Evaluation of Efficacy and Safety of Adult Diabetic Ketoacidosis (DKA) Treatment Protocol at a Tertiary Health Care Center

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Evaluation of Efficacy and Safety of Adult Diabetic Ketoacidosis (DKA) Treatment Protocol at a Tertiary Health Care Center

Submitted in Partial Fulfillment of the Requirements for the Degree of Doctor of Nursing Practice at the University of Kentucky

By
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Lexington, Kentucky
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Abstract

BACKGROUND: Hypoglycemia can be a complication of diabetic ketoacidosis (DKA) protocols. This prolongs time to DKA resolution, increasing hospital stay and mortality risk. Does a revised DKA protocol reduce the incidence of hypoglycemia and reopening of the anion gap due to inappropriate transition to subcutaneous insulin? There is a lack of published data in the U.S. on factors affecting time to resolution of DKA and LOS in the ICU. This review was focused on evaluation of safety outcomes and protocol effectiveness by comparing hypoglycemia and hypokalemia events and instances of anion gap reopening for the duration of DKA treatment.

PURPOSE: To evaluate the effectiveness and safety of a diabetes ketoacidosis (DKA) protocol at UK Healthcare in patients with diabetes type 1: whether time to AG resolution, hypoglycemia, hypokalemia and anion gap reopening incidences different following transition from old protocol to a revised protocol.

METHODS: Retrospective chart review of patients managed with a DKA protocol before and after protocol revision. Protocol efficacy was evaluated by assessing time to resolution of AG, length of stay (LOS) in the hospital. Protocol safety evaluated by assessing the number of incidences of hypoglycemic, hypokalemic events and events of anion gap reopening.

ANALYSIS: Comparison was done using descriptive statistics as well as parametric and nonparametric tests to determine incidences of hypoglycemia, hypokalemia, anion gap that reopened, time to anion gap resolution difference of 2 protocols. Comparisons of demographic and clinical data of cohorts: t-test for continuous variables and the Mann-Whitney U tests.
**RESULTS:** 67 patients met biochemical inclusion criteria for DKA: median ages 32 and 31 years, 55% were males and 45% were females on average. The revised protocol (group 2, n=42) did not show to be safer than old algorithm (group 1, n=28) in hypoglycemia events for duration of the treatment with 44% (n=11) in the first group and 53% (n=22) for the second group. It did not show to be safer in terms of hypokalemia, 40% (n=10) of hypokalemia incidences in the first group and 50% (n=21) in the second group (p=0.458). But it showed time in to anion gap resolution was 3 hours faster when no hypoglycemia happened in the second cohort compared to the first cohort and that the length of stay in ICU decreased by 1 day when no incidences of anion gap reopening happened in the second group as compared to the first cohort. The protocol showed to be safer for patients in terms of faster DKA resolution and shorter ICU LOS but not in terms of incidences of adverse events. Individual factors associate with slower resolution of DKA were lower admission pH (p=.029) in the first group but no correlation found in the second group (p=0.735).

**IMPLICATION/CONCLUSION:** This project showed no difference in safety outcomes such as hypoglycemia or hypokalemia but improved effectiveness outcomes such as faster AG resolution between two groups. But it showed that increased safety (avoidance of hypoglycemia and AG reopening) of the protocol leads increase in effectiveness and shorter ICU LOS in the second group. Future studies should focus on the staff and providers compliance with following protocol and timely transition from IV insulin infusion to SC insulin.
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Dedication

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BACKGROUND AND SIGNIFICANCE OF PROPOSED PROJECT

Problem Identification and Expected outcomes

Every year, more than 100,000 patients are admitted to U.S. hospitals for diabetic ketoacidosis (DKA), and treatment costs exceed $1 billion (Bull et al., 2007). The mean cost of hospitalization is about $7,500 per stay (Fayfman et al., 2017). DKA is a serious complication of diabetes, which requires emergent interventions and treatments (Islam et al., 2018). DKA is a metabolic disorder that includes hyperglycemia with ketoacidosis caused by excessive production of ketones (Islam et al., 2018). DKA protocols are designed to efficiently treat the condition. Adverse events associated with the DKA treatment protocol can prolong the time it takes to resolve the condition. Hypoglycemia and hypokalemia are the most common complications of the treatment for DKA (Hirsch & Emmett, 2020). Protective strategies recommended against treatment complications are low-dose intravenous insulin treatment and thorough monitoring of potassium and blood glucose (Hirsch & Emmett, 2020).

Hypoglycemia can prolong time to DKA resolution and increase length of hospital stay and mortality risk. Lorenson et al. (2019) investigated the incidence of hypoglycemia at 34 U.S. hospitals, and determined that 35% of patients receiving standard DKA care developed the condition. According to Dhatariya (2015), 28% of patients developed hypoglycemia after about 14.7 hours of treatment. Hypoglycemia has been associated with an 85% increase in the risk of inpatient death, as well as a 2.5 day increase in LOS for each day of hypoglycemia (Turchin et al, 2009). Suboptimal compliance with the DKA protocol with regard to inadequate monitoring of K+ resulted in hypokalemia in a study by Kennedy et al. (2018). Two DKA protocols (old and
revised) at a tertiary care center in Kentucky addressed hypoglycemia and hypokalemia problems, and the objective of this project was to evaluate the differences in these outcomes.

The revised DKA protocol was a hospital-wide change for which implementation began at the end of November 2018. As with the old protocol, the revised protocol addresses the problem of hypoglycemia by: 1) the addition of 5% dextrose to fluid infusion when the threshold for blood glucose (BG) is < 200mg/dL, and 2) insulin infusion rate reduction by half if BG falls by >150mg/dL from the last BG concentration. This correlates with the American Diabetes Association (ADA) guideline, which directs providers to change IVF with 5% dextrose 0.45% NaCl at 150-250 ml/hr (Kitabchi, 2009). The revised protocol addresses hypoglycemia with 5% dextrose fluids when BG is less than or equal to 250mg/dL, and a 50% reduction in insulin infusion when BG is between 101-149 mg/dL. This simplifies the calculation step and places the threshold for starting 5% dextrose at an earlier point. This also follows the Joint British Diabetes Societies (JBDS) recommendation with the addition of glucose when blood sugar reaches 250 mg/dL. However, the JBDS recommends adding 10% glucose rather than 5%, and at a slower rate of 125 ml/hr to run with 0.9% of NaCl plus KCl in order to avoid fluid overload and hypokalemia. According to Lorensen et al. (2019), reducing the rate of insulin infusion when initiating dextrose is protective against hypoglycemia. The 2009 ADA has indicated that a bolus of insulin is not necessary if patients receive an hourly insulin infusion of 0.14 units/kg body weight (equivalent to 10 units/h in a 70-kg patient), with a goal of reducing blood sugar by 50-75 mg from the previous value every hour after beginning treatment (Kitabchi, 2009). This correlates with the revised protocol, which recommends the same insulin infusion rate but a slightly higher threshold for the blood sugar goal: 50-100 mg/dL. According to 2009 ADA guidelines, potassium replacement should be started when serum concentration is <5.2 to
maintain a level of 4-5 mEq, as patients are total body depleted despite normal or elevated serum results. Insulin infusion must be stopped when hypoglycemia or hypokalemia occurs (Kitabchi, 2009). According to Fayfman et al. (2017), this can cause rebound hyperglycemia, ketogenesis and recurrent acidosis within about 10 minutes after abrupt cessation of insulin (half-life of insulin is <10 min). Consequently, hypoglycemia or hypokalemia can both prolong DKA resolution and increase risk of mortality due to cardiac arrhythmias and lack of BG to supply the cells in the body. Potassium concentrations <3.3 can lead to life-threatening arrhythmias and respiratory muscle weakness (Kitabchi, 2009). Also, during treatment, many patients with DKA do not experience adrenergic manifestations of sweating, nervousness, fatigue, hunger, and tachycardia—i.e., the signs and symptoms of hypoglycemia. This can lead to death; it is crucial to check blood sugar every hour (Fayfman et al 2017). Hypoglycemic episodes can cause seizures, arrhythmias and cardiovascular events. The aim of DKA protocols and guidelines is to resolve DKA and reduce the incidence of hypoglycemia and hypokalemia. In this project, the PI evaluated time to resolution of anion gap as a primary outcome and hypoglycemia (BG <70mg/dL), hypokalemia (K+ <3.3 mmol/L) and anion gap (AG) reopening as safety outcomes of a new DKA protocol at a tertiary care center in Kentucky.

The gap in the literature is that the recommendation for DKA management is often based upon clinical judgment in the absence of scientific evidence. The gap in practice is the high rate of dangerous hypoglycemic events and AG reopening, so a tertiary care center in KY revised its DKA protocol to attempt to resolve these problems. This project included a thorough review of published, databased literature about the most common adverse events associated with DKA treatment protocols, such as hypoglycemia and hypokalemia. This body of literature included numerous randomized controlled studies as well as the currently available ADA and JBDS
recommendations on treatment modalities for DKA in order to facilitate faster resolution of the problem. The PI compared studies, appraised evidence and uncovered data from a review of the electronic medical record to determine incidences of hypoglycemia and hypokalemia at the tertiary hospital in Kentucky and analyzed the findings to determine if the current protocol was more effective at ensuring safe care for patients.

