

# A Potassium Result Is Not Necessary Before Insulin Administration in Patients with Hyperglycemia

Adam Munn<sup>1</sup>, Rubayet Hossain MD<sup>2</sup>, Jon Schrock MD, FACEP<sup>1,3,\*</sup>

<sup>1</sup>Case Western Reserve University, School of Medicine, Cleveland, OH, United States of America

<sup>2</sup>The Mount Sinai Health System, The Department of Emergency Medicine, Icahn School of Medicine, New York, New York, United States of America

<sup>3</sup>The MetroHealth System, The Department of Emergency Medicine, Case Western Reserve University School of Medicine, Cleveland, OH 2500 MetroHealth Drive Cleveland, OH 44109, United States of America

\***Corresponding Author:** Jon Schrock, The MetroHealth System, The Department of Emergency Medicine, Case Western Reserve University School of Medicine, Cleveland, OH 2500 MetroHealth Drive Cleveland, OH 44109, United States of America, Tel.: 216-778-5747, E-mail: jschrock@metrohealth.org

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## Abstract

**Background:** Hyperglycemia is a common condition that is treated in the emergency department (ED). Hyperglycemia is often treated with intravenous fluids and insulin. Current guidelines recommend obtaining potassium levels prior to the initiation of insulin therapy. This often delays insulin therapy for several hours.

**Objectives:** To compare the rate of hypokalemia in patients with hyperglycemia who were treated with insulin before and after initial potassium levels resulted.

**Methods:** A retrospective chart review was performed with all adult patients who presented to the ED from 2005 to 2022, with hyperglycemia and were treated with insulin therapy. By comparing the time of insulin administration to the time that the metabolic panels resulted, the encounters were separated in two groups, those who received insulin before initial potassium levels resulted (referred to as the early insulin group) and those who received insulin after initial potassium levels resulted (referred to as the late insulin group). Primary outcomes were the rates of mild hypokalemia (defined as potassium levels < 3.5) and moderate hypokalemia (defined as potassium levels < 2.5) after the first and second repeat potassium levels. Secondary outcomes were the development of arrhythmias, hypotension and subjective weakness. Rates of hypokalemia were compared using Chi-square analysis and rates of secondary outcomes were compared using logistic regression.

**Results:** 1446 patient encounters in the ED were reviewed and 1284 were included for analysis. During 275 of these ED encounters (21.4%) patients received insulin prior to their initial serum potassium levels having resulted. The rate of mild hypokalemia after the first repeat potassium among the early insulin group was 7.64% compared to a rate of 7.63% among the late insulin group (p=1) The rate of mild hypokalemia after the second repeat potassium among the early insulin group was 25.5% compared to a rate of 26.3% among the late insulin group (p=0.98; difference of 0.01%; 95% CI: -1.59 to 0.61%). The rate of moderate hypokalemia after the first repeat potassium among the early insulin group was 0.36% compared to a rate

of 0.30% among the late insulin group ( $p=0.99$ ; difference of 0.001%; 95% CI: -0.38 to 1.38%). The rate of moderate hypokalemia after the second repeat potassium among the early insulin group was 17.5% compared to a rate of 18.7% among the late insulin group ( $p=0.95$ ; difference of 0.02%; 95% CI: -1.52 to 0.56%). There was a positive association between the early insulin group and the development of hypotension (Odds Ratio [OR] 1.65; 95% CI: 1.10 to 2.50). There was no association between the early insulin group and subjective weakness (OR 0.75; 95% CI: 0.52 to 1.70) or arrhythmias (OR 0.71; 95% CI: 0.28 to 1.80).

**Conclusion:** Patients who received insulin prior to a potassium lab value have the same rates of mild and moderate hypokalemia. There was a positive association between the early insulin group and the development of hypotension. Given this information we see no reason to delay moderate doses of insulin in patients with hyperglycemia.

