Published in final edited form as:
Surgery. 2008 October ; 144(4): 629–637. doi:10.1016/j.surg.2008.07.001.

Intensive Insulin Therapy is Associated with Reduced Infectious Complications in Burn Patients

Mark R. Hemmila, MD
Department of Surgery, University of Michigan Medical Center, Ann Arbor, Michigan

Michael A. Taddonio, BS
Department of Surgery, University of Michigan Medical Center, Ann Arbor, Michigan

Saman Arbabi, MD, MPH
Department of Surgery, Harborview Medical Center, University of Washington, Seattle, Washington

Paul M. Maggio, MD, MBA
Department of Surgery, Stanford University School of Medicine, Stanford, California

Wendy L. Wahl, MD
Department of Surgery, University of Michigan Medical Center, Ann Arbor, Michigan

Abstract

Background—Intensive insulin therapy to control blood glucose levels has reduced mortality in surgical, but not medical intensive care unit (ICU) patients. Control of blood glucose levels has also been shown to reduce morbidity in surgical ICU patients. There is very little data for use of intensive insulin therapy in the burn patient population. We sought to evaluate our experience with intensive insulin therapy in burn injured ICU patients with regard to mortality, morbidity, and use of hospital resources.

Study Design—Burn patients admitted to our American College of Surgeons Level 1 verified Burn Center ICU from 7/1/2004 to 6/30/2006 were studied. An intensive insulin therapy protocol was initiated for ICU patients admitted starting 7/1/2005 with a blood glucose target of 100–140 mg/dL. The two groups of patients studied were control (7/1/2004 to 6/30/2005) and intensive insulin therapy (7/1/2005 to 6/30/2006). All glucose values for the hospitalization were analyzed. Univariate and multivariate analyses were performed.

Results—152 ICU patients admitted with burn injury were available for study. No difference in mortality was evident between the control and intensive insulin therapy groups. After adjusting for patient risk, the intensive insulin therapy group was found to have a decreased rate of pneumonia, ventilator-associated pneumonia, and urinary tract infection. In patients with a maximum glucose value > 140 mg/dL, the risk for an infection was significantly increased (OR 11.3, 95% CI 4–32, *p*-value <0.001). Presence of a maximum glucose value > 140 mg/dL was associated with a sensitivity of 91% and specificity of 62% for an infectious complication.

Manuscript Correspondence: Mark R. Hemmila, MD Department of Surgery, University of Michigan Medical Center 1B407 University Hospital 1500 E. Medical Center Drive, SPC 5033 Ann Arbor, MI 48109-5033 mhemmila@umich.edu Business Tel: (734) 936-9666 Home Tel: (734) 761-7094 Fax: (734) 936-9657.

Conclusion—Intensive insulin therapy for burn injured patients admitted to the ICU was associated with a reduced incidence of pneumonia, ventilator associated pneumonia, and urinary tract infection. Intensive insulin therapy did not result in a change in mortality or length of stay when adjusting for confounding variables. Measurement of a blood glucose level > 140 mg/dL should heighten the clinical suspicion for presence of an infection in patients with burn injury.

INTRODUCTION

A prominent component of the stress response to burn injury is hyperglycemia.[1] This sympathetic nervous system mediated elevation in blood glucose has traditionally been treated expectantly given the belief that this was a beneficial "fight or flight" stress response to injury. In 2001, publication of the first Van den Berghe paper challenged the conventional wisdom that stress related elevations in blood glucose were not harmful.[2] The study demonstrated a reduction in mortality from 8.0% to 4.6% for mechanically ventilated surgical intensive care unit patients treated with intensive insulin therapy to control hyperglycemia. The two groups studied were the intensive insulin therapy group who received intravenous insulin to maintain a blood glucose level between 80 and 110 mg/dL and a control group who received infusion of insulin if the blood glucose level exceeded 215 mg/dL with a target range of 180–200 mg/dL. A reduction in morbidity was also demonstrated with intensive insulin therapy patients experiencing reduced rates of acute renal failure, hyperbilirubinemia, and sepsis.

