Original Article

Evaluation of a Computerized Insulin Dosing Tool for the Treatment of Diabetic Ketoacidosis

Journal of Pharmacy Practice
1-6

DOI: 10.1177/0897190019834367
journals.sagepub.com/home/jpp
SAGE

Aubrey A. Defayette, PharmD[1], Lisa M. Voigt, PharmD[2], Kimberly T. Zammit, PharmD[2], Jamie N. Nadler, MD[3], and Brian P. Kersten, PharmD[2]

Abstract

Purpose: Computerized insulin dosing tools (CIDT) have been shown to improve the care of critically ill patients with hyperglycemia. Application of a CIDT in addition to a diabetic ketoacidosis (DKA) order set for the treatment of DKA has not been evaluated. Our goal was to determine the effects the CIDT would have on the treatment of a patient with DKA. **Methods:** In this retrospective, pre–post chart review, a provider-driven insulin dosing strategy (pregroup) was compared to the CIDT (postgroup) with 24-hour pharmacist monitoring. The CIDT utilized an equation that incorporated a patient's most recent blood glucose (BG) value and recommended a rate of insulin (units/hour) every hour. **Results:** All baseline characterizes were similar between the 2 groups. There were no significant differences in average time to anion gap closure ($\leq$ 12 mEq/L) or intensive care unit length of stay between the pregroup and postgroup (12.5 [6] hours vs 10.5 [7] hours, $P = 0.235$; 40.6 [24] hours vs 40.8 [24] hours, $P = 0.945$). Although not statistically significant, 17 hypoglycemic events (BG < 70 mg/dL) occurred in the pregroup with 4 being severe (BG < 50 mg/dL) while 5 hypoglycemic events occurred in the postgroup, none of which were severe. **Conclusion:** This study suggests, when compared to a provider-driven insulin dosing strategy, the CIDT with 24-hour pharmacist monitoring is efficacious and safe for treatment of patients with a primary diagnosis of DKA.

Keywords

diabetic ketoacidosis, computerized insulin dosing tool, hypoglycemia, hypokalemia, safety, and efficacy

Diabetic ketoacidosis (DKA) is an acute metabolic complication of type 1 and type 2 diabetes mellitus (DM) which can be potentially fatal.[1,2] Although deaths due to DM continue to decline, the prevalence of DKA remains high.[3,4] The 2017 National Diabetes Statistic Report published by The Center for Disease Control and Prevention states, in 2014, there were 168 000 adult hospitalizations for DKA and 207 000 emergency department visits for a hyperglycemic crisis.[4]

The management of DKA recommended by the American Diabetes Association (ADA) includes administration of intravenous (IV) fluids, insulin, and electrolyte supplementation to correct metabolic derangements that accompany this disorder.[5] Treatment of DKA is a meticulous process requiring frequent monitoring and follow-up to avoid complications, particularly hypoglycemia and hypokalemia. Timely adjustments in therapy are necessary based on laboratory results obtained as frequently as every hour.

When caring for critically ill patients, comprehensive protocols and order sets have been shown to decrease intensive care unit (ICU) morbidity, mortality, ICU length of stay (LOS), hospital LOS, errors, and cost.[2,6-11] There is increasing evidence that a computerized insulin dosing tool (CIDT) reduces the number of hypoglycemic events, time to target blood glucose (BG), and variation in BG over time when treating hyperglycemia in critically ill patients.[12-15] Although promising results have been seen, application of a CIDT in addition to a DKA order set for the treatment of DKA has not been evaluated. Our objective was to determine the potential benefits and risks a CIDT would have on the treatment of patients with DKA.

Methods

Study Design, Setting, and Populations

This retrospective, pre–post observational chart review study was conducted at Buffalo General Medical Center in Buffalo, NY. The University at Buffalo institutional review board approved this study.

