Correction of Serum Potassium Level in Hypokalaemic Patients with Hypomagnesaemia and Normomagnesaemia

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Abstract

Objective: To determine the extent of increase in potassium level after intravenous infusion of potassium chloride in hypokalaemic patients with hypomagnesaemia and normomagnesaemia and to overview the impact of different concentrations and dilutions of potassium chloride infusion for rapid correction of hypokalaemia.

Methods: A prospective, cohort study was conducted in Abbasi Shaheed Hospital, Karachi from January to March 2016. Convenience sampling was done, 46 patients were included who had a Serum Potassium level less than 3.5 meq/L at the time of admission to the hospital. Protocols of potassium chloride infusion such as such as 20 mEq/200 ml, 30 mEq/300 ml, 40 mEq/400 ml and 50 mEq/500 ml were given to three groups of hypokalaemic patients having hypomagnesaemia, normomagnesaemia and hypermagnesaemia to figure out the correlation of potassium correction with serum magnesium level. The pre and post-infusion serum potassium levels were checked along with the outcome of the extent of increase in potassium levels.

Results: For 46 patients (mean age 60 ± 3 (r= 21-96 years), the mean pre-infusion serum potassium and magnesium levels were found to be 3.12 ± 0.04 (r= 2.30-3.5) mmol/L and 0.81 ± 0.03 (r= 0.52-1.58) mmol/L respectively. The difference in the pre/post-infusion serum potassium levels in hypokalaemic patients with hypomagnesemia (n= 46) was not found be significant ($p>0.05$) whereas the pre/post-infusion serum potassium level was significant ($p<0.05$) in hypokalaemic patients with normomagnesaemia or hypermagnesaemia.

Conclusion: Serum magnesium level needs to be concurrently monitored and corrected in mild to moderate hypokalaemic patients as low magnesium levels were found to have profound effect on serum potassium level in patients receiving potassium supplement for correction of potassium level back to normal.

Keywords: Hypokalaemia, hypomagnesaemia, electrolytes, potassium chloride, pharmacology.

IRB: Approved by Abbasi Shaheed Hospital. **Dated:** 24th Feruary 2017.

Citation: Ishaqi AA, Raza ML, Muhammad IN, Hyder N, Iqbal A, Zehra N. Correlation of Serum Potassium Level in Hypokalaemic Patients with Hypomagnesaemia and Normomagnesemia [Online]. 2017;22:20-5. Available from: www.annals-ashkmdc.org.

(ASH & KMDC 22(3):208;2017)

Introduction

Hypokalaemia occurs in about 20% of hospitalised patients. Four to five percent of these patients may develop clinically significant hypokalaemia, which is defined as a serum potassium level of less than 3 mEq/L[1-3]. A study reported that 16% of all elderly patients requiring hospitalisation were found to have hypokalaemia; however, no significant difference in incidence was found between those patients receiving diuretics and the non-diuretic group[4].

Higher incidence of hypokalaemia has been reported in asthmatics (due to beta-agonist administration), pregnant patients (due to terbutaline), thyrotoxic patients (due to catecholamine excess), and in children (due to diarrhoea). Diuretics are the

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Date of Submission: 28th April 2017
Date of Acceptance: 12th September 2017

most common cause of hypokalaemia[2,5]. Diuretic-induced hypokalaemia more likely occurs if salt intake is high or if diuretics are used for congestive heart failure, nephrotic syndrome, or hepatic cirrhosis rather than hypertension[6,7]. Most diuretics (thiazides, furosemide, ethacrynic acid) will increase renal tubular flow, resulting in loss of potassium flow down the concentration gradient[8]. Serum potassium levels may fall significantly approximately 10 days after initiation of diuretic therapy such mechanism is unclear. However, hypokalaemia can occur in patients receiving combination therapy with angiotensin-converting-enzyme inhibitor (ACE inhibitor) and diuretics. One of the studies revealed that 33% of initially normokalaemic patients developed hypokalaemia when receiving combination therapy[9].

Patients with a magnesium deficiency may develop impairment in their ability to conserve potassium. Hypokalaemia is present in about 40% of hospitalised patients with hypomagnesaemia[7,10]. Hypomagnesaemia is often associated with hypokalaemia (due to urinary potassium wasting) and hypocalcaemia (due to lower parathyroid hormone secretion and end-organ resistance to its effect).