The patients in the Van den Berghe study represented a mixed surgical intensive care unit population with only 4% being multiple trauma or burn patients. The positive results from this prospective randomized trial triggered interest in applying intensive insulin therapy to other groups of critically ill patients. However, when intensive insulin therapy was studied in a medical intensive care unit the results were varied with mortality increasing in some groups and decreasing in others.[3] Because of this difficulty in extrapolation of the reduction in mortality and morbidity seen in a mixed group of surgical patients who received intensive insulin therapy to other patient populations considerable interest has arisen in studying the effect of intensive insulin therapy in trauma and burn patients.

Minimal data on hyperglycemia in burn patients is currently available, and what data exists is primarily in the pediatric burn population. In pediatric patients with ≥ 60% total body surface area burn, poor glucose control (≥ 40% of all plasma glucose values ≥ 140 mg/dL) was associated with bacteremia, fungemia, reduced skin graft take, and increased mortality.[4] Intensive insulin therapy to maintain blood glucose levels of 90 to 120 mg/dL in pediatric patients with a ≥ 30% total body surface area burn has been compared to "conventional insulin therapy".[5] In the intensive insulin therapy group there was a reduced rate of urinary tract infections and a trend was seen towards the experimental group having increased survival in a logistic regression model. Because there is very little data for use of intensive insulin therapy in the burn patient population, especially with regard to adult patients, we sought to evaluate our experience with intensive insulin therapy in burn injured ICU patients with regard to mortality, morbidity, and use of hospital resources.

METHODS

Patient Data

From July 1, 2004 to June 30, 2006, 152 burn patients were admitted to the Burn intensive care unit on the University of Michigan Burn Service. Patients with concomitant burn and trauma injuries were excluded. Those patients with desquamating skin diseases such as toxic epidermal necrolysis or calciphylaxis were also excluded. All blood glucose values recorded either at the bedside or in the central chemistry laboratory were available for analysis from

the computerized medical record. Demographic and outcome data were obtained from the Trauma Registry (NTRACS v3.4) and confirmed on retrospective chart review. Abstracted data included age, gender, hospital length of stay, intensive care unit length of stay, ventilator days, % total body surface area burn, % 3rd degree burn, % 2nd degree burn, type of burn (scald, flame, chemical, etc.), presence of inhalation injury, and disposition.

For infectious complications, the presence of a ventilator-associated pneumonia (VAP) diagnosed by bronchoalveolar lavage, bloodstream infection or urinary tract infection were defined using Centers for Disease Control (CDC) definitions. These infections were collected prospectively by our Infection Control Liaison and verified on retrospective chart review. Superficial and deep wound infections, organ space infections, were classified by the National Surgical Quality Improvement Project (NSQIP) definitions. Quantitative wound culture results were considered positive if they grew ≥ 1 × 105 cfu/g of tissue. All infectious complications and microbiology results were reviewed and confirmed from the medical record.

For the time period from July 1, 2004 to June 30, 2005, the Burn ICU had a suggested insulin drip protocol for use in ICU patients with sustained blood glucose levels (> 12 hours) over 150 mg/dL. A mandatory hospital-wide policy for use of insulin drips for mechanically ventilated patients in the ICU, with a blood glucose > 140 mg/dL, was formally initiated on July 1, 2005 in the Burn ICU. The goal was maintance of a blood glucose level between 100–140 mg/dL with a target of 120 mg/dL. Adjustments to the insulin drip rate in units/hour were based on hourly blood glucose checks and a clinical nomogram. If the blood glucose was between 100–140 mg/dL for three consecutive hours and changing < 40 mg/dL per hour, then blood glucose checks were done every two hours. The policy was begun in the winter/spring of 2005 and an educational program was conducted for the nurses, technicians, and physicians prior to formal implementation of the intensive insulin therapy policy. In non-intubated patients or following extubation, insulin drip therapy or sliding scale was used as necessary to maintain a target blood glucose level of < 140 mg/dL until the patient left the ICU or became floor status. For this study the patients admitted between July 1, 2004 to June 30, 2005 served as the historical control group and the patients admitted between July 1, 2005 to June 30, 2006 comprised the intensive insulin therapy group.

