

Original Research

Evaluation of Intravenous Insulin Lispro for Hyperkalemia Treatment in Emergency Department Patients

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Background/Purpose

Although intravenous (IV) regular insulin has been the main treatment option for management of acute hyperkalemia, our institution utilizes IV insulin lispro as the preferred rapid-acting insulin. Little data currently exists on the safety or efficacy of insulin lispro for this indication. This study aims to evaluate the safety and efficacy of this alternative.

Methods

This study is a retrospective chart review of adult patients who received IV insulin lispro in an academic medical center Emergency Department (ED) for the treatment of hyperkalemia. The main efficacy and safety outcomes evaluated within 6 hours post-insulin administration were: change in serum potassium concentration and the incidence of hypoglycemia.

Results

One hundred and thirteen IV insulin lispro administrations were included. For evaluation of efficacy, the mean serum potassium before insulin administration was 6.6 mmol/L. The mean first serum potassium concentration after insulin administration was 5.5 mmol/L, with a serum potassium decrease of 1.1 mmol/L. As for safety, the mean blood glucose before insulin administration was 147.8 mg/dL. The mean first blood glucose after insulin administration was 149.9 mg/dL. Dextrose was co-administered 90.2% of the time. There were a total of 18 hypoglycemic events (15.9%), including 3 events that met the criteria for severe hypoglycemia (2.7%).

Conclusion

For treatment of hyperkalemia in ED patients, IV insulin lispro appears to be an efficacious alternative to IV insulin regular. However, a further review of its safety profile is warranted.

BACKGROUND

Hyperkalemia is a common electrolyte disorder that can be potentially life-threatening and affect 1 to 10% of hospitalized patients and 2 to 3% of patients seen in the Emergency Department (ED).^{1,2} It is most commonly associated with renal insufficiency, particularly in patients with chronic kidney disease (CKD), medications that are potassium-sparing or act on the renin-angiotensin-aldosterone system, and diets with potassium-rich foods. Patients can be asymptomatic or present with a variety of symptoms, including muscle weakness and/or life-threatening arrhythmias.

Management of acute hyperkalemia may include stabilization of cardiac membranes with intravenous (IV) cal-

cium, temporary redistribution of potassium into cells with IV insulin and nebulized beta-agonists, and enhanced elimination from the body with IV loop diuretics, sodium-potassium exchange resins, and emergent hemodialysis.³

Insulin is known to lower serum potassium concentrations by driving extracellular potassium intracellularly through the sodium-potassium-ATPase pump in skeletal muscle cells.⁴ IV regular insulin has been the main treatment choice for this temporary redistribution; its potassium-shifting effects typically occur within 15 minutes of administration and may persist up to 4 hours or longer.⁵

The institution at which this study was conducted utilizes IV lispro insulin as the preferred rapid-acting insulin in management of acute hyperkalemia to reduce insulin products stocked in the automated dispensing cabinets to

minimize errors. Limited current data exists evaluating the use of IV lispro insulin for this indication. The purpose of this study was to determine the efficacy and safety of this alternative when used for treatment of hyperkalemia in ED patients.

METHODS

This study was a retrospective chart review of a convenience sample conducted at a single-site academic medical center in the Midwest. It was submitted to the university's Institutional Review Board (IRB) and determined to be exempt from IRB approval.

Patients 18 years and older were included if they had received IV lispro insulin at a dose of 5 units for the treatment of acute hyperkalemia in the ED at University Hospital (UH) between January 1, 2022, to January 1, 2023. They were excluded if: they had received continuous IV insulin or dextrose infusions (either concurrently or within 6 hours of the IV lispro insulin administration), there were additional intermittent IV or subcutaneous (SQ) insulin doses administered, the doses were administered at an outside hospital before transfer, or there were no follow-up serum potassium or blood glucose levels within 6 hours from the IV insulin dose. Patients with multiple ED visits within the year were considered eligible if they met the inclusion criteria.

