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Impact of Adding Reduced and Weight-based Insulin Dosing Options to the Emergency Department and Inpatient Hyperkalemia Order-set

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ABSTRACT

PURPOSE: To compare the effects of weight-based, reduced, and standard IV insulin doses on potassium reduction and hypoglycemia incidence in the treatment of acute hyperkalemia.

METHODS: The hyperkalemia treatment order-set was updated to include reduced and weight-based insulin dose options. Patients ≥ 18 years old with acute hyperkalemia treated with insulin using the order-set were included. Patients with missing data or who started dialysis before follow-up potassium monitoring were excluded. The primary efficacy outcome was reduction in serum potassium. The primary safety outcome was incidence of hypoglycemia and severe hypoglycemia. Secondary outcomes included insulin dose administered, completion of hourly glucose checks, and dextrose use.

RESULTS: The pre-protocol group included 60 patients and the post-protocol group included 76 patients. Potassium reduction was similar with a mean reduction of 0.9 mEq/L in the pre-protocol group and 0.85 mEq/L in the post-protocol group. The incidence of hypoglycemia was 18% in the pre-protocol group with 2% of patients developing severe hypoglycemia. The incidence of hypoglycemia was 13% in the post-protocol group with 3% of patients developing severe hypoglycemia. The mean insulin dose administered was 9.5 units in the pre-protocol group and 7.7 units in the post-protocol group. In the post-protocol group, weight-based and reduced insulin doses were administered to 84% and 13% of patients, respectively. Less than 25% of patients completed all glucose checks. Only about 50% of patients with hypoglycemia were treated with dextrose.

CONCLUSIONS: Using weight-based and reduced insulin doses in the treatment of acute hyperkalemia results in comparable potassium reduction and reduced hypoglycemia incidence.

KEYWORDS: hyperkalemia, insulin, hypoglycemia

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BACKGROUND

Hyperkalemia is a common electrolyte abnormality defined by an elevated serum potassium level greater than 5 mEq/L. The clinical presentation of hyperkalemia is often asymptomatic. In severe cases, EKG changes and life-threatening cardiac arrhythmias may occur. Risk factors for hyperkalemia include renal impairment, heart failure, uncontrolled diabetes, and certain medications. Potential causes of hyperkalemia include impaired potassium excretion, abnormal extracellular potassium distribution, and excess potassium intake.[1-4] The treatment options for acute hyperkalemia include medications to provide cardioprotective effects, shift potassium intracellularly, and remove excess potassium. In patients with severe hyperkalemia or EKG changes, IV calcium gluconate or IV calcium chloride can be administered to provide cardioprotective effects and prevent cardiac arrhythmias. IV insulin, albuterol nebulizers, or IV sodium bicarbonate can be administered to shift potassium intracellularly and reduce the serum concentration of potassium. IV loop diuretics and oral potassium binders can be given to remove excess potassium through the urine and feces, respectively. Hemodialysis can also be initiated to renally eliminate excess potassium.[1,5] Hypoglycemia is a common adverse effect associated with insulin use. In the treatment of acute hyperkalemia, 10 unit doses of IV insulin are commonly used, leading to an increased risk of iatrogenic hypoglycemia. Multiple studies have found that using lower IV

Table 1. Pre-Protocol Hyperkalemia Treatment Order-Set

Pre-Protocol Hyperkalemia Treatment Order-Set
Insulin regular U-100, 10 units IV
Dextrose 50% (D50W), 25 g (with insulin)
D50W, 25 g PRN for glucose < 70 or 50 g PRN for severe hypoglycemia or mental status changes (for first 6 hours)
Hourly fingerstick glucose for 6 hours
Additional options: albuterol nebulizer, calcium gluconate, furosemide, sodium bicarbonate, potassium binders

