***ENDOCRINE PRACTICE*** **Rapid Electronic Article in Press**
Rapid Electronic Articles in Press are preprinted manuscripts that have been reviewed and accepted for publication, but have yet to be edited, typeset and finalized. This version of the manuscript will be replaced with the final, published version after it has been published in the print edition of the journal. The final, published version may differ from this proof.
DOI:10.4158/EP-2019-0510
© 2020 AACE.

Original Article EP-2019-0510

# SAFETY AND EFFICACY OF GLUCOSTABILIZER IN THE MANAGEMENT OF DIABETIC KETOACIDOSIS

*Anna Y. Groysman, MD[1]; Virginia Peragallo-Dittko, RN, CDE, BC-ADM, FAADE, FAAN[2]; Shahidul Islam, DrPH, PStat®[3]; Stanislaw Klek, MD[4]*

From: [1]Department of Internal Medicine, NYU Winthrop Hospital, Mineola, New York; [2]Diabetes and Obesity Institute, NYU Winthrop Hospital, Mineola, New York; [3]Department of Biostatistics, NYU Winthrop Hospital, Mineola, New York; [4]Division of Endocrinology, Diabetes and Metabolism, NYU Winthrop Hospital, Mineola, New York

Running Title: Glucostabilizer in DKA Management

Corresponding Author: Anna Y Groysman, MD
NYU Winthrop Hospital, Internal Medicine
Address: 259 First Street, Mineola, NY 11501
Email: Anna.Groysman@nyulangone.org

DOI:10.4158/EP-2019-0510
© 2020 AACE.

**ABSTRACT**

***Objective*:** To evaluate the safety and efficacy of GlucoStabilizer software intravenous insulin (IV) dosing in comparison to American Diabetes Association (ADA) protocol-directed provider-guided insulin dose adjustment (PGIA).

***Methods*:** GlucoStabilizer calculates the dose of IV insulin required to reach a prescribed target glucose range. GlucoStabilizer has not been fully studied in DKA. This retrospective study compared outcomes in patients with DKA before and after implementation of GlucoStabilizer. Insulin doses were administered based on GlucoStabilizer calculations or PGIA. The analysis evaluated before-after changes in amount of insulin used, time to target, hypoglycemia or hypokalemia events, and time to DKA resolution.

***Results*:** We studied 77 patients with insulin doses calculated by GlucoStabilizer and 69 patients with PGIA dosing. GlucoStabilizer was superior to PGIA. Patients treated with GlucoStabilizer-calculated doses did not experience hypoglycemia (N=0 vs. N=10; p<0.001). The 10 unique PGIA patients had a total of 18 episodes with 17 between 55 to 69 mg/dL; 1 <54 mg/dL, and no episodes <40 mg/dL. The GlucoStabilizer group required less insulin to reach DKA resolution (59.2 vs. 101.2 units; p<0.001). Time to glycemic target and DKA resolution were similar (6.7 vs. 4.6 hours; p=0.132) and (9.8 vs. 9.9 hours; p=0.803), respectively. No difference in incidence of hypokalemia was seen (N=9 vs. N=11; p=0.48).

***Conclusions:*** This study demonstrates the GlucoStabilizer settings that can be successfully used in the management of DKA with the avoidance of hypoglycemia. Patients treated with GlucoStabilizer-

DOI:10.4158/EP-2019-0510
© 2020 AACE.

calculated doses experienced no hypoglycemia and required less insulin as compared to those managed with PGIA.

**Abbreviations:**

**ADA**=American Diabetes Association; **PGIA**= protocol-directed provider-guided insulin dose adjustment; **DKA**= diabetic ketoacidosis; **IV**= intravenous; **eGMS**= electronic glycemic management systems; **ISF**= insulin sensitivity factor; **ED**= Emergency Department; **EMR**= electronic medical record; **SGLT2**= sodium-glucose co-transporter 2.

DOI:10.4158/EP-2019-0510
© 2020 AACE.