**Context, Scope and Consequences**

In a survey conducted in over 70 hospitals across the United Kingdom, adverse outcomes such as hypoglycemia occurred in 27.6% of patients undergoing DKA treatment, and hypokalemia in 55% of these patients (Dhatariya et al 2015). Because these adverse reactions are so prevalent, it is important to follow recent, evidence-based guidelines when treating DKA. Incidences of hypoglycemia and hypokalemia are higher when providers do not adhere to the ADA and the JBDS recommendations (Gupta et al.2017, Munir et al.,2017; Thuzar et al.,2014 Dhatariya et al 2015). Also, following recommendations of the 2009 ADA guidelines yielded better outcomes in hypoglycemia reduction than the JBDS recommendations (Lorenson et al, 2019). Researchers have shown that hospital and Intensive Care Unit (ICU) Length of Stay (LOS) are longer when DKA treatment protocols do not follow clinical guidelines (Bull, et al., 2007; Islam et al., 2018; Ramakkishnan et al., 2013). Additionally, the literature shows that the time to DKA resolution is longer when non-protocolized treatment modalities or outdated protocols are used (Fusco et al., 2015; Islam., 2018; Laliberte et al., Ramakrishnan et al., 2013; Munik et al., 2017; Hara et al., 2013; Brown et al,2018).

Centers for Disease Control (CDC) reported age-adjusted DKA hospitalizations rates steadily increasing from 2009 to 2014 at an average annual rate of 6.3% (Benoit et al., 2018). Delays in DKA resolution and hypoglycemia put patients at a higher risk for prolonged
hospitalization. Turchin at al. (2009) showed statistically significant increases in LOS and patient death for every day of hypoglycemia. Longer term problems identified with poor blood sugar control included kidney failure, cardiovascular problems, vision problems and stroke (McCary, 2018).

**Evidence-Based Interventions**

Despite available literature and multiple studies recommendation and the 2009 ADA guideline consensus statement, it is not clear which protocol is best for DKA management, because DKA protocols are based on clinical judgment rather than scientific evidence. DKA protocol therapy is aimed at correcting hypovolemia, hyperglycemia, metabolic acidosis and electrolyte imbalances (Bull et al., 2007). This project is important because of the lack of clear studies in this area, and the numerous problems during DKA treatment such as high incidences of adverse effects and a lack of consensus on standards of care among providers.

The revised protocol at this medical center was simplified, and the Primary Investigator (PI) evaluated how efficient the protocol was to reach faster AG resolution and to avoid most common complications, such as hypoglycemia and hypokalemia. The PI reviewed the hospital's DKA protocol, compared it with recommendations from the literature, and highlighted the main changes from the previous protocol. The new protocol has only two fluid options rather than eight (isotonic 0.9% NaCl and 5% Dextrose 0.45% NaCl), which makes it more practical to use. Also, it specifies K+ replacement before the start of the protocol, which correlates with the ADA recommendation to replace K+ to reach at least 3.3 mmol/L before starting the insulin and a goal to maintain K+ between 4-5 mmol/L. The change to the electrolyte replacement part of the protocol (from premixed electrolytes and IV fluids to an electrolyte replacement sliding scale) simplified the electrolyte replacement process and made it easier to keep K+ at goal. The old
protocol required electrolytes to be premixed with IV fluids before treatment by the pharmacist resulting in the need for constant IV fluid bags changes. The change eliminated possible interruptions in treatment continuation caused by fluid bags not being readily available on the ward. The multi-step insulin-dosing algorithm was modified to a two-step table with simplified calculations on titration adjustments. The new protocol is easier to follow for the staff as its instructions are clearer, simpler to follow and less time consuming, especially for the nurses who are assigned higher acuity patients.

The first stage of the revised DKA protocol specifies titration adjustments when BG >250 with the goal of a 50-100mg/hr BG decline and electrolyte replacement based on biochemical profiles. The second stage: specifies IV fluids and insulin titrations if BG < or 250 with the goal of a 150-250 BG concentration. IV fluids are adjusted based on BG and serum sodium concentration thresholds. Two types of IV fluids are isotonic 0.9% solution in the first stage and 5% dextrose 0.45% NaCl in the second stage. When BG concentration reaches less than 250 mg/dL then the IV fluids from the second stage are started. The ADA guidelines recommended the fluid change after intravascular volume is restored and sodium (Na+) concentration is normal (135mEq or >) or elevated, and addition of dextrose when BG reaches 200mg/dL with the goal that BG be >200 mg/dL. The revised protocol addressed Na+ correction with 0.9% NaCL infusion (when corrected Na+ less than 135) or 0.45% NaCl (when corrected Na+ more of equal to 135). Recent evidence showed that the outcome is not different when continuous insulin infusion at rate of 0.14 units/kg/hr administered without bolus versus adding bolus for faster blood sugar correction. Also, the literature recommends insulin infusion continuation until ketoacidosis resolved, with serum BG < 200mg/dL and AG closure based on the laboratory ranges of the individual facilities; and switch to subcutaneous (SC) insulin
coverage after DKA resolution and 1-2 hours before infusion stopped (Hirsh & Emmet, 2018).

Current DKA protocol have only continuous insulin infusion without insulin bolus and have references on when to switch to SC insulin and insulin drip discontinuation follows the most available recent recommendation. The new protocol addresses the ADA’s goals for hypokalemia and hypoglycemia prevention and uses the same fluid modalities and strategies for electrolyte replacement, insulin infusion titration and monitoring as the ADA guideline.

**Objectives/Purpose**

The purpose of this project was to evaluate outcomes of currently used treatments for hyperglycemic crisis in patients with type 1 diabetes and DKA.

**Objective 1**: First, to investigate the use of a new DKA protocol at tertiary care center in KY in decreasing the number of hypoglycemic episodes.

**Objective 2**: Secondly, to investigate the number of episodes of hypokalemia that occurred with the revised protocol and compare that to the number of episodes associated with the old protocol.

**Objective 3**: Finally, to investigate whether the revised DKA could close the AG sooner than the old protocol.

The revised protocol, designed for use with adult patients with DKA, came into effect on November 28, 2018 at the tertiary hospital. The PI evaluated whether outcomes improved, and hypokalemia and hypoglycemia episodes decreased six months after and six months prior to implementation of the new protocol. Outcomes evaluated included the timeline to AG closure timelines and blood sugar resolution (from time of insulin infusion start to first BG<250mg/dL, and AG < or = 16 mEq/L).
Theoretical Framework

The Framework for Continual Improvement of Health Care emphasizes continued nursing education and by its application it is possible to define practice problems that can lead to solving them (Batalden & Stoltz, 1995, see Appendix G).

In order to achieve medical advances and continue to improve practice, nurses must combine knowledge with professional experience. For example, it is crucial to know anatomy and microbiology, and to understand the nursing discipline and its values. Because of concerns about the quality and efficacy of a protocol nurses must work with other health care disciplines to make continual improvements.

Continual improvement involves a team approach. For instance, nurses working at their best cannot meet their goal without the pharmacists working at their best as well. A single department meeting their improvement goals is not enough; the whole healthcare team must be involved in order to achieve lasting change. Leaders have to help workers understand the system to facilitate this teamwork.

Variation or defect of event need to be understood in order to properly respond to the problems. Is it common or special variation? Is AG resolution time increasing because of a common variation, such as a faulty protocol that requires fundamental change in the process? Or it is a special variation, such as provider’s non-adherence to the protocol or a late transition from IV to SC insulin? By removing special causes or fixing common variations, improvements can be made. Leaders must understand the psychology of change in order to help their followers achieve it. Finally, the theory of knowledge involves the combination of an action with a theory. If hypothesis about the cause of the problem or variation and attempted solution to the variation
are close to actual response or desired outcomes, then the treatment is probably effective, and this project evaluation is testing if the treatment of DKA is effective (Batalden & Stoltz, 1995).

**Synthesis of the Evidence in the Literature**

Diabetes ketoacidosis (DKA) is an acute complication of diabetes with increased production and decreased clearance of serum ketones due to uncontrolled hyperglycemia. Patients are severely dehydrated and develop metabolic acidosis. The PICOT question was: In adults 18 years and older, how do evidence-based DKA treatment protocols based on recent guidelines predict DKA resolution during a hospital stay, compared to DKA treatments that are not based on guidelines?

The search started with a thorough review of the most recent articles about recommended treatments for DKA, other conditions that can lead to metabolic acidosis and monitoring standards to DKA resolution. The databases searched included PubMed, Ovid, National Medical Library, CINAHL with Full Text, EMBASE, BMJ Clinical Evidence, Medline and UpToDate system. Search terms included: DKA, hyperglycemic crisis, DKA protocol, diabetes management, with narrowing to diabetic ketoacidosis, diabetic emergencies, hyperglycemic emergencies searches to find information specific for insulin infusion treatments of DKA. The search resulted in the selection of 15 articles from 2007 to 2019 and the ADA guidelines and the JBDS. About 50% of the searched literature includes articles published between 2017 and 2018. Eleven articles were evidence from guidelines developed from systematic reviews or evidence from well-designed cohort studies, and the rest of the articles were quality improvement, descriptive survey, and review designs. The search did not yield many randomized controlled trials design studies to answer the PICOT question, so cohort studies were mostly the only evidence to evaluate the practice.
Evidence-Based Recommendations

The PI reviewed the literature focusing on treatment modalities and its outcomes, such as a timeline for correction of ketoacidosis as well as safety indicators such as episodes of hypoglycemia and hypokalemia.