Table 2. Post-Protocol Hyperkalemia Treatment Order-Set

Post-Protocol Hyperkalemia Treatment Order-Set
Insulin regular U-100, 0.1 units/kg IV (max 10 units), 5 units, or 10 units • Default dose option = 0.1 units/kg • Criteria included to help identify patients at high risk for hypoglycemia
Dextrose 50% (D50W), 25 g (with insulin)
D50W, 25 g PRN for glucose < 70 or 50 g PRN for severe hypoglycemia or mental status changes (for first 6 hours)
Hourly fingerstick glucose for 6 hours
Serum potassium level
Additional options: albuterol nebulizer, calcium gluconate, furosemide, sodium bicarbonate, potassium binders

insulin doses in the treatment of acute hyperkalemia results in lower rates of hypoglycemia and similar effects on potassium reduction. A recent meta-analysis published in Pharmacotherapy compiled results from 10 studies evaluating the effects of reduced (< 10 units) or weight-based (0.1 units/kg, maximum 10 units) IV insulin doses in the treatment of acute hyperkalemia. Overall, the studies found no difference in potassium reduction and a lower incidence of hypoglycemia with reduced and weight-based insulin doses compared to standard doses. The findings of these studies suggest that using reduced or weight-based insulin doses in the treatment of acute hyperkalemia results in a potential safety benefit without impacting efficacy.[6,7] The purpose of this study is to compare the effects of reduced (5 units), weight-based (0.1 units/kg, maximum 10 units), and standard (10 units) IV insulin doses on potassium reduction and hypoglycemia incidence in the treatment of acute hyperkalemia.

METHODS

This study was a retrospective single-center quality improvement initiative conducted at Reading Hospital. The Institutional Review Board (IRB) at Reading Hospital approved the study as a quality improvement initiative. Pre-protocol data was collected from July 1, 2022 through September 30, 2022 to determine baseline data utilizing standard insulin doses. Post-protocol data was collected from December 20, 2022 through March 21, 2023 to assess the impact of weight-based and reduced insulin doses.

The pre-protocol hyperkalemia treatment order-set included regular insulin 10 units IV as the default (standard) dosing option to be administered with 25 g of IV dextrose. The pre-protocol order-set also contained hourly fingerstick glucose checks for the first 6 hours after insulin administration and additional dextrose doses to be given as needed for hy-

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Table 3. Baseline Demographics

	Pre-Protocol (n=60)	Post-Protocol (n=76)	P-value
Age (years), median (range)	68 (30-92)	69 (24-98)	0.877
Female, n (%)	29 (48)	28 (37)	0.177
Renal Impairment, n (%)	33 (55)	49 (65)	0.531
Diabetes, n (%)	39 (65)	43 (57)	0.219
Overweight/Obese, n (%)	41 (68)	58 (76)	0.326
Pre-Treatment Potassium (mEq/L), median (range)	6.4 (5.2-8.4)	6.3 (4.9-8.2)	0.505

Renal Impairment: history of CKD
Diabetes: history of type 1 or type 2 diabetes
Overweight/Obese: BMI > 29.5 kg/m^2

poglycemia (25 g IV for blood glucose < 70 and 50 g IV for severe hypoglycemia or mental status changes). Additional treatment options available in the pre-protocol order-set included IV calcium gluconate, IV sodium bicarbonate, albuterol nebulizers, IV furosemide, and oral potassium binders (*Table 1*). The post-protocol hyperkalemia treatment order-set included weight-based (0.1 units/kg, maximum 10 units), reduced (5 units), and standard (10 units) IV regular insulin dose options. The weight-based insulin dose was selected as the default dose option. Criteria was included to help providers identify patients at higher risk for hypoglycemia (females, low body weight, renal impairment, or pre-treatment hypoglycemia) to guide the selection between 5 unit or 10 unit doses if a patient's weight was not readily available. The post-protocol order-set also included an optional serum potassium level to be ordered by providers as clinically indicated. The fingerstick glucose checks, as needed dextrose doses, and additional treatment options remained the same in the pre- and post-protocol order-sets (*Table 2*).

Patients ≥ 18 years old with acute hyperkalemia treated with IV insulin using the order-set were included in the study. Patients with missing data (weight, follow-up potassium level, no blood glucose levels) and patients who started dialysis before follow-up potassium level measurement were excluded from the study. Data collected included patient demographics (age, sex, height, weight), past medical history (CKD, diabetes), serum potassium levels, blood glucose levels, insulin doses ordered, and dextrose orders/administrations.

The primary efficacy outcome was reduction in serum potassium from baseline; pre-treatment (before insulin administration) and post-treatment (within 24 hours of insulin administration) serum potassium levels were assessed. The primary safety outcome was incidence of hypoglycemia (glucose less than 70 mg/dL) and severe hypoglycemia (glucose less than 40 mg/dL); blood glucose levels were measured at baseline and hourly post-treatment for 6 hours. Secondary outcomes included insulin doses ordered, completion of hourly glucose checks, and dextrose use.

