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Original Contributions

THE ASSOCIATION OF EMERGENCY DEPARTMENT TREATMENTS FOR HYPERGLYCEMIA WITH GLUCOSE REDUCTION AND EMERGENCY DEPARTMENT LENGTH OF STAY

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☐ **Abstract—Background: Hyperglycemia is frequently encountered in the emergency department (ED), and insulin and intravenous fluid are commonly administered to reduce glucose prior to discharge. Objectives: We sought to determine the magnitude of the association between glucose-lowering therapies and 1) actual glucose reduction and 2) ED length of stay (LOS). Methods: We performed a retrospective chart review study of patients with any glucose level ≥ 400 mg/dL who were discharged from the ED between January 2010 and December 2011. Generalized estimating equation models were created for the ED outcomes of glucose reduction and ED LOS with primary predictors of insulin and intravenous fluids administered. Results: The cohort consisted of 422 patients with 566 encounters. Median arrival and discharge glucose were 473 mg/dL and 326 mg/dL, respectively, with median glucose reduction of 144 mg/dL. Median length of stay was 253 min. After adjustment, 10 units of subcutaneous insulin and 1 liter of intravenous fluid were associated with 33 mg/dL and 27 mg/dL glucose reduction, respectively. Every liter of intravenous fluid administered was associated with a 45-min increase in ED LOS; insulin administration was not associated with ED LOS. Conclusion: In patients with type 2 diabetes who present with moderate to severe hyperglycemia, both insulin and intravenous fluids are associated with a modest glucose reduction. Intravenous fluids were associated with a significant increase in ED LOS, but insulin was not. These results should be considered when determining whether to administer therapies that reduce glucose in the ED.** © **2017 Elsevier Inc. All rights reserved.**

☐ **Keywords—hyperglycemia; diabetes; endocrine; metabolic; treatment**

Previous presentation: This study was presented in abstract form at the 2014 Annual Meeting of the Society of Academic Emergency Medicine in Dallas, TX, May 2014.

INTRODUCTION

Hyperglycemia is commonly encountered in the emergency department (ED), and comprises approximately 1% of encounters (1). Because most patients with hyperglycemia do not have diabetic ketoacidosis or a hyperosmolar hyperglycemic state, the majority of patients with hyperglycemia do not require hospital admission and are eligible for discharge from the ED (2). There is no consensus on the effect of glucose reduction on these patients or what care should be provided to this patient population, and recent work demonstrated that treating hyperglycemia in the ED may lack value (3,4).

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The effectiveness of insulin and intravenous fluids in reducing glucose has not been extensively studied in the ED. One small study suggests that oral or intravenous fluid therapy reduces glucose by approximately 40 mg/dL per liter administered (5). Because glucose-lowering therapies may lack value, and because many of these patients are asymptomatic, it would be helpful for emergency physicians to better characterize the association between therapies that lower glucose levels and ED length of stay (LOS).

Study Objectives

We sought to determine the magnitude of the association between glucose-lowering therapies and 1) actual glucose reduction and 2) ED LOS.

MATERIALS AND METHODS

Study Design and Setting

This chart review study was set in an urban academic Level I trauma center with an annual census of approximately 100,000 patients. During the study period there was no ED protocol for patients with hyperglycemia. Demographic information, laboratory values, medications, and fluids administered, as well as time stamps for a patient's flow through the ED are stored in a comprehensive electronic medical record. We followed best practices for retrospective study design (6). The institutional review board of Hennepin County Medical Center declared this to be exempt from review.

Selection of Participants

The electronic medical record was searched to find all ED patients aged 18 years or older who were cared for and discharged directly from the ED between January 1, 2010 and December 31, 2011 who had a glucose value of $\geq$ 400 mg/dL at any point during the ED encounter. Patients were excluded if they had type 1 diabetes or if the chief complaint was hypoglycemia. A patient was considered to have type 1 diabetes only if this was explicitly listed in their medical history.

Data Collection and Processing

A comprehensive chart review of eligible ED encounters was performed, including review of physician and nursing notes, laboratory values, and medications and fluids administered. Specific data points to collect were designated a priori. Four trained investigators reviewed all eligible charts and entered data onto a standardized Excel spreadsheet (version 14.0; Microsoft Corporation, Redmond, WA). Abstractors were blinded to these study questions. Abstractors first reviewed a standard set of 20 records to check for errors. They met periodically to review progress and ensure uniform variable definitions. In the event of conflicting data, two independent reviewers performed a consensus review of the patient chart. Missing data were left as such.