## INTRODUCTION

The pursuit of safer and more effective management of diabetic ketoacidosis (DKA) stems from it being one of the most serious metabolic complications of diabetes that requires intensive monitoring. Maghrabi et al.(1) demonstrated that standardization of DKA management yields superior outcomes. They performed a retrospective chart review of patients with DKA managed before and after implementation of an algorithm-based protocol. Utilization of an algorithm-based protocol resulted in reduced time to resolution of DKA and fewer hypoglycemic episodes without compromising electrolyte imbalance. Another study demonstrated that the use of a standardized protocol for management of DKA reduced the frequency of inappropriate discontinuation of intravenous insulin and recurrence of DKA (2).

The American Diabetes Association (ADA) consensus statement provides algorithm-based recommendations for the treatment of DKA including intravenous (IV) insulin dosing (3). The IV insulin dosing protocol includes a weight-based starting dose followed by dosing guidelines linked with the rate of glucose decline.

A review article analyzed a total of 85 articles published between 1973 and 2016 and found that “intravenous insulin rates remain contentious” and cite a lack of studies guiding insulin dosing (4).

DOI:10.4158/EP-2019-0510
© 2020 AACE.

In effort to manage DKA, many institutions have relied on either the ADA dosing guidelines or standardized paper-based algorithms to dose intravenous insulin infusion rates. Paper-based insulin-dosing algorithms do not usually take into account patient-specific blood glucose trends and result in oscillation between hypoglycemia and hyperglycemia (5). In addition, the commonly used (original and updated IIP) Yale insulin infusion protocol clearly states that it should not be used in the treatment of DKA (6).

Currently, four electronic glycemic management systems (eGMS) are commercially available for intravenous insulin infusion dosing (7). Glucommander ™(Glytec® Systems, Waltham, MA), EndoTool®(Monarch Medical Technologies, Charlotte, NC), GlucoCare™ (Pronia Medical Systems, Louisville, KY and GlucoStabilizer® (Indiana University Health Inc, Indianapolis, IN, MDN LLC.) software programs have been cleared by the US Food and Drug Administration (7). Among myriad factors considered, interoperability with the inpatient electronic medical record (EMR) was a deciding factor when NYU Winthrop chose GlucoStabilizer over other eGMS software available at the time of purchase.

Software-guided insulin dosing calculators have been studied widely demonstrating substantial evidence that that they can be safely and effectively used to treat hyperglycemia in both ICUs and general medical or surgical units. Moreover, numerous studies have demonstrated superiority and/or non-inferiority of software-guided insulin dosing calculators as compared to use of manual protocols or provider guided dosing in attaining prescribed target glucose levels and avoiding hyper/hypoglycemia and electrolyte derangements (5,8-12). These eGMS systems do not use the same algorithms and to date, there have been no head-to-head studies comparing the

DOI:10.4158/EP-2019-0510
© 2020 AACE.

systems. GlucoStabilizer and other insulin infusion dosing software programs were designed to maintain blood glucose in a target range for effective treatment of hyperglycemia but have been sparsely tested for management of DKA in adults (9, 13, 14).

## GlucoStabilizer Settings for the Treatment of DKA

GlucoStabilizer is a software-guided insulin dosing system that calculates the required dose of IV insulin based on target glucose range and adjusts rates based on an individual's response to treatment with the use of an insulin sensitivity factor (ISF) called a multiplier. The multiplier is an key component of the insulin dose calculation as it models the patients glycemic response to insulin (11). For example, a multiplier of 0.03 increases the insulin dose by 0.03 units/hour for each mg/dL increase in the blood glucose. When the next blood glucose value is entered, the software calculates the next multiplier and infusion rate.

eGMS programs such as GlucoStabilizer are capable of reliably calculating insulin doses to maintain blood glucose in target range and alert nurses when to measure patients' blood glucose thereby reducing hypoglycemia and errors (7, 9, 10, 13).