The statistical analysis utilized the group t-test, chi-square test, and Fishers exact test. The group t-test was used for continuous data including change in potassium from baseline, insulin doses administered, completion of glucose checks, and baseline characteristics (age, overweight/obese). The chi-square test was used for discrete data with larger sample sizes including hypoglycemia incidence, dextrose use, and baseline characteristics (sex, renal impairment, diabetes history). The Fishers exact test was used for discrete data with smaller sample sizes including severe hypoglycemia incidence. Statistical significance was determined using an alpha level of 0.05.

RESULTS

In the pre-protocol group, 68 patients were screened and 60 patients were included in the analysis. In the post-protocol group, 92 patients were screened and 76 patients were included in the analysis. In both groups, patients were excluded for missing data or dialysis initiation (*Figure 1*). Baseline characteris-

Figure 1. Patient Screening

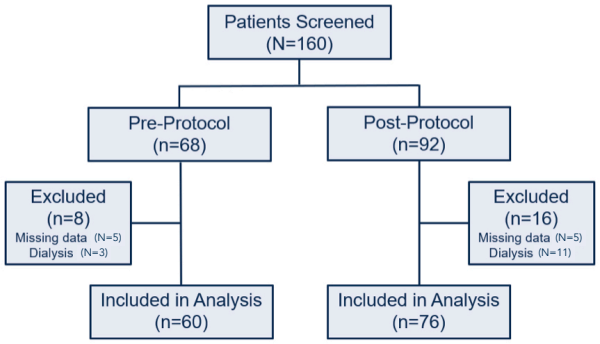


Figure 2. Primary Efficacy Endpoint – Potassium Reduction

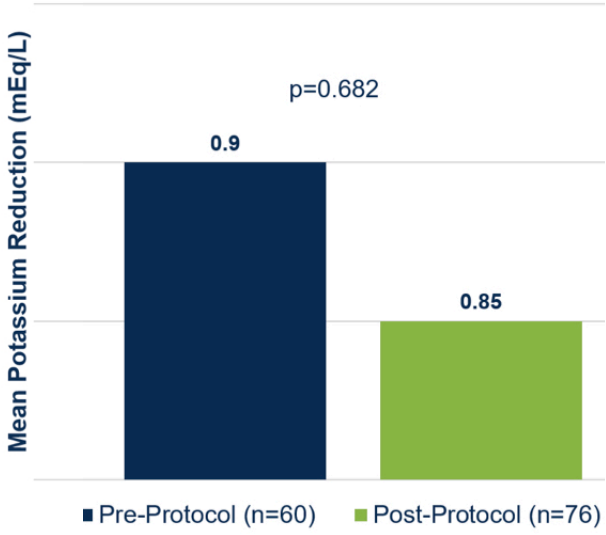
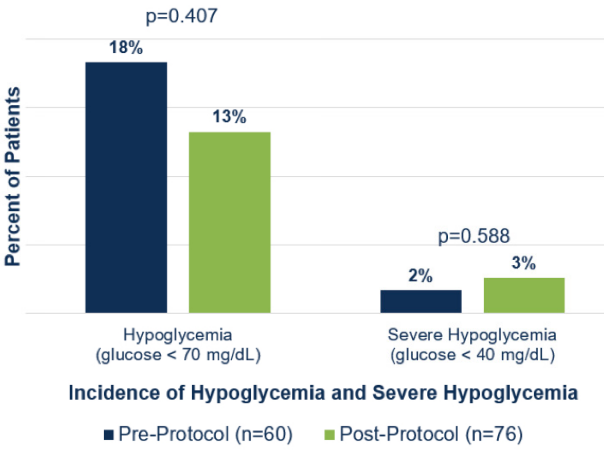


Figure 3. Primary Safety Endpoint – Hypoglycemia and Severe Hypoglycemia



tics were similar between groups, with no statistically significant differences identified (*Table 3*).

Potassium reduction from baseline was similar between groups with a mean (SD) potassium reduction of 0.9 (0.88) mEq/L in the pre-protocol group and 0.85 (0.71) mEq/L in the post-protocol group. The difference in potassium reduction between groups was not statistically significant (p=0.682) (*Figure 2*). Follow-up potassium levels were obtained within 24 hours of insulin administration in both groups. The median time to follow-up potassium level was 5 hours in the pre-protocol group and 6 hours in the post-protocol group.