Age, sex, chief complaint, and ED LOS were extracted from the electronic medical record directly. Arrival glucose level, discharge glucose level, whether a urinalysis or a basic chemistry panel test were obtained, amount of intravenous fluids administered, amount of subcutaneous aspart or regular insulin administered (aspart insulin was much more commonly utilized), and previous hemoglobin A1c level (within 6 months) were abstracted by manual chart review.

The two main outcomes were total ED glucose reduction during the encounter and ED LOS. Glucose reduction was defined as the first glucose value minus the last glucose value. LOS was defined as from the time the patient was roomed in the ED to the time the discharge order was placed by the physician.

To assess interobserver agreement for arrival and discharge glucose, and the amount of intravenous fluids and insulin administered, 20% of the charts were reviewed by a second abstractor.

Data Analysis

Baseline characteristics and ED management of hyperglycemia were analyzed descriptively, with proportions and medians presented, with associated interquartile ranges or 95% confidence intervals. We completed a univariate (unadjusted) analysis of those who did and did not receive insulin and intravenous fluids with the median ED glucose reduction and LOS.

Table 1. Baseline Data

Parameter	Value (n = 566)
Age, years; median (IQR)	48 (40–54)
Male gender, n (%)*	244/422 (58)
Chief complaint	
Hyperglycemia	247 (49)
Alcohol intoxication	61 (11)
Abdominal pain	35 (6)
Abscess	22 (4)
Other	169 (30)
Arrival glucose, mg/dL; median (IQR)	473 (425–560)
Recent hemoglobin A1c*, mmol/mol; median (IQR)	10.4 (8.6–13)
Urinalysis obtained, n (%)	367 (65)
Urine ketones present, n (% of obtained)	85 (23)
Basic chemistry obtained, n (%)	414 (73)

IQR = interquartile range.
* There were 566 encounters with 422 unique patients.

Table 2. ED Management of Hyperglycemia and Response

Parameter	Value (n = 566)
Intravenous fluid administered, n (%; 95% CI)	448 (79; 76–82)
Amount of intravenous fluid administered, if received, liters; median (IQR)	2 (1, 2)
Subcutaneous insulin administered, n (%; 95% CI)	389 (69; 65–73)
Amount of subcutaneous insulin administered, if received, units; median (IQR)	10 (0, 10)
Glucose reduction, mg/dL; median (95% CI)	144 (132–162)
Discharge glucose, mg/dL; median (95% CI)	326 (318–336)
Length of stay, minutes; median (95% CI)	253 (241–267)

ED = emergency department; CI = confidence interval; IQR = interquartile range.

We then conducted analyses to determine the association between insulin and intravenous fluids and 1) ED glucose reduction and 2) ED LOS. To perform this, we created multivariable generalized estimating equations. We utilized this method to account for patients with more than one visit during the study period, rather than multiple linear regression, which assumes all observations are independent. For glucose reduction, a Gaussian distribution was used; for LOS, a gamma distribution was used to account for the right-skewed nature of the outcome. A robust variance estimator was utilized. To construct the generalized estimating equation models, covariates that could plausibly affect the outcomes were selected a priori for inclusion into the respective models. For glucose reduction, covariates included arrival glucose, age, the amount of intravenous fluids administered, and the amount of subcutaneous insulin administered. For LOS, covariates included arrival glucose, glucose reduction, age, the amount of intravenous fluids administered, the amount of subcutaneous insulin administered, and whether a basic metabolic panel was obtained. Whether a basic metabolic panel was obtained was included to account for any delay in obtaining a blood test as part of the ED evaluation. In the glucose reduction model, patients with only a single glucose value were excluded (i.e., glucose reduction could not be calculated).

From each generalized estimating equation model, we report the coefficients with associated 95% confidence intervals. No a priori sample size was calculated. Stata 12.1 (StataCorp, College Station, TX) was used for all data analyses.

RESULTS

Of 706 encounters identified, 140 were excluded (135 due to type 1 diabetes mellitus; five with a chief complaint of hypoglycemia), leaving 566 ED encounters for analysis, with 422 unique patients. Baseline data and ED management of hyperglycemia are displayed in Tables 1 and 2. The unadjusted univariate analysis comparing the outcomes stratified by the treatment received is presented in Table 3. The generalized estimating equation results for both outcomes are displayed in Table 4. Interobserver agreement was assessed: arrival and discharge glucose had 95% ($\kappa = 0.84$) and 91% ($\kappa = 0.74$) agreement, respectively; the amount of intravenous fluids and insulin administered had 89% ($\kappa = 0.70$) and 92% ($\kappa = 0.76$) agreement, respectively.