According to the ADA, DKA diagnosis defined when BG > 250mg/dl, presence of ketones in serums or urine and pH < 7.3 or bicarbonate < or= 18.0 mmol/L. The JBDS (2013) recommends protocolized management of DKA, including fluid repletion with 0.9% NaCl as initial IV fluids and aiming for ketone clearance with a weight-based fixed rate insulin IV drip (Phillips & Sinha, 2018). The guideline states to infuse fluids within 24-36 hours and complete half of those IV fluids within 8-12 hours of admission to correct dehydration (Islam et. al., 2018). Bicarbonate administration is not recommended for metabolic acidosis correction unless pH <6.9 (Islam et al. 2018). Discontinuation of IV insulin should happen 2-4 hours after subcutaneous (SC) insulin administration to avoid rebound hyperglycemia (Kitabchi, 2009). The ADA noted a six-fold increase in the rate of hypoglycemia occurrence with the use of intensive insulin therapy in medical ICU patients (n=1200) are not recommended except surgical ICU patient population (Moghissi et al., 2009). Boluses of IV insulin, tight glycemic control and fixed rates are considered intensive insulin therapies as referenced in the literature. When a patient is treated with regular insulin, a starting threshold of glucose concentration should be ≤180 mg/dl. IV insulin therapy should be kept at goal of 140 and 180 mg/dL from the time it is initiated and targets <110 not recommended in critically ill patients in order to prevent hypoglycemia (Moghissi et al., 2009).

The two-bag protocol is the addition of 10% dextrose IV fluids to a NaCl solution rather than using one bag with only NaCl isotonic solution throughout the whole DKA treatment time.
This has been associated with faster hyperglycemia resolution and reduction in hospital and ICU LOS by more than 20%. Using boluses in aiding faster hyperglycemia correction did not show any differences in time for DKA resolution (Islam et al., 2018). In a randomized controlled study, Brown et al. (2018) evaluated the effect of an insulin bolus compared to no bolus on the management of DKA. They noted no difference in time to DKA resolution between the two groups, no increase in incidences of hypoglycemia (no statistically significant findings) and no difference in hospital LOS. Brown et al's study had a low sample size (n=145) and the potential for inaccurate record keeping. One conclusion from this study is that it is safer to use the protocol without insulin boluses because it has no benefit in faster resolution, but it can theoretically increase the risk of hypoglycemic events.

**Evidence-Based Protocol**

In a randomized controlled study (RCS), Turchin et al. (2009; n=2582) found that hypoglycemia occurs in an average of 8% of all admissions, and is strongly linked to increased LOS and risk of mortality. The 2006 ADA guidelines recommended that the DKA drip include an insulin bolus in addition to the fixed-rate insulin infusion, and this could have contributed to an increase in hypoglycemia incidences. Hypoglycemia episodes were reduced when the insulin infusion was titrated based on the 2009 ADA guidelines (Lorenson et al., 2019, Gupta et al., 2016, Thuzar et al., 2014). Laliberte et al., (2017) noted no difference in hypoglycemia rates with insulin infusion adjustments with bolus insulin administration as compared to insulin titration without bolus. Conversely, a RCS by Thuzar et al. (2014) showed faster DKA resolution, shorter LOS, and fewer hypoglycemic and hypokalemic events (p<0.05) by titration of the IV insulin with a goal of BG between 160 to 250 mg/dl, addition of 10% dextrose (100ml/hr) when BG reached 250 mg/dl or less, and replacement of K+ when serum K+ was less
than 5. In their large RCS (n=256), Hara et al. (2013) noted a nine hour decrease in time to DKA resolution with a similar treatment to the one used by Thuzar et al. (2014). However, they did not find the difference in safety outcomes, such as reduction of hypoglycemia and hypokalemia, compared to the treatment without protocol (p<0.05). Choosing the right IV fluids is important for better efficacy and safety outcomes. In their RCS, Munir et al. (2017; n=383) evaluated outcomes of one bag versus two bag protocols and noted clinically significant results, such as faster AG closure and BG resolution and fewer hypoglycemia episodes with the two bag protocol.

The protocol can be an effective tool to manage DKA and following the protocol closely can improve outcomes, as the following studies show. Researchers have found that compared to no protocol, DKA protocols yield faster DKA resolution (Bull et al., 2007; Ramakrishana et al., 2013; Thuzar et al., 2014); reduce rebound DKA episodes (Ramakrishana et al., 2013), and significantly reduce hypoglycemia and hypokalemia (Thuzar et al., 2014). A QI study (n=30) by Kennedy (2018) showed that suboptimal compliance with the DKA protocol led to hypokalemia (n=8). Ronsley et al. (2017; n=157) also noted low compliance in their study on a pediatric population. Hence, better outcomes were related to protocol adherence.

Finally, in a large national study, Dhatariya et al. (2015; n=281) gathered data on DKA management in 72 hospitals across the UK. They reported mixed findings, suggesting that the fixed rate of insulin infusion could be too aggressive, resulting in increased hypoglycemia rates. It was also confounding if high rates of hypokalemia and hypoglycemia were due to poor adherence or faulty guidelines. The study evaluated DKA management with 70% of providers following JBDS guidelines. The researchers noted 28% of patients receiving the DKA protocol developed hypoglycemia with a median time of development at 15 hours after treatment started.
They also found that 55% of patients receiving the DKA protocol developed hypokalemia (Dhatariya et al., 2015).

In conclusion, the literature review revealed that DKA treatments based on the 2006 ADA guidelines cause high rates of hypoglycemia and hypokalemia, but researchers have noted mixed results with the 2009 ADA guidelines as well. The rates of hypoglycemia and hypokalemia are also prevalent with DKA treatment based on the JBDS guidelines. The review revealed inconclusive results with regard to safety outcomes, and this could result from faulty guidelines or poor adherence. Hence, there are no clear recommendations for providers. However, resolution outcomes related to DKA seem to be better with slow insulin titration, and with the right type of IV fluids (2 bag protocol over 1 bag protocol), based on biochemical markers and electrolyte replacement to maintain BG and K+ at safe and steady levels. There is a need to constantly evaluate outcomes and compare protocols to find the best possible evidence to achieve better patient results. With these findings in mind, the PI chose to evaluate the variables of time to AG resolution, AG reopening, hypokalemia, and hypoglycemia to better understand the efficiency of the current protocol in use at the medical center in Kentucky.

**Agency Description**

**Setting**

The project focused on outcome evaluation of a DKA protocol at UK HealthCare in Lexington Kentucky. The project focused on UK HealthCare Hospital, which is a 945-bed medical center. It is a Level 1 Trauma center with approximately 40,000 patient visits to the ED each year. The hospital serves Fayette and surrounding counties, with the largest population from Eastern Kentucky (UK HealthCare). This organization is comprised of 9,000 healthcare professionals, including physicians, nurses, pharmacists and other providers.
The project involved the collection of data from all inpatient wards that treat patients with DKA, including progressive units, ICUs and the ED. Registered nurses work closely with advanced care providers, physicians and nursing care technicians to deliver critical care to DKA patients. Critical care trained nurses can autonomously manage hyperglycemia crises with the help of protocols. Care is provided continuously, 24 hours a day. Each unit can have its own specific care guidelines in addition to the hospital-wide guidelines. Critical care units at UK Chandler Hospital include cardiothoracic vascular intensive care unit, a clinical decision unit, emergency and trauma services, medical intensive care units, progressive care units, and the stroke center. There are 206 critical care beds at UK Healthcare that make up cardiothoracic, medical, surgical, neurosciences and compose the setting for this project.

**Target Population and Recruitment**

UK Chandler Medical Center provides health care to all Kentucky counties. UK HealthCare discharged 37,789 patients in 2016 (UK HealthCare, 2016). The target population for this study was adults with type 1 diabetes who were admitted to the hospital with DKA as their primary diagnosis and received DKA protocol treatment. The diagnosis of DKA is based on ADA biomarker concentration obtained from venous blood gas and a serum chemistry panel (Menchine, 2011). For safety outcome evaluation, the PI included a comparison of number of episodes of hypoglycemia (blood sugar less than 70 mg/dL) and hypokalemia (potassium less than 3.3 mEq/L; Kitabchi, et. al., 2008) and efficacy of the protocol was evaluated through calculation of duration in hours for AG to reach 16 or less and calculation of duration of BG to reach 250mg/dL. Other variables evaluated were admission pH <7.3 to determine relation to AG closure.
The PI collected laboratory values and demographic data through retrospective chart reviews six months before November 28, 2018 (revised DKA protocol implementation day) and six months after this day. According to data collected using the REDCap research informatics tool, six months before November 28, the sample population included 25 subjects; six months after implementation of the revised protocol, there were 42 subjects, for a total of 67 individuals.

The inclusion criteria were patients with diabetes mellitus type 1 (DM1). The exclusion records of subjects included conditions such as DM2, uncompensated liver failure, uncompensated kidney failure, myocardial infarction, fluid overload or severe impairment of a vital organ during protocol examination days; pregnancy; and children under the age of 18 years. Also, the PI excluded patients admitted to the hospital who used non-insulin treatments to treat hyperglycemia and alcohol in their blood. The reason for exclusion was that all of the listed problems could lead to erroneous interpretation of relevant laboratory results.

