Effect of varied insulin dosing on serum potassium reduction in acute management of hyperkalemia: a systematic review and meta analysis of retrospective cohort studies

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ABSTRACT

Hyperkalemia, is a commonly encountered electrolyte derangement in the healthcare setting. It can be managed in a number of ways. One of which is forced intracellular shift of potassium using insulin. Standard of care recommendation is ten units of regular insulin typically given with a bolus of dextrose to guard against hypoglycemia which can result from insulin administration. There are studies suggesting that a lower dose of five units will be just as effective as ten units, with a lower risk of the side effect of hypoglycemia. This will be especially advantageous in patients are higher risk of hypoglycemia such as lower weight, non diabetic, end stage renal disease and female patients. Hence we performed this meta analysis and systematic review to evaluate if lower dosing of insulin has the same efficacy as the standard ten units of insulin for the reduction of potassium in hyperkalemia.

INTRODUCTION

Hyperkalemia is commonly encountered in various hospital settings. It is defined by lab values above 5.0 mEq/L to 5.5 mEq/l [1]. Although mild elevations may be of benign consequence, higher levels may have catastrophic results including sudden cardiac death [2].

Management of hyperkalemia is steered by level of elevation above normal range, and clinical status of the patient. One treatment method of hyperkalemia is the use of injectable insulin which causes intracellular shift of potassium. Till date, the standard of care recommendation is 10 - 20 units of insulin, administered with D50W to offset risk of hypoglycemia [3,4,5]. Some studies however, have used lower dosing of insulin to manage hyperkalemia and reported lower rates of hypoglycemia.

We conducted a meta-analysis to evaluate the efficacy of low versus standard (higher) dose insulin on potassium, and clinical outcomes including rates of adverse effects.

METHODS AND MATERIALS

We searched electronic databases from inception to August 2020 for prospective and retrospective cohort studies.

We calculated weighted mean difference (MD) and their 95% corresponding confidence intervals for continuous variables using an inverse variance test.

For dichotomous variables, we calculated the odd ratios (OR) along with corresponding 95% confidence intervals (CI) using the random Mantel-Haenszel method. We included 9 retrospective cohort studies with a total of 3,298 events.

RESULTS

Author	Mean age low insulin group (years)	Mean age low insulin group (years)	Mean weight low insulin group (kg)	Mean weight high insulin group (kg)	Cohort total	Female cohort	Number of IDDM	Number of NIDDM	Number of ESRD/Dialysis dependent patient low insulin group	Number of ESRD/Dialysis dependent patient high insulin group
Brown et al	55.6 (15.1)	56.6 (16.7)	90	82.9	350	118	13	148	84	32
Garcia et al	62.3 ± 19.7	58.9 ± 16.3	77.4 ± 21.5	79 ± 20	401	119	N/A	N/A	N/A	N/A
K.P. Keeney et al.	Median = 65 IQR (51–75)	Median = 60 IQR (49-71)	Median = 79	Median = 80	442	188	138	91	30	61
LaRue et al	59.6 ± 17.6	62.3 ± 16.2	80.9	80.9	675	317	169	323	68	189
Moussavi et al	N/A	N/A	N/A	N/A	700	N/A	N/A	N/A	N/A	N/A
Pierce et al	62 (15)	58 (15)	89	75	149	49	N/A	N/A	31	21
Vinh Tran et al	56.9 (17.0)	58.6 (14.4)	75.7	78.8	370	138	N/A	131	N/A	N/A
Wheeler et al	61.9 (17.6)	55.7 (15.7)	74.2	69.9	132	54	N/A	N/A	16	20
Zuern et al	60.7 ± 17.7	59.3 ± 16.3	84.4	88	165	59	N/A	N/A	N/A	N/A

Figure 1: Study characteristics

Figure 2: PRISMA flowchart outlining literature search

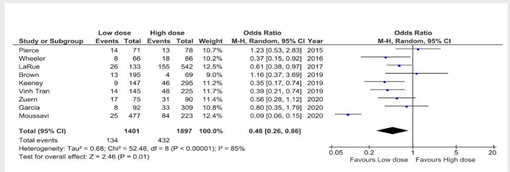

Figure 4: Forest plot comparing rates of mild hypoglycemia

RESULTS

There was no significant difference between low dose insulin and high dose insulin groups in the decrease of serum potassium. [MD = 0.03; 95% confidence interval (CI) - 0.06 - 0.11; p = 0.53].

There were significant differences between the groups in the clinical outcome of mild hypoglycemia [OR = 0.48; 95% confidence interval (CI) 0.26-0.86; p = 0.01], and severe hypoglycemia [OR = 0.41; 95% confidence interval (CI) 0.27-0.65; p = < 0.0001].

There was no significant difference between groups in the clinical outcome of rebound hyperkalemia [OR 0.85; 95% confidence interval (CI) 0.6-1.21; p = 0.37].

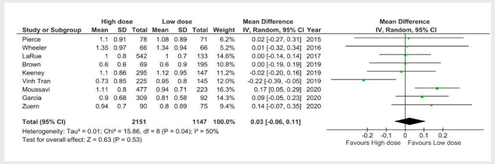

Figure 3: Forest plot of primary outcome, comparing change in potassium between standard and low insulin dose protocol

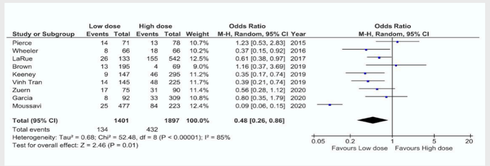

Figure 5: Forest plot comparing rates of severe hypoglycemia

DISCUSSION

Our meta analysis showed no statistically significant difference between decrease in potassium between low insulin dose group and standard dose group. Decrease in potassium however did favor the low insulin group.
Patients were more likely to suffer hypoglycemia in the standard dose insulin group. This was statistically significant.
Four out of nine studies reported data on rebound hyperkalemia. The difference between both insulin groups was not statistically significant.
One study included cardiac adverse events as well as mortality in both low and standard dosed insulin groups. Both of these events were reported greater in the standard insulin dose group, however it was not statistically significant.
All studies in our meta analysis were adequately matched in baseline characteristics. All studies accounted for diabetic patient cohorts, and patients with end stage renal disease including those on dialysis.
Some limitations include the lack of blinding, as a result of the type of studies included. Also, time to recheck of potassium was not uniform across studies. Third, although all studies did administer other treatments to manage hyperkalemia, the studies did not uniformly employ the same agents and at comparable doses.

CONCLUSIONS

This meta-analysis showed that lower injectable insulin dosing strategy for treatment of hyperkalemia is as effective as standard, higher dosing strategy.
Based on the current analysis and given the increased risk of hypoglycemic events, low dose insulin strategies such as 5 units or weight based 0.1 U/kg should be considered in management of hyperkalemia. Further adequately powered studies, including randomized controlled trials are needed however.

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