In the adjusted glucose reduction model, administration of 1 liter of intravenous fluid was associated with a mean glucose reduction of 27 mg/dL; administration of 10 units subcutaneous insulin was associated with a mean glucose reduction of 33 mg/dL (Figure 1).

In the adjusted ED LOS model, administration of 1 liter of intravenous fluid was associated with a 45-min increase in LOS; administration of insulin was not associated with a change in LOS (Figure 2).

DISCUSSION

Hyperglycemia is a common diagnosis in the ED, and although glucose reduction in the ED may lack value, it is common to attempt to reduce glucose levels prior to discharge, even in asymptomatic patients (3,4). This investigation suggests that glucose-lowering therapies in the ED may have only a modest effect, on average, and may prolong ED LOS.

In this investigation, both insulin and intravenous fluid were associated with only modest glucose

Table 3. Unadjusted Analysis of ED Treatments with Glucose Reduction and ED LOS

Outcomes	IV Fluids Received	No IV Fluids	Insulin Received	No Insulin
Glucose reduction* (mg/dL)	180 (164–196)	101 (59–146)	196 (181–213)	117 (91–133)
ED LOS (min)	275 (264–288)	147 (122–170)	282 (262–291)	212 (188–230)

ED = emergency department; LOS = length of stay; IV = intravenous fluids.
All values are median (95% confidence interval).
* This examines the 492 subjects who had both an arrival and discharge glucose value, excluding those with a single glucose value.

Table 4. Generalized Estimating Equation Models

	Outcomes			
	Glucose Reduction (mg/dL)*		ED LOS (min)	
Predictors	Coefficient	95% CI	Coefficient	95% CI
Age (years)	0.47	−0.47 to 0.48	0.99	0.15–1.83
IV fluids received (L)	26.7	16.8–36.7	45.3	32.8–57.8
Insulin received (10 units)	32.8	18.1–47.4	7.6	−6.8 to 22.1
Arrival glucose (mg/dL)	–	–	−0.08	−0.21 to 0.04
Basic chemistry obtained (yes/no)	–	–	45.2	15.4–74.9

ED = emergency department; LOS = length of stay; CI = confidence interval; IV = intravenous.
* This examines the 492 subjects who had both an arrival and discharge glucose value, excluding those with a single glucose value.

reduction. However, these results should not be viewed as an accurate prediction of how much glucose will be lowered for any individual patient; Figure 1 clearly demonstrates that glucose reduction as a function of insulin and intravenous fluid will vary significantly patient to patient. This is not intuitive; traditionally, patients are thought to have a predictable response to insulin or intravenous fluids (7). This does not seem to be true when applied to a heterogeneous ED population with type 2 diabetes mellitus. Data from this study suggest that insulin and fluids administered may not be the primary determinants of glucose reduction, which is likely influenced by individual insulin resistance, food/drink consumed in the ED, and other confounding variables.

The modest reduction of glucose with intravenous fluids (27 mg/dL per liter of fluid) observed in this study is similar to a recent randomized trial that demonstrated

