

Management of hospitalized patients with mild to moderate diabetic ketoacidosis using a continuous insulin infusion protocol on a medical surgical ward and observation level of care

A retrospective cohort study

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Abstract

Although the practice of using rapid-acting subcutaneous insulin for the management of mild-to-moderate diabetic ketoacidosis is becoming increasingly popular, the continuous insulin infusion remains widely utilized, and its real-world applicability and safety on a medical surgical unit (Med Surg) and observation level of care are unclear. We assessed whether a continuous insulin infusion protocol for mild-to-moderate diabetic ketoacidosis on Med Surg/observation level of care over a 6.5-year period was associated with adverse outcomes.

A retrospective cohort study of adults hospitalized with mild-to-moderate diabetic ketoacidosis was conducted at 2 community hospitals in Northern California, USA, from January 2014 to May 2020. Demographic and clinical variables were collected using an electronic health record. Admission to Med Surg/observation was compared to intensive care unit admission for the outcomes of 30-day readmission, presence of hypoglycemia, rate of hypoglycemic episodes, in-hospital and 30-day mortality, and length of stay using bivariate analysis.

Among 227 hospital encounters (mean age 41 years, 52.9% women, 79.3% type 1 diabetes, 97.4% utilization of continuous insulin infusion), 19.4% were readmitted within 30 days, and 20.7% developed hypoglycemia. For Med Surg/observation encounters compared to the intensive care unit, there were no statistically significant differences in the risk of readmission (RR 1.48, 95% CI, 0.86–2.52), hypoglycemia (RR 1.17, 95% CI, 0.70–1.95), or increased length of stay (RR 0.71, 95% CI, 0.55–1.02); there was a lower risk of hypoglycemic events during hospitalization (RR 0.69, 95% CI, 0.54–0.96).

Continuous insulin infusion utilization may be a safe option for treatment of mild-to-moderate diabetic ketoacidosis on Med Surg/observation level of care. Further investigation is needed.

Abbreviations: ADA = American Diabetes Association, CI = confidence intervals, ED = emergency department, DKA = diabetic ketoacidosis, ICU = intensive care unit, KPNC = Kaiser Permanente Northern California, Med Surg = medical surgical ward, RR = relative risk, SRO = Santa Rosa, SRF = San Rafael, SD = standard deviations.

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1. Introduction

While admission to an intensive care unit (ICU) remains the standard of care for severe diabetic ketoacidosis (DKA), the safety of managing mild-to-moderate DKA outside of the ICU is unclear. nonICU management of DKA could save considerable costs and prevent ICU overcrowding during times of crisis.^[1] Small, randomized trials have shown no differences in outcomes on a medical surgical unit (Med Surg) or observation level of care compared to the ICU, using either a continuous insulin infusion or subcutaneous rapid-acting insulin.^[2–6] In this study, Med Surg refers to patients who have been admitted to the hospital as inpatient status, whereas observation level of care refers to patients who are being monitored as outpatient status for potential early discharge. The location of observation level of care varies, occurring in the emergency department (ED), hospital unit, or elsewhere, and may or may not be confined to designated areas. Of note, most nonICU encounters in the studies mentioned previously were ED observation stays and not Med Surg.^[2–5] The trials enrolled limited numbers, some with hourly glucose monitoring protocols that may not be generalizable to Med Surg.^[7] Despite guidelines that uncomplicated DKA may be managed with subcutaneous rapid-acting insulin,^[8] the continuous insulin infusion remains widely utilized.^[9] Thus, many are concerned about managing DKA outside of an ICU or intermediate care unit, where a continuous insulin infusion requires adequate nursing for glucose monitoring and adjustments in insulin and intravenous fluids to prevent errors and adverse events. Potential negative in-hospital events and postdischarge sequelae include readmission, hypoglycemia, increased length of stay, and death.