[1] D'Youville School of Pharmacy, Buffalo, New York, USA
[2] Kaleida Health, Buffalo General Medical Center, Buffalo, New York, USA
[3] Jacobs School of Medicine and Biomedical Sciences, University at Buffalo, Buffalo, NY, USA

Corresponding Author:
Aubrey A. Defayette, D'Youville School of Pharmacy, 320 Porter Avenue, DAC 336, Buffalo, NY 14201, USA.
Email: gawrona@dyc.edu

Patients were included if they were 18 years or older with a primary diagnosis of DKA defined as a plasma glucose > 250 mg/dL, anion gap > 10, and positive urine and/or serum ketones.[5] All patients were admitted to a closed 34-bed medical ICU and received treatment with the DKA order set (Appendix A). The pregroup included patients whose insulin regimens were managed by provider-driven insulin dosing from April 1, 2014, through October 31, 2015. These data were part of a quality assurance initiative started by the pharmacy department. The CIDT, GlucoStabilizer™ (Medical Decisions Network, Charlottesville, Virginia), was implemented on March 15, 2016. The postgroup included patients who were managed with the CIDT from March 15, 2016, through November 30, 2016. The CIDT was unavailable in the emergency department therefore patients in the postgroup were not started on the program until they were transferred to the medical ICU. Pharmacists monitored the postgroup 24 hours a day, 7 days a week.

All patients admitted were evaluated for inclusion in the pre and postgroup required initiation of the DKA order set (Appendix A) at the time of ICU admission. The order set followed standardized ADA treatment recommendations and was ordered electronically through a computerized physician order entry (CPOE) system.[5] Patients were excluded if they had a primary diagnosis of hyperosmolar hyperglycemic state (HHS), sepsis, septic shock, respiratory failure, active coronary artery disease, acute stroke, end-stage liver or kidney disease, pregnancy, or pancreatitis.

Intervention and Training

In the pregroup, nurses communicated all BG values to the provider who then made a decision on how the rate of insulin was adjusted. There was no comprehensive insulin dosing paper protocol for nurses to follow. In the CIDT group, a web-based software program used mathematical modeling to provide insulin dosing based on BG values and targeted a prespecified BG range.[13] It calculated an insulin infusion rate in units/hour based on the patient's most recent BG value; (BG [mg/dL] − 60) × multiplier. The multiplier, an insulin sensitivity factor, was set at an initial default of 0.02. The multiplier is not a constant; rather, it will adjust based on factors such as attainment of the target BG range and the rate of BG decline over time. Prior to using the CIDT for management of DKA, consultation with an endocrinologist provided assistance in establishing the target BG, multiplier, and frequency of BG testing for the DKA population. The BG target chosen was 100 to 160 mg/dL.

Frequency of BG monitoring was hourly, with an audible alarm alerting the nurse to obtain the scheduled BG. The Abbott Precision Xceed Pro (Abbott Diabetes Care Inc, Alameda, California) BG meter was utilized to obtain BG values unless they were outside the recommended limits of accuracy for the meter (<50 mg/dL or > 400 mg/dL). If either of these criteria were met, a serum BG was drawn and sent to the laboratory for interpretation.

Pharmacists responsible for verifying provider orders were incorporated into the management of the DKA protocol. They were responsible for ensuring the DKA order set was utilized and patients were entered into the CIDT properly. Furthermore, they assisted with transition to subcutaneous insulin when indicated, which was pharmacist- or provider-driven. A monitoring form (Appendix B) was provided to all pharmacists for their reference with key interventions. The pharmacists monitored these patients in conjunction to their other required activities which included order verification, answering phone calls, attending cardiac arrests, and checking filled medication orders. Pharmacists were asked to complete the monitor forms and follow up 24 hours a day, 7 days a week. The majority of time spent on this task occurred upon initial verification of the insulin order.

Prior to implementation of the CIDT intervention, the providers and nurses were trained on the pertinent updates to the DKA treatment pathway. The providers also received education on the functionality of the CIDT and to avoid interrupting the insulin infusion if a rate of zero units/hour was calculated unless the patient was hypoglycemic (<70 mg/dL). Nurses were trained to initiate dextrose containing fluids when the first BG was less than 250 mg/dL and call the provider if the program recommended an insulin infusion rate of zero units/hour. Pharmacists were provided information regarding appropriate treatment of DKA, how the CIDT functioned, and the key interventions they were expected to perform.

Data Collection

The patients in the pregroup were identified by querying the electronic medical record for patients in whom the DKA order set was selected. The patients in the postgroup were identified through a report generated by the CIDT database. A random number generator was used to select patients in the pregroup to be compared to a similar number of patients in the postgroup. Once patients were identified, all data were collected via the institution's electronic medical record. In addition to efficacy and safety outcomes data, demographic and relevant baseline laboratory data including information to calculate an Acute Physiology and Chronic Health Evaluation (APACHE) II score and to determine severity of DKA as defined by the ADA[5] were collected.