Utilization of software programs for insulin dosing in the treatment of DKA has limitations that must be appreciated. Residents who are largely responsible for dosing insulin in academic institutions can misconstrue the difference in the primary role of insulin for treating hyperglycemia as compared to the role of insulin in the management of DKA. In treating hyperglycemia, the role of an intravenous insulin infusion is to reduce blood glucose levels to a designated target range. However, when managing DKA, the primary role of the continuous intravenous insulin infusion is to

DOI:10.4158/EP-2019-0510
© 2020 AACE.

resolve acidosis, with improvement in glucose values as a secondary benefit. A more gradual decline in blood glucose is desired to prevent episodes of hypoglycemia while attaining resolution of ketoacidosis (15). Thus, the rates of insulin infusion based on tested insulin sensitivity factors and target blood glucose ranges used in managing hyperglycemia will not apply when managing patients with DKA.

Traditionally, studies have used time to resolution of DKA as a surrogate endpoint for patient outcomes. However, thus far, no studies have demonstrated that faster correction of DKA leads to better outcomes. In fact, the opposite is likely true. Lower rates of insulin infusion result in more gradual reduction in plasma osmolality, fewer complications including episodes of hypoglycemia, hypokalemia, cerebral edema, and no difference of time spent in the ICU (4, 15). Rapid resolution of DKA is an endpoint that does not necessarily correlate with better clinical outcomes.

When NYU Winthrop began using GlucoStabilizer for IV insulin dosing in the treatment of DKA, there were no published studies recommending insulin sensitivity factors or glucose target ranges. The team chose an initial multiplier of 0.01 and target range of 140-200 mg/dL to allow for a more steady decline in blood glucose and minimize hypoglycemia. There was no IV insulin bolus given prior to initiation of GlucoStabilizer. It is important to note that insulin infusion software is focused solely on glucose values and maintaining them in target range. Thus, potentially if glycemic target range is attained but the patient is still in acidosis, the software may recommend reducing the infusion rate to 0 units/hr. Doing so prior to resolution of acidosis in DKA would prolong treatment. Instead, the staff is educated and instructed to override the GlucoStabilizer-guided dose

DOI:10.4158/EP-2019-0510
© 2020 AACE.

of zero to continue IV insulin infusing at the rate of 0.3 units/hr and increase the rate of dextrose infusion to support continued IV insulin infusion.

The staff of NYU Winthrop successfully utilizes GlucoStabilizer to manage hyperglycemia for patients admitted to the ICU, post cardiac surgery, antepartum and intrapartum (16). Our aims were: to modify the settings of GlucoStabilizer and apply them to successfully manage DKA in the ICU; and to evaluate the safety and efficacy of GlucoStabilizer software dosing in comparison to ADA protocol-directed provider-guided insulin dose adjustment.

**METHODS**

This study used a quasi-experimental design involving before and after period (17). The "before" period extended from October 2015 through May 2017 and the "after" period was July 2017 to April 2018. NYU Winthrop hospital implemented GlucoStabilizer software in June 2017 to calculate insulin doses to manage DKA, which provided a natural opportunity to study the effect of this software guided insulin adjustment compared to ADA protocol-directed provider-guided insulin dose adjustment that was in place prior to June 2017. The research team had no control over subjects who received intervention. We report our experience with non-pregnant adult patients, 18 years of age or older, irrespective of established diagnosis of diabetes mellitus, with a diagnosis of DKA admitted between October 2015 and April 2018. The protocol was reviewed by the Institutional Review Board. MDN, the GlucoStabilizer parent company, was not involved in any aspect of the study including funding.

Prior to June 2017, DKA was managed at NYU Winthrop Hospital according to the DKA protocol from the 2009 ADA Consensus Statement on Hyperglycemic Crises in Adult Patients with Diabetes (3). As described in the protocol, insulin doses were adjusted hourly, with a goal of decreasing plasma glucose by 50-75 mg/dL per hour, a process labeled ADA protocol-directed provider-guided insulin dose adjustment (PGIA).

The intervention group (after period) included 77 patients who were admitted for treatment of DKA with IV insulin infusion doses calculated by GlucoStabilizer software since its implementation in June 2017. The pre-intervention comparison group (before period) included 69 similar patients admitted prior to June 2017 whose initial IV insulin infusion dose was weight-based at 0.1 units/kg/hour without IV insulin bolus and whose subsequent doses were based on the ADA protocol.