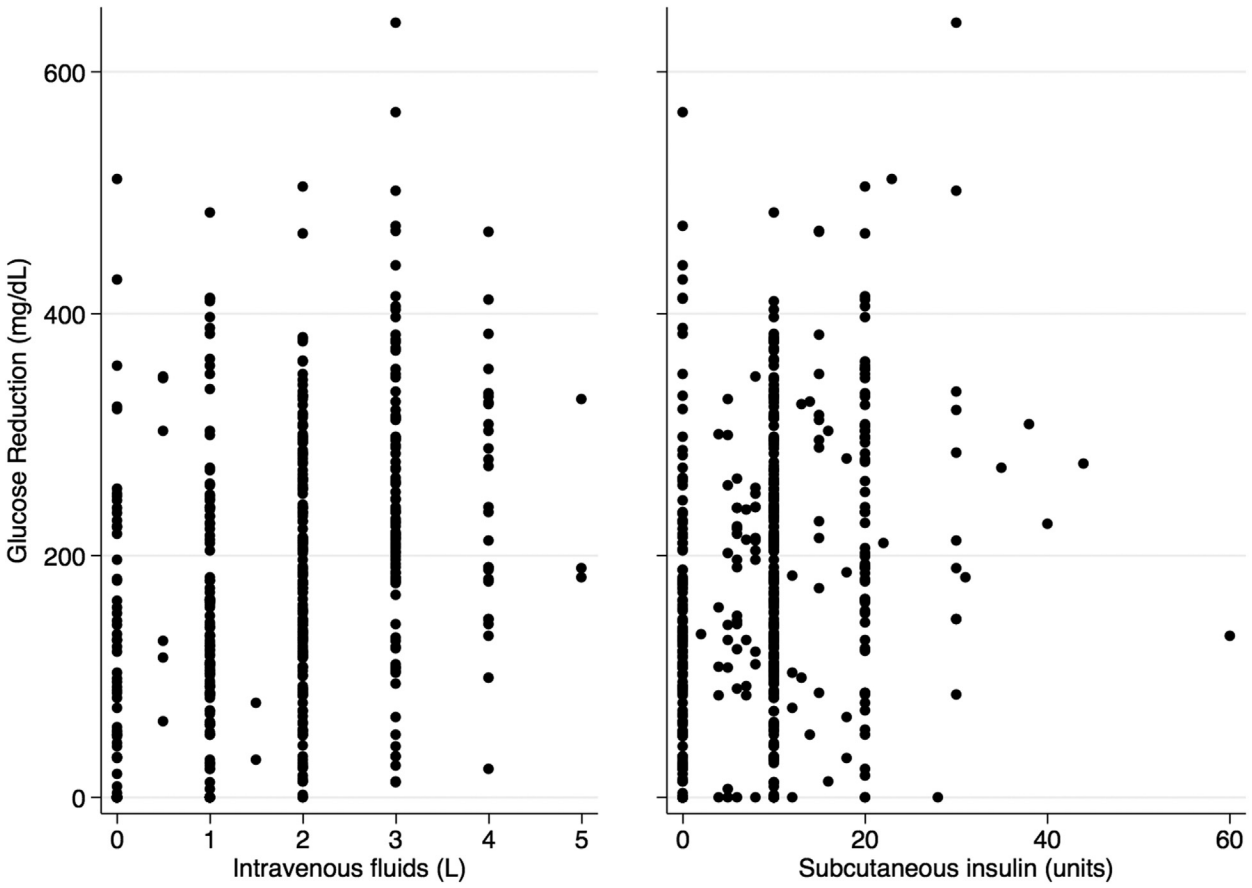

Figure 1. Scatterplot of glucose reduction by intravenous fluid and insulin administered. Patients with an increase in glucose during the emergency department stay are not pictured on this graph (n = 25).