Patient demographics, baseline characteristics, pertinent comorbidities, and additional hyperkalemia treatments, including need for emergent hemodialysis, were collected to identify potential confounding variables.

The primary efficacy outcome was the change in potassium concentration within 6 hours of IV lispro insulin administration. As for safety, the incidence of hypoglycemia, defined as a blood glucose level of <70 mg/dL was recorded. Additionally, the incidence of severe hypoglycemia, defined as a blood glucose level of <40 mg/dL, was also recorded. Per the institution's protocol, a 25 g IV dextrose bolus was co-administered with IV lispro insulin to all patients with a blood glucose level of <250 mg/dL. A subgroup analysis of IV lispro insulin administrations that led to hypoglycemia was also completed.

RESULTS

A total of 148 IV insulin administrations that met the inclusion criteria were identified in the study period. Thirty-five administrations of IV insulin were excluded as follows: 14 occurred at an affiliated hospital before transfer to UH, 11 had additional IV or SQ insulin administered within 6 hours of IV lispro insulin, 4 received IV regular insulin instead of lispro, 4 had an insulin infusion started within 6 hours, and 2 did not have a follow-up blood glucose reported in the electronic health record. Subsequently, 110 unique patients and 113 IV lispro insulin administrations were included in the analysis.

Patient demographics and comorbidities are presented in [table 1](#). The majority included were male (60.1%), with a mean age of 62 years. Almost half had no history of dia-

betes (46.9%) and nearly three-fourths had no insulin use at baseline (72.6%). Although the mean recorded serum creatinine (SCr) at the time of IV insulin administration indicated some level of acute kidney injury, the mean baseline SCr was also elevated, highlighting the baseline prevalence of CKD amongst the study population. In fact, 64.6% of the patients included had CKD stage 3 or higher.

The efficacy and safety data for IV insulin lispro are presented in [table 2](#). The mean serum potassium before insulin administration was 6.6 mmol/L. The mean first serum potassium concentration after insulin administration was 5.5 mmol/L, with a serum potassium decrease of 1.1 mmol/L. As for safety, the mean blood glucose before insulin administration was 147.8 mg/dL. The mean first blood glucose after insulin administration was 149.9 mg/dL. There was a total of 18 hypoglycemic events (15.9%), including 3 that met the criteria for severe hypoglycemia (2.7%). Intravenous dextrose, at a dose of 25 g, was co-administered with IV insulin 90.2% of the time. The mean time to follow-up potassium was approximately 2 h. The mean time to follow-up blood glucose was 1.5 h. Other treatments administered as part of acute hyperkalemia management are presented in [table 3](#).

Hypoglycemia occurred in 18 different patients ([table 4](#)). These patients had a lower mean BMI (26.7 kg/m² compared to 28.2 kg/m²). They were also less likely to use insulin at baseline, 88.9% of these patients did not have any insulin use at baseline, compared to 72.6% overall. They also had a higher mean baseline (2.96 mg/dL) and recorded (5.72 mg/dL) SCr at the time of IV insulin lispro administration and their mean blood glucose before IV insulin was also lower (111.4 mg/dL compared to 147.8 mg/dL).

Three patients experienced severe hypoglycemia ([table 4](#)). All were men, with a lower BMI, and with no use of insulin at baseline. Two of them had stage 5 CKD and were recipients of intermittent hemodialysis. Their mean blood glucose before IV insulin lispro was 81.3 mg/dL. A dose of IV dextrose 25 g was co-administered with IV lispro insulin for all 3 patients.