The incidence of hypoglycemia was 18.3% in the pre-protocol group with 1.7% of patients developing severe hypoglycemia. The incidence of hypoglycemia was 13.2% in the post-protocol group with 2.6% of patients developing severe hypoglycemia. There was a 5.1% absolute risk reduction and 27.9% relative risk reduction in hypoglycemia incidence in the post-protocol group. Differences in the incidence of hypoglycemia (p=0.407) and severe hypoglycemia (p=0.588) between groups were not statistically significant (*Figure 3*).

The mean (SD) insulin dose administered decreased from 9.5 (1.5) units in the pre-protocol group to 7.7 (2.0) units in the post-protocol group. The reduction of the average insulin dose administered in the post-protocol group was statistically significant (p<0.001). In the pre-protocol group, standard insulin doses were used in most patients (90%). In the post-protocol group, weight-based (84%) and reduced (13%) insulin doses were used in most patients (*Figure 4*).

Less than 25% of patients in both groups completed all hourly post-treatment glucose checks. There was a wide range in the number of glucose checks completed; patients in both groups completed between 1 and 9 glucose checks after insulin treatment. The mean number of hourly glucose checks completed was 4 in both groups (*Figure 5*).

As needed dextrose doses for the treatment of hypoglycemia were ordered for 100% of patients in both groups. As needed dextrose doses were administered to 45.1% of patients with hypoglycemia in the pre-protocol group and 59.8% of patients with hypoglycemia in the post-protocol group. The difference in dextrose administration was not statistically significant (p=0.794) (*Figure 6*).

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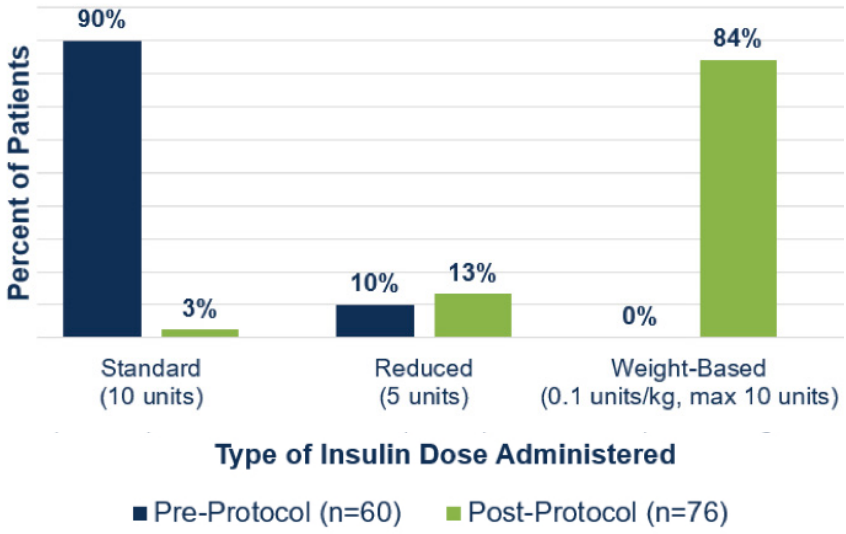
DISCUSSION