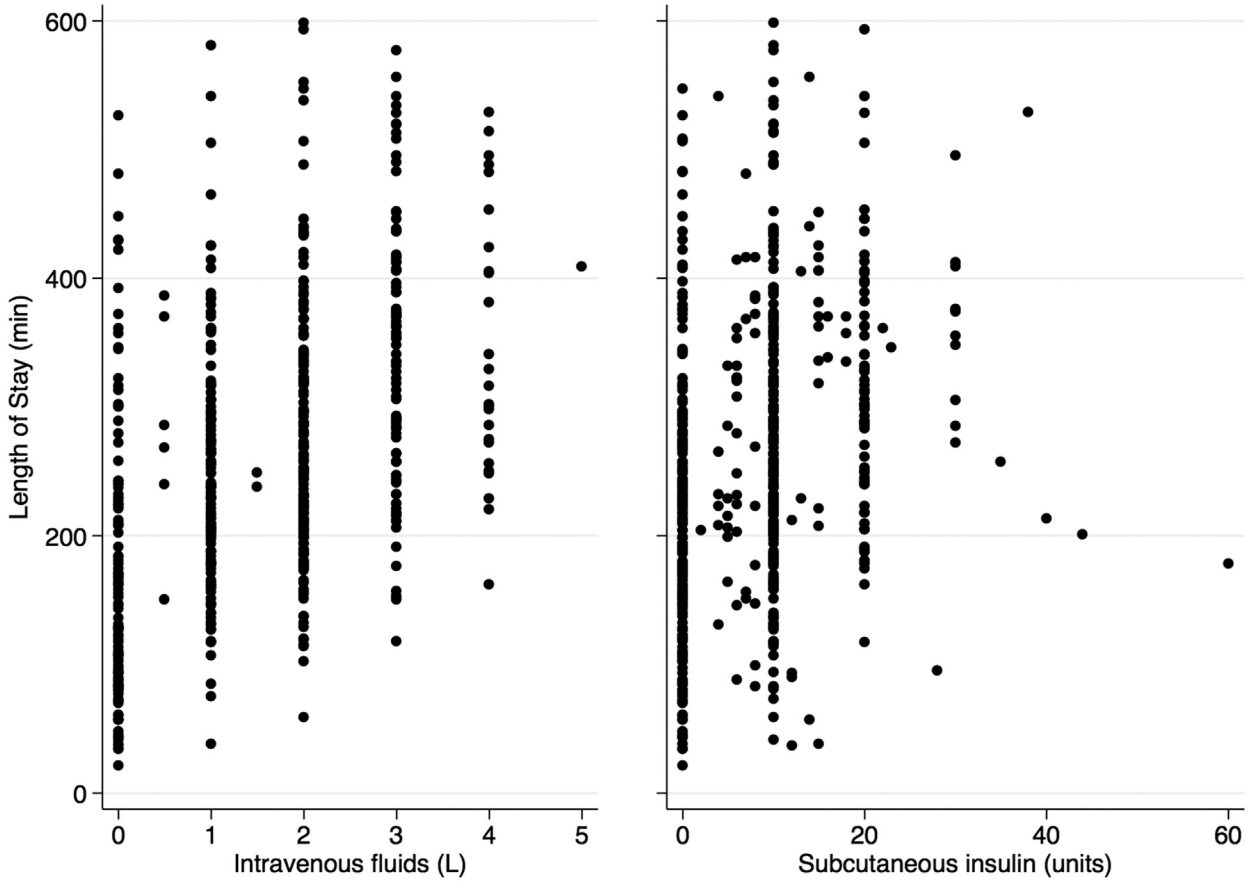

Figure 2. Scatterplot of emergency department length of stay by intravenous fluid and insulin administered.

approximately 39 mg/dL of glucose reduction per liter of oral or intravenous fluid (5). This indicates that fluid administration should probably not be viewed as an important glucose reduction therapy for ED patients with hyperglycemia; instead it would be reasonable to reserve intravenous fluid administration for those with hypovolemia.

LOS is an important quality metric in the ED (8,9). In this study, insulin had no association with LOS, perhaps because not much time is required to administer insulin. In contrast, each liter of intravenous fluid administered was associated with a 45-min increase in LOS, highlighting the limitation of this intervention when administered for ED hyperglycemia.

Because glucose reduction for ED patients who are well enough to be discharged seems to lack value and is not associated with a reduction in short-term adverse outcomes, and because this study provides evidence that insulin and intravenous fluids are, on average, modestly effective and prolong ED LOS, it is possible that efforts to reduce glucose in the ED in patients who are otherwise well are not worthwhile (4). It is desirable, additionally, to avoid complications such as hypoglycemia, which occurs in 2% of patients (4).

Limitations

There are several limitations to this investigation. This was a retrospective study, which has inherent biases (6). We mitigated this by following sound chart review practices, and all outcomes were numerical without allowances for subjective interpretation.

The arrival and glucose reduction were defined as the first and last ED glucose values, respectively, and may not represent the actual arrival and discharge glucose values. This limitation may underestimate the association between treatments administered and ED glucose reduction if the last glucose value was obtained shortly after a treatment was administered, though that is not the usual practice in our ED.

Although we adjusted for certain variables that could have affected the outcomes, unmeasured confounders likely contributed to both glucose reduction and length of stay. Therefore, the magnitudes of the associations should not be considered accurate values. However, the small glucose reduction with intravenous fluids is consistent with prior literature, and it is intuitive that administering a liter of fluids will prolong ED LOS, so the

results, although not necessarily accurate, have face validity (5). Future prospective work in ED patients with hyperglycemia will help overcome many of these limitations.

CONCLUSION

In patients with type 2 diabetes who present with moderate to severe hyperglycemia, both insulin and intravenous fluids are associated with only a modest glucose reduction. Every liter of intravenous fluids administered is associated with a 45-min increase in ED LOS. Because reducing glucose in patients well enough to be discharged may lack value, these current results should be considered when determining whether to administer therapies that reduce glucose in the ED. It may be reasonable to reserve intravenous fluids for patients with hypovolemia.

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ARTICLE SUMMARY

1. Why is this topic important?

Hyperglycemia is commonly encountered in the emergency department (ED). Although treatments to reduce glucose are often employed, the effectiveness of these treatments and their association with ED length of stay are not known.

2. What does this study attempt to show?

The goal of this study is to determine how much glucose reduction and ED length of stay are associated with common treatments for hyperglycemia.

3. What are the key findings?

Our study suggests that, on average, intravenous fluids and insulin result in only modest glucose reduction in the ED. Administration of intravenous fluids was associated with a 45-min increase in ED length of stay.

4. How is patient care impacted?

Because reducing glucose in patients well enough to be discharged may lack value and does not change short-term outcomes, these current results should be considered when determining whether to administer therapies that reduce glucose in the ED. It may be reasonable to reserve intravenous fluids for patients with hypovolemia.