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Insulin for HyperKalemia in Renal Insufficiency

Introduction

- Insulin with dextrose is an effective method to lower potassium levels quickly in acute hyperkalemia.
- Literature shows ranges of potassium reduction by 0.5-1.0 mEq after administration of a single dose.
- Patients with renal insufficiency and end stage renal disease (ESRD) have a higher incidence of hypoglycemia after treatment with insulin for hyperkalemia due to:
    - Reduced insulin clearance (prolonged insulin action)
    - Reduced hepatic glucose production
    - Reduced renal gluconeogenesis
- The appropriate dose of insulin to minimize hypoglycemic events when using for the treatment of hyperkalemia in patients with renal insufficiency is still debated.

Pharmacology	
Medication	Insulin (human regular)
Mechanism	Cause an intracellular shift of potassium via exchange of sodium ions via the Na+/K+ ATPase pump
Dose	5-10 units Doses of 0.1 units/kg (max 10 units) have also been considered
Administration	IV push
PK/PD	Onset: 15-30 minutes for initial potassium lowering effects Duration: 4-6 hours, prolonged duration in ESRD
Adverse Effects	Hypoglycemia, hypokalemia, hypersensitivity
Compatibility	Can dilute in normal saline to increase volume for ease of administration
Pearls	Must be given with dextrose (25g IV) to prevent hypoglycemia - Some patients require repeated dextrose; rare exceptions for those already extremely hyperglycemic The most common used product is regular human insulin given IV to ensure fast onset of potassium lowering effects and prevent variable absorption

Overview of Evidence			
Author, Year	**Design (Sample Size)**	**Intervention & Comparison**	**Outcomes**
Verdier et al., 2021	Single center, retrospective (n =174)	5 units vs 10 units IV regular insulin in ICU patients	• Hypoglycemia was more frequent with 10 unit vs 5 units of IV insulin (19.5 vs 9.2%, p=0.052) • No difference in rates of severe hypoglycemia or change in serum potassium

Moussavi et al., 2020	Retrospective, observational (n=700)	10 units vs <10 units IV regular insulin	• Significantly lower frequency of hypoglycemia with lower insulin doses (11.2 vs 17.6%, p=0.008) • Greater reduction in serum potassium with insulin doses <10 units (mean reduction 0.94 vs 0.8, p=0.008)
Keeney et al., 2019	Single center, retrospective (n=442)	5 units vs 10 units IV regular insulin	• Hypoglycemic events in patients with reduced eGFR were higher in patients receiving 10 units of insulin (17.4 vs 7.9%, p=0.02) • Similar potassium reductions in both groups
McNicholas et al., 2018	Single center, retrospective (n=99)	Evaluate hypoglycemia risk based on usage of hyperkalemia protocol	Subgroup analysis showed trend towards hypoglycemia with higher doses of insulin in ESRD. (5 units: 28% vs 10 units: 54%)
LaRue et al., 2017	Single center, retrospective (n=675)	5 units vs 10 units IV regular insulin	• Hypoglycemia was significantly increased in patients receiving 10 units of insulin (28.6 vs 19.5%, 95% CI -16.8% to -1.3%) • No significant difference in potassium decrease
Pierce et al., 2015	Single center, retrospective (n=149)	5 units vs. 10 units with low eGFR	No significant difference in hypoglycemia between those receiving 10 units or 5 units of inuslin (19.7 vs 16.7%)
Apel et al., 2014	Single center, retrospective (n=221)	Hypoglycemia risk in patients receiving IV regular insulin (4-10 units) in patients with ESRD on HD	• 90% of patients received 10 units of insulin • 13% of patients experienced hypoglycemia (IV insulin doses not specified) • Patients who were not diabetic had a higher risk of hypoglycemic events (OR 2.3, 95% CI 1.0–5.1, p=0.05)
Schafers et al., 2012	Single center, retrospective (n=89)	Evaluated evidence of hypoglycemia in any patient receiving 5 -10 units regular insulin	• 61 patients had renal insufficiency (69%) • 19 patients had hypoglycemia (21%) • 15/19 patients who became hypoglycemic had renal insufficiency (79%)

Conclusions

- Hypoglycemia risk seems to be elevated in those patients with renal insufficiency, especially those who are insulin-naive
- Consideration should be made to lower the initial dose of IV insulin for patients with AKI or CKD

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