Alignment with Organizational Goals

The organization's mission corresponds with that of this project, specifically, to look for cutting edge services on the level of the best providers in the nation, and lead the way to ensure quality, safety and value for every patient. The protocol could be an effective way to resolve DKA, or the project could produce new data so that any deficiencies can be improved. Also, the project can lead to further studies to improve the protocol, encourage additional training, and to encourage other researchers to work on improving knowledge about DKA treatment. The project aligned with a strategic plan to reduce patients’ LOS and hence improve their experiences. So, the actions to correct the problems can be developed with future studies that can result in a reduction in a patient stay and bettering the quality of care and patient experiences. The strategic plan addresses patient care by potentially limiting high-cost patient care expenses for treating the
sickest. This means expansion of ambulatory patient care and a higher number of healthier patients. DKA patients require emergent treatment and are included in the category of the sickest patients. Additionally, UK HealthCare reported 810 patients on insulin for treatment of DKA and non-DKA hyperglycemia who experienced hypoglycemia (blood sugar < 51) in 2018, and the goal is to lower this number. If complications such as hypoglycemia can be avoided with an efficient protocol, this can reduce the sickest patients’ expenses. This project served as knowledge tool that indicated how well the DKA protocol aligns with the ADA guidelines and the JBSG. This project was designed to support the academic role of the organization to advance research and adopt evidence-based practices.

**Stakeholders**

There were multiple stakeholders or people who would be interested in protocol evaluation. The primary stakeholders were nurses, nurses' techs and patients because they were the targets of the efforts. Nurses implemented the DKA protocol and adjusted DKA treatments based on MDs’ or other providers’ orders. NCTs were charting intake and output and checking BG hourly. There were secondary stakeholders as well: medical doctors, advanced care providers, nurse managers, and pharmacists who were directly responsible for reviewing orders and adjusting orders based on biochemical results. Other key stakeholders included senior clinical experts, Critical Care Services Councils, policy makers (those who sit on the committees to approve the protocol), those who can influence others (CEOs) and those with academic or research interests (Community ToolBox). These last groups of stakeholders were remotely involved in the process of DKA implementation but were mostly working on safety improvement and necessary changes to the DKA protocol at the population level.
Facilitators and Barriers

Facilitators helped this evaluation project to be conducted efficiently. They involved leadership support, IRB approval, and hospital mission alignment with the project goals and outcomes. One of the main facilitating factors was the persistence of the evaluator and unfolding results. But the biggest facilitator was that this protocol was already used hospital-wide; and it was a change that need to be evaluated for effectiveness. The stakeholders who used the protocol were interested to know if what they were implementing was actually working. Some barriers included delays in data retrieval, staff shortage to retrieve the data, other research projects, and technical problems.

Design

The PI used a retrospective cohort design for the chart review. This design was chosen because chart evaluation involved comparison of sample groups available in records. Retrospective chart reviews were used to see the outcomes of the protocol before it was revised, for the time between 2018-05-28 and 2018-11-28 and after the change, for dates between 2018-11-28 and 2019-05-28.

Methods

Project Interventions

This project involved the collection of data from patient charts and included all inpatient areas that treat patients with DKA, such as progressive care units, ICUs, and the ED. The study includes only data extraction and interpretation without any intervention. Old and revised DKA protocols were compared with the review of stored data, and outcomes of DKA treatments were evaluated, such as episodes of hypoglycemia, hypokalemia, and the timeline for correction of AG.
IRB and Ethical Concerns

A letter of approval was received from the Nursing Research Council on June 12, 2019. IRB approval was obtained on 10/2/2019 (#53236) in order to access the patients’ information. After IRB approval, the PI reviewed patients’ extracted data done by CCTS with variables of interest. CCTS practices and rules of compliance with HIPAA ensured the protection of participants’ health information. It was not practical to obtain consent because the PI was doing a fully retrospective EMR review. This project was granted exempt status because the PI used de-identified data of the patients’ records and the project was not defined as clinical research, so consent was not required. The PI was not required to submit a waiver of authorization for approval of data extraction, as data was de-identified by CCTS. The study did not include any prospective data; therefore, there was no access to patients and no opportunity to seek informed consent. The application was approved by IRB and a nonmedical type exemption was granted.

The risk to patients was minimal and did not pose any additional threat than the other ethically reviewed studies. The only possible risk for the study was a breach of personal information due to unforeseen breaches of privacy. The only people that had access to the data were the University of Kentucky IRB, CCTS specialists, a statistician and the PI. This data for this study will be kept for six years and the destruction of all research data will be done per UK HealthCare policy. After IRB approval, the PI reviewed patients’ extracted data with variables of interest.

The CCTS data extractor uploaded the data into REDCap. About two weeks after the request was submitted the PI received an email that included a link to access the data. The data were released to the PI in de-identified format. The PI did not make any attempt to identify the subjects.
The PI compared old and revised DKA protocols with the review of stored data, evaluated outcomes of DKA treatments such as episodes of hypoglycemia, hypokalemia, and timeline for correction of AG before change for the time between 2018-05-28 and 2018-11-28 and after change for dates between 2018-11-28 and 2019-05-28. Data collection included: demographics (race, gender, age, ethnicity), length of ICU and non-ICU stay, lab values (venous blood pH, K+, BG values, AG), LOS, admission disposition, discharge disposition.

**Sample**

The sample population included adult patients with diabetes type 1 as their primary diagnosis for admission who received DKA protocol treatment at the Medical Center. The PI chose convenience sampling because it was a review of all the patients' charts over a period of 6 months before and after the set date. The number of patients selected for chart review happened to be at the hospital during the time period and were not randomly assigned. No other hospitals' protocols were evaluated. The PI evaluated the difference between the "exposed" cohort (the charts of patients treated with the revised protocol) and the "unexposed" cohort (the charts of those treated with the old protocol). Two samples had an unequal number of participants.

The information collected included adults aged 18 and older, of both sexes, and the sample population includes 25 and 42 patients in each group respectively. It excluded records of subjects less than 18 years old, as well as cases with other conditions, such as uncompensated liver failure, uncompensated kidney failure and evidence of alcohol intoxication because of the possibility of data interpretation errors. Minors and pregnant women were excluded because of variations in variables characteristics that can compromise laboratory results interpretation. The sample evaluated was similar to the general population of patients with DKA, with the exclusion
of conditions that can affect a proper evaluation of ketoacidosis resolution but no other comorbidities.

**Measures and Instruments. Implementation. Data Collection**

The PI relied solely on objective data of biochemical tests that make my project valid. Specifically, the PI examined patient outcomes by measuring a number of episodes of ↓BG (BG < 70 dL), ↓K (hypokalemia, K < 3.3) and timeline for AG closure (<16 mmol/L) and timeline to BG resolution of 250 dL or less.

After data collection was completed by CCTS technicians, the PI reviewed the data and further excluded cases based on DKA treatment noncompliance or misleading data when laboratory values such as glucose were collected at longer than a 1-hour interval. This was viewed as treating the patient with modalities other than the protocol, or as the use of a different treatment to resolve DKA. Therefore, the excluded cases were identified and not counted in statistical analysis. SPSS software was used to compare the data of two different protocols using descriptive and inferential statistics and displayed the results of the findings with the help of tables. After the findings interpretation, the results were shared with members of the project committee.

Physical resources needed for chart review included a personal computer, since all patient information was stored in electronic health records. The International Statistical Classification of Disease and Related Health problems, 10th revision (ICD-10) was used to classify and code all diagnoses for inclusion and exclusion criteria. Diagnosis search from 2019 ICD-10-CM included code E10.10 (type 1 diabetes mellitus with ketoacidosis without coma). Admission type was "emergency," because patients admitted to emergency are sent to other units when a bed becomes available. So, the patients either stayed in the ED or transferred to subsequent units for
treatment continuation. Exclusion criteria for the search included diagnosis coded as Z33, Z34, Z3A (pregnant state) and K76.6 (decompensated alcoholic cirrhosis), R74.0 (lactic acidosis), F10, (ingestion of drugs such as aspirin, methanol, ethylene glycol) and T45 (advanced chronic kidney disease).

**Data analysis**

The PI compared the number of episodes of hypoglycemia, hypokalemia and an average time to AG closure in both sample groups from the time of hospital admission until AG resolution. This was based on biochemical results, and the PI used descriptive statistics (means and standard deviations or frequency distributions) to summarize study variables. Using SPSS software, the PI analyzed data and compared study variables with a two-sample t-test, chi-square test of association or Mann-Whitney U test. All data analysis was conducted using SPSS, version 24 with an alpha level of .05.

Descriptive statistics were used to translate the characteristics of the sample into measurable numerical data. AG resolution was counted as the serum AG reaching 16 or less mmol/L. The PI compared number of patients, age, race, gender, glucose, adverse incidences of low potassium and pH levels to evaluate differences in both groups at baseline and throughout the timeframe of DKA treatment.

**Results (demographics and findings)**

Cohort 1 or group 1 included all patients who received treatment before the protocol change and cohort 2 or group 2 included all patients who received treatment after the protocol change occurred.

A higher proportion of patients were Caucasian compared to cohort 2 (92% vs. 74%, p=.032). The majority of patients were in their early 30s (mean 32 vs. 31, p=.830). The
progressive care unit was the most frequently admitted service with 48% for the patients in cohort 1 and 52% in cohort 2 (p=.300). The average number of days spent in the hospital for treatment of DKA with the old protocol was 5 days (p=.472), 3.5 with the new protocol, and 2 days in the ICU in both cohorts (p=.656).