Outcome Measures

The primary efficacy outcome included time to anion gap closure (≤12 mEq/L) from admission. The secondary outcomes evaluated were ICU and emergency department LOS, number of hypoglycemic events (<70 mg/dL), and severe hypoglycemic events (<50 mg/dL) while on the insulin infusion, number of IV dextrose (25 g) boluses administered, dextrose 5% water (D5 W) ordered, appropriate initiation of D5 W (within 1 hour after the first BG reading below 250 mg/dL), number of hypokalemic events (potassium < 3.5 mEq/L) while on the insulin infusion, time to subcutaneous insulin ordered, reopening of

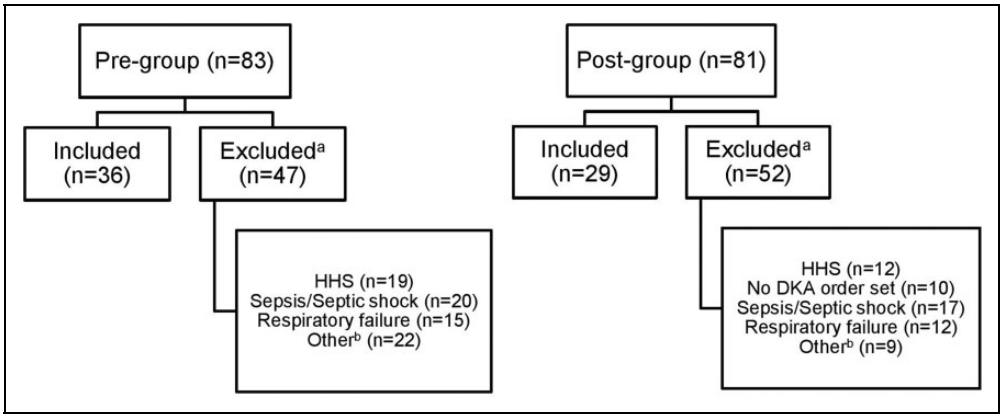

Figure 1. Study population selection. DKA indicates diabetic ketoacidosis; HHS, hyperosmolar hyperglycemic state. [a]All exclusion criteria were evaluated for each patient, thus multiple patients met more than one of the exclusion criteria; [b]Active coronary artery disease, acute stroke, end-stage liver or kidney disease, pregnancy, and pancreatitis.

the anion gap (>12 mEq/L), and the number of interventions made by a pharmacist in the postgroup.

Statistical Methods

Continuous data are reported as mean and standard deviation and categorical data are reported as frequencies and percentages. The unpaired *t* test was used to compare means and the Pearson Chi-Square test or Fisher's exact test was used to compare categorical data. A *P* value of less than 0.05 was considered statistically significant. Analyses were performed using SPSS version 23 (IBM SPSS Statistics, IBM Corporation, Armonk, New York).

Results

Of the 164 patients evaluated for this study, a total of 65 met inclusion criteria, 36 in the pregroup and 29 in the postgroup (Figure 1). The average age of the study population was 45 (17) years old with 38 (58.5%) patients having a diagnosis of type 1 DM. Baseline characteristics and laboratory values which were collected upon presentation were similar in both groups including the mean APACHE II score and the severity of DKA (Table 1).

The average time to anion gap closure was similar between the groups (Table 2). There was no difference between the pregroup and postgroup in ICU LOS either (40.6 [24] hours vs 40.8 [24]; $P = 0.84$). For those admitted through the emergency department, there was no difference in the mean LOS in the emergency department between the pregroup and postgroup, respectively (n = 30, 7.1 [6.5] hours vs n = 23, 4.7 [3.4] hours; $P = 0.115$).

There were 12 patients in the pregroup and 4 patients in the postgroup who experienced at least 1 hypoglycemic event ($P = 0.087$; Figure 2). Four severe events occurred in 3 patients prior to the CIDT intervention and none after implementation of the new tool ($P = 0.247$). Nurses administered seven 25 g IV dextrose boluses to the pregroup and 3 to the postgroup. There were a similar number of patients in each group who had an order placed for a continuous D5 W infusion (n = 33 vs n = 24; $P = 0.45$) upon verification of the insulin infusion. Despite more hypoglycemic events, a greater percentage of patients

Table 1. Baseline Characteristics Upon Admission to the Emergency Department.