Statistical Analysis

Data were compared using both univariate and multivariate statistical measures. Continuous variables were analyzed using an unpaired two-tailed Student's *t*-test for data with a normal distribution. Continuous data exhibiting a skewed distribution such as length of stay were analyzed using the Wilcoxon Rank Sum test. Patients who died were excluded from hospital length of stay calculations. Discrete variables were compared using a Chi-square analysis. Multivariate analysis of outcome variables were performed using multiple logistic or linear regression and adjusting for confounding variables such as age, gender, % total body surface area burned, presence of inhalation injury, and history of diabetes. Database management and querying were performed using Microsoft Access software (Microsoft Corporation, Redmond, WA). All statistical analysis was performed using STATA SE 9.2 software (Stata Corporation, College Station, TX). Results are presented as mean values ± standard deviation unless otherwise noted. Statistical significance was defined as a p-value ≤ 0.05. Approval for this study was obtained from the University of Michigan Health System Institutional Review Board.

RESULTS

Patient demographics

The historical control group consisted of 81 burn patients who were treated in the ICU between July 1, 2004 and June 30, 2005. A hospital-wide policy regarding use of insulin drips for mechanically ventilated patients in the ICU was formally initiated on July 1, 2005. The intensive insulin therapy group consisted of 71 burn patients who were admitted to the ICU between July 1, 2005 and June 30, 2006. Data describing the demographics for various patient characteristics between these two groups is listed in Table 1. Patient characteristics in the control and treatment group were reasonably well matched.

Glucose values

Following institution of the intensive insulin therapy protocol, the average number of glucose checks per patient did not change (Table 2). There was no difference in the average admission glucose value between the two groups. The mean of all measured glucose values obtained for the control and intensive insulin therapy patient groups was different, 142 vs. 130 mg/dL ($p<0.0001$). To examine this result further, a mean daily patient glucose value was calculated. There was a difference in the proportion of days that the mean daily patient glucose was greater than 140 mg/dL for the two groups, 35% for the control and 22% for intensive insulin therapy group ($p<0.0001$). The average of the mean daily patient glucose was 135 vs. 129 mg/dL for the control vs. intensive insulin therapy groups ($p=0.0007$). However, calculating a mean glucose for each patient for their entire hospital stay and comparing these values between the control and intensive insulin therapy groups demonstrated no calculated difference in the mean patient glucose level, 127 vs. 126 mg/dL ($p=0.9$).

A maximum measured glucose value for each patient during their hospital stay was obtained. There was no difference between the control and intensive insulin therapy groups for the maximum measured glucose values. There was also no difference in the proportion of days that the maximum patient glucose was greater than 140 mg/dL (54 vs 51%, $p=0.3$). However, there was a difference in the proportion of days that the maximum patient glucose was greater than 200 mg/dL (17 vs 11%, $p=0.006$).

Hypoglycemia was defined as a glucose value less than 70 mg/dL and severe hypoglycemia as a glucose value less than 40 mg/dL. The proportion of days in which a patient experienced a measured hypoglycemic episode out of the total number of days that a glucose value was checked was 4.5% for the control and 6.4% for the intensive insulin therapy group ($p=0.09$). A total of 7 episodes of severe hypoglycemia occurred in the control group and 3 events occurred in the intensive insulin therapy group ($p=0.7$). No adverse clinical sequela was noted in any of the patients following the episodes of measured severe hypoglycemia.

Clinical outcomes

Mortality was 9% for the control group and 7% for the intensive insulin therapy group. No difference was appreciated in mortality between the two groups in both univariate and multivariate analysis. The mean hospital stay decreased from 17 to 10 days ($p=0.01$) when intensive insulin therapy was initiated, however the statistical difference in univariate analysis did not hold up when multivariate analysis was performed adjusting for age, gender, % total body surface area burned, presence of an inhalational injury, and history of diabetes (Table 3). Similarly, there was no difference in multivariate analysis for mean ICU length of stay or mean ventilator days when adjusted for confounding variables.