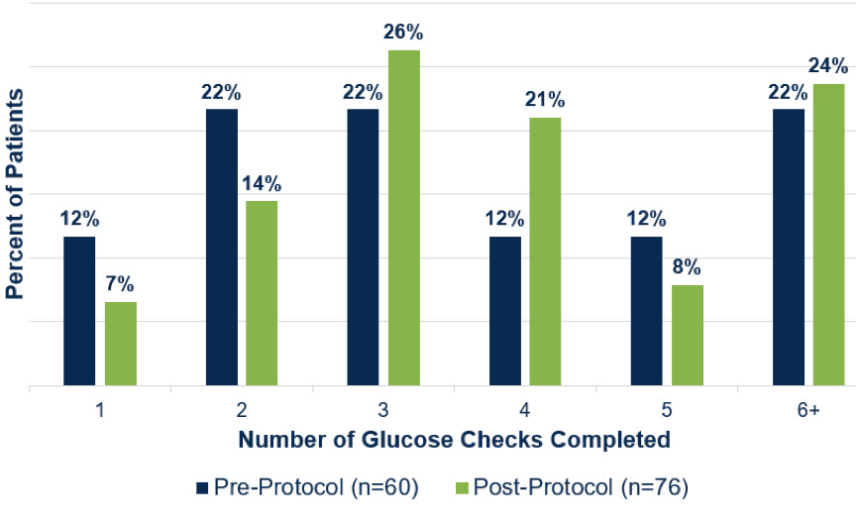
The use of weight-based and reduced insulin doses resulted in similar potassium reduction compared to standard insulin doses in the treatment of acute hyperkalemia, indicating that the use of lower insulin doses does not impact efficacy. There was no statistically significant difference in potassium reduction between groups. Additionally, weight-based and reduced insulin doses were associated with a 5% absolute risk reduction and 28% relative risk reduction in hypoglycemia incidence, indicating a safety benefit with lower insulin doses. However, the reduction in hypoglycemia incidence using weight-based and reduced insulin doses was not statistically significant. After the order-set was updated, high utilization of weight-based and reduced insulin doses was observed. The mean insulin dose administered decreased from 9.5 units in the pre-protocol group to 7.7 units in the post-protocol group, which was a statistically significant reduction. Fingerstick glucose checks were not completed every hour in most patients; only about 25% of patients in both groups had 6 or more hourly glucose checks completed after insulin treatment. Most patients in both groups were administered initial dextrose doses with insulin and ordered additional dextrose doses as needed for hypoglycemia. However, less than 60% of patients with hypoglycemia in both groups were treated with dextrose as clinically indicated.

Figure 4. Secondary Endpoint – Insulin Dose Administration



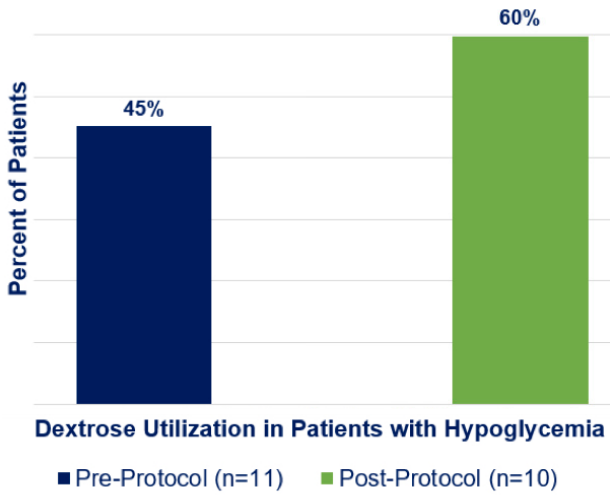
	Pre-Protocol (n=60)	Post-Protocol (n=76)	P-value
Mean Insulin dose administered (units)	9.5	7.7	<0.001

Figure 5. Secondary Endpoint – Glucose Monitoring



The major limitation for this study was the use of additional potassium-lowering treatment options that may have impacted the assessment of efficacy. However, the use of additional treatment options was similar in both groups with most patients receiving multiple hyperkalemia treatment options. Additionally, there was variability in the timing of potassium monitoring and completion of hourly glucose monitoring in both groups. Since there is currently no standardized follow-up potassium level contained in the order-set, follow-up potassium levels were re-

Figure 6. Secondary Endpoint – Dextrose Utilization in Hypoglycemia



checked within 24 hours of insulin treatment with a median time to follow-up potassium level of 5-6 hours in both groups. Standardized follow-up potassium level timing was not established due to provider preference to guide hyperkalemia treatment and monitoring on patient-specific conditions. Glucose monitoring was not completed consistently, with patients in both groups completing between 1 and 9 glucose checks in the first 6 hours after insulin administration. Other limitations to this study included the limited sample size and single-center design, which reduce its generalizability.

Future plans for this study include continued assessment of weight-based and reduced insulin dosing options for the treatment of acute hyperkalemia. Additionally, education will be given to providers and nurses regarding the benefits of using weight-based and reduced insulin doses in the treatment of acute hyperkalemia, use of initial and as needed dextrose doses, and completion of hourly fingerstick glucose checks. Future studies can be conducted on the effectiveness of weight-based versus reduced insulin doses, completion of hourly glucose monitoring, and utilization of dextrose in hypoglycemia.

CONCLUSION

The findings of this study show that using reduced and weight-based insulin doses compared to standard doses in the treatment of acute hyperkalemia resulted in similar efficacy through comparable potassium reduction (no statistically significant difference identified) and improved safety through reduced hypoglycemia incidence (not statistically significant).

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