The mechanisms responsible for hypokalaemia associated with hypomagnesemia includes redistribution, renal loss and gastrointestinal loss. Redistribution is a shifting of potassium from the extracellular space to the intracellular space and is caused by alkalosis, catecholamine, cellular incorporation, insulin infusion, aldosterone, and hyper osmolality (e.g. hypokalaemic periodic paralysis)[11]. The following mechanisms of renal loss are as follows: increased aldosterone, excessive unabsorbed anions, enhanced sodium delivery to the distal nephrons, higher tubular flow and alkalaemia[12]. Reduced intracellular magnesium, due to magnesium scarcity, causes the magnesium-mediated inhibition of renal outer medullary potassium channel (ROMK) channels and increases potassium secretion. Notably reduced magnesium alone does not cause hypokalaemia. An increase in distal sodium delivery or increment in aldosterone levels may be needed for exacerbating potassium wasting in magnesium deficiency[13]. Excessive aldosterone results in hypokalaemia by increasing the active transport of potassium into the nephron in an exchange with sodium. Potassium then flows down the concentration gradient and thus subsequently into the urine. Magnesium may influence the incidence of cardiac arrhythmias by a direct effect, an effect on potassium metabolism or by an effect as a calcium blocking agent[14].

The treatment of hypokalaemia is focused on minimising ongoing potassium loss and providing replacement of potassium. The aggressiveness of replacement therapy is dependent on the severity of the patient's symptoms, the presence of ECG abnormalities, and serum potassium level[15]. If hypokalaemia is a result of the intracellular shifting of potassium, aggressive replacement may result in hyperkalaemia. Intravenous access should be obtained in moderate hypokalaemia so that parenteral replacement can be given. Central access should be obtained in severe hypokalaemia so that more concentrated infusions of potassium may be administered[1,16-18].

The purpose of this study is to determine the extent of increase in potassium level after intravenous infusion of potassium chloride in hypokalaemic patients with hypomagnesemia and normomagnesaemia because hypomagnesaemia is considered as one of the factors that could delay and interrupt in the correction of patients with hypokalaemic state inspite of using higher doses of potassium. The study also overviews the impact of different concentrations and dilutions of potassium chloride infusion for rapid correction of hypokalaemia.

Methods

A prospective cohort study was conducted in cardiology ward within the Department of Medicine of tertiary care public sector teaching hospital (Abbasi Shaheed Govt. Hospital, Karachi, Pakistan) from January to March 2016. The cardiology ward is provided with the facility of cardiac monitoring of

patients during and after the potassium chloride infusion to monitor any infusion related side effects. The potassium chloride infusions used were in mEq/ml. However the paient's potassium or magnesium levels were expressed in mmol/L in the texxt as well as in the table. Sample size was based on the primary analysis which involves comparison of change in pre- and post-potassium serum level with respect to serum magnesium level considering p=0.05, study power= 80%, effect size= 0.3. For all the patients who were admitted to the cardiology ward, a basic screening of all essential elements/ electrolytes was done as a routine practice. The study included those patients who were secondarily diagnosed with hypokalaemia, whom potassium serum level was found below 3.5 mEq/L at the time of admission to the hospital and were given potassium chloride infusion for rapid correction of hypokalaemia. The serum magnesium levels were also noted for all the patients enrolled to check the impact of hypomagnesaemia and normomagnesaemia on the correction of serum potassium level post-infusion of potassium chloride. The serum potassium level was checked before the commencement of intravenous infusion and 1-2 h after the completion of the intravenous infusion. The outcome of different dosing protocols of potassium chloride was analysed. These protocols include different concentrations of potassium chloride such as 20 mEq/200 ml, 30 mEq/300 ml, 40 mEq/400 ml and 50 mEq/500 ml etcetera. The administration time of potassium chloride intravenous infusion was also monitored to figure out the optimum administration time for rapid correction of potassium levels in hypokalaemic patients. Inclusion criteria was: age>20 year, Potassium levels $\leq$3.5mmol/L, patients on intravenous infusion of potassium chloride either given through peripheral or central line, and patients on constant monitoring of arrhythmia to observe dose and administration time-related side effects.

Exclusion criteria included patients with massive tissue breakdown (rhabdomyolysis, burns, trauma), the patients who received any potassium chloride infusion within last 48 h, patients previously on oral potassium supplement within last 3 days, and patients who have taken potassium-sparing diuretics in last 3 days.

Statistical analysis was performed byusing clinical data of hypokalaemic patients and analysed using Paired *t*-test using SPSS statistical software (SPSS, v.17.0, Chicago). The level of significance was set at $p<0.05$. Data is presented as the Mean ± SEM (standard error mean) for age (year), potassium level (mEq) and infusion time (hours) except otherwise stated.

