Medication use evaluation for prevalence of hyperchloremia and acute kidney injury in patients with diabetic ketoacidosis

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Introduction

What is diabetic ketoacidosis?

- Diabetic ketoacidosis (DKA) is a complication of uncontrolled diabetes that features hyperglycemia, metabolic acidosis, and increased ketone production.[1]

How does this relate to hyperchloremia?

- Normal saline (0.9% NaCl) and half-normal saline (0.45% NaCl) are commonly initiated fluids for DKA treatment to increase intravascular volume and tissue perfusion.[1]
- Observational studies have found that 0.9% NaCl in DKA management has been associated with hyperchloremia.[2,3]
- According to the most recent American Diabetes Association (ADA) guideline on DKA management (2009), hyperchloremic acidosis is a known complication during recovery but was considered to have few clinical effects.[1]

Why is this significant?

- Hyperchloremia may be associated with poor clinical outcomes such as increased risk for acidosis and acute kidney injury (AKI), therefore leading to prolonged hospital length of stay (LOS).[2,3,4]
- The SCOPE-DKA trial indicated that 0.9% NaCl had worse clinical outcomes when compared to Plasmalyte-148, which included prolonged hospital LOS, increased adverse events, and longer time to DKA resolution.[5]
- A retrospective cohort found that patients with hyperchloremia received significantly more fluid volume, particularly with 0.9% NaCl or 0.45% NaCl, which led to longer resolution times for DKA, prolonged hospital LOS, and increased incidence of AKI.[3]
- No guidance exists for non-saline based fluids in DKA, especially in the setting of hyperchloremia.

Objectives

Primary: To assess the prevalence of hyperchloremia and in-hospital AKI among critically ill patients with DKA .

Secondary: The time to DKA resolution, total time of insulin infusion, total amount of normal saline and overall intravascular fluids administered to each patient, hospital length of stay.

Methods

A retrospective medication use evaluation of 95 critically-ill adult patients admitted between July 1, 2020 and April 30, 2021 at Atrium Health Cabarrus was performed. Data were stored and analyzed in REDCap®.[6]

Inclusion Criteria: DKA diagnostic criteria (plasma glucose >250 mg/dL, arterial/venous pH ≤ 7.3, serum bicarbonate ≤ 18 mEq/L, positive urine or serum ketones, and anion gap > 10 mEq/L), located in critical care units with an ICD-10 code for DKA (E08.10, E08.11, E09.11, E10.10, E10.11, E11.11, E13.10, E,13.11) who received insulin-R 100 units/NS 100 mL. Only the first episode was included.

Exclusion Criteria: End-stage renal disease receiving renal replacement therapy, septic shock, acute pancreatitis, patients within a protected population (incarcerated, pregnant, etc.), and those who received subcutaneous insulin monotherapy

Data Collection: Age, sex, blood glucose, blood urea nitrogen, anion gap, serum sodium and potassium, serum creatinine (SCr), serum bicarbonate, urine or serum ketones, arterial or venous pH, prevalence of AKI (defined as a ≥ 0.3 mg/dL SCr increase from baseline within 48 hours or ≥ 50% in the previous 7 days) on admission,[7] length of hospital stay (hours), development of hyperchloremia, and in-hospital AKI, time to development of AKI, time to resolution of DKA, length of insulin infusion, and types of volumes of IV fluid administered. Hyperchloremia was defined as serum chloride > 109 mEq/L.[3]

Statistical Analysis: Descriptive statistics were reported as median (IQR) or n (%).

Results

Figure 1. Patient Screening

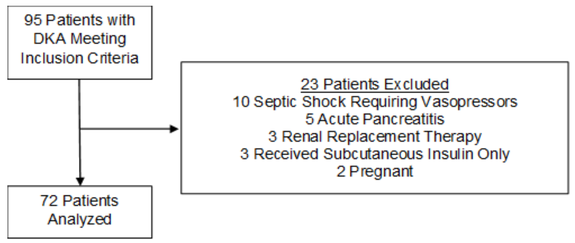


Table 1. Patient Baseline Characteristics (N=72)