Baseline Characteristics	Pregroup (n = 36)	Postgroup (n = 29)	*P*
Age, years, mean (SD)	43 (17)	47 (17)	0.34
Male, no. (%)	16 (44.4)	15 (51.7)	0.56
Type 1 DM, no. (%)	22 (61.1)	16 (55.2)	0.63
APACHE II score, mean (SD)	13 (7)	14 (6)	0.53
Severity of DKA, no. (%)			0.94
Mild	0 (0)	0 (0)	
Moderate	22 (61.1)	18 (62.1)	
Severe	14 (38.9)	11 (37.9)	
GCS, mean (SD)	14.7 (1.1)	15 (0)	0.1
Heart rate, bpm, mean (SD)	110 (24)	110 (18)	0.92
Mean arterial pressure, mm Hg, mean (SD)	92 (22)	100 (20)	0.11
Arterial pH, mean (SD)	7.23 (0.2)	7.23 (0.1)	0.89
Anion gap, mmol/L, mean (SD)	24.1 (6)	22.8 (7.2)	0.45
Serum bicarbonate, mmol/L, mean (SD)	12.6 (5.5)	12.9 (5.3)	0.83
Blood glucose, mg/dL, mean (SD)	600 (196)	614 (187)	0.78
Serum ketones, mmol/L, mean (SD)	7.7 (3.3)	7.1 (3.9)	0.6
Urine ketones, mg/dL, mean (SD)	63.7 (24.5)[a]	55.2 (22)[b]	0.16

Abbreviations: APACHE, Acute Physiology and Chronic Health Evaluation; DKA, diabetic ketoacidosis; DM, diabetes mellitus; GCS, Glasgow Coma Scale; SD, standard deviation.
[a]n = 35.
[b]n = 28.

Table 2. Primary Outcome Results.

Primary Outcome	Pregroup (n = 36)	Postgroup (n = 29)	*P*
Time to anion gap closure (hour); mean (SD)	12.5 (6)	10.7 (7)	0.24

Abbreviation: SD, standard deviation.

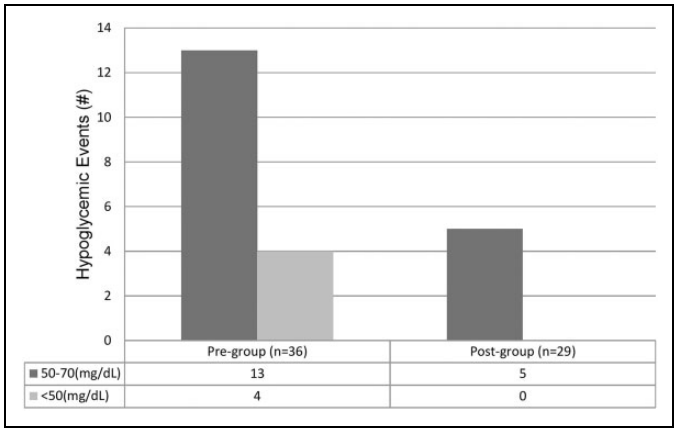

Figure 2. Hypoglycemic events in the pregroup and postgroup.

Table 3. Comparing Intensive Care Unit Length of Stay and Time to Anion Gap Closure to Studies That Evaluated Comprehensive Paper Protocols.

	ICU LOS (hour); mean (SD)			Time to Anion Gap Closure (hour); Mean (SD)		
Study	Pre	Post	*P* Value	Pre	Post	*P* Value
Bull et al[11]	44 (28)	34 (18)	0.007	15.4 (13.3)	10.3 (4.6)	<0.001
Beik et al[2]	64.8 (19)	37.1 (74.8)	<0.01	13 (9)	9.3 (7.4)	<0.01
Defayette et al	40.6 (24)	40.8 (24)	0.84	12.5 (6)	10.5 (7)	0.24

Abbreviations: ICU, intensive care unit; LOS, length of stay; SD, standard deviation.

in the pregroup had appropriate initiation of a continuous D5 W infusion when compared to the postgroup, but this was not statistically significant (n = 19 vs n = 10; $P = 0.14$).