Results

A total of 46 patients were examined which fulfilled the inclusion criteria as specified above. All of the patients developed hypokalaemia prior to the hospital admission and were secondarily diagnosed with hypokalaemia on the basis of a first basic screening test of electrolytes after the hospital admission. Out of 46 patients, 22 patients (47.8%) were female and 24 patients (52.2%) were male. The mean age of patients was 60 ± 3.0 (21-96) years with an average Body Mass Index of 31.73 ± 1.40 (17.09-58.9) kg/m^2. The total serum potassium deficit among the patients studied was 20.17 ± 1.58 mEq with a total daily deficit of 94.44 ± 4.39mEq.

The mean pre-infusion serum potassium and magnesium levels were found to be 3.12 ± 0.04 (2.30-3.5) mmol/L and 0.81 ± 0.03 (0.52-1.58) mmol/L respectively. Hypomagnesaemia was detected in total 14 patients, whereas, hypermagnesaemia and normomagnesaemia were diagnosed in 12 and 20 patients respectively. For a baseline serum potassium level of 3.8 mmol/L, a mean deficit of 20.17 ± 1.58 (6.40-49.92) mmol/L, while the total daily requirement of 94.44 ± 4.39 (46.40-160) mmol/L serum potassium was found in the examined patients. The infusion protocol of 40mEq/400 ml was used in 50% (n= 23) patients for correction of hypokalaemia. Other infusion protocols used were 20 mEq/200 ml (n= 11), 30 mEq/ 300 ml (n= 8) and 50 mEq/500 ml (n= 4). The corrected serum potassium level after potassium chlo-

Table 1. Summarised details of patients having both hypokalaemia and hypomagnesemia

	Mean ± S.E	Range
Age	52.93 ± 5.22	26-91
[K+] Pre-Infusion	3.04 ± 0.81	2.70-3.9
[K+] mEq Given	32.14 ± 2.81	20-50
Mean Infusion Time	3.50 ± 0.60	2-10
[K+] Post-Infusion	3.28 ± 0.07	2.90-4.1
[Mg+] Pre-Infusion	0.60 ± 0.01	0.52-0.69
[K+] 0.24 ± 0.03	0.10 - 0.5	
Paired t-test :P-value > 0.05 (0.072)		

Age (years); [K+] potassium level in mmol/L before start of infusion; [Mg+] Magnesium level in mmol/L; [K+] difference between pre- and post-infusion potassium level in mmol/L; Mean infusion time (hours). S.E: Standard Error

Table 2. Summarised details of patients having hypokalaemia and hypermagnesemia

	Mean ± S.E	Range
Age	68.33 ± 5.40	21-86
[K+] Pre-Infusion	3.15 ± 0.91	2.30-3.5
[K+] mEq Given	35.83 ± 2.29	20-50
mean infusion time	4.42 ± 0.65	2-10
[K+] Post-Infusion	3.63 ± 0.12	2.70-4.4
[Mg+] Pre-Infusion	1.05 ± 0.05	0.92-1.58
[K+]	0.48 ± 0.11	0-1.3
Paired t-test: P-value < 0.05 (0.007)		

*Age (years); [K+] potassium level in mmol/L before start of infusion; [Mg+] Magnesium level in mmol/L; [K+] difference between pre- and post-infusion potassium level in mmol/L; Mean infusion time (hours)
S.E: Standard Error

Table 3. Summarised details of patients having hypokalaemia and normomagnesaemia

	Mean ± S.E	Range
Age	59.05 ± 5.35	32-96
[K+] Pre-Infusion	3.17 ± 0.71	2.50-3.5
[K+] mEq Given	36.50 ± 3.10	20-80
mean infusion time	4.30 ± 0.46	2-10
[K+] Post-Infusion	3.53 ± 0.09	2.80-4.4
[Mg+] Pre-Infusion	0.81 ± 0.01	0.71-0.91
[K+]	0.36 ± 0.07	-0.20-1
Paired t-test: P-value < 0.05 (0.002)		

*Age (years); [K+] potassium level in mmol/L before start of infusion; [Mg+] Magnesium level in mmol/L; [K+] difference between pre- and post-infusion potassium level; Mean infusion time (hours)

Table 4. Showing pre- and post-infusion protocol of K+ and its impact of potassium level

Increase In Potassium Level By Different Infusion Protocols			
KCl infusion	N	Mean[K+]	Range
20mEq/200ml	11	0.2	0-0.6
30mEq/300ml	8	0.2	0-0.5
40mEq/400ml	23	0.45	0.1-1.3
50mEq/500ml	4	0.57	0.5-0.8

Where N= Number of Patient, [K+] difference between pre- and post-infusion potassium level;

ride infusion was found to be 3.48 ± 0.06 (2.70-4.4) mEq.