Characteristic	Values
Age (years)*	48 (23)
Race*	
Caucasian	42 (58)
African-American	27 (38)
Other	3 (4)
Female*	30 (42)
History of Diabetes*	
Type 1 Diabetes	25 (35)
Type 2 Diabetes	38 (53)
No Prior History	9 (12)
Chronic Kidney Disease*	7 (10)
Stage 1	0 (0)
Stage 2	1 (1.4)
Stage 3	6 (8.3)
Stage 4	0 (0)
Stage 5	0 (0)
Blood Glucose (mg/dL)†	558 ± 389
Sodium (mmol/L)†	133 ± 8
Potassium (mmol/L)†	4.6 ± 1.3
Chloride (mmol/L)†	96 ± 10
Hyperchloremia on Admission*	1 (1)
Creatinine (mg/dL)†	1.52 ± 1.02
Blood Urea Nitrogen (mg/dL)†	26 ± 22
AKI on Admission*	52 (72)
Initial Fluid Bolus Type*	
Normal Saline	11 (15.3)
Lactated Ringer's (LR)	60 (83.3)
Plasma-Lyte	1 (1.4)

* Data presented as n (%); † Data presented as median ± IQR

Table 2. Intravenous Fluids Administered (N=72)

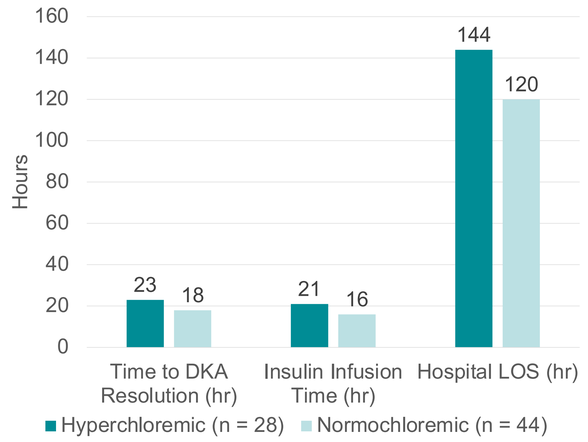
Fluid Type	n (%)	Volume (mL), median ± IQR
Normal Saline (0.9% NaCl)	58 (81)	1100 ± 2238
Half-Normal Saline (0.45% NaCl)	29 (40)	510 ± 1079
Lactated Ringer's	61 (85)	2000 ± 2035
Plasma-Lyte	4 (6)	1300 ± 1188
Dextrose 5% in Water (D5W)	11 (15)	843 ± 1715
0.9% NaCl-D5W	6 (8)	2021 ± 823
0.45% NaCl-D5W	53 (74)	1646 ± 2005
LR-D5W	2 (3)	1415 ± 698
Total IV Volume	72 (100)	5460 ± 3697

Table 3. Outcomes (N=72)

Outcomes	All (N=72)	Normal Saline Received (n=59)	No Normal Saline Received (n=13)
Hyperchloremia*	28 (38.9%)	24 (40.7%)	4 (30.8%)
In-Hospital AKI*	0 (0%)	0 (0%)	0 (0%)
AKI on Admission*	52 (72.2%)	44 (74.6%)	8 (61.5%)
AKI on Admission Resolved*	49 (94.2%)	42 (95.5%)	7 (87.5%)
Time to DKA Resolution (hr)†	19 ± 12	19 ± 12	18.5 ± 27.3
Insulin Infusion Time (hr)†	18 ± 10	18 ± 10	16 ± 10
Hospital LOS (hr)†	120 ± 96	120 ± 120	96 ± 132

*Data presented as n (%); † Data presented as median ± IQR

Figure 2. Outcomes by Chloride Status (N=72)



Discussion

- Of the patients treated for DKA, 82% received 0.9% NaCl solution.
- For patients that received fluid replacement therapy:
  - Approximately 40% developed hyperchloremia after treatment.
  - No episodes of AKI developed after treatment.
  - Majority (94%) of AKI present on admission resolved.
- Of the 28 patients that developed hyperchloremia:
  - Majority (86%) of patients received normal saline.
  - Median time to DKA resolution was 23 hours.
  - Median insulin infusion time was 21 hours

Conclusion

- Similar outcomes were seen between patients who received normal saline versus patients that did not receive normal saline during fluid replacement including:
  - Median length of hospital stay
  - Time to DKA resolution
  - Frequency of AKI development
- The results of this MUE are a snapshot of patients admitted to the ICU at Atrium Health Cabarrus.
  - DKA order sets changed from normal-saline based to LR-based in mid-2021 among Atrium Health facilities.
    - Outcomes pertaining both order sets may be compared
- Future investigation across multiple institutions also may enhance the assessment of the benefits in using balanced crystalloids for the treatment of DKA in critically ill patients.

Resources

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Disclosures

All authors have nothing to disclose.