DKA was defined according to the diagnostic criteria published in the ADA consensus statement (3): blood glucose of 250mg/dL; arterial pH of ≤7.30; serum bicarbonate level of ≤18mEq/L; anion gap >10 mEq/L; and positive β-Hydroxybutyrate or acetone. Resolution of DKA was determined as a blood glucose level of less than 200mg/dL plus two of the following: pH>7.3, serum bicarbonate level ≥15 mEq/L, anion gap ≤ 12 mEq/L (3).

Hypoglycemia was defined as blood glucose <70mg/dL, clinically significant hypoglycemia was defined as blood glucose < 54 mg/dL (18) and severe hypoglycemia was defined as blood glucose <40mg/dL. Metabolic profile was measured routinely, every 4-6 hours and hypokalemia was defined as potassium levels <3.3 mEq/L. The evaluation of the efficacy and safety of GlucoStabilizer

DOI:10.4158/EP-2019-0510
© 2020 AACE.

as compared to PGIA was based on time-to-target blood glucose level of ≤180 mg/dL; time to resolution of DKA; total number of insulin units received as documented in GlucoStabilizer history for the intervention group or in the IV insulin flow sheet for the comparison group; number of unique patients who had at least one hypoglycemic episode with blood glucose <40mg/dL; <54 mg/dL and 55 to 69 mg/dL, number of hypoglycemic episodes and the number of patients experiencing hypokalemic episodes. Subcutaneous insulin administered prior to intravenous infusion was not included in the total number of insulin units received.

Demographic measures included total number of patients studied, age, sex, height, weight, BMI, prior history of diabetes mellitus, anion gap, serum bicarbonate level, creatinine, baseline serum blood glucose on admission to Emergency Department (ED), pH on admission, potassium level on admission, insulin given prior to IV insulin infusion start, and causes of DKA.

Age was calculated based on birth year. Sex and prior history of diabetes were self-reported. Anthropometric measurements were conducted with participants wearing hospital gowns. Body weight was recorded in kilograms using a scale-bed. Body height was self-reported and recorded in inches. BMI was automatically calculated by the electronic medical record (EMR) system as kilograms per meter squared (kg/m2). Anion gap was calculated as ([Na+] − ([Cl−] + [HCO3−]). Levels of serum bicarbonate (mEq/L), creatinine (mg/dL), and potassium (mEq/L) were resulted by the hospital laboratory. Causes of DKA were based on patient feedback and assessment as entered in patients' progress notes.

DOI:10.4158/EP-2019-0510
© 2020 AACE.

Patients with end-stage renal disease, those diagnosed with hyperosmolar hyperglycemic state (defined as plasma glucose >600mg/dL; arterial pH>7.3; serum bicarbonate >18mEq/L; effective serum osmolality >320mOsm/Kg) and those with sodium-glucose co-transporter 2 (SGLT2) inhibitor-associated euglycemic DKA were excluded from the study. Patients managed by both methods of insulin infusion during same hospital stay were also excluded.

### Statistical Methods

Data were summarized using descriptive statistics such as mean (SD), median (Q1-Q3) frequency and percentage as appropriate. Continuous variables were assessed for normality using histogram and Kolmogorov-Smirnov test. Bivariate comparisons were performed for continuous variables using Wilcoxon rank-sum test if non-normality was assumed, two-sample t-test was used otherwise. Fisher's exact test was used to compare categorical variables. A multivariable general linear model was developed for log-transformed insulin units. This model considered study groups, gender, age, BMI, HbA1c, PH in ED and bicarbonate measured in ED as the potential confounders. For the final model reported, an exhaustive search of the model space was conducted and models were ranked on the basis of their adjusted $R^2$ values. All analyses were conducted using SAS 9.4 (SAS Institute Inc, Cary, NC) and results were considered significant if $p<0.05$.