The average difference between pre/post-infusion serum potassium level was 0.35 ± 0.04 (-0.20-1.3) mmol/L. The patients with hypokalaemia and hypomagnesemia did not show significant improvement in post-infusion serum potassium level with p=0.072 (Table 1). However, hypokalaemic patients having hypermagnesaemia and normomagnesaemia with p=0.007 and p=0.002 respectively, showed a significant increase in serum potassium levels after potassium chloride infusion (Table 2 and 3). Increase in serum potassium level by different protocols of potassium chloride infusion is summarised in Table 4.

Discussion

The duration and degree of hypokalaemia and hypomagnesaemia have a strong influence on the clinical manifestations associated with hypokalaemia. One of the important clinical manifestations associated with hypomagnesaemia is depletion of serum potassium level. Most of the patients with hypokalaemia remain asymptomatic especially with mild hypokalaemia with serum potassium level above 3 mEq/L.

The potassium chloride infusion protocols of 20 mEq and 30 mEq were found to be ineffective in increasing the serum potassium level with a mean difference in pre- and post- infusion potassium level of 0.2 mmol/L. James et al. also reported a similar result with a mean increment of 0.2 mmol/L after infusion of 20mEq infusion[19]. Douglas et al. also reported similar increase when 20 mEq potassium was given via an intravenous (0.25 mmol/L) and enteral route (0.27 mmol/L)[20]. In contrast, Hamill et al. reported a mean increase of 0.5 mmol/L and 1.1 mmol/L after giving 20 mEq and 40 mEq potassium infusion respectively[21].

Infusion protocols of 40 mEq and 50 mEq were found to be most effective with a mean increase in post infusion potassium level of 0.45 mmol/L and 0.57 mmol/L respectively. Distinctive results were reported by Melissa et al. who stated that potassium chloride infusion of 20 mEq is more effective than 40mEq infusion in correcting the state of hypokalaemia to normokalaemia[22]. None of the infusion protocol tended to move any of the patients towards the hyperkalaemic state. The usual time interval used for the potassium chloride infusion was 10 mEq per hour.

In this prospective cohort observational study, potassium chloride infusion was given to patients for the correction of hypokalaemia. These hypokalaemic patients were divided into three groups based on their serum magnesium levels. The hypokalaemic patients with normal magnesium level showed a significant increase in mean serum potassium level ($p<0.05$) with 55% of the patients improved to normal baseline serum potassium level i.e. 3.5mmol/L.

The hypokalaemic patients with hypermagnesaemia also showed a significant increase in potassium serum level ($p<0.05$) while, hypokalaemic patients with concurrent hypomagnesaemia did not show significant improvement ($p>0.05$) with a mean increase of 0.24 mEq rejecting the alternate hypothesis that low magnesium serum level has no impact on the correction of hypokalaemic state. In contrast to 48.4% of hypokalaemic patients with hypermagnesaemia, only 21.4% of the hypokalaemic patient with the coexisting condition of hypomagnesaemia attained the normal baseline serum of 3.5 mmol/L.

Hence, it is recommended to monitor the serum magnesium levels in patients with low serum potassium levels as low serum magnesium levels affect potassium correction via intravenous potassium chloride infusion. The usage of higher volume protocols of potassium chloride infusions such as 40 mEq/400 ml and 50 mEq/500 ml was found to be more effective in rapid correction of hypokalaemia rather than small volume infusion protocols.

Limitations of the study include, lack of data in connection with a variety of medical conditions such as shock (hypovolemia, cardiogenic), phaeochromocytoma, nephrotic syndrome etc.

These clinical conditions need to be further studied, as alteration of electrolyte levels may occur. Secondly, this study did not cover co-morbidities and further studies are required to analyse the consequence when various pathologies are present together.

Conclusion

Potassium chloride infusion protocol with a concentration of 40 mEq/400 ml or 50 mEq/500 ml at a rate of 10 mEq per hour can be used for the correction of moderate to severe hypokalaemia of the patients. Magnesium level should be corrected if the normal magnesium serum was below the normal range in patients with concurrent hypokalaemic and hypomagnesemia for rapid and timely correction of hypokalemia.

Conflict of Interest

Authors have no conflict of interests and received no grant/funding from any organisation for this study

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