

## 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           |                                                                                                                                                                                                                                                                                                                               |
|------------------------|-------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| <b>Medication</b>      | Insulin (human regular)                                                                                                                                                                                                                                                                                                       |
| <b>Mechanism</b>       | Cause an intracellular shift of potassium via exchange of sodium ions via the Na <sup>+</sup> /K <sup>+</sup> ATPase pump                                                                                                                                                                                                     |
| <b>Dose</b>            | 5-10 units<br>Doses of 0.1 units/kg (max 10 units) have also been considered                                                                                                                                                                                                                                                  |
| <b>Administration</b>  | IV push                                                                                                                                                                                                                                                                                                                       |
| <b>PK/PD</b>           | Onset: 15-30 minutes for initial potassium lowering effects<br>Duration: 4-6 hours, prolonged duration in ESRD                                                                                                                                                                                                                |
| <b>Adverse Effects</b> | Hypoglycemia, hypokalemia, hypersensitivity                                                                                                                                                                                                                                                                                   |
| <b>Compatibility</b>   | Can dilute in normal saline to increase volume for ease of administration                                                                                                                                                                                                                                                     |
| <b>Pearls</b>          | Must be given with dextrose (25g IV) to prevent hypoglycemia<br>- Some patients require repeated dextrose; rare exceptions for those already extremely hyperglycemic<br><br>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                                                                                                                                                                                                                                                                                            |
|-------------------------|--------------------------------------|-----------------------------------------------------------------------------------------------------|-----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| Moussavi et al., 2021   | Meta-analysis (n = 3437)             | 10 units vs <10 units IV regular insulin                                                            | <ul style="list-style-type: none"> <li>&lt;10 units IV regular insulin had lower pooled odds of hypoglycemia odds ratio [OR] 0.55 and severe hypoglycemia OR 0.41</li> <li><b>No difference in potassium reduction</b> was detected mean difference -0.02 mmol/L</li> </ul>                         |
| Verdier et al., 2021    | Single center, retrospective (n=174) | 5 units vs 10 units IV regular insulin in ICU patients                                              | <ul style="list-style-type: none"> <li>Hypoglycemia was more frequent with 10 unit vs 5 units of IV insulin (19.5 vs 9.2%, p=0.052)</li> <li>No difference in rates of severe hypoglycemia or change in serum potassium</li> </ul>                                                                  |
| Moussavi et al., 2020   | Retrospective, observational (n=700) | 10 units vs <10 units IV regular insulin                                                            | <ul style="list-style-type: none"> <li>Significantly lower frequency of hypoglycemia with lower insulin doses (11.2 vs 17.6%, p=0.008)</li> <li>Greater reduction in serum potassium with insulin 10 units (mean reduction 1.11 vs 0.94, p=0.008)</li> </ul>                                        |
| Keeney et al., 2019     | Single center, retrospective (n=442) | 5 units vs 10 units IV regular insulin                                                              | <ul style="list-style-type: none"> <li>Hypoglycemic events in patients with reduced eGFR were higher in patients receiving 10 units of insulin (17.4 vs 7.9%, p=0.02)</li> <li>Similar potassium reductions in both groups</li> </ul>                                                               |
| 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                                                              | <ul style="list-style-type: none"> <li>Hypoglycemia was significantly increased in patients receiving 10 units of insulin (28.6 vs 19.5%, 95% CI -16.8% to -1.3%)</li> <li>No significant difference in potassium decrease</li> </ul>                                                               |
| 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 insulin (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 | <ul style="list-style-type: none"> <li>90% of patients received 10 units of insulin</li> <li>13% of patients experienced hypoglycemia (IV insulin doses not specified)</li> <li>Patients who were not diabetic had a higher risk of hypoglycemic events (OR 2.3, 95% CI 1.0–5.1, p=0.05)</li> </ul> |
| Schafers et al., 2012   | Single center, retrospective (n=89)  | Evaluated evidence of hypoglycemia in any patient                                                   | <ul style="list-style-type: none"> <li>61 patients had renal insufficiency (69%)</li> <li>19 patients had hypoglycemia (21%)</li> </ul>                                                                                                                                                             |

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|  |  | receiving 5 -10 units regular insulin | • 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-naïve
- Consideration should be made to lower the initial dose of IV insulin for patients with AKI or CKD

## References

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