## RESULTS

In this study of a total of 146 patients, 77 had IV insulin infusion doses calculated by GlucoStabilizer software and 69 had ADA protocol-directed PGIA. The demographics and clinical characteristics of the study patients are shown in Table 1. There were no differences in the mean

DOI:10.4158/EP-2019-0510
© 2020 AACE.

age, BMI, weight, gender, HbA1c, pH in ED, or bicarbonate level between the intervention and comparison groups.

In the intervention group, the mean time to DKA resolution 9.8 (6.8-17.3) hours and time to blood glucose target 6.7 (4.1-9.8) hours were not statistically different than the comparison group 9.9 (6.1-15.8) hours and 4.6 (3.1-10.30) hours, respectively. There was no difference in number of episodes of hypokalemia between groups 9 (11.7%) vs 11 (15.9%) p=0.48. (Table 2).

Ten patients in the ADA protocol-directed PGIA group had at least one episode of hypoglycemia (14.5%) defined as blood glucose < 70 mg/dL compared to no hypoglycemia in the GlucoStabilizer group (p<0.001). The 10 unique patients in the ADA protocol-directed PGIA group had a total of 18 episodes with one episode < 54 mg/dL, and 17 episodes between 55 to 69 mg/dL.

The GlucoStabilizer group used a median of 59.2 units of insulin which was significantly different compared to 101.2 units used by the PGIA group (p<0.001) (Table 2). A multivariable model confirmed this finding. The GlucoStabilizer group had a 44% reduction in the number of insulin units used compared to the PGIA group (slope=-0.584, p<0.0001) after adjusting for age, BMI and bicarbonate measured in ED (R-square=0.30).

**DISCUSSION**

This study has demonstrated that management of IV insulin dosing in adult patients with DKA using GlucoStabilizer software is superior to that of ADA protocol-directed PGIA in preventing hypoglycemia. It is non-inferior in meeting time to reaching glycemic target, time to DKA resolution, and preventing hypokalemia. There was no negative impact on safety in our patient population.

DOI:10.4158/EP-2019-0510
© 2020 AACE.

Hypoglycemia is a major parameter in evaluating the safety of an IV insulin dosing method in the treatment of DKA. It remains a significant concern in hospitalized patients as it may be an independent risk factor for increased mortality and poor clinical outcomes. Hypoglycemia can cause brain metabolic dysfunction due to impaired glucose metabolism and increase the risk of ventricular arrhythmias due to QT interval prolongation (8). Other feared consequences of hypoglycemia include seizures and hypoglycemic coma (19). For these reasons, management of DKA requires an insulin dosing approach that reduces the risk of hypoglycemia and its complications, a goal that GlucoStabilizer software has successfully accomplished in this study (N=0 patients with hypoglycemia compared to N=10 on ADA protocol-directed PGIA).

This study targeted rate of hypokalemia as a measure of safe DKA management since disturbance in serum potassium concentration can have fatal arrhythmogenic potentials. Hypokalemia is one of the most commonly encountered electrolyte abnormalities in medicine and with a higher risk during insulin infusion as insulin causes a flux of potassium into cells. There was no difference in the rate of hypokalemia between the intervention and comparison group ($p$=0.48). Since medical residents were largely responsible for measuring and repleting electrolytes, the use of GlucoStabilizer vs. ADA protocol-directed PGIA may not have been a significant factor in regulating serum potassium concentrations. A higher powered research study would be needed to evaluate if this was a type II error of our study.

When DKA was managed viaADA protocol-directed provider-guided insulin dosing, there was a delay in timely insulin dose adjustment because medical residents were interrupted in their care of other patients when called with the hourly blood glucose results. This lag in time could have

DOI:10.4158/EP-2019-0510
© 2020 AACE.

contributed to episodes of hypoglycemia electrolyte derangements and amount of insulin prescribed. Management of DKA with GlucoStabilizer, however, allows for adjustment of insulin rates immediately as needed without the need for hourly input from medical residents. In addition, software-generated reminders for nurses to check blood glucose every 60 minutes along with data fields and reports that emphasize overdue glucose checks contribute to timely dose adjustment with eGMS. Similarly, the broad dosing guidelines in the ADA protocol are not as sensitive as the eGMS software-determined doses which may have contributed to the greater number of insulin units presecribed in the PGIA group.