The control group of burn patients experienced proportionately more infectious complications when compared to the intensive insulin therapy group (Table 3). In univariate analysis this was true for any infection, pneumonia, ventilator-associated pneumonia, bacteremia, and urinary tract infection. When adjusted for potential confounding variables a difference in rate of infection between the control and intensive insulin therapy groups was found for pneumonia, ventilator-associated pneumonia, and urinary tract infection.

Mortality and infectious risk

Mortality risk for admission, mean patient, maximum, and minimum glucose values obtained throughout the hospital stay for each patient was assessed. In univariate analysis admission glucose > 200 mg/dL, mean patient glucose > 140 mg/dL and maximum glucose > 200 mg/dL were all associated with a significant risk of mortality (Table 4). Minimum glucose < 70 mg/dL was not associated with an increased risk of mortality. None of these parameters were found to correlate with an increased risk for mortality in burn patients when adjustments were made for age, gender, TBSA burn, and inhalational injury using multivariate analysis.

To further asses the affect of elevated blood glucose on infections, we analyzed the results by stratifying patients by maximum measured glucose values. Experiencing an elevation of blood glucose greater than 200 mg/dL was associated with a significant risk of infectious complications in burn patients (Table 5). This was true for quantitative wound culture > 10^5 cfu/g, pneumonia, ventilator-associated pneumonia, and bacteremia.

Burn patients who had at least one measured maximum glucose value > 140 mg/dL also had a significantly increased risk of infection (OR 11.3, 95% CI 4–32, p-value < 0.001). Of a total of 59 patients who had a maximum glucose ≤ 140 mg/dL, 53 did not experience an infection, and six had a bacterial infection diagnosed. Ninety-three burn patients had at least one maximum glucose value > 140 mg/dL during their hospitalization. Of these patients, 32 did not experience an infection, and 61 patients did have an infectious complication requiring antimicrobial treatment. Therefore, the presence of a maximum glucose value > 140 mg/dL was associated with a sensitivity of 91% and a specificity of 62% for an infectious complication in burn patients treated in the ICU.

DISCUSSION

The use of intensive insulin therapy to maintain a target glucose level 100–140 mg/dL reduced infectious complications in our burn patients. A glucose value > 140 mg/dL is a non-specific marker of potential infection and should heighten clinical suspicion. In addition, glucose values that exceed 200 mg/dL are associated with a substantially increased risk for the following infections in burn patients: quantitative wound culture > 10^5 cfu/g, pneumonia, ventilator-associated pneumonia, and bacteremia. The use of intensive insulin therapy was not associated with a reduction in mortality or use of hospital resources by burn patients.

This study is limited by the fact that it is an observational study and not a prospective randomized clinical trial. The control and intensive insulin therapy groups were well matched however, and the study was conducted over two years, which is a short time period. It was not surprising that no difference in mortality was found as the study would need at least 10-fold more patients to have a power of 0.8 to detect a 40% reduction in mortality. The number of patients who died in each group was small (<9%) and therefore no conclusions can be reached regarding the effect of intensive insulin therapy on burn patients with regard to mortality. Another limitation is that our intensive insulin therapy protocol targeted a blood glucose value of 100–140 mg/dL rather than “tight glucose control”

between 80 and 110 mg/dL as described in other studies. Our hospital was not comfortable with an insulin infusion protocol that would target a blood glucose level of < 110 mg/dL due to the risk of profound hypoglycemia.