In general, AG reopening was not associated with longer overall stay in the hospital (p=.96). AG reopened in about 28% of patients in both cohorts and hypoglycemia episodes noted for the overall duration of hospital stay were more than 96%, vs 93% in the first and second groups respectively. Hypoglycemia that happened on the DKA drip before AG closure was slightly higher in the 2nd group than in the 1st group, with 29% vs 24% (p=.683), so the revised protocol did not result in fewer hypoglycemic episodes. But the rate of hypoglycemia on the DKA drip for the duration of IV insulin infusion almost doubled in both groups (24%->44%-> and 29%->53%; p=.510). This may indicate that the patients were on the insulin drip after AG closure, and this resulted in large increase in hypoglycemic episodes. Data suggest that the transition to SC insulin was not timely.

Instances of hypokalemia were 40% in the 1st cohort and 50% in the second cohort (p=.427). So, the revised protocol showed higher number of hypokalemic episodes, suggesting that a sliding scale for K+ replacement could have resulted in more autonomy for the staff, but also higher noncompliance either among providers or staff.

As compared to literature findings, hypoglycemia and hypokalemia rates were higher at this medical center than what was found in the literature. For example, the rate of hypokalemia was 28.6% (p=.038), and the rate of hypoglycemia was 8.6 % (p=.036) in the study by Thuzar et al., (2014). Hara et al. (2013) had a 30.1% rate of hypokalemia (p=.413) and an 8% rate of hypoglycemia (p=.259).
Time to resolution of AG was 11.8 hours in the 1st group and 10.43 hours in the 2nd group (p=.219), time to blood sugar resolution on average was 6.6 hours (1st group) vs 6.5 hours (2nd group) in both cohorts (p=.883). Time to AG resolution was close to findings noted in the literature. Patients treated with the 2009 ADA consensus statement protocol, had 13.6 hours for DKA to resolve (n=113, p<.01) in Hara et al., study (2013) and 15 hours to DKA resolution (n=35, p=.01), in Thuzar et al., study (2014).

For the adverse events and associated ICU LOS analysis, there was no significant difference (p=0.643) when adverse events occurred (AG reopened) and when treatment had no adverse events (as measured by ICU LOS) in the first group (n=25). For adverse event of AG reopening in relation to ICU LOS, there was 3 ICU days on average when no event happened and 4 ICU days when such event occurred. The AG reopening in this sample did not indicate longer ICU stay (in days), compared to the cases when no AG reopening happened. For the second group (n=42), there was a significant difference (p=.031) between incidences of AG reopening and ICU length of stay (as measured by ICU LOS). In particular, the mean length of ICU stays for patients whose AG reopened was 4 days compared to 2 days for patients who had no instances of AG reopening. The AG reopening in this sample indicated longer ICU stay (in days), on average, compared to the cases with no AG reopening. More patients required ICU level of care in the second group 40.5 %, compared to the first group 30.8 % (p=.333)

Problem resolution analysis showed that in the first group of patients (n=25), the time to AG resolution was not much different (11.5 vs 11.89 hours) when hypoglycemia episodes occurred versus when there were no occurrences of hypoglycemia. There was no difference between the timeline for AG resolution and hypoglycemia before AG closure (p=0.847) for the first cohort. For the second cohort (n=42), the PI concluded that in those cases with no instances
of hypoglycemia before AG resolution resulted in faster AG resolution, and this was statistically significant (p=0.05). The majority of cases in the second cohort (n=30) had on average 9 hours to AG resolution when there were no hypoglycemic episodes before AG closure. When hypoglycemia did occur, the time to AG resolution increased by almost 4 hours, for a total of 13 hours.

Also, there was positive moderate association between incidences of pH less than 7.3 and AG resolution for the first group, n=25 (Spearman’s rho .436, p=.029). But no association was found between incidences of pH less than 7.3 and time to AG resolution in the second group, n=42 (Spearman’s rho .055, p=.735)

**Discussion**

There was no significant difference in hypoglycemia episodes between cohorts. Hypoglycemia episodes while on the protocol before AG closure were 24% for the first cohort and 29% for the second cohort, with more patients in second cohort (p=.683). Interestingly, patients had 96% and 92% of hypoglycemia episodes in the first and second groups throughout the whole time spent in the hospital. This suggests that the protocol change did not result in a smaller number of hypoglycemia episodes, and hypoglycemia rates were high for the duration of the entire hospital stay. The study showed that hypoglycemia events between both groups were not different for the first objective of the project.

The second objective was satisfied by calculating the number of hypokalemia episodes that were higher in the 2nd cohort (40% vs 50%) but there was no statistically significant difference between groups (p=.427).

Finally, for the third objective, AG resolution in hours was almost 2 hours faster in the 2nd group, (12 vs 10 hours; p=.22). AG closure was not related to hypoglycemia episodes within
AG resolution in the second cohort (p=.847). It showed that the first cohort had 12 hours on average for AG to close when no episodes of hypoglycemia occurred. However, there was faster AG resolution in the second group when no hypoglycemia occurred during treatment before AG closure (p=.05). Hypoglycemia incidences affected time to AG closure in the second cohort (n=30), which was statistically significant. On average, it took 9 hours for the AG to close. Also, in the second group, length of ICU stay was twice as long when AG reopened during the hospital stay (p=.031). So, avoidance of hypoglycemia and AG reopening can help with faster problem resolution and fewer days spent in the ICU.

Also, instances where venous pH was less than 7.3 were higher in the second cohort 64% (n=16) and 75% (n=30; p=.343) were not statistically different between the two groups. But a moderate positive association between low pH and time to treatment resolution was found. It means an association between lower pH and longer time to treatment resolution (p=.029), when no such association was found in the second group (p=.735). That can suggest that low pH was attributed to other conditions rather than ketoacidosis, possibly affecting the laboratory values.

**Limitations and Strength of the study**

Small sample size was a significant limitation of this study. Sample size could increase if the observation timeframe for both cohorts was broadened, but due to time constraints it was not possible to achieve.

The number of people in both cohorts were not equal. There was a smaller sample size than anticipated. Future studies could be done to evaluate compliance with the protocol adherence among providers and staff as well as to evaluate comorbidities. Another study could survey nurses about their attitudes about the protocol and provide feedback for improvement.
The strength of the study is that there is no known DKA protocol treatment evaluation study done at UK HealthCare.

**Implications for practice, education, policy, and future research**

Future studies should focus on hypoglycemia and AG reopening reduction as those preventive strategies have been shown to promote faster AG resolution and shorter ICU LOS. The next study can focus on a larger sample and employ a two-year timeframe for evaluation before and after the revised protocol with inclusion of prospective study design; this should help to better clarify the differences in protocols. The incidences of medication errors during drip infusion were not evaluated in this study; future researchers could focus on that, since it can influence the effectiveness of the treatment.

The protocol addressed hypoglycemia with low-dose insulin infusion without bolus and addition of dextrose to IV fluids when blood sugar reached less than 250mg/dL. This follows the 2009 ADA guidelines, but there were no improvements in hypoglycemia cases between the two groups. This raises questions about whether other factors may be affecting high rates of hypoglycemia, such as staff nonadherence, and the need for accountability when following the protocol. These factors should be evaluated in future studies. Also, the time from AG closure to transition from DKA insulin drip to sliding scale can be evaluated because it can affect hypoglycemia outcomes. Since, the results suggested long time to transition to SC insulin after AG resolution occurred. A system alert is needed to notify the providers when AG closure occurs, and it could be done by the pharmacists to reduce hypoglycemia with a timely transition to SC insulin. These alerts can be a valuable tool and an important protective strategy since this institution is a teaching hospital and many junior providers might not be aware of the specifics of DKA management. Finally, future studies can focus on ways to reduce hypoglycemia, regardless
of insulin drip infusion or sliding scale use. This number is very high throughout the hospital stay, and on average occurs almost on every patient who is affected by diabetes.

Potassium replacement orders should be easily available for the nurses, with clear instructions to start replacing potassium when values are between 4.1-5 or less than 4.1. There is a need for a timely K+ replacements. It can be achieved by timely notifications or call back from lab personnel to alert nursing. Also, pharmacists can verify orders for K+ replacement sooner. Instructions about potassium K+ replacement and doses parameters should be included on the algorithm in the same table next to IV fluids and IV insulin titration for better visualization. Proactive, timely potassium replacement can help prevent hypokalemia, pauses in insulin drip infusion and AG reopening.

Further research can evaluate the sustainability of the DKA protocol. In the next study, researchers can examine costs and mortality numbers and compare those numbers after every 2 years of protocol implementation.

**Summary/Conclusion**

Outdated evidence-based DKA treatment modalities can lead to high numbers of adverse outcomes. New evidence-based practices become available with time and there is a need to implement that in the current practice.

This project was a retrospective review to assess the effectiveness and safety of the currently used protocol in order to see what can be done to implement better protocols in the future. There was no improvement in safety outcomes noted, such as less hypoglycemia or hypokalemia, but the project did reveal better effectiveness outcomes, such as faster AG closure timelines. However, the study noted that increased safety of the protocol can increase its effectiveness and shorter ICU LOS. The study showed that AG resolution was on average 9
hours when no hypoglycemia occurred, and it was about 4 hours faster than when hypoglycemia occurred in the second sample group. Also, ICU LOS was two times shorter when incidences of AG reopening did not happen in the second group. Biochemical results with lower pH were related to longer AG resolution in the first group.

Since AG reopening was shown to significantly increase ICU LOS, strategies focused on hypoglycemia rebound hyperglycemia, and hypokalemia should be explored since all of these factors can cause AG reopening. Also, diabetic educators should be alerted when the lab values are hitting or approaching critical values so as to actively participate in DKA management teaching and helping staff and providers to understand the specifics of treatment. The review revealed that labs to determine ketones in the blood serum were inconsistently ordered. The majority of the providers ordered this laboratory on admission, and then very few ordered follow up on ketone disappearance.