**Keywords:** Hyperglycemia; Potassium; Hypokalemia; Insulin; Diabetes; Emergency Department

## Background

Patients with diabetes mellitus and associated hyperglycemia requiring intervention is commonly encountered in the emergency department (ED). The prevalence of diabetes in the United States has continued to increase since 1988 with an estimated 15.9% of adults aged 20 and over having diabetes as of 2015-2018 [1]. In 2020 there were approximately 507,000 visits to the emergency department with type II diabetes listed as the primary diagnosis [2]. Diabetic ketoacidosis (DKA) and hyperglycemic hyperosmolar state (HHS) are two hyperglycemic crises that arise as complications of diabetes mellitus and can occur in patients with both type I and II diabetes mellitus [3]. The underlying pathogenesis in DKA and HHS are a lack of (DKA) or reduced (HHS) action of insulin, increased levels of counter regulatory hormones, and dehydration secondary to osmotic diuresis [3, 4, 5]. While the underlying cause of hyperglycemia during a hyperglycemic crisis in individuals with diabetes mellitus is multifactorial, the primary abnormalities stem from an absolute or relative insulin deficiency [4]. Patients can have elevated blood glucose with or without Diabetic ketoacidosis (DKA) or hyperglycemic hyperosmolar state (HHS).

The mainstay of treatment for hyperglycemia in the ED is intravenous fluids and insulin therapy. However, current guidelines recommend that insulin therapy only be initiated after obtaining a serum potassium level  $> 3.3$  mEq/L. In a hyperglycemic state secondary to insulin deficiency, serum potassium levels can initially be elevated. The serum hyperosmolality results in a shift of potassium from the intracellular to extracellular space. This process can lead to a total body potassium deficit as potassium is then lost via osmotic diuresis and cells are unable to uptake potassium without the action of insulin [5, 6]. It has been estimated that 5-10 units of insulin will lower potassium by 1 mEq/L in patients with End Stage Renal Disease (ESRD) who receive insulin [7]. However, it is not clear that this potassium shift would be the same for patients with normal renal function or for patients not in DKA. The concern is that initiation of insulin therapy will promote a rapid shift of potassium into the intracellular space resulting in symptomatic hypokalemia, and possible cardiac arrest [4]. Therefore under current guidelines the definitive treatment of hyperglycemia in the ED is delayed by approximately 1 hour and 45 minutes until an initial metabolic panel containing the serum potassium level has resulted. This study attempted to determine the rates of hypokalemia in patients with hyperglycemia who were treated with insulin before and after initial potassium levels resulted.

## Methods

This retrospective chart review was performed at an academic medical center with a large urban main campus ED that receives more than 100,000 visits annually. The study was reviewed and approved by our institutions' Institutional Review Board.

All patients aged 18 or older who presented to the ED, were diagnosed with hyperglycemia or diabetes, and had laboratory evaluation performed in the ED from 2005 to 2022 were reviewed. Exclusion criteria included euglycemia ( $<200$  mg/dL) at presen-

tation, patients who eloped or were transferred prior to laboratory evaluation being performed, patients who did not receive a repeat metabolic panel, and patients who did not receive insulin therapy within 12 hours of arrival to the ED. A research assistant manually reviewed all patient encounters. For each eligible patient encounter, the following data was obtained from the EMR: initial and repeat insulin administration (including dose, type, route, and time), initial and repeat lab values, dates, and times (including glucose, blood urea nitrogen, potassium, bicarb, and carbon dioxide), initial vital signs, and new clinical findings including measurable weakness, muscle cramps, hypotension, EKG changes (prolonged QRS or flat T waves), and new onset arrhythmias. Demographics, medical history, and ED visit or admission information for each patient were also recorded.

Primary outcomes were the rates of mild hypokalemia (defined as potassium levels  $< 3.5$ ) and moderate hypokalemia (defined as potassium levels  $< 2.5$ ) after the first and second repeat potassium levels. Secondary outcomes were the development of new clinical findings such as arrhythmias, hypotension and subjective weakness. By comparing the time of insulin administration to the time that the metabolic panels resulted, the encounters were separated in two groups, those who received insulin before initial potassium levels resulted (referred to as the early insulin group) and those who received insulin after initial potassium levels resulted (referred to as the late insulin group).

All data was analyzed using Stata V 14 (State College, Tx) statistical software. Rates of hypokalemia were compared using Chi-square analysis and rates of secondary outcomes were compared using logistic regression.

## Results

1446 patient encounters in the ED met the original inclusion criteria. Of these, 68 met one or more exclusion criteria, and an additional 94 encounters were removed as they were duplicate entries. 1284 patient encounters were included for analysis. The mean age of our study was 49.4 and 53.3% of patient encounters were male. See table 1 for additional demographic information.