DISCUSSION

This study investigated the efficacy and safety of IV lispro insulin in the management of acute hyperkalemia in patients presenting to the ED. It demonstrated that IV insulin lispro effectively reduced serum potassium concentration by 1.1 mmol/L at 2 hours post administration. Although several recent studies have compared various IV regular insulin dosing strategies, including 5 units vs. 10 units or 0.1 units/kg vs. 10 units, few studies have compared the effectiveness of IV lispro insulin in this context.^{6,7} The potassium-lowering effects of these dosing regimens have been reported as ranging from 0.96 to 1.02 mmol/L, which is comparable to the decrease in serum potassium concentration found in this study.⁷

The incidence of hypoglycemia in this study was 15.9%, while the incidence of severe hypoglycemia was 2.7%. The patients at our institution received a mean IV dextrose dose of 25 g at the time of IV insulin administration and addi-

Table 1. Patient demographics and comorbidities

	N = 113
Mean age, y	62 (SD 14.7)
Male, No. (%)	68 (60.1)
Mean weight (kg)	80.5 (SD 24.8)
Mean height (cm)	169.1 (SD 12.1)
Mean BMI (kg/m ²)	28.2 (SD 8.2)
No history of diabetes, No. (%)	53 (46.9)
History of type I diabetes, No. (%)	4 (3.5)
History of type II diabetes, No. (%)	56 (49.6)
No insulin use at baseline, No. (%)	82 (72.6)
Mean eGFR at time of IV insulin, mL/min/1.73m ²	27.2 (SD 28.2)
Mean baseline SCr, mg/dL	2.1 (SD 2.1)
Mean recorded SCr at time of IV insulin, mg/dL	4.9 (SD 4.6)
iHD at baseline, No. (%)	16 (14.2)
PD at baseline, No. (%)	5 (4.4)
Stage 1 CKD at baseline, No. (%)	21 (18.6)
Stage 2 CKD at baseline, No. (%)	19 (16.8)
Stage 3 CKD at baseline, No. (%)	37 (32.7)
Stage 4 CKD at baseline, No. (%)	13 (11.5)
Stage 5 CKD at baseline, No. (%)	23 (20.4)

Abbreviations: BMI, body mass index; eGFR, estimated glomerular filtration rate; SCr, serum creatinine; iHD, intermittent hemodialysis; PD, peritoneal dialysis; CKD, chronic kidney disease

Table 2. Efficacy and safety of IV insulin lispro when used for temporary serum potassium reduction in acute hyperkalemia

	N = 113
Mean serum potassium before IV insulin, mmol/L	6.6 (SD 0.7)
Mean serum potassium after IV insulin, mmol/L	5.5 (SD 0.8)
Decrease in serum potassium with IV insulin, mmol/L	1.1
Mean time of follow-up potassium, h:mm	2:03 (SD 1:19)
Mean blood glucose before IV insulin, mg/dL	147.8 (SD 66.4)
Mean blood glucose after IV insulin, mg/dL	149.9 (SD 76.2)
Mean time of follow-up blood glucose, h:mm	1:34 (SD 1:16)
Incidence of hypoglycemia, No. (%)	18 (15.9)
Incidence of severe hypoglycemia, No. (%)	3 (2.7)

tional doses were given after hypoglycemia was identified. The incidence of hypoglycemia is comparable to a retrospective study by LaRue et al. In this study 675 patients received either regular insulin 5 units (133 patients) or 10 units (542 patients).⁶ Per the protocol at this institution, dextrose 25 g (either oral or IV) was to be co-administered with the IV insulin, followed by another 25 g dose an hour later, and a third, 25 g dose could be given 3 hours after IV insulin administration, if the blood glucose was less than 70 mg/dL. Hypoglycemia, defined as a blood glucose <70 mg/dL, occurred in 19.5% of the patients that received the 5-units dose compared to 28.6% of the patients that received the 10-units dose. Severe hypoglycemia, defined as a

blood glucose of <40 mg/dL, occurred in 3% of the patients that received the 5-units dose, compared to 6.8% of the patients that received the 10-units dose.

Various risk factors for the development of hypoglycemia after IV insulin therapy have been identified. Recognizing these risk factors can guide proactive management to prevent the development of hypoglycemia. Lower pretreatment blood glucose levels of ≤140 mg/dL and of ≤120 mg/dL have been associated with an increased risk of hypoglycemia.^{8,9} The mean pretreatment blood glucose level in the patients that experienced hypoglycemia in this study was 111.4 mg/dL and it was even lower, 81.3 mg/dL, for the patients that developed severe hypoglycemia.