At Kaiser Permanente Santa Rosa Medical Center, mild-to-moderate DKA has been managed with a continuous insulin infusion protocol on Med Surg and observation level of care since 2014. Home oral hypoglycemic medications and home subcutaneous insulin regimens were discontinued per protocol upon initiation of the continuous insulin infusion. The insulin infusion was continued until the ketoacidosis had resolved (i.e., normalization of anion gap) and the hyperglycemia had corrected (i.e., glucose <200 mg/dL). Management is based on 2-hour glucose and 4-hour laboratory monitoring, both feasible on Med Surg. Our continuous insulin infusion utilization on Med Surg/observation level of care represents a practice variation, with outcomes unknown compared to other Kaiser Permanente Northern California (KPNC) hospitals who manage DKA in the ICU with higher nurse-to-patient ratios and hourly glucose monitoring. For additional noninsulin treatments in the management of DKA such as intravenous fluids and electrolytes, the Med Surg/observation DKA protocol followed the American Diabetes Association (ADA) guidelines.^[8] To our knowledge, data are limited on associations between outcomes and Med Surg/observation continuous insulin infusion utilization for mild-to-moderate DKA.

We therefore undertook this study as part of a quality improvement project, at our hospital, to evaluate the safety of our continuous insulin infusion protocol on Med Surg/observation and to test the hypothesis that it might be associated with adverse outcomes compared to the ICU.

2. Methods

2.1. Study design

We surveyed hospital medicine chiefs within KPNC to identify the admitting level of care for DKA patients. We then conducted a retrospective cohort study at 2 KPNC hospitals—Santa Rosa (SRO) and San Rafael (SRF) medical centers—of adults hospitalized with mild-to-moderate DKA. Patients were followed from January 1, 2014, through May 31, 2020. KPNC is an integrated healthcare system that includes 21 hospitals and serves a

community-based population of > 4.4 million members. Kaiser Permanente SRO has had a continuous insulin infusion protocol since 2014 for mild-to-moderate DKA on Med Surg/observation, whereas SRF has managed these patients in the ICU. This study was approved by the KPNC Institutional Review Board with a waiver of informed consent.

2.2. Hospital encounters

We identified DKA encounters through an electronic health record using Datavision™ software. Encounters were excluded if patients were < 18 years, treated as an outpatient or ED visit, admitted to Labor & Delivery, admitted to a KPNC hospital other than SRO or SRF, had an admission pH < 7.00, anion gap ≤ 10, or blood glucose ≤ 250 mg/dL (ADA laboratory criteria for severe DKA).^[8] Charts were reviewed by clinicians for accuracy.

2.3. Exposure

Our exposure of interest was the admitting level of care. As mild-to-moderate DKA is managed at SRO outside of the ICU in both an observation unit and on Med Surg, we compared nonICU (Med Surg/observation) to ICU level of care.

2.4. Outcomes

The primary outcome was 30-day readmission. The secondary outcomes were the presence of hypoglycemia (defined as a blood glucose < 70 mg/dL), rate of hypoglycemic episodes, in-hospital and 30-day mortality, and length of stay.

2.5. Demographic and clinical variables

Demographic variables included age, sex, race/ethnicity, insurance type, and facility. Clinical variables included diabetes type, continuous insulin infusion utilization, initial serum glucose, bicarbonate, anion gap, and pH.

2.6. Statistical analysis

We used descriptive statistics for cohort characteristics. We reported means (with standard deviations [SD]) for continuous variables and numbers/proportions for categorical variables. Differences between Med Surg/observation versus ICU were evaluated using T-tests for continuous variables and chi-square tests for categorical variables. To evaluate the association between level of care and outcomes, we conducted bivariate analysis and reported relative risk (RR) with 95% confidence intervals (CI). We used Poisson regression to characterize the rate of hypoglycemic episodes.

3. Results

Of the 21 hospital medicine chiefs surveyed within KPNC, 14 (66.7%) responded. SRO was the only facility that treated mild-to-moderate DKA on Med Surg/observation. The other 13 of 14 (92.9%) facilities, including SRF, admitted DKA patients to the ICU only.

3.1. Cohort characteristics

We identified 142 patients and 227 total encounters for mild-to-moderate DKA between January 1, 2014 and May 31, 2020. Table 1 describes baseline characteristics of patients. The mean age (SD) was 40.7 (19.7) years, 120 (52.9%) were female, 180 (79.3%) had type 1 diabetes, and a continuous insulin

Table 1
Patient characteristics of study cohort by level of care on admission.