Hyperglycemia in burn patients is multifocal in etiology. These patients have increased hepatic gluconeogenesis, resistance to the action of insulin to clear glucose into muscle, and the ability of insulin to act as a muscle protein anabolic agent is markedly reduced.[6,7] Harmful effects of hyperglycemia have been demonstrated in prior animal studies in which elevated glucose levels resulted in impairments of immune function and wound healing.[8,9] Elevations in plasma glucose impair immune function by altering cytokine production from macrophages, reducing lymphocyte proliferation, and attenuating the intracellular bactericidal activity of leukocytes.[10–13] At glucose levels > 220 mg/dL immunoglobulins become glycosylated causing a reduction in opsonin activity.[8] In a rabbit burn model, mortality was reduced in animals that maintained normoglycemia independent of insulin levels.[14] Maintaining normoglycemia also prevented endothelial dysfunction, as well as liver and kidney injury. In these hyperglycemic burned rabbits, leukocyte dysfunction was present and could be rescued by insulin treatment.

Intensive insulin therapy exerts an antiinflammatory effect on patients by reducing levels of C-reactive protein, improving the systemic inflammatory response, and suppressing the hepatic acute phase response.[15,16] Insulin therapy also counteracts the adverse effect of low mannose-binding lectin levels. In diabetic patients who underwent major noncardiac surgery, good preoperative glycemic control defined as a HbA(1c) level less than 7% was associated with a decreased rate of postoperative infectious complications (OR 2.1, 95%CI 1.2–3.7).[17] Early hyperglycemia in trauma patients (glucose ≥ 200 mg/dL) measured during day 1 or 2 following injury was found to be an independent predictor of infection in a multiple regression analysis that controlled for the effect of age, injury severity score, and base deficit.[18] These findings were not true for cutoffs defining hyperglycemia as ≥ 110 mg/dL or ≥ 150 mg/dL. In our study of burn patients we established a similar result with presence of an elevated glucose level > 200 mg/dL being associated with a significant risk of infectious complications.

For burn patients, the incidence of split thickness skin graft take has been found to be reduced from 85% in patients with normoglycemia to 60% in patients with hyperglycemia.[19] Within the pediatric burn population there has been identified a significant association between persistent and severe hyperglycemia to a reduction in skin graft take.[4] Gore, et al noted that pediatric burn patients who had poor glucose control, defined as ≥ 40% of all plasma glucose values ≥ 140 mg/dL, also had an increased incidence of fungemia and mortality. Maintenance of euglycemia (serum glucose 100 to 140 mg/dL) in pediatric burn patients resulted in improved lean body mass, and less peripheral muscle wasting.[20] Infusion of insulin ≥ 1.5 μU/kg/min to maintain euglycemia reduced hepatic acute phase protein levels after a severe burn injury.[21] This effect was most pronounced at days 21 and 28 following thermal injury. The burn patients in our study that received intensive insulin therapy had a reduced rate of bacteremia (4 versus 14%), but this difference was not statistically significant in multivariate analysis. We did find that a glucose level > 200 mg/dL was associated with an odds-ratio of 8.8 for bacteremia among all of the patients studied. We did not collect formal data on graft take, patient nutritional status, or draw blood samples to measure immune response so no conclusions can be made about our results in these areas relative to other studies.

In addition to the known toxic effect of elevated glucose levels the presence of hyperglycemia may also be a marker for infection. Neonates with invasive fungal infections had higher rates of hyperglycemia (serum glucose > 215 mg/dL) in the first month of life

than a control group with late onset sepsis caused by bacteria (47% vs. 24%, p=0.008).[22] Carbohydrate intolerance episodes typically occurred 72 hours prior to the onset of an invasive fungal infection. In trauma patients the hourly and 24-hour insulin requirements significantly increased from the time before to the time after developing a positive bronchoalveolar lavage culture in patients with pneumonia.[23] The 24-hour insulin requirement increased from 7.6 units in the non-pneumonia group to 26.2 units in the pneumonia group. Our findings that burn patients who had a glucose value > 140 mg/dL experienced a significant increased risk of infection lends further support to the hypothesis that hyperglycemia may be a marker of infection. It is conceivable that in the future an algorithm could be created that evaluates dynamic glucose levels and changes in insulin infusion rates over time to predict when a clinical alert should be sent to the physician to perform a bedside physical exam and initiate an infection workup. Suspicion and prompt diagnosis of pneumonia is important because patients who receive adequate and timely antibiotic therapy based on bronchoalveolar lavage results when a ventilator-associated pneumonia is suspected have a markedly improved rate of survival (62% vs. 9%).[24]