The study didn’t find that the revised protocol is less effective than the old algorithm. Even though no improvements in safety outcomes were noted, there was faster DKA resolution, which is consistent with other researchers’ findings on effects of the 2009 guidelines-based protocols. Looking back at theoretical framework, the variation can be caused by special circumstances, such as providers being unaware of the best time to transition to SC insulin, and responding to this problem could reduce incidences of hypoglycemia. Also, nurses and laboratory staff should work together to ensure more timely potassium monitoring, as well as proactive and timely replacement.

Neither adherence to the protocol nor medical errors were evaluated in this project, and should be evaluated in the next studies. Looking back at theoretical framework, the project yielded valuable information and this information should be brought to the attention of the
committee that is working on revision of the protocol so they can take these findings into consideration. Strategies to avoid hypoglycemia and hypokalemia should combine knowledge of DKA management as well as knowledge of the system, communicating and working with providers, pharmacists, diabetic educators and nursing in order to explore possible solution for improvement in safety outcomes. All three objectives were met as the number of hypoglycemic and hypokalemic episodes was evaluated, as well as time to AG closure.
References


UK ADULT DKA ALGORITHM

INITIAL DKA IV INSULIN

Baseline FSBS
Start insulin infusion once $K > 3.3\text{mEq/L}$ at 0.14 units/kg/hr (round to the nearest 1/2 unit)

Begin FSBS monitoring q1hr

If FSBS does not fall by 10% in 1st hour, give insulin 0.14 units/kg IV bolus ***

- FSBS decreases by $> 50\text{mg/dL}$ after IV bolus
  - Continue current infusion rate
- FSBS decreases by $< 50\text{mg/dL}$ after IV bolus
  - Double infusion rate

- FSBS decreases by $> 50\text{mg/dL}$ after doubling infusion
  - Continue current infusion rate
- FSBS decreases by $< 50\text{mg/dL}$ after doubling infusion
  - Repeat Insulin 0.14 units/kg IV bolus

IV DKA INSULIN MAINTENANCE INSTRUCTIONS

- INSULIN TITRATION-RAPID DECREASE
- INSULIN TITRATION-WO PROGRESS
- INSULIN TITRATION-RAPID INCREASE
- INSULIN TITRATION-AT GOAL

- FSBS decreases by $>150\text{mg/dL}$ since last check
- FSBS increases by $<100\text{mg/dL}$
  - Increase infusion rate by 25%
- FSBS increases by $>100\text{mg/dL}$ since last check
  - Increase infusion rate by 50%
- FSBS decreases by 50-150 mg/dL per hour since last check
  - Continue current infusion rate

Use INITIAL TITRATION on left first
*** IF FSBS decreases by $>150\text{ mg/dL}$ from the last FSBS check during the initial titration, reduce the rate by 50%
Add DS if FSBS fall $<200\text{ mg/dL}$

Once you reach a ‘continue current infusion rate’ or ‘Call Prescriber’ & move to the other INSULIN TITRATION directions unless Prescriber orders otherwise.
UK ADULT DKA ALGORITHM

Fluid selection is based on the patient’s correct serum sodium, serum glucose, and serum potassium concentrations.

Key points:

- If serum sodium is < 135mEq/L, use 0.9% sodium chloride; if serum sodium is > 135mEq/L, use 0.45% sodium chloride
- When the glucose concentration falls below 200mg/dl, change IV fluids to add dextrose 5%
- If serum potassium is < 5.2mEq/L, add 20mEq KCl to each liter of IV fluid
- Flow rate for IVFs ranges from 150-250 ml/hr as determine by order
## Appendix C: Revised DKA Protocol

### Nursing guideline gNU-27 Adult DKA and HHS Guideline: ICU, ED and Progressive Use Only

<table>
<thead>
<tr>
<th>Blood Glucose</th>
<th>Insulin</th>
<th>IV Fluid</th>
</tr>
</thead>
<tbody>
<tr>
<td>251 mg/dL and higher</td>
<td>If BG decreases ≤ 101 mg/dL, within 1 hour (From last FBS) Decrease current infusion rate by 50% (Multiply current rate by 0.5)</td>
<td>Fluid per physician order</td>
</tr>
<tr>
<td>250 mg/dL and lower</td>
<td>If BG decreases ≤ 49 mg/dL, within 1 hour (From last FBS) Increase current infusion rate by 50% (Multiply current rate by 1.5)</td>
<td>For electrolyte replacement, use Electrolyte Replacement Protocol if ordered. If not ordered contact provider to get replacement orders as electrolyte values result in SCM.</td>
</tr>
<tr>
<td></td>
<td>If there is any increase in BG or if BG decreases &lt; 49 mg/dL, within 1 hour (From last FBS)</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Check BG every 1 hour. Follow titration table</td>
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</tbody>
</table>

### Insulin and Fluid Titration

Do NOT start insulin infusion if initial K ≤ 3.3 mEq/L, implement replacement per Electrolyte Replacement Protocol or notify provider for potassium orders AND regarding delay in starting insulin infusion.

Initial DKA Insulin Infusion Rate: 0.14 units/kg/hr (maximum: 14 units/hr) – Use DKA Insulin setting on Alaris® Pump

#### Stage 1 – Begin when BG > 250 mg/dL (For BG 251 mg/dL and higher)

<table>
<thead>
<tr>
<th>Stage 1 – Follow titration table</th>
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</thead>
<tbody>
<tr>
<td>BG decreases ≤ 101 mg/dL, within 1 hour (From last FBS) Decrease current infusion rate by 50% (Multiply current rate by 0.5)</td>
</tr>
<tr>
<td>BG decreases ≤ 49 mg/dL, within 1 hour (From last FBS) Increase current infusion rate by 50% (Multiply current rate by 1.5)</td>
</tr>
<tr>
<td>There is any increase in BG or if BG decreases &lt; 49 mg/dL, within 1 hour (From last FBS)</td>
</tr>
</tbody>
</table>

Stage 2 – Begin when BG < 250 mg/dL (For BG 250 mg/dL and lower); Target glucose during stage 2 is 150-250 mg/dL. Activate order for stage 2 insulin. Initiate D5W-0.45% NaCl @ 100 ml/hr and discontinue all other IV fluids ordered with Stage 1 of DKA/HHS treatment. Continue electrolyte replacement described above.

### Stage 2

<table>
<thead>
<tr>
<th>Blood Glucose 250 mg/dL and lower</th>
</tr>
</thead>
<tbody>
<tr>
<td>If BG &gt; 250 mg/dL, within 1 hour Follow Stage 2 titration guidelines above. Increase current infusion rate by 50% (Multiply current rate by 1.5)</td>
</tr>
<tr>
<td>If BG 150-250 mg/dL, within 1 hour Continue current infusion rate</td>
</tr>
<tr>
<td>If BG 101-149 mg/dL, within 1 hour Decrease current infusion rate by 50% (Multiply current rate by 0.5)</td>
</tr>
<tr>
<td>If BG 70-100 mg/dL, within 1 hour Decrease current infusion rate by 50% (Multiply current rate by 0.5, recheck BG in 30 minutes)</td>
</tr>
<tr>
<td>If BG &lt; 70 mg/dL STOP insulin infusion. Give 25 g of dextrose 50% per hypoglycemia management protocol, notify provider.</td>
</tr>
<tr>
<td>When BG &gt; 100 mg/dL, restart insulin infusion at 50% previous rate (multiply previous rate by 0.5).</td>
</tr>
</tbody>
</table>

### Stage 3

Transition to subQ insulin per provider order. Turn off insulin infusion 2 hours after first dose of subQ insulin. IVFs at the discretion of the provider.
### Table 1: Synthesis of the Literature