Three published reports have focused on managing DKA in adults with the use of software-guided insulin infusion. The first retrospective chart review focused on the use of Glucommander to manage DKA in the emergency department (ED) and demonstrated its utility in distinguishing those patients who need admission to inpatient care versus those who can be discharged from the ED (13). Of the 35 patients included, 16 patients were discharged from the ED directly and 19 were admitted. The authors report 18 episodes of hypoglycemia (<70 mg/dL) with no episodes less than 40 mg/dL. The authors describe the glucose target range and multiplier as physician selected but these settings were not included in the paper.

A retrospective multicenter study involving 1750 patients treated with eGMS compared the use of Glucommander versus column-based protocols such as the Yale or Leuven protocols in adult patients admitted to the ICU or step-down floors to dose IV insulin infusions in the management of DKA (9). The study included various glucose target ranges in Glucommander chosen by individual sites (100- 140 mg/dL; 120-160 mg/dL; 140-180 mg/dL; 160-180 mg/dL) and

DOI:10.4158/EP-2019-0510
© 2020 AACE.

initial multipliers of 0.01, 0.02 or 0.03. In the Glucommander group, 12.9% of patients had blood glucose <70 mg/dL and the rate of severe hypoglycemia defined as blood glucose <40 mg/dL was 0.46%. The authors report that comparison of the best treatment outcomes among the varied Glucommander glucose target ranges and multipliers was the group with an initial multiplier of 0.01 and glucose target range of 120 to 180 mg/dL with 7.9% of patients experiencing hypoglycemia.

A recently published, underpowered pilot study that included 24-hour pharmacist oversight of DKA management, compared the use of GlucoStabilzer for insulin dosing to provider-driven insulin dosing using a diluted concentration of 50 units Regular insulin/100 mL 0.9% sodium chloride (14). The glucose target range was set at 100 to 160 mg/dL with an initial multiplier of 0.02. IV insulin infusion dosing was calculated by GlucoStabilizer for 29 patients and there were 5 episodes of hypoglycemia (50 to 70 mg/dL). The provider-driven arm had 36 patients and there were 17 episodes of hypoglycemia with 4 < 50mg/dL and 13 episodes 50 to 70 mg/dL.

Despite the differences in algorithms, target ranges, multipliers and insulin concentration, studies citing use of eGMS in the treatment of DKA consistently report less hypoglycemia than column-based algorithms or provider-driven IV insulin dosing.

**Assumptions and Limitations**

This study has several limitations. It was not a randomized controlled trial. This is a (retrospective) quasi-experimental study without control. A more robust quasi-experimental study would include a parallel control hospital where intervention was not implemented. We did not

DOI:10.4158/EP-2019-0510
© 2020 AACE.

adjust for factors that could impact time to resolution of DKA. These include choice of fluids and insulin therapy prior to the initiation of IV insulin infusion, patients experiencing trauma or other illness, and/or holding the insulin infusion due to hypokalemia.

The authors have made numerous assumptions as follows. There was no malfunction of intravenous insulin infusion via BD Alaris$^{TM}$ Pumps in the hospital influencing outcomes. Consistent with policy, all patients were given nothing by mouth during insulin initiation. Intervention and comparison groups represent random samples from the same larger population to which we apply our conclusions.

## Clinical Implications and Future Studies

While software-guided insulin infusion programs reduce staff responsibility for performing laborious and error prone dose calculations, management of electrolytes and fluid infusion rates still needs to be actively managed by hospital medical staff. Thus, it is imperative that healthcare practitioners participate in DKA management training with emphasis on fluid management, electrolyte replacement and avoiding hypoglycemia, and hypokalemia.

Clinical information technology companies are challenged to design more sophisticated algorithms that meet the unique requirements of DKA treatment. Future studies should include a cost-benefit analysis of eGMS vs columnar or provider-guided methods to dose IV insulin including not only the rate of hypoglycemia but nursing satisfaction, trust and time involved in dose adjustment.