There were 27 hypokalemic events occurring in 14 patients in the pregroup and 18 events occurring in 8 patients in the postgroup. In the pregroup, 9 patients had 1 event, 3 had 3 events, 1 had 4 events, and 1 had 5 events. In the postgroup, 3 patients had 1 event, 2 had 2 events, 2 had 3 events, and 1 had 5 events. This was not statistically significant ($P = 0.35$).

The average time to placement of an order for subcutaneous insulin was shorter in the postgroup when compared to the pregroup, but this was not statically significant (14.9 [8.5] hours vs 21.8 [18.3] hours, $P = 0.078$). The anion-gap reopened in 2 patients in the pregroup and 1 patient in the postgroup. In the pregroup, the anion gap reopened after 1 patient refused subcutaneous insulin administration. A dose of subcutaneous insulin that was considerably lower than their home basal regimens was given to the 2 remaining patients.

The postgroup had an average of 1 pharmacist-initiated intervention per patient. Common interventions included educating providers about the DKA order set, educating the nurse about the CIDT, calling providers to recommend ordering the continuous D5 W infusion, and calling nurses to recommend initiation of the continuous D5 W infusion.

Discussion

To our knowledge, this is the first study to evaluate the CIDT for the treatment of patients with DKA exclusively. While this study did not compare the CIDT to a comprehensive insulin dosing paper protocol, but rather a provider driven approach, our average time to anion gap closure and ICU LOS were numerically similar to those reported in previous studies (Table 3).[2,11] Additionally, recurrence of ketosis was uncommon with the intervention. Although time to anion gap closure may represent a surrogate end point for the management of DKA, it was chosen as the primary outcome for the study as a way to measure efficacy of the CIDT. We believe this addresses the efficacy of the CIDT with 24-hour pharmacist monitoring as this was the only change made to the management of DKA during the study period.

Neither Beik et al[2] nor Bull et al[11] were able to find a statistically significant decrease in the total number of hypoglycemic events with implementation of a comprehensive paper protocol. Similarly our study was unable to show a statistically significant difference in hypoglycemic events. There were 33% of patients in the pregroup and 14% of patients in the postgroup who experienced a hypoglycemic event (Figure 2). This could be considered a significant improvement in clinical care despite the postgroup having a greater number of patients with inappropriate initiation of D5 W. Although there were more patients in the postgroup with inappropriate initiation of D5 W, this may have been a documentation error, as the smart pumps and electronic medical record do not communicate with one another. These results validate the decision to lower our target BG to accommodate the limitations of the CIDT.

In previous studies, the reported percentage of patients experiencing at least 1 hypoglycemic event was comparable to the events in our study.[11,16] Bull et al who evaluated implementation of a comprehensive paper protocol found 18 (16.2%) of 111 patients experienced at least 1 hypoglycemic event in their intervention group.[11] Sandler et al evaluated hypoglycemic events using the CIDT for management of stress hyperglycemia in a medical or surgical ICU population.[16] An admission diagnosis of DKA or HHS were not evaluated; however, a small percentage of patients with end-stage renal disease were included. Sixteen percent of patients in the medical ICU experienced 1 or more episodes of moderate hypoglycemia (<70 mg/dL) and zero patients experienced severe hypoglycemia (<40 mg/dL).

In our study, 39% of patient in the pregroup and 28% of patients in the postgroup experienced at least 1 hypokalemic event. Similarly, Beik et al found no difference in the number of patients who experienced a hypokalemic event with implementation of their comprehensive protocol.[11] Furthermore, these authors found a statistically significant decrease in the mean number of hypokalemic events per person (2.1 vs 1.3, $P = 0.016$).[11] Our study found no difference between groups in

the number of patients who experienced at least one hypokalemic event during the insulin infusion ($P = 0.43$). There were 27 hypokalemic events in the pregroup and 18 in the postgroup. Our data suggest that the CIDT had similar or perhaps improved safety outcomes with respect to hypoglycemia and hypokalemia when compared to other comprehensive protocols.[2,11]

Providers and pharmacists were eager to utilize the CIDT because of its unique features, but continuing education was an important component of this project and will be necessary to ensure sustained success. The majority of interventions executed by pharmacists centered on educating providers and nurses concerning the availability and utilization of the CIDT. Pharmacist's involvement provided an added layer of safety as the CIDT had not been used previously in this patient population. As the end users have become more comfortable with this technology, 24-hour pharmacist oversight has moved toward clinical rather than technical interventions. Additionally, quality improvement strategies are necessary to maintain continued efficacy and safety of the CIDT. Utilization and adherence is monitored periodically and presented at our institution's Pharmacy and Therapeutic Committee meeting.