CONCLUSIONS

Intensive insulin therapy in burn patients to a target of 100–140 mg/dL reduced infectious complications in burn patients. Presence of hyperglycemia was found to be a non-specific marker of infection in burn patients and increased the risk of infections such as quantitative wound culture > 10^5 cfu/g, pneumonia, ventilator-associated pneumonia, and bacteremia.

Acknowledgments

Financial Support: Mark R. Hemmila was supported by a Central Surgical Association Foundation Enrichment Grant and an American Association for the Surgery of Trauma Research and Education Foundation Scholarship.

ABREVIATIONS

ICU	Intensive Care Unit
TBSA	Total Body Surface Area Burn
VAP	Ventilator Associated Pneumonia

REFERENCES

1. Gore DC, Chinkes DL, Hart DW, Wolf SE, Herndon DN, Sanford AP. Hyperglycemia exacerbates muscle protein catabolism in burn-injured patients. Crit Care Med. 2002; 30:2438–2442. [PubMed: 12441751]
2. Van den Berghe G, Wouters P, Weekers F, Verwaest C, Bruyninckx F, Schetz M, et al. Intensive insulin therapy in critically ill patients. N Engl J Med. 2001; 345:1359–1367. [PubMed: 11794168]
3. Van den Berghe G, Wilmer A, Hermans G, Meersseman W, Wouters PJ, Milants I, et al. Intensive insulin therapy in the medical ICU. N Engl J Med. 2006; 354:449–461. [PubMed: 16452557]
4. Gore DC, Chinkes D, Heggers J, Herndon DN, Wolf SE, Desai M. Association of hyperglycemia with increased mortality after severe burn injury. J Trauma. 2001; 51:540–544. [PubMed: 11535907]
5. Pham TN, Warren AJ, Phan HH, Molitor F, Greenhalgh DG, Palmieri TL. Impact of tight glycemic control in severely burned children. J Trauma. 2005; 59:1148–1154. [PubMed: 16385293]
6. Jahoor F, Herndon DN, Wolfe RR. Role of insulin and glucagon in the response of glucose and alanine kinetics in burn-injured patients. J Clin Invest. 1986; 78:807–814. [PubMed: 2875083]
7. Jahoor F, Shangraw RE, Miyoshi H, Wallfish H, Herndon DN, Wolfe RR. Role of insulin and glucose oxidation in mediating the protein catabolism of burns and sepsis. Am J Physiol. 1989; 257:E323–E331. [PubMed: 2675628]

