Insulin 5 units or 0.1 units/kilogram v 10 units for Hyperkalemia

Introduction

1. Severe hyperkalemia is a potentially life-threatening condition and should be treated immediately due to risk of muscle paralysis and lethal cardiac arrhythmias.[1]
2. Serum potassium is elevated primarily for one of two reasons:
   (1) Extracellular potassium shifts
   (2) Decreased renal excretion
3. Insulin is one of many rapid treatment methods of hyperkalemia because of its potential to shift potassium intracellularly by increasing Na+-K+ ATPase activity in a dose-dependent manner.[1]
4. Other treatment and stabilization methods for hyperkalemia include calcium, beta-agonists, sodium bicarbonate, exchange resins, diuretics, and hemodialysis.[1]
5. The use of Insulin + glucose as a treatment modality for hyperkalemia is popular in an acute care setting, but patients should be monitored closely for hypoglycemia and other potential adverse drug reactions.

	Regular Insulin
How Supplied	U-100 vials → 100 units per 1 mL[2] U-500 vials → 500 units per 1 mL[2]
Category	Short-acting[2]
Administration	Intravenous[2]
PK/PD	Onset: ~15-20min[2] Duration: ~1.5-2hrs[2] Half-life: ~30min-1hr (dose-dependent)[2]
Adverse Effects	Hypoglycemia, irritation at site of infusion/injection, edema, hypokalemia[2]
Drug Interactions and warnings	Caution with medications that may alter glucose regulation[2] (ex. Diabetes medications, fluoroquinolones, octreotide, hydroxychloroquine, ACEs/ARBs, corticosteroids, antipsychotics) Caution with medications that may mask signs/symptoms of hypoglycemia[2] (ex. Beta-blockers, clonidine, lithium)
Compatibility	NS, D5W, D10W, D5/½NS, LR, D5LR[2]

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Overview of Evidence

Author, year	Design/ sample size	Intervention & Comparison	Outcome
Pierce et al. 2015	Retrospective ED, ICU, & non-ICU patients with low eGFR and hyperkalemia (K>6). (n=149)	10u (n=78) v **5u (n=71)**	Safety: No difference in rate of hypoglycemia (BG ≤ 70) or severe hypoglycemia (BG < 50). [About 30% of the hypoglycemic episodes in the 10u group occurred outside the 4hr monitoring window.]
LaRue et al. 2017	Retrospective ED patients with renal insufficiency and hyperkalemia (K>5). (n=675)	10u (n=542) v **5u (n=133)**	Efficacy: Serum potassium was reduced to the same extent between groups. Safety: Lower rates of hypoglycemia with 5u.
McNicholas et al. 2018	Retrospective ED patients with CKD/ESRD and hyperkalemia (K≥6). (n=139)	10u (n=76) v **5u (n=63)**	Safety: Less instances of hypoglycemia and no instances of severe hypoglycemia with 5u.
Garcia et al. 2020	Retrospective ED, ICU, & non-ICU patients with hyperkalemia (K>5.1). (n=401)	10u (n=309) v **5u (n=92)**	Efficacy: No difference in potassium reduction between groups. [Patients with K+ > 6 had a 0.23 greater reduction in K+ with 10u.]
Keeney et al. 2020	Retrospective ED patients with hyperkalemia. (n=442)	10u (n=295) v **5u (n=147)**	Efficacy: No difference in potassium reduction between the groups regardless of renal function. Safety: Lower occurrence of hypoglycemia with 5u, especially when eGFR < 45.
Wheeler et al. 2016	Retrospective ED, ICU, & non-ICU patients with hyperkalemia. (n=132)	10u (n=66) v **0.1u/kg [max 10u] (n=66)** (69.9±14.2kg) **(74.2±12.6kg)**	Efficacy: No difference in potassium reduction between the groups. Safety: Less hypoglycemia episodes with 0.1u/kg [Increased hypoglycemia in female patients and patients with BG < 140.]
Brown et al. 2018	Retrospective ED, ICU, & non-ICU patients with hyperkalemia (K>5). (n=264)	10u (n=69) v **0.1u/kg [max 10u] (n=195)** (82.9±28.3kg) **(90±28.3kg)**	Efficacy: No difference in potassium reduction between the groups. Safety: Lower rates of hypoglycemia with 0.1u/kg.
Tran et al. 2020	Observational/Prospective ED, ICU, & non-ICU patients with hyperkalemia. (n=370)	10u (n=225) v **0.1u/kg [max N/A] (n=145)** (78.8±26.9kg) **(75.7±25.4kg)**	Safety: Decreased episodes of hypoglycemia with 0.1u/kg dosing and ordersets. [The greatest risk factors for hypoglycemia was poor renal function (SCr > 2.5), high doses of insulin (>0.14u/kg), insulin use with low BG (BG < 140).]
Zuern et al. 2020	Retrospective ED, ICU, & non-ICU patients with hyperkalemia (K>5). (n=165)	10u (n=90) v **0.1u/kg [max 10u] (n=75)** (88kg:72.5-110) **(84.4kg:75.3-106.6)**	Efficacy: Both groups had similar potassium reduction. Safety: Fewer hypoglycemic and severe hypoglycemic episodes with 0.1u/kg.

All studies allowed additional standard of care for treatment of hyperkalemia

Conclusions

- There is **no difference** in the extent of **potassium reduction** with various insulin dosing strategies for hyperkalemia treatment.
- The use of **5u insulin** for hyperkalemia resulted in **less episodes of hypoglycemia** compared to 10u insulin, which is approximately 0.1u/kg, based on the weight of the general patient population.
- Hyperkalemia treatment order panels/sets may be useful to **ensure cautious monitoring of hypoglycemia** for patients treated with insulin and renal dysfunction.

References

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