There are several limitations to this study. The first comes with its design, as it was a retrospective, pre–post observational chart review at a single center. Although a trend toward improved outcomes was observed, the study may not be adequately powered to detect a statistical difference. Screening may have limited the sample size if the CPOE order set was not utilized in the pregroup and if the CIDT was not utilized in the postgroup. However, as a pilot study, our results suggest the CIDT provides similar efficacy and safety when compared to the provider driven dosing strategy. In addition, the CIDT was unable to be implemented until patients were admitted to the ICU; therefore, patients in the CIDT group were initially managed with the provider insulin dosing. It is unclear how the program would have affected the time to anion gap closure if it were initiated in the emergency department.

It is important to point out that the CIDT was utilized at our institution for treatment of stress hyperglycemia prior to implementation of treatment for DKA; therefore, there was no additional cost for our institution to use the CIDT in this population. Cost may be a factor when implementing a CIDT and would be institution-specific.

Finally, the target BG range of 100 to 160 mg/dL was below the recommended ADA target of 150 to 200 mg/dL[5] and may limit generalizability of the CIDT. A lower than recommended target range was chosen to prevent the CIDT from directing the nurse to hold the insulin infusion prior to resolution of DKA. This could have potentially occurred when the BG was below the low target of 100 mg/dL and the multiplier had decreased to zero. However, the likelihood of this occurring with a higher target of 150 to 200 mg/dL would have been significantly greater. It is important to note that although we chose a lower target BG, there were numerically less hypoglycemic events when compared to patients in the pregroup who had a target BG of 150 to 200 mg/dL.

Conclusion

This study suggests the CIDT is efficacious and safe for treatment of patients with a primary diagnosis of DKA when compared to provider-driven insulin dosing. Further studies are needed to evaluate the efficacy and safety of the CIDT if implemented in the emergency department or if used in patients with DKA and other concomitant diagnoses.

Appendix A. Diabetic ketoacidosis order set

Intravenous Fluids (These orders are NOT to be used in patients with end-stage renal disease.)

IV Bolus. 0.9% sodium chloride bolus 1000 mL, intravenous (IV) piggyback, infuse over: 60 minutes, once, or 1000 mL, IV piggyback, infuse over: 60 minutes, q1 hour.

IV Maintenance Fluids. 0.9% sodium chloride IV continuous, mL/h, 1000 mL.

0.45% sodium chloride IV continuous, mL/h, 1000 mL.

If potassium is < 5.2 mmol/L, consider a potassium containing solution:

0.9% sodium chloride with potassium chloride 20 mEq/L IV continuous, mL/h, 1000 mL.

0.45% sodium chloride with potassium chloride 20mEq/L IV continuous, mL/h, 1000 mL.

For glucose < 250 mg/dL:

Dextrose 5% in water IV continuous, mL/h, 1000 mL, comments: Start when glucose is < 250 mg/dL.

Medications

Antiemetics. Metoclopramide 10 mg, injection, IV push, q6 h, as needed (PRN) nausea/vomiting

Ondansetron 4 mg, injection, IV push, q6 hour, PRN nausea/vomiting.

Insulin. NOTE: Do not start insulin until potassium is > 3.3 mEq/L.

Insulin regular 0.15 U/kg, injection, IV push once.

Then insulin regular 50 units in 0.9% sodium chloride 100 mL, IV continuous, unit/h.

Potassium replacement (These orders are NOT to be used in patients with end-stage renal disease.). Potassium chloride 10 mEq in 0.9% sodium chloride 50 mL, 10 mEq, injection, IV piggyback, q1 hour, PRN other (comment: potassium < 2.8 mEq/L give 10 mEq q1 hour × 8 doses. For potassium 2.8-3.3 mEq/L give 10 mEq q1 hour × 6 doses. For potassium 3.4-3.9 mmol/L give 10 mEq q1 hour × 4 doses.).

Laboratory

Immediate (STAT) one time orders. Complete blood count with differential, comprehensive metabolic panel, venous or arterial blood gas, hemoglobin A1c, osmolality, phosphate level,

magnesium Level, urinalysis with microscopy, blood glucose fingersticks, human chorionic gonadotropin qualitative, lactate whole blood, amylase level, lipase Level, and ketones beta-hydroxybutyrate.

