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Case Series

Serum potassium response to intravenous potassium chloride in severely hypokalemic patients from Ethiopia: A case series

Zablon Mesfin Anbessie[1], Dawit Kebede Huluka[2], Seifemichael Getachew Abebe[3]

[1]Bethzatha General Hospital, Addis Ababa, Ethiopia.
[2]College of Health Sciences Addis Ababa University Addis Ababa, Ethiopia
[3]St. Paul Millennium Medical college, Addis Ababa, Ethiopia
Corresponding author*: Zabalon22@hotmail.com

Abstract

Introduction : *One out of five admitted patients has hypokalemia, among which a similar number has severe hypokalemia, a life-threatening condition. The therapy and response of severe hypokalemia is mainly based on findings from other countries and in Ethiopia patients may have lower than recommended potassium replacement requirements, and as there have been no publications, this series was conducted to guide the clinical management of severely hypokalemic patients.*

Methods: *A nine-month prospective case series in Bethzatha general hospital ICU in Ethiopia were reviewed.*

Case presentation*-Six patients with a median age of 45 years were included. The range of admission serum potassium level was (1 to 1.8) meq/l. An average of 383 meqs of intravenous potassium chloride was infused to raise the serum potassium level by 2.57 meq/l. To raise the serum potassium level by 0.27meq/l an average of 39.4meq of potassium chloride was needed.*

Conclusion: *There was more than a half dose reduction in the potassium chloride infusion required to raise the serum potassium to the same target in the literature.*

Keywords: *Potassium chloride, Potassium response, Severe hypokalemia, Hypokalemia treatment*
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Introduction:

Hypokalemia or low serum potassium level is defined as serum potassium below 3.5meq/l. It is classified as mild (3-3.5meq/l), moderate (2.5-3meq/l), and severe (<2.5 meq/l) based on serum potassium levels(1,2). It is among the most prevalent laboratory abnormality occurring in hospitalized patients, accounting for 12-20% of those patients(1–3). It is estimated that one out of five hypokalemic patients has severe hypokalemia, which can induce muscle paralysis, respiratory failure, and life-threatening cardiac arrhythmias.

In-hospital mortality for hospitalized hypokalemic patients can range from 20-34%, which in large part is attributed to the 31% mortality observed in severely hypokalemic patients.(1,2,4)

Treatment of severe hypokalemia requires intravenous potassium chloride (IV KCL) which itself can lead to serious cardiac arrhythmias and severe infusion site reactions if overdosed or dosed too fast (4,5).

Most publications dealing with the dose, route, and concentration of IV KCL as well as the response to treatment of severe hypokalemia, are empiric guidelines, rather than evidence-based.(1,3–8)

Infusion rates of 10-20meq/l/hr. peripherally and 40 to 60meq/l/hr. centrally are recommended for severe hypokalemia treatment(4,5,8). The rate of response of serum potassium to the different infusion rates recommended above varies, with some studies reporting a rise in serum potassium of 0.4-0.43meq/l for 20meq of IV KCl (7), while others have reported the response to be from 0.27-0.4meq/l for 95-100meq of IV KCL infused (8).

The management of severe hypokalemia is based on retrospective chart reviews and case series with patient populations having significant variability in their demographics and comorbidities. This resulted in varying recommendations on the amount of IV KCL required by different populations(1–5,8). In the Ethiopian context, routine clinical practice suggests lower doses of potassium chloride, and to the author's knowledge, as there has been no publication to guide clinical management and serve as a baseline for further studies, this series was performed to shed some light on the issue.

Methods and Materials

Study Site: Bethzatha general hospital ICU.in Addis Ababa, Ethiopia.

Study Duration- October 2018 to June 2019

Study type-Prospective case series of severly hypokalemic patients managed by standard guidelines

Sample size-A total of six patients met inclusion criteria and were included

Inclusion criteria: All patients with serum potassium below 2.5meq/l, and required ICU care.

Exclusion criteria: Patients who had serum potassium below 2.5meq/l, but did not need ICU admission.

Consent- Informed oral and written consent was taken from patients or next of kin.

Ethical clearance :

was taken from Addis Ababa health bureau as part of a large ICU registry being run in the hospital's ICU (BIRD project) (A/A/H/2464/227)

Data collection: Demographic, clinical, and therapeutic data were collected prospectively using a structured data collection format by the treating physician in the ICU.

Out come

1. The rate of change of serum potassium to IV KCL infusion.
2. The amount of IV KCL required to get to a normal serum potassium level.

