of SSI may be explained by multiple factors. Many studies that indicated the lack of success with use of SSI were conducted in patients with severe hyperglycemia and with diabetes [29-35] or had a significant proportion of diabetics in their population [36-40]. In contrast to these studies, only 12% of our population who received SSI therapy had diabetes and none had severe hyperglycemia at initiation of PN or EN. Patients with diabetes and severe hyperglycemia prior to initiation of continuous nutrition therapy were given a continuous IV RHI infusion[14] and were excluded from study entry. The low incidence of diabetes mellitus in our study population is important to interpreting our data as critically ill, hyperglycemic patients with diabetes who receive continuous EN or PN exhibit more BG variability, require more insulin, and may not achieve similar effectiveness in glycemic control when compared to non-diabetics with stress-induced hyperglycemia [14]. In contrast to our study, the majority of published studies examining efficacy of SSI made no effort to exclude severely hyperglycemic patients with the exception of some studies excluding those with diabetic ketoacidosis or hyperosmolar non-ketotic coma. Studies reporting failure of SSI therapy included patients whose baseline BG exceeded 180 mg/dL, with the average initial BG concentrations ranging from 178 mg/dL to 229 mg/dL [29,30,32,33,36,38-40] in contrast to 123 mg/dL and 164 mg/dL for our SSI dosing algorithms.

All patients in this study were ICU patients and required intense BG monitoring every 3 to 6 hours

while nutrition therapy was being initiated and advanced to goal. In contrast, some previous studies excluded patients in the ICU [32,33,36,39] with less frequent BG monitoring and less insulin dosing opportunities to reduce hyperglycemia [35,38,41]. The most commonly reported BG determination interval for SSI dosing from the literature is every 6 hours [29-31,35,37,39]. With more frequent BG monitoring, patients who fail SSI and who require more intensive insulin therapy can be identified sooner. In addition, patients can receive RHI doses more frequently in an effort to maintain glycemic control.

The success or failure of SSI therapy may also be attributable to the dosage design of the SSI regimen itself. Most published SSI algorithms do not prescribe short-acting insulin therapy until the BG is greater than 150 or 200 mg/dL [29-31,35,37,39]. The usual initial dosage of RHI or insulin aspart in other published algorithms is 2 units and the dosage is escalated by an additional 2 units for every 50 mg/dL increase in BG above the baseline BG intervention range [29-31,35,37,39]. In contrast, the SSI algorithms employed in our practice are more intensive with incremental increases in RHI dosage by either 2 or 3 units for every 25 mg/dL above a BG of 125 mg/dL (Table **1**). Therefore, in addition to our stringent patient selection and exclusion criteria for who receives SSI, our efficacy in glycemic control may also be partially attributed to more intensive insulin dosing and BG monitoring.

Safety of our SSI algorithms are evident by the low incidence of hypoglycemia (Table **3**). None of the patients in the lower intensity SSI and two patients (5%) in the higher intensity SSI group experienced an episode of severe hypoglycemia (BG < 40 mg/dL). It may be argued that some patients in the low intensity SSI may not have required insulin therapy due to the 11% incidence of mild to moderate hypoglycemia (BG 40 to 69 mg/dL) despite receiving only an average of 4 units/day. These data indicate that it is difficult to anticipate who will or will not require insulin therapy during advancement of the carbohydrate-containing nutrition regimen for this population, as 21% of patients whom SSI therapy was thought to be adequate actually required more intensive insulin therapy and 10% of all patients receiving SSI therapy experienced an episode of mild to moderate hypoglycemia.

This study has limitations. Data were collected retrospectively and decisions regarding selection for initial SSI therapy and/or escalation in insulin therapy were at the careful discretion of the interdisciplinary NSS. Patients with severe hyperglycemia at initiation of PN or EN were excluded from the analysis due to early identification and provision of more aggressive insulin therapy. The rationale for receiving less than 3 days of SSI without escalation to more aggressive insulin therapy was most likely due to achievement of goal nutrition intake without the need for a significant amount of insulin supplementation as it is common practice to discontinue SSI therapy under these circumstances at our institution. Eighteen patients who failed the lower intensity SSI and given the higher intensity SSI group resulted in inclusion in both groups which may be a source of error in the data. The assumption was made that a single BG concentration reflected the BG for the entire time period until the next BG determination. This assumption may be erroneous particularly if the patient was given RHI therapy in response to the BG concentration. Not all patients achieved BG concentrations within the target range for the entire day. The low and high intensity SSI regimens were able to achieve target BG concentrations for a mean of 20 and 16 hours daily, respectively. However, this duration of glycemic control is favorable considering that even a continuous IV RHI infusion or subcutaneous NPH with SSI averages 20 and 15 hours daily, respectively, in a continuously-fed, trauma ICU population with severe hyperglycemia [14,23]. Finally, it is unknown whether use of SSI for controlling mild to moderate hyperglycemia improves clinical outcomes during critical illness following traumatic injury and requires further study.

CONCLUSIONS

Despite bias against the use of SSI in inpatient settings, there is no evidence to refute the role of SSI therapy as a means for identifying critically ill patients who develop severe hyperglycemia (BG > 180 mg/dL) requiring intensive insulin therapy or for management of mild to moderate hyperglycemia during continuous EN or PN therapy. Prescribing SSI ensures that BG concentrations are assessed frequently to facilitate evaluation for initiation of change in the current glycemic control methodology to a more aggressive regimen. For those who do not require escalation to a more aggressive regimen, our intermittent RHI sliding scale algorithms are safe and effective for controlling mild to moderate hyperglycemia for the majority of critically ill patients with traumatic injuries who require continuous nutrition therapy. SSI is a viable mode of therapy for achieving glycemic control in patients who are not at highest risk for severe hyperglycemia.

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