| | Med surg/observation (N = 107, 47.1%) | Intensive care unit (N = 120, 52.9%) | Total (N = 227) | P value |
|---------------------------|--|---|--------------------|---------|
| Age (yr), mean (SD) | 40.0 (19.4) | 41.4 (20.1) | 40.7 (19.7) | 0.162 |
| Gender | | | | 0.98 |
| Female | 72 (31.7%) | 48 (21.1%) | 120 (52.9%) | |
| Male | 35 (15.4%) | 72 (31.7%) | 107 (47.1%) | |
| Race/ethnicity | | | | 0.192 |
| Asian | 0 (0%) | 3 (1.3%) | 3 (1.3%) | |
| Black | 3 (1.3%) | 3 (1.3%) | 6 (2.6%) | |
| Hispanic | 17 (7.5%) | 12 (5.3%) | 29 (12.8%) | |
| White | 87 (38.3%) | 97 (42.7%) | 184 (81.1%) | |
| Native American | 0 (0%) | 3 (1.3%) | 3 (1.3%) | |
| Other/unknown | 0 (0%) | 2 (0.9%) | 2 (0.9%) | |
| Diabetes type | | | | 0.173 |
| Type 1 | 89 (39.2%) | 91 (40.1%) | 180 (79.3%) | |
| Type 2 | 18 (7.9%) | 29 (12.8%) | 47 (20.7%) | |
| Facility | | | | <0.001 |
| Santa Rosa | 103 (45.4%) | 48 (21.1%) | 151 (66.5%) | |
| San Rafael | 4 (1.8%) | 72 (31.7%) | 76 (33.5%) | |
| Insurance type | | | | 0.897 |
| Missing | 10 (4.4%) | 17 (7.5%) | 27 (11.9%) | |
| Commercial/self-funded | 62 (27.3%) | 68 (30.0%) | 130 (57.3%) | |
| Medicare | 28 (12.3%) | 26 (11.5%) | 54 (23.8%) | |
| Medicaid | 7 (3.1%) | 9 (4.0%) | 16 (7.0%) | |
| Insulin infusion utilized | | | | N/A* |
| Yes | 101 (94.4%) | 119 (99.2%) | 220 (97.4%) | |
| No | 6 (5.6%) | 1 (0.8%) | 7 (2.6%) | |
| Glucose†, mean (SD) | 532 (190.6) | 588 (240.4) | 561 (219.7) | 0.053 |
| pH‡, mean (SD) | 7.22 (0.12) | 7.23 (0.13) | 7.22 (0.123) | 0.555 |
| Bicarbonate‡, mean (SD) | 13.6 (5.5) | 12.1 (6.8) | 12.8 (6.3) | 0.066 |
| Anion gap‡, mean (SD) | 23.1 (6.2) | 25.9 (6.4) | 24.6 (6.45) | 0.001 |

*P value was calculated but the expected counts were too low for the result to be valid.

†Initial value on presentation.

‡Missing n = 58.

infusion was used in 220 (97.4%) encounters. ICU admission for DKA was significantly higher at SRF (72 of 76 [94.7%]) than SRO (48 of 151 [31.8%]) ($P < .001$). Overall, 107 encounters (47.1%) were Med Surg/observation (59 Med Surg, 48 observation) and 120 (52.9%) were ICU. The mean anion gap for Med Surg/observation was significantly lower than the ICU (23.1 vs 25.9, $P = .001$). There were no other significant differences between the 2 groups, though Med Surg had lower mean glucose (532 vs 588, $P = .053$) and higher mean bicarbonate (13.6 vs 12.1, $P = .066$) compared to ICU.

3.2. Outcomes

In total, 44 patients (19.4%) were readmitted during 30-day postdischarge follow-up. 23.4% (N = 25) of Med Surg/observation patients were readmitted compared to 15.8% (N = 19) of ICU patients. There was no difference in readmission risk between Med Surg/observation vs ICU (RR 1.48, 95% CI, 0.86–2.52) (Table 2).

For our secondary outcomes, 22.4% (N = 24) of Med Surg/observation patients were hypoglycemic during hospitalization compared to 19.2% (N = 23) of ICU patients. There were 55 hypoglycemic episodes per 107 encounters on Med Surg/observation compared to 89 per 120 encounters in the ICU. The mean length of stay was 2.3 days for Med Surg/observation versus 3.3 days for ICU. For Med Surg/observation versus ICU, there were no differences in the risk of hypoglycemia (RR 1.17, 95% CI, 0.70–1.95) nor increased length of stay (RR 0.71, 95% CI, 0.55–1.02), but there was a lower risk of recurrent hypoglycemic episodes during hospitalization (RR 0.69, 95% CI, 0.54–0.96) (Table 2). No patients died during hospitalization. For 30-day mortality, there was no difference between Med Surg/observation (0 of 107 deaths) versus ICU (2 of 120 deaths) ($P = .258$).