<table>
<thead>
<tr>
<th>Author, Year</th>
<th>Study Design Purpose</th>
<th>Sample Characteristics &amp; Setting</th>
<th>Variables: Independent Dependent</th>
<th>Data Analysis</th>
<th>Main Findings</th>
</tr>
</thead>
<tbody>
<tr>
<td>1. Bull et al., 2007</td>
<td>Design: RCS to determine the effect of a mandatory protocol for treating diabetic ketoacidosis</td>
<td>Sample: N= 241 (btw 2000-2005) IG= 111(postprotocol) CG= 130 (preprotocol) Jan 1, 2000- Dec 31, 2002 (preprotocol), and Jan 1, 2003-Dec 31, 2004 (postprotocol), with a principal DKA diagnoses</td>
<td>IV = the protocol DV1 = ICU LOS DV2 = hospital LOS DV3 = time to correction of AG and ketone clearance DV4 = # hypoglycemic episodes</td>
<td>Power analysis for this outcome performed before beginning the study and use of a two-sided test with an alpha of .05 and a power of 85%. Two groups compared using Student’s t-test from SPSS version 12.0 (SPSS, Chicago, IL) for Windows; p &lt; .05 was considered to be significant.</td>
<td>Before protocol implementation, the mean SD ICU and hospital LOS were 44 and 28 hrs and 91 and 73 hrs. After implementation, ICU and hospital LOS ↓ 23% and 30%, to 34 and 18 hrs and 64 and 41 hrs, (both p &lt; .007). Time to AG closure ↓ (both p &lt; .05). Number of hypoglycemic episodes - no difference observed.</td>
</tr>
<tr>
<td>2. Gupta et al., 2016</td>
<td>Design: RCS to assess the efficacy of a unified hyperglycemia and DKA insulin infusion protocol, based on an algorithm aimed at glycemic targets and minimizing hypoglycemia</td>
<td>Sample: N=62 Surgical care implementation project n=20; MICU n=42</td>
<td>IV = insulin infusion protocol DV = blood glucose numbers</td>
<td>M data analyzed by t-tests or ANOVA, post-hoc analysis was performed by the Fisher LSD procedure for subgroup analysis. Correlation and regression analysis was performed using Pearson’s correlation coefficient. Statistics on proportions were performed by Chi square analysis. Statistical procedures performed with Statistica for Windows (Version 5, Statsoft Inc., Tulsa OK). Significance was defined as a P &lt; 0.05 by two-tailed testing</td>
<td>BG targets of 100–180 mg/dL in majority patient population. No episodes of hypoglycemia blood 4–6 weeks. The two year pre-institution of the protocol, # of hypoglycemic events ↓ (BG &lt;70MG/dL pre-protocol 2.87% vs post-protocol 2.30% &lt; 0.001 (statistically significant)</td>
</tr>
<tr>
<td>3. Fuso et al, 2015</td>
<td>Design: RCS for the treatment of DKA between July 1, 2007 and June 30, 2010</td>
<td>Sample: N=60 (satisfying guidelines n=12; not satisfying guidelines n=48)</td>
<td>IV = Diabetes CG DV1: IVF DV2: insulin gtt rate DV3: transition to SC insulin DV4: # rebound DKA, # hypoglycemia</td>
<td>Descriptive statistics: demographic information. Nominal data analyzed based on the sample size using the chi-square test and Fisher Exact test. Two-sample student’s t-tests were used to evaluate differences between 2 groups for continuous discrete data. The Mann-Whitney U test - evaluate differences between groups for nonparametric discrete data. Statistical analysis using StatPlus 2009 (AnalystSoft, Alexandria, VA). A two-sided p-value of &lt;0.05 statistically significant</td>
<td>Low compliance with the 2006 ADA CG. Sixteen (26.7%) patients were treated in compliance CG with IVF infused. 10 (83.3%) out of 12 (by CG) patients were appropriately transitioned to SC insulin from insulin gtt vs 22 (45.8%) out of 48 (not treated by CG) were transitioned to SC insulin from an insulin gtt (p = 0.045). 5 (41.6%) of patients treated by CG experienced an episode of rebound DKA compared to 11 (22.6%) patients not treated by CG (p = 0.342).</td>
</tr>
<tr>
<td>4. Islam et al, 2018</td>
<td>Design: Review to review</td>
<td>Sample: N=NA</td>
<td>IV=NA DV=NA MEDLINE (via PubMed)</td>
<td>NA</td>
<td>treated with protocol -resolution of DKA in 10 h. After protocols, ICU LOS ↓ 23% to 34+18 h. M hospital LOS ↓ 30% to 64+41 h. Initial bolus dose of insulin -&gt; no significant benefit to DKA</td>
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<td>Author, Year</td>
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<td>7. Ronksley et al.</td>
<td>Study design: RCS September-December 2013</td>
<td>Sample: N=157 Setting: University of British Columbia Children's Hospital</td>
<td>IV: DKA protocol DV1: initial lab values</td>
<td>Log-linear regression analysis with SAS/STAT Software version 9.4.</td>
<td>Health care providers' adherence to the DKA protocol is poor, poor adherence to protocol's IVF. The length of time on insulin infusion was 21.5 and 24.1 hours in pediatrics</td>
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<td>5. Lali et al., 2017</td>
<td>Design: RCS</td>
<td>Sample: compliance with 2006 guidelines group: PRE n=12 (60 total); POST n=14 (55 total). Compliance with 2009 guidelines group: PRE-order n=19 (60 total); POST-order n=36 (55 total) Setting: MICU at a large academic medical center</td>
<td>IV1: PRE-2006 CG IV2: POST 2009 CG DV1a: 24 h volume in ml, mean (PRE-), mean (POST) DV1b: hypoglycemia, (%) (PRE) DV1c: time to DKA resolution in hours, M (IQR) DV2a: receipt of insulin bolus (PRE and POST) DV2b: insulin gtt M (PRE&amp; POST)</td>
<td>Hypothesized ↑ compliance to 50%, 52 patients required, a power of 90% and a two-sided level of 0.05. Descriptive statistics - demographic information and individual outcome measures, IV, insulin administration and compliance rates. Continuous variables - Student's t-test or Wilcoxon signed-rank test. The chi-square or Mantel–Haenszel test was utilized for categorical variables. To control for confounding, a multivariate analysis performed with a logistic regression model. Statistical analyses performed utilizing GraphPad Prism (GraphPad San Diego, CA, USA).</td>
<td>20% in the PRE group received treatment compliant with the 2006 and 25.5% in the POST group Compliance to the 2009 CG was significantly ↑ in the POST group (31.7% vs 65.5%, OR 4.44 95% CI 1.8 to 10.92, P = 0.0004). Time to DKA resolution ↓ (P = 0.04), and hypoglycemia↓ (P = 0.0022). Only 20% of patients received treatment compliant with the guidelines. DKA treatment in the POST group was 4.44 times more compliant to the 2009 ADA DKA guidelines (contain the most updated recommendations in the US for the care of patients with hyperglycemic crises. Also, significantly ↑ compliance to 24-h IVF, initial insulin gtt rate, time to DKA resolution and appropriate transition to SC insulin in the POST group. Limitations: small sample size, confounding variables not assessed</td>
</tr>
<tr>
<td>Author, YEAR</td>
<td>Study Design</td>
<td>Sample Characteristic &amp; Setting</td>
<td>Variables: Independent Dependent</td>
<td>Data Analysis</td>
<td>Main Findings</td>
</tr>
<tr>
<td>-------------</td>
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</tr>
<tr>
<td>11.Thuzar et al., 2014</td>
<td>Study design: RCS</td>
<td>Purpose: to review adherence to a provincial DKA protocol and the length time on an insulin infusion</td>
<td>Sample: N=71 (Jan 2008-Mar 2012) protocol group n=35 (Jan 2010-Mar 2012) control group n=36 (Jan 2008-Dec 2009)</td>
<td>IV: DKA protocol DV: incidence of hypoglycemia (protocol vs control) DV2: incidence of hypoglycemia (control vs protocol) DV3: hospital mortality DV4: hospital LOS</td>
<td>Data compared using two-tailed Student's <em>t</em>-test, Chi-square and Mann–Whitney <em>U</em> tests as applicable. Quantitative data were expressed as mean ± SD.</td>
</tr>
<tr>
<td>8.Turc hin et al., 2009</td>
<td>Study design: RCS</td>
<td>Purpose: if hypoglycemia associated with mortality in diabetic patients</td>
<td>Sample: N=2582 Setting: 734-bed teaching hospital</td>
<td>IV= # of days with hypoglycemia DV1= hospital mortality DV2= LOS</td>
<td>Frequencies, proportions, means, SD, median ranges; Summary stats for pt. demographics’ Wilcoxon test (# days and mortality, LOS continuous variables); Fisher’s exact test for binary var.; logistic regression for inpatient death probability; SAS stat. software</td>
</tr>
<tr>
<td>9.Ram akrish nan et al., 2013</td>
<td>Study design: RCS</td>
<td>Purpose: to analyze the impact of the standardized order set on the management of patients with DKA</td>
<td>Sample: N=165 (Oct 2005-Nov 2012): before(n=80), after(n=85), the date of introduction order set (Oct 2009) Setting: MICU</td>
<td>IV: ‘Critical Care DKA Protocol’ DV1: time to achieve AG closure DV2: # of hypoglycemia episodes DV3: time to attain blood glucose level of 200 mg/dL DV4: LOS in ICU</td>
<td>Following outcomes were compared between the two groups using unpaired <em>t</em> test: 1. Time needed to achieve AG closure, 2. Time needed to attain a BG of 200 mg/dl, 3. LOS in ICU solely for the purpose of management of DKA, 4. # of hypoglycemic episodes. Not statistically significant</td>
</tr>
<tr>
<td>10.Mu nir et al 2017</td>
<td>Study Design: RCS from 2008-2015</td>
<td>Purpose: compared the conventional ‘one-bag protocol’ of management of diabetic ketoacidosis (DKA) with the ‘two-bag protocol’</td>
<td>Sample: N=383: one-bag treatment n=249 two-bag n=134 Setting: Riverside University Health System Medical Center</td>
<td>IV: one bag DKA treatment IV2: two bags DKA treatment DV1= AG closure (resolution of DKA) DV2= BG &lt;250mg/dL DV3= time to reach HCO3 &gt; 18 mmol/L DV4= LOS</td>
<td>Two-independent samples <em>t</em>-test for continuous variables and χ² test for proportions for categorical variables Outcome measures comparing the 1-bag vs 2-bag protocols used to compare the time to AG closure (primary outcome measure) and time to reach BG &lt;250 mg/dl, time to reach HCO₃ level &gt;18 mmol/L, and hospital LOS (secondary outcome measures). The relationship between the time to AG closure and admission variables assessed using Pearson product–moment correlation. ANCOVA using AG closure time as the DV, and admission variables as covariates: patient’s age, weight, BMI, admission pH and AG, BHB, BUN, Cr, BG, HgbA1c, and the Charlson Comorbidity Index. Data entered into a Microsoft Excel spreadsheet and analyzed using SAS V.9.3.</td>
</tr>
<tr>
<td>Setting: a tertiary Townsville teaching hospital in Australia</td>
<td>Sample: N=256; nonprotocol n =143; protocol n=113</td>
<td>IV= DKA protocol</td>
<td>Protocol efficacy -time to resolution of DKA or HHS, LOS in the ICU, and LOS in the hospital. Protocol safety evaluated for hypoglycemic and hypokalemic events</td>
<td>the protocol group vs. 28% in the control group for hypoglycemia ( ( P = 0.036 )).</td>
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</tr>
<tr>
<td><strong>Study design:</strong> RCS</td>
<td><strong>Purpose:</strong> evaluate the efficacy and safety of protocol based upon the 2009 American Diabetes Association (ADA) consensus statement</td>
<td><strong>Sample:</strong> N=145 Bolus group n=58, no bolus group n=87</td>
<td><strong>IV:</strong> DKA protocol</td>
<td>Patients on the hyperglycemic crises protocol experienced a 9.2 hour (95% confidence interval (CI): 4.70-13.70; ( P&lt;.001 )) decrease in time to resolution, with nonprotocol patients. No difference in safety outcomes, including the number of patients with moderate hypoglycemia. Protocol decreased times to resolution of DKA without increasing the rate of hypoglycemia or hypokalemia.</td>
<td></td>
</tr>
<tr>
<td><strong>Study design:</strong> RCS</td>
<td><strong>Purpose:</strong> to evaluate the effect of an insulin bolus, as compared to no bolus, on the management of DKA.</td>
<td><strong>Setting:</strong> Grady Memorial Hospital, 953 bed academic medical center</td>
<td><strong>DV1:</strong> DKA resolution variables (BG&lt;200, pH&lt;7.3, AG &lt;12mEq, Bicarb&gt;15 mEq)</td>
<td><strong>DV2:</strong> Incidence of hypoglycemia, incidences of hypokalemia</td>
<td></td>
</tr>
<tr>
<td><strong>Study design:</strong> Descriptive study/research problem: survey method</td>
<td><strong>Purpose:</strong> to conduct national survey on DKA management and compare them against national standards with JBDS guidelines</td>
<td><strong>Sample:</strong> N=281</td>
<td><strong>DV:</strong> JBDS guidelines</td>
<td><strong>Descriptive statistics</strong> (mean, SD) Surveys of providers (yes, no) with questions to determine compliance (biochemistries, DKA resolution) with JBDS; SPSS software</td>
<td></td>
</tr>
<tr>
<td><strong>Study design:</strong> RCS</td>
<td><strong>Purpose:</strong> to evaluate hypoglycemia episodes reduction in adult DKA treatment differ with fixed insulin protocol</td>
<td><strong>Sample:</strong> 155 Cohort 1 n=77; Cohort 2 n= 78</td>
<td><strong>IV1:</strong> fixed rate insulin infusion DKA protocol</td>
<td><strong>Logistic regression</strong> -incidence of hypoglycemia difference of 2 protocols; <strong>Multiple regression</strong> -incidence of severe hypoglycemia, administration of D50W, rebound hyperglycemia). Continuous outcomes - <strong>ordinary linear regression</strong> (LOS in ICU, time to AG&lt;or=12, time until serum bicarbonate &gt; or=15, serum glucose prior to hypoglycemia, etc.) - <strong>t-test</strong> for continuous variables (age and weight)</td>
<td></td>
</tr>
</tbody>
</table>