Table 3. Therapies co-administered with IV insulin lispro in management of hyperkalemia

	N = 113
IV dextrose, No. (%)	102 (90.3)
Calcium gluconate, No. (%)	101 (89.4)
Potassium binder, No. (%)	49 (43.4)
IV diuretic, No. (%)	47 (41.6)
Nebulized albuterol, No. (%)	42 (37.2)
IV sodium bicarbonate, No. (%)	23 (20.4)
Emergent iHD, No. (%)	11 (9.7)

Abbreviations: iHD, intermittent hemodialysis

Table 4. Characteristics of patients that experienced hypoglycemia with IV insulin lispro

	Hypoglycemia (n = 18)	Severe hypoglycemia (n = 3)
Female, No. (%)	6 (33.3)	0 (0)
Mean BMI, (kg/m ²)	26.7 (SD 7.6)	23.0 (SD 5.3)
No history of diabetes, No. (%)	9 (50)	2 (66.6)
History of type I diabetes, No. (%)	0 (0)	0 (0)
History of type II diabetes, No. (%)	9 (50)	1 (33.3)
No insulin use at baseline, No. (%)	16 (88.9)	3 (100)
Insulin use at baseline, No. (%)	2 (11.1)	0 (0)
Mean eGFR at time of IV insulin, mL/min/1.73m ²	23.8 (SD 27.8)	44.0 (SD 64.1)
Mean baseline SCr, mg/dL	2.96 (SD 2.70)	4.93 (SD 3.58)
Mean recorded SCr at time of IV insulin, mg/dL	5.72 (SD 4.26)	5.57 (SD 4.75)
No dialysis at baseline, No. (%)	12 (66.7)	1 (33.3)
iHD at baseline, No. (%)	5 (27.8)	2 (66.6)
PD at baseline, No. (%)	1 (5.6)	0 (0)
Stage 1 CKD at baseline, No. (%)	4 (22.2)	1 (33.3)
Stage 2 CKD at baseline, No. (%)	2 (11.1)	0 (0)
Stage 3 CKD at baseline, No. (%)	5 (27.8)	0 (0)
Stage 4 CKD at baseline, No. (%)	1 (5.6)	0 (0)
Stage 5 CKD at baseline, No. (%)	6 (33.3)	2 (66.6)
Mean blood glucose before IV insulin, mg/dL	111.4 (SD 41.5)	81.3 (SD 1.2)
IV dextrose administered, No. (%)	17 (94.4)	3 (100)
Mean IV dextrose dose administered, g	25 (SD 0)	25 (SD 0)

Abbreviations: BMI, body mass index; eGFR, estimated glomerular filtration rate; SCr, serum creatinine; iHD, intermittent hemodialysis; PD, peritoneal dialysis; CKD, chronic kidney disease

Additionally, abnormal renal function is a known risk factor for hypoglycemia due to decreased insulin clearance.⁸ Patient's experiencing hypoglycemia in this study had higher mean baseline and recorded SCr at the time of IV insulin administration and were more likely to be on dialysis. Other reported risk factors for development of hyperkalemia include no history of diabetes, and female sex.^{10,11} These risk factors were not evident in this study as more men tended to develop hypoglycemia than women. However, the absence of a history of diabetes was roughly equal between groups.

Based on the results of this study, lower pretreatment blood glucose levels, in the setting of severe renal dysfunc-

tion, lower BMI, and history of no baseline insulin use, may be used proactively to guide IV dextrose dosing decisions.