Statistical analysis

The collected data was entered into SPSS V25. the mean and median along with the standard deviations were calculated. Initial serum potassium level adjustment was done using a web-based calculator.(9)

Case Summary

Case-1

A 45 years old hypertensive and diabetic female presented with progressively increasing fatigue, vomiting, headache, and fever. On examination, she had pulsus alternans and a regularly irregular pulse. Her investigations showed a sodium of 126meq/l, a potassium of 1.0meq/l, chloride of 67meq/l,magnesium of 2.2mg/dl, phosphate of 1.9mg/dl, creatinine of 1.46mg/dl, and urea of 38mg/dl. Her blood gas analysis showed a PH of 7.59, a PO_2 of 119mmHg, a PCO_2 of 62.8mmHg, an HCO_3 of 60mmol/L, lactate of 0.86mg/dl, and anion Gap of 6.5. Her ECG had a persistent bigeminal rhythm with intermittent bursts of non-sustained ventricular tachycardia. After a central line was secured, 30meq/l/hr. of potassium chloride was infused for four hours after which, the serum potassium became 2.37meq/l, so, the infusion rate was decreased to 20 meq/l/hr. for the next nine hours, and the serum potassium became 3.43meq/l.

Case-2

A 35 years old male patient was admitted to the ICU for hypersplenism and severe diabetic ketoacidosis. On admission he was dehydrated, his random blood sugar was 350mg/dl, and his urine had +3 ketones. Eighteen hours into the management of diabetic ketoacidosis, his blood gas analysis showed a PH of 7.57, HCO_3 of 22.3mmol/L, PO_2 of 67mmHg, PCO_2 of 24.8mmHg, lactate of 0.57mg/dl, anion gap of 7, and the serum potassium dropped to 1.8 meq/l from 2.2 meq/l. The patient had declined to get a central venous line, so, potassium chloride at a rate of 10meq/l/hr. was infused for 12 hours after which the serum potassium became 2.66meq/l. After another 13 hours at the same rate, the serum potassium rose to 2.89meq/l, and after an additional 13 hours, the serum potassium became 3.67meq/l.

Case-3

An 80 years old male patient was readmitted five days post-discharge for possible hospital-acquired pneumonia after he presented with cough and shortness of breath. He was a known diabetic, hypertensive, and adrenal insufficiency patient on follow-up. After admission, the patient developed respiratory failure and septic shock for which ventilatory and vasopressor support was provided. After extubation and discontinuation of vasopressor support, the patient developed polyuria of five liters per day. The arterial blood gas at this time showed a PH of 7.53, HCO_3 of 41.7mmol/L, PO_2 of 62mmHg, PCO_2 of 50.6mmHg, lactate of 2.6mg/dl, and an anion gap of 2. His serum potassium at this time was 1.5meq/l, with serum magnesium of 1.2mg/dl, and serum phosphate of 1.9mg/dl. His ECG showed frequent premature ventricular contractions.

After a central line was inserted intravenous potassium chloride, at a rate of 20meq/hr. was given along with intravenous magnesium sulfate. Twelve hours later, the serum potassium rose to 4.48meq/l and potassium chloride infusion was discontinued.

Case-4

A 56 years old diabetic patient was brought to the hospital after he was found unconscious at a roadside. On evaluation, he had repeated episodes of generalized tonic -clonic seizures with vomiting of coffee ground material. His blood pressure was 140/80mmHg, his pulse rate was 130 beats per minute, and he had a respiratory rate of 42 breaths per minute with an oxygen saturation of 70% on a 15L face mask oxygen. He had diffuse rhonchi and fast deep breaths. His Glasgow coma scale was 8/15. He was admitted to the ICU and was intubated for type I respiratory failure. On the second day of intubation, the patient was producing three to five liters of urine output, his serum sodium rose from 136 meq/l to 155meq/l, his serum creatinine rose from 1.6mg/dl to 2.6mg/dl, and his serum potassium dropped from 4.04meq/l to 1.5meq/l. The arterial blood gas showed a PH of 7.18, a PO_2 of 72mmHg, an $HCO_3$of 11.5mmol/L, a PCO_2 of 31mmHg, a lactate of 1.6mg/dl, and anion gap of 7. A central catheter was inserted and potassium chloride was infused at a rate of 20meq/hr. for six hours. The repeat serum potassium after six hours of infusion was 4meq/L, so intravenous potassium chloride was stopped.