© 2020 AACE.

## CONCLUSION

This study demonstrates the GlucoStabilizer settings that can be successfully used in the management of DKA with the avoidance of hypoglycemia. The GlucoStabilizer software-guided insulin dosing system with settings configured to the unique goals of DKA treatment was superior to ADA protocol-directed provider-guided insulin adjustment. Patients treated with GlucoStabilizer-calculated doses experienced no hypoglycemia and required less insulin as compared to those managed with ADA protocol-directed provider-guided insulin adjustment.

## DISCLOSURE

No competing financial interests exist.

DOI:10.4158/EP-2019-0510
© 2020 AACE.

**REFERENCES**


1. **Maghrabi A, Hamoudeh E, Hassan T, et al.** Safety and efficacy of an algorithm-based protocol in the management of diabetic ketoacidosis. *Endocr Pract*. 2012;18:842-846.

2. **Karajgikar ND, Manroa P, Acharya R, et al**. Addressing pitfalls in management of diabetic ketoacidosis (dka) with a standardized protocol. *Endocr Pract.* 2019;25:407-412.

3. **Kitabchi AE, Umpierrez GE, Miles JM, Fisher JN.** Hyperglycemic crises in adult patients with diabetes. *Diabetes Care*. 2009;32:1335-1343.

4. **Tran TTT, Pease A, Wood AJ, et al**. Review of evidence for adult diabetic ketoacidosis management protocols. *Front Endocrinol.* 2017;8:106.

5. **Yamashita S, Ng E, Brommecker F, et al**. Implementation of the Glucommander method of adjusting insulin infusions in critically ill patients. *Can J Hosp Pharm.* 2011;64:333-339.

6. **Shetty S, Inzucchi SE, Goldberg PA, et al.** Adapting to the new consensus guidelines for managing hyperglycemia during critical illness: the updated Yale insulin infusion protocol. *Endocr Pract*. 2012;18:363-370.

7. **Salinas PD, Mendez CE.** Glucose management technologies for the critically ill. *J Diabetes Sci Technol*. 2019:1-9.

8. **Newton CA, Smiley D, Bode BW, et al.** A comparison study of continuous insulin infusion protocols in the medical intensive care unit: computer-guided vs. standard column-based algorithms. *J Hosp Med*. 2010;5:432-437.


DOI:10.4158/EP-2019-0510
© 2020 AACE.

9. **Ullal J, Aloi JA, Reyes-Umpierrez D, et al.** Comparison of computer-guided versus standard insulin infusion regimens in patients with diabetic ketoacidosis. *J Diabetes Sci Technol.* 2018;12:39-46.

10. **Bouw JW, Campbell N, Hull MA, et al.** A retrospective cohort study of a nurse-driven computerized insulin infusion program versus a paper-based protocol in critically ill patients. *Diabetes Technol Ther*. 2012;14:125-130.

11. **Juneja R, Roudebush C, Kumar N, et al.** Utilization of a computerized intravenous insulin infusion program to control blood glucose in the intensive care unit. *Diabetes Technol Ther.* 2007;9:232-240.

12. **Marvin MR, Inzucchi SE, Besterman BJ.** Computerization of the Yale insulin infusion protocol and potential insights into causes of hypoglycemia with intravenous insulin. *Diabetes Technol Ther*. 2013;15:246-252.

13. **Ullal J, McFarland R, Bachand M, et al.** Use of a computer-based insulin infusion algorithm to treat diabetic ketoacidosis in the emergency department. *Diabetes Technol Ther*. 2016;18:100-103.

14. **Defayette AA, Voigt LM, Zammit KT, et al.** Evaluation of a computerized insulin dosing tool for the treatment of diabetic ketoacidosis. *J Pharm Pract* 2019; https://doi.org/10.1177%2F0897190019834367.