### Limitations
- Non-randomized cohort design, assignments by provider preference, confounding variables not ruled out. Potential for inaccurate record keeping, missing data, possibility of resolution to occur prior to labs collected, not ruled out.
- Unclear if the development of low K and pH is due to the poor adherence to the CG vs CG are wrong.

### Hypoglycaemia
- 27.6% of patients developing overt hypoglycaemia at median time of 14.7 h after treatment was started. Possible that currently used insulin drip regimen is too aggressive when BG drop. Unclear if the development of low K and BG levels is due to the poor adherence to the CG vs CG are wrong.

- Hypoglycaemia was 19.2% in cohort 2 ver-sus 32.5% in cohort 1; use of dextrose 50% in water (D50W) was also reduced in cohort 2. No differences were seen in AG or bicarbonate correction, rebound hyperglycaemia or ICU length of stay.
### Table 2: Comparison of time to resolution and adverse outcomes between cohorts. Descriptive statistics was used for each variable of interest

<table>
<thead>
<tr>
<th>Variable</th>
<th>n=25 Protocol #1 Mean (SD)</th>
<th>n=42 Protocol #2 Mean (SD)</th>
<th>p value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Time for AG to close (in hours)</td>
<td>11.8 (4.23)</td>
<td>10.43 (4.46)</td>
<td>.22</td>
</tr>
<tr>
<td>Time for glucose to normalize (in hours)</td>
<td>6.6 (2.31)</td>
<td>6.5 (2.88)</td>
<td>.883</td>
</tr>
</tbody>
</table>

Protocol #1 (before change), Protocol #2 (after change)
Table 3: Comparison of demographic and clinical characteristics between cohorts

<table>
<thead>
<tr>
<th>Variable</th>
<th>Cohort 1 (n=25)</th>
<th>Cohort 2 (n=42)</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, Mean (SD)</td>
<td>32 (13)</td>
<td>31 (11)</td>
<td>.830</td>
</tr>
<tr>
<td>Gender, n (%)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Male</td>
<td>14 (56%)</td>
<td>23 (55%)</td>
<td>.921</td>
</tr>
<tr>
<td>Female</td>
<td>11 (44%)</td>
<td>19 (46%)</td>
<td></td>
</tr>
<tr>
<td>Race, n (%)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Af. American</td>
<td>2 (8%)</td>
<td>8 (19%)</td>
<td>.032</td>
</tr>
<tr>
<td>Other</td>
<td>0 (0%)</td>
<td>3 (7%)</td>
<td></td>
</tr>
<tr>
<td>Caucasian</td>
<td>23 (92%)</td>
<td>31 (74%)</td>
<td></td>
</tr>
<tr>
<td>Service, n (%)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Pulmonary ICU</td>
<td>8 (32%)</td>
<td>17 (41%)</td>
<td>.300</td>
</tr>
<tr>
<td>PCU</td>
<td>12 (48%)</td>
<td>22 (52%)</td>
<td></td>
</tr>
<tr>
<td>Other</td>
<td>5 (20%)</td>
<td>3 (7%)</td>
<td></td>
</tr>
<tr>
<td>Discharge disposition</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Home</td>
<td>19 (76%)</td>
<td>35 (83%)</td>
<td>.434</td>
</tr>
<tr>
<td>Other</td>
<td>6 (24%)</td>
<td>7 (17%)</td>
<td></td>
</tr>
<tr>
<td>Hospital LOS, median (IQR) in days</td>
<td>5 (9.5)</td>
<td>3.5 (9)</td>
<td>.472</td>
</tr>
<tr>
<td>ICU LOS, median (IQR) in days</td>
<td>2(4.5)</td>
<td>2 (4)</td>
<td>.656</td>
</tr>
</tbody>
</table>
Table 4: Comparison of adverse outcomes between cohorts

<table>
<thead>
<tr>
<th>Variable</th>
<th>Cohort 1 (n=25) n (%)</th>
<th>Cohort 2 (n=42) n (%)</th>
<th>( p )</th>
</tr>
</thead>
<tbody>
<tr>
<td>Incidences of AG reopening</td>
<td>7 (28%)</td>
<td>12 (29 %)</td>
<td>.960</td>
</tr>
<tr>
<td>Hypoglycemia Yes</td>
<td>24 (96%)</td>
<td>39 (93%)</td>
<td>.599</td>
</tr>
<tr>
<td>Hypokalemia Yes</td>
<td>10 (40%)</td>
<td>21 (50%)</td>
<td>.343</td>
</tr>
<tr>
<td>Hypoglycemia for duration DKA drip treatment before AG closed</td>
<td>6(24%)</td>
<td>12 (29%)</td>
<td>.683</td>
</tr>
<tr>
<td>Hypoglycemia for duration of DKA drip treatment</td>
<td>11 (44%)</td>
<td>22 (53%)</td>
<td>.510</td>
</tr>
</tbody>
</table>
Table 5: Comparison of treatment resolution within each group based on blood sugar
Independent sample T test

| Time to AG resolution (in hours) when hypoglycemia occurred within AG resolution timeframe | Cohort 1 (n=25) Mean (SD) | P | Cohort 2 (n=42) Mean (SD) | P |
|---|---|---|---|---|---|
| Yes (n=6) | 11.50 (3.39) | .847 | Yes (n=12) | 13.17 (5.81) | .050 |
| No (n=19) | 11.89 (4.54) | | No (n=30) | 9.33 (3.30) | |

Table 6: Comparison ICU LOS and adverse event (AG reopening) within each group

| ICU LOS (in days) when AG reopened | Cohort 1 (n=25) Mean (SD) | P | Cohort 2 (n=42) Mean (SD) | P |
|---|---|---|---|---|---|
| Yes (n=7) | 4.43 (2.07) | .643 | Yes (n=12) | 4.25 (3.44) | .031 |
| No (n=18) | 3.17 (6.91) | | No (n=29) | 1.69 (2.19) | |
Figure 1: Framework for the Continual Improvement of Health Care, Batalden & Stoltz (1995)