4. Discussion

To our knowledge, this is the largest study addressing safety concerns about using a continuous insulin infusion protocol for

Table 2
Outcomes of patients hospitalized with mild to moderate diabetic ketoacidosis: med surg/observation vs intensive care unit level of care.

| | RR (95% CI)* | P value |
|--|-------------------|---------|
| 30-day readmission | 1.48 (0.86, 2.52) | 0.53 |
| Patients hypoglycemic during hospitalization (%) | 1.17 (0.70, 1.95) | 0.545 |
| Hypoglycemic episodes during hospitalization (mean)† | 0.69 (0.54, 0.96) | 0.038 |
| Length of stay (d) | 0.71 (0.55, 1.02) | 0.063 |

*Relative risk and 95% confidence intervals.

†Hypoglycemic episode defined as blood glucose < 70.

mild-to-moderate DKA among Med Surg/observation patients. In this retrospective cohort study, we did not detect an association between Med Surg/observation level of care and 30-day readmission. We had hypothesized that patients on a Med Surg/observation continuous insulin infusion protocol would be at higher risk for readmission and hypoglycemia compared to the ICU. What we found instead was a lower risk of hypoglycemic episodes on Med Surg/observation, though this finding might reflect confounding as ICU patients had increased severity of lab markers. Thus, while nonsignificant, ICU patients in our study might represent a population with higher acute physiology compared to Med Surg patients. We also noted a nonsignificant but improved length of stay among Med Surg/observation patients which likely reflects the proportion of observation encounters (44.9%), but nevertheless has positive implications for health-care utilization.

Strengths of our study include sample size, Med Surg representation, and real-world applicability. Previous trials comparing ICU to nonICU care had small sample sizes with few Med Surg patients included.^[2–6] To our knowledge, this is the largest study to date (N = 227) evaluating the association of level of care on outcomes in DKA management, with 59 of 107 (56.7%) nonICU encounters admitted to Med Surg. Adequate Med Surg representation is important to address increased ward utilization during times of crisis such as the COVID-19 pandemic, where strain on critical care capacity was associated with increased mortality.^[10] Our study findings are generalizable to the broader hospitalized population, as our Med Surg/observation continuous insulin infusion protocol has been in clinical practice at a community hospital since 2014 and not under the premises of a trial.

This study had some limitations. Despite data collection since the inception of our protocol, the study was likely underpowered to detect a difference in readmission between Med Surg/observation versus ICU. Another limitation was that we had 227 encounters from 142 patients. Thus, several patients had multiple hospitalizations for DKA over the duration of our study period. We opted to count each hospitalization as a distinct encounter even if the patient had been previously hospitalized for DKA, given that the level of care and treatment could differ from previous encounters. While this limits the interpretation of our data, our findings reflect real-world healthcare utilization in that patients admitted for DKA are known to experience frequent rehospitalizations for DKA.^[11] While predictors and causes for readmission among patients hospitalized for DKA are multifactorial and require further study, previous studies have shown this population to be at high readmission risk and have elucidated some of these risk factors including preexisting medical comorbidities, age, malnutrition, and leaving against medical advice.^[11,12] Thus, investigation on multidisciplinary interventions to mitigate risk and prevent readmissions in DKA patients is needed. Additional limitations include potential downstream crossover in levels of care that may be unaccounted for; a considerable proportion of SRO patients (31.8%) with

mild-to-moderate DKA managed in the ICU for reasons not addressed; and patients admitted to Med Surg at SRF without an established nonICU continuous insulin infusion protocol in place. These SRF patients (4 of 76) made up a small proportion (5.3%) of admissions and were included in the total Med Surg/observation group for our analysis.

5. Conclusions

In summary, the continuous insulin infusion remains widely used in clinical practice for management of mild-to-moderate DKA. In our retrospective cohort study, we did not detect associations between continuous insulin infusion utilization for DKA on Med Surg/observation level of care with adverse outcomes. Larger studies are needed.

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