Recurring orders. Blood glucose fingersticks every 1 hour and venous or arterial blood gas, basic metabolic panel, comprehensive metabolic panel, lactate whole blood, magnesium level, and phosphate level every 4 hours.

Support services/ Referrals

Referral to Nutritionist Adult

Appendix B. Diabetic Ketoacidosis Monitoring Form for Pharmacists

Pharmacist name	
Patient name	
Medical record number	
	Yes or No
Order set ordered	
Called to get order for order set	
Patient entered into the CIDT	
Called nurse to put patient into the CIDT	
Blood glucose < 250 mg/dL; dextrose initiated	
Recommended dextrose initiation	
Recommended potassium replacement	
Recommended phosphate replacement	
Insulin drip inappropriately turned off	
Recommended reinitiation of insulin drip	
Recommended subcutaneous insulin	
Additional comments/interventions	

Abbreviation: CIDT, computerized insulin dosing tools.

Declaration of Conflicting Interests

The author(s) declared no potential conflicts of interest with respect to the research, authorship, and/or publication of this article.

Funding

The author(s) received no financial support for the research, authorship, and/or publication of this article.

References

1. Westerberg DP. Diabetic ketoacidosis: evaluation and treatment. *Am Fam Physician*. 2013;87:337-346.
2. Beik N, Anger KE, Forni AA, et al. Evaluation of an institution-wide guideline for hyperglycemic emergencies at a tertiary academic medical center. *Ann Pharmacother*. 2013;47:1260-1265.
3. Kochanek KD, Murphy SL, Xu JQ, et al. *Deaths: Final Data for 2014. National Vital Statistics Reports*. Hyattsville, MD: National Center for Health Statistics; 2016;65:1-121.
4. Centers for Disease Control and Prevention. *National Diabetes Statistics Report, 2017*. Atlanta, GA: Centers for Disease Control and Prevention, US Department of Health and Human Services; 2017. www.cdc.gov/diabetes/pdfs/data/statistics/national-diabetes-statistics-report.pdf. Accessed May 15, 2018.
5. Kitabchi AE, Umpierrez GE, Miles JM, et al. Hyperglycemic crises in adult patients with diabetes. *Diabetes Care*. 2009;32:1335-1343.
6. East TD, Heermann LK, Bradshaw RL, et al. Efficacy of computerized decision support for mechanical ventilation: results of a prospective multi-center randomized trial. *Proc AMIA Symp*. 1999:251-255.
7. Evans RS, Pestotnik SL, Classen DC, et al. A computerized-assisted management program for antibiotics and other antiinfective agents. *N Engl J Med*. 1998;338:232-238.
8. Keetch DW, Buback D. A clinical-care pathway for decreasing hospital stay after radical prostatectomy. *Br J Urol*. 1998;81:398-402.
9. Morris AH. Developing and implementing computerized protocols for standardization of clinical decisions. *Ann Intern Med*. 2000;132:373-383.
10. Meade M, Ely E. Protocols to improve the care of critically ill pediatric and adult patients. *JAMA*. 2002;288:2601-2603.
11. Bull SB, Douglas IS, Foster M, et al. Mandatory protocol for treating adult patients with diabetic ketoacidosis decreases intensive care unit and hospital lengths of stay: results of a nonrandomized trial. *Crit Care Med*. 2007;35:41-46.
12. Saur NM, Kongable GL, Holewinski S, et al. Software-guided insulin dosing: tight glycemic control and decreased glycemic derangements in critically ill patients. *Mayo Clin Proc*. 2013;88:920-929.
13. Juneta 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.
14. Crocket SE. Glucose control in the critically ill patient utilizing computerized intravenous insulin dosing. *US Endocrinology*. 2009;5:45-48.
15. Juneja R, Roudebush CP, Nasraway SA, et al. Computerized intensive insulin dosing can mitigate hypoglycemia and achieve tight glycemic control when glucose measurement is performed frequently and on time. *Crit Care Med*. 2009;13:1-10.
16. Sandler V, Misiasz MR, Jones J, et al. Reducing the risk of hypoglycemia associated with intravenous insulin: experience with a computerized insulin infusion program in 4 adult intensive care units. *J Diabetes Sci Technol*. 2014;8:923-929.