**Table 1:** Demographics of Patient Encounters

Race	Frequency (%)
American Indian	2 (0.16)
Asian	2 (0.16)
African American	614 (47.82)
Hispanic	43 (3.35)
Caucasian	520 (40.50)
Declined to Answer	103 (8.02)

During 275 of these ED encounters (21.4%) patients received insulin prior to their initial serum potassium levels having resulted. The rate of mild hypokalemia after the first repeat potassium among the early insulin group was 7.64% compared to a rate of 7.63% among the late insulin group ( $p=1$ ; difference of 0.00%, 95% confidence interval [CI]: -1.45 to 0.45). The rate of mild hypokalemia after the second repeat potassium among the early insulin group was 25.5% compared to a rate of 26.3% among the late insulin group ( $p=0.98$ ; difference of 0.01%; 95% CI: -1.59 to 0.61%). The rate of moderate hypokalemia after the first repeat potassium among the early insulin group was 0.36% compared to a rate of 0.30% among the late insulin group ( $p=0.99$ ; difference of 0.001%; 95% CI: -0.38 to 1.38%). The rate of moderate hypokalemia after the second repeat potassium among the early insulin group was 17.5% compared to a rate of 18.7% among the late insulin group ( $p=0.95$ ; difference of 0.02%; 95% CI: -1.52 to 0.56%).

There was a positive association between the early insulin group and the development of hypotension (Odds Ratio [OR] 1.65; 95% CI: 1.10 to 2.50); 14.2% in the early insulin group developed hypotension during their ED visit compared to 9.32% in the late insulin group. There was no association between the early insulin group and subjective weakness (OR 0.75; 95% CI: 0.52 to 1.70) or arrhythmias (OR 0.71; 95% CI: 0.28 to 1.80).

## Discussion

This study demonstrated that there were no statistically significant differences in the rate of mild or moderate hypokalemia in patients who received insulin early compared to patients who received insulin late after both the first repeat potassium level and the second repeat potassium level obtained in the ED. Additionally, there was a positive association between the early insulin group and the development of hypotension. There were no other associations between the early insulin group and the clinical events used to evaluate for symptomatic hypokalemia including subjective weakness and arrhythmias (see table 2).

**Table 2:** Logistic Regression Analysis of Symptomatic Patients in Insulin First Group

	Odds Ratio (95% CI)
<b>Weakness</b>	<b>0.748 (0.523 – 1.069)</b>
<b>Prolonged QRS</b>	<b>1.230 (0.534 – 2.833)</b>
<b>QT Prolongation</b>	<b>1.42497 (0.990 – 2.049)</b>
<b>Arrhythmia</b>	<b>0.708 (0.278 – 1.801)</b>
<b>Numbness</b>	<b>2.135 (0.521 – 8.757)</b>
<b>Hypotension</b>	<b>1.652 (1.095 – 2.491)</b>

Our results show a similar rate of hypokalemia, around 7%, as another study evaluating insulin use in the ED [9]. The risk of severe hypokalemia was very small and was shown by the very low rate of adverse events. This suggests that significant time delays in awaiting lab results may not be necessary which would potentially increase throughput of patients within the department.

The underlying etiology of hyperglycemia is a lack of insulin, an insufficient response to insulin, an increased need for insulin or a combination of the three. Therefore, insulin serves as a definitive treatment to hyperglycemia. In DKA, insulin is required to stop lipolysis and ketone production. Prior studies have shown that improved ED protocols for DKA have resulted in decreased time to anion gap closure and reduced hospital length of stay [10]. In general, shorter ED length of stays have been linked to improved quality of care and decreased inpatient costs [11].

Given the lack of differences in the rate of hypokalemia and minimal association with clinical events possibly related to hypokalemia, there may not be a need to delay insulin therapy until after receiving an initial potassium result. Metabolic panels can take several hours to result thereby delaying definitive treatment of hyperglycemia and prolonging time to disposition.

There are limitations to this study. This was a retrospective study performed at a single academic institution with a large urban main emergency department which may limit its generalizability to other populations. As it was a retrospective study the dosing and route of administration of insulin as well as the time between repeat potassium values was not standardized. Future research should evaluate the change in potassium in intravenous versus subcutaneously administered insulin both with and without intravenous fluids with respect to changes in potassium and total time spent in the ED.

## Conclusion

Our study found that patients who received insulin prior to obtaining a potassium lab value have the same rates of mild and moderate hypokalemia as those who received insulin after obtaining a potassium lab value. The rates of significant complications were low between the two groups and do not support withholding insulin therapy prior to obtaining a potassium level. Given this information we see no reason to delay moderate doses of insulin in patients who present to the ED with hyperglycemia.

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