15. **Wagner A, Risse A, Brill L, et al.** Therapy of severe diabetic ketoacidosis. zero- mortality under very-low-dose insulin application. *Diabetes Care*. 1999;22:674-677.

DOI:10.4158/EP-2019-0510
© 2020 AACE.

16. **Dinglas C, Muscat J, Adams T, et al.** Software-guided insulin dosing improves intrapartum glycemic management in women with diabetes mellitus. *Am J Obstet Gynecol*. 2018;219:191.e-191.e6.

17. **Harris AD, McGregor JC, Perencevich EN, et al.** The use and interpretation of quasi-experimental studies in medical informatics. *J Am Med Inform Assoc.* 2006;13:16-23.

18. **Agiostratidou G, Anhalt H, Ball D, et al.** Standardizing clinically meaningful outcome measures beyond HbA1c for type 1 diabetes: a consensus report of the American Association of Clinical Endocrinologists, the American Association of Diabetes Educators, the American Diabetes Association, the Endocrine Society, JDRF International, the Leona M. and Harry B. Helmsley Charitable Trust, the Pediatric Endocrine Society, and the T1D Exchange. *Diabetes Care*. 2017;40:1622-1630.

19. **Krinsley JS, Grover A.** Severe hypoglycemia in critically ill patients: risk factors and outcomes. *Crit Care Med*. 2007;35:2262-2267.

DOI:10.4158/EP-2019-0510
© 2020 AACE.

**Table 1**

**Demographics and Clinical Characteristics**

| Variable | GlucoStabilizer N=77 | PGIA N=69 | P-value† |
|---|---|---|---|
| Age (Year) | 50(28-64) | 44(29-62) | 0.242 |
| Gender (Male), n (%) | 41(53.3) | 38(55.1) | 0.869 |
| BMI (kg/m2) | 25.6(22.5-29.1) | 25.8(22.1-30.8) | 0.994 |
| Weight (kg) | 70.0(60.5-82.2) | 72.5(61.0-90.7) | 0.419 |
| HbA1c (%) | 11.2±2.8 | 11.4±2.8 | 0.710 |
| HbA1c(mmol/mol) | 99.4±30.9 | 101.4±31.0 | 0.710 |
| pH in ED | 7.2(7.1-7.3) | 7.2(7.1-7.3) | 0.852 |
| Bicarbonate in ED | 11.2(7.3-17.0) | 11.6(7.7-14.6) | 0.502 |
| Baseline Blood glucose in ED (mg/dL) | 538(424-691) | 522(418-705) | 0.897 |

Abbreviations: PGIA=provider-guided insulin adjustment; ED=emergency department; BMI=body mass index

Continuous variables were presented as median (1st quartile-3rd quartile) for non-normally distributed variables and mean ± SD otherwise.

†P values are from Wilcoxon rank-sum test for non-normally distributed variables, t-test for normally distributed variables and Fisher's exact test for categorical variables.

DOI:10.4158/EP-2019-0510
© 2020 AACE.

**Table 2**
**Bivariate Comparisons of Outcome Variables**

| Variable | GlucoStabilizer N=77 | PGIA N=69 | P- value† |
|---|---|---|---|
| Time to DKA Resolution (hours) | 9.8(6.8-17.3) | 9.9(6.1-15.8) | 0.803 |
| Time to blood glucose target (≤180 mg/dL) (hours) | 6.7(4.1-9.8) | 4.6(3.1-10.3) | 0.132 |
| Total insulin units used (units) | 59.2(35.2-101.6) | 101.2(69.0-162.2) | <0.001 |
| Hypoglycemia (<70 mg/dL), n (%) | 0(0) | 10(14.5) | <0.001 |
| Hypokalemia (<3.3 mEq/L), n (%) | 9(11.7) | 11(15.9) | 0.48 |

Abbreviations: PGIA= provider-guided insulin adjustment
†P values are from Wilcoxon rank-sum test for continuous variables and Fisher's exact test for categorical variables.
Continuous variables are presented as median (1st quartile-3rd quartile) as the data are not normally distributed.

DOI:10.4158/EP-2019-0510
© 2020 AACE.