This study has several limitations; it was conducted at a single center with a small sample size which may limit its generalizability. The retrospective nature of the study may have also introduced bias. Additionally, since repeat doses of IV insulin within 6 hours of the initial dose were excluded, there is a potential a chance that there was selection bias in favor of patients that initially responded to single IV insulin lispro dose. Future research with a larger, multi-centered study that compares IV insulin lispro to insulin regular is warranted to validate the efficacy and safety of this treatment alternative.

CONCLUSION

For treatment of acute hyperkalemia in ED patients, IV insulin lispro appears to be an equally efficacious alternative to IV insulin regular. However, a further review of its safety profile in comparison to IV insulin regular is warranted.

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PREVIOUS AFFILIATIONS

At the time of the study, Dr. Lee was affiliated with University of Wisconsin Health (Madison, WI).

CONFLICT OF INTEREST STATEMENT

The authors have declared no potential conflicts of interest.

DATA AVAILABILITY

The data underlying this article cannot be shared publicly due to HIPAA privacy laws without a mutually agreed upon data use agreement for this limited data set.

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REFERENCES

1. Singer AJ, Thode HC Jr, Peacock WF. A retrospective study of emergency department potassium disturbances: severity, treatment, and outcomes. *Clin Exp Emerg Med*. 2017;4(2):73-79. doi:[10.15441/ceem.16.194](https://doi.org/10.15441/ceem.16.194)
2. Moore ML, Bailey RR. Hyperkalaemia in patients in hospital. *N Z Med J*. 1989;102(878):557-558.
3. Mahoney BA, Smith WA, Lo DS, Tsoi K, Tonelli M, Clase CM. Emergency interventions for hyperkalaemia. *Cochrane Database Syst Rev*. 2005;2005(2):CD003235. doi:[10.1002/14651858.CD003235.pub2](https://doi.org/10.1002/14651858.CD003235.pub2)
4. Clausen T, Everts ME. Regulation of the Na,K-pump in skeletal muscle. *Kidney Int*. 1989;35(1):1-13. doi:[10.1038/ki.1989.1](https://doi.org/10.1038/ki.1989.1)
5. *Humulin R U-100*. Lilly USA, LLC; 2011.
6. LaRue HA, Peksa GD, Shah SC. A Comparison of Insulin Doses for the Treatment of Hyperkalemia in Patients with Renal Insufficiency. *Pharmacotherapy*. 2017;37(12):1516-1522. doi:[10.1002/phar.2038](https://doi.org/10.1002/phar.2038)
7. Beard MM, McKenzie JJ, Potter TG, Varney Gill K. Evaluating Risk Factors for Developing Hypoglycemia During Treatment of Hyperkalemia With Intravenous Regular Insulin. *J Pharm Pract*. Published online January 4, 2024. doi:[10.1177/08971900231223025](https://doi.org/10.1177/08971900231223025)
8. Wheeler DT, Schafers SJ, Horwedel TA, Deal EN, Tobin GS. Weight-based insulin dosing for acute hyperkalemia results in less hypoglycemia. *J Hosp Med*. 2016;11(5):355-357. doi:[10.1002/jhm.2545](https://doi.org/10.1002/jhm.2545)
9. Coca A, Valencia AL, Bustamante J, Mendiluce A, Floege J. Hypoglycemia following intravenous insulin plus glucose for hyperkalemia in patients with impaired renal function. *PLoS One*. 2017;12(2):e0172961. doi:[10.1371/journal.pone.0172961](https://doi.org/10.1371/journal.pone.0172961)
10. Apel J, Reutrakul S, Baldwin D. Hypoglycemia in the treatment of hyperkalemia with insulin in patients with end-stage renal disease. *Clin Kidney J*. 2014;7(3):248-250. doi:[10.1093/ckj/sfu026](https://doi.org/10.1093/ckj/sfu026)
11. Schafers S, Naunheim R, Vijayan A, Tobin G. Incidence of hypoglycemia following insulin-based acute stabilization of hyperkalemia treatment. *J Hosp Med*. 2012;7(3):239-242. doi:[10.1002/jhm.977](https://doi.org/10.1002/jhm.977)