8. Black CT, Hennessey PJ, Andrassy RJ. Short-term hyperglycemia depresses immunity through noenzymatic glycosylation of circulating immunoglobulin. J Trauma. 1990; 30:830–833. [PubMed: 2380999]
9. Moulin V, Lawny F, Barritault D, Caruelle JP. Platelet releasate treatment improves skin healing in diabetic rats through endogenous growth factor secretion. Cell Mol Biol (Noisy-le-grand). 1998; 44:961–971. [PubMed: 9763200]
10. Losser MR, Bernard C, Beadeux JL, Pison C, Payen D. Glucose modulates hemodynamic, metabolic, and inflammatory responses to lipopolysaccharide in rabbits. J Appl Physiol. 1997; 1566:1574.
11. Reinhold D, Ansorge S, Schleicher ED. Elevated glucose levels stimulate transforming growth factor-beta 1 (TGF-beta 1), suppress interleukin IL-2, IL-6 and IL-10 production and DNA sysnthesis in peripheral blood mononuclear cells. Horm Metab Res. 1996; 28:267–270. [PubMed: 8811326]
12. Gregory R, McElveen J, Tattersall RB, Todd I. The effects of 3-hydroxybutyrate and glucose on human T cell responses to Candida albicans. FEMS Immunol Med Microbiol. 1993; 7:315–320. [PubMed: 8136782]
13. Moises RS, Heidenreich KA. Glucose regulates the expression of Gi-proteins in cultured BC3H-1 myocytes. Biochem Biophys Res Commun. 1992; 182:1193–1200. [PubMed: 1540164]
14. Ellger B, Debaveye Y, Vanhorebeek I, Langouche L, Giulietti A, Van Etten E, et al. Survival benefits of intensive insulin therapy in critical illness: impact of maintaining normoglycemia versus glycemia-independent actions of insulin. Diabetes. 2006; 55:1096–1105. [PubMed: 16567534]
15. Hansen TK, Thiel S, Wouters PJ, Christiansen JS, Van den Berghe G. Intensive insulin therapy exerts antiinflammatory effects in critically ill patients and counteracts the adverse effect of low mannose-binding lectin levels. J Clin Endocrinol Metab. 2003; 88:1082–1088. [PubMed: 12629088]
16. Jeschke MG, Klein D, Herndon DN. Insulin treatment improves the systemic inflammatory reaction to severe trauma. Ann Surg. 2004; 239:553–560. [PubMed: 15024317]
17. Dronge AS, Perkal MF, Kancir S, Concato J, Aslan M, Rosenthal RA. Long-term glycemic control and postoperative infectious complications. Arch Surg. 2006; 141:375–380. [PubMed: 16618895]
18. Laird AM, Miller PR, Kilgo PD, Meredith JW, Chang MC. Relationship of early hyperglycemia to mortality in trauma patients. J Trauma. 2004; 56:1058–1062. [PubMed: 15179246]
19. Mowlavi A, Andrews K, Milner S, Herndon DN, Heggers JP. The effects of hyperglycemia on skin graft survival in the burn patient. Ann Plast Surg. 2000; 45:629–632. [PubMed: 11128762]
20. Thomas SJ, Morimoto K, Herndon DN, Ferrando AA, Wolfe RR, Klein GL, et al. The effect of prolonged euglycemic hyperinsulinemia on lean body mass after severe burn. Surgery. 2002; 132:341–347. [PubMed: 12219032]
21. Wu X, Thomas SJ, Herndon DN, Sanford AP, Wolf SE. Insulin decreases hepatic acute phase protein levels in severely burned children. Surgery. 2004; 135:196–2002. [PubMed: 14739855]
22. Manzoni P, Castagnola E, Mostert M, Sala U, Galletto P, Gomirato G. Hyperglycemia as a possible marker of invasive fungal infection in preterm neonates. Acta Paediatr. 2006; 95:486–493. [PubMed: 16720499]
23. Martin RS, Smith JS, Hoth JJ, Miller PR, Meredith JW, Chang MC. Increased insulin requirements are associated with pneumonia after severe injury. J Trauma. 2007; 63:358–364. [PubMed: 17693836]
24. Luna CM, Vujacich P, Niederman MS, Vay C, Gherardi C, Matera J, et al. Impact of BAL data on the therapy and outcome of ventilator-associated pneumonia. Chest. 1997; 111:676–685. [PubMed: 9118708]

Table 1

Patient demoqraphics.

Patient Characteristic	Control	Intensive Insulin Rx	*p* -value
N (%)	81 (53)	71 (47)	--
Mean Age, y	42	43	0.9
Gender			
Male	70%	79%	0.2
Female	30%	21%	
%TBSA Burn	19%	15%	0.1
%TBSA 3rd Degree Burn	7%	5%	0.3
%TBSA 2nd Degree Burn	12%	10%	0.2
Inhalation Injury	37%	31%	0.4
History of Diabetes	5%	10%	0.2
TPN	7%	4%	0.4
Insulin Drip	15%	23%	0.2
Other Hyperglycemic Medications	42%	38%	0.6
Steroid Therapy for Sepsis	12%	9%	0.4

TBSA, total body surface area; TPN, total parenteral nutrition.

Table 2

Glucose values.

Measurement	Control	Intensive Insulin Rx	*p* -value
Total Number of Glucose Checks	4455	3451	--
Mean Number of Glucose Checks per Patient	55	49	0.7
Total Number of Days Glucose Checked	1083	621	--
Mean Admission Patient Glucose, mg/dL	128	151	0.3
Mean Glucose, mg/dL	142	130	<0.001
Number of Days Mean Daily Patient Glucose > 140 mg/dL, N (%)	383 (35)	137 (22)	<0.001
Mean of Mean Daily Patient Glucose, mg/dL	135	129	<0.001
Mean of Mean Patient Glucose, mg/dL	127	126	0.9
Mean of Maximum Patient Glucose, mg/dL	199	186	0.5
Number of Days Maximum Daily Patient Glucose > 140 mg/dL, N (%)	582 (54)	316 (51)	0.3
Number of Days Maximum Daily Patient Glucose > 200 mg/dL	189 (17)	70 (11)	<0.001
Mean of Minimum Patient Glucose, mg/dL	87	92	0.4
Number of Days with Hypoglycemia Episode (Glucose < 70 mg/dL), N (%)	49 (4.5)	40 (6.4)	0.09
Number of Days with Severe Hypoglycemia Episode (Glucose < 40 mg/dL), N (%)	7 (0.6)	3 (0.4)	0.7

Table 3

Outcomes.

Parameter	Control	Intensive Insulin Rx	*p* -value	
			Univariate	Multivariate*
N	81	71	--	--
Mortality, %	9	7	0.7	0.9
Mean Hospital LOS, days	17 ± 18	10 ± 14	0.01	0.3
Mean ICU LOS, days	9 ± 12	5 ± 10	0.03	0.08
Mean Ventilator days	6 ± 9	3 ± 9	0.02	0.054
Any Infection	52%	35%	0.04	0.1
Positive Quantitative Wound Culture	11%	4%	0.1	0.3
Pneumonia	37%	16%	0.003	0.009
Ventilator-Associated Pneumonia	31%	10%	0.002	0.009
Bacteremia	14%	4%	0.047	0.1
Urinary Tract Infection	22%	6%	0.004	0.01

LOS, length of stay; ICU, intensive care unit.

*Adjusted for age, gender, tbsa, inhalation injury, history of diabetes.

Table 4

Mortality risk.

Parameter	N (%)	Univariate		Multivariate*	
		OR (95% Cl)	*p* -value	OR (95% Cl)	*p* -value
Admission Glucose > 200 mg/dL	13 (9)	11.8 (3.1–46)	<0.001	2.0 (0.2–18)	0.6
Mean Glucose > 140 mg/dL	34 (22)	4.0 (1.2–13.3)	0.02	1.0 (0.2–5.4)	0.9
Maximum Glucose > 200 mg/dL	54 (36)	10.9 (2.3–52)	0.003	2.1 (0.3–15)	0.5
Minimum Glucose < 70 mg/dL	33 (22)	1.9 (0.5–6.8)	0.3	0.6 (0.1–3.3)	0.5

OR, odds ratio; Cl, confidence interval.

*Adjusted for age, gender, tbsa, inhalation injury.

Table 5

Risk of infection if maximum glucose > 200 mg/dL

Parameter	Multivariate Analysis*	
	OR (95% CI)	*p* -value
Any Infection	4.9 (2.1–12)	<0.0001
Positive Quantitative Wound Culture	6.7 (1.2–38)	0.03
Pneumonia	4.1 (1.5–11)	0.005
Ventilator-Associated Pneumonia	7.2 (2.4–22)	<0.0001
Bacteremia	8.8 (1.6–48)	0.01
Urinary Tract Infection	1.1 (0.4–3.4)	0.8

OR, odds ratio; CI, confidence interval.

*Adjusted for age, gender, tbsa, inhalation injury.