Case-5

A 37 years old known HIV patient for the past five years presented to the hospital complaining of watery diarrhea, intermittent vomiting, and a loss of 13 kilograms of weight over the past month. Two days before his presentation he was unable to move his extremities and became bedridden. On examination, he had cachexia with generalized hypotonia, hyporeflexia, and muscle power of 1/5 in all muscle groups including the neck muscles.His serum sodium was135meq/L, serum potassium was 1.13meq/l, serum magnesium was 4.4mg/dl, and serum phosphate was 1.3mg/dl. His ECG showed ST segment depression and U waves. After ICU admission, a central line was inserted and intravenous potassium chloride was infused at a rate of 20mq/l/hr. for 15 hours, after which the serum potassium became 1.19meq/L. So, the rate of infusion was increased to 30meq/hr. and the serum potassium was checked after six hours. At that time, the level was 1.31meq/l., and another three hours of infusion at the same rate was allowed, after which the potassium became 2.04meq/l. The infusion rate was maintained, as the patient had massive ongoing diarrhea for 14 more hours, and the potassium determined then became 4.26meq/l.

Case-6

An 85 years old hypertensive and diabetic female presented to the hospital complaining of a productive cough for one month with frequent episodes of seizures for 24 hours. On examination, she was agitated and confused with a puffy face, right lung lower lobe crepitation, and an irregularly irregular distant heart sound. She had a serum sodium of 120meq/l, potassium of 1.4meq/l, magnesium of 1.6mg/dl, a chloride of 69meq/l, and phosphate of 3.7mg/dl. Her blood gas showed a PH of 7.53, a PO_2 of 51mmHg, a PCO_2 of 75mmHg, an HCO_3 of 61mmol/l, lactate of 1.18mg/dl, and an anion gap of zero. After a central line was inserted, potassium chloride at a rate of 20meq/l/hr. was infused for six hours after which the serum potassium became 2.2meq/l, and after an additional eight hours at the same rate, the serum potassium became 3.9meq/l.

Results

The median age of the patients was 45 years (35-85), with one-third being females. The commonest comorbidities were diabetes and hypertension. The range mean of baseline serum potassium was from 1 to 1.8meq/l . (Table-1)

The mean IV KCL infusion rate between admission and the first retest time was 20meq/l (10-30meq/l). The median time that elapsed before the first retest was done was 9 hours, 4/6 patients required retesting two times while only 2/6 required retesting three times (Table-2)

A mean of 383.3 meq/l (120-990) IV KCL was infused over 20 hours (6-38) to bring about a change in the serum potassium by 2.57meq/l. The mean change in serum potassium between the first and last retest was 3.96 meq/l (3.43-4.48 meq/l). The mean IV KCl amount needed to raise the serum potassium by 1meq/l, was 146 meq when the baseline serum potassium was not corrected for PH, and 212meq when the baseline serum potassium was corrected for PH. (Table-3, Figure-1)

Table-1 Baseline demographic and clinical characteristics

Patient	**1**	**2**	**3**	**4**	**5**	**6**
Age	45	35	80	56	37	85
Sex	F	M	M	M	M	F
Comorbidity	Diabetes Hyper-tension	Diabetes DKA** Hypersplen-ism	Diabetes Hypertension Malignancy Dementia Heart failure	Diabe-tes	HIV infec-tion††	Hypertension Diabetes
Potassium (meq/l)	1	1.8	1.5	1.5	1.1	1.4
PH	7.59	7.57	7.53	7.18	7.40	7.53
HCO_3 (mmol/l) *	60.00	22.3	41.7	11.5	17.6	61
PCO_2 (mmHg) †	62.8	24.8	50.6	31	28.6	75
Magnesium (mg/ dl)	2.2	2.1	1.2	1.8	4.4	1.6
Phosphate (mg/dl)	1.9	1.1	1.9	2.0	1.3	3.7
Creatinine (mg/ dl)	1.46	0.74	0.8	2.6	0.5	0.8
IV access‡	Central line	Peripheral line	Central line	Central line	Central line	Central line
Hydration status	Dehy-drated	Dehydrated	Dehydrated	Dehy-drated	Dehydrated	Dehydrated
Ongoing loss	Present	Absent	Present	Present	Present	Absent
Loss Site	GI§	No	Renal	Renal	GI	No
Neurologic find-ing	Absent	Absent	Absent	Absent	Generalized hypotonia	Absent
Cardiac finding	Bigeminy NSVT‖	None	PVC¶	None	ST depression U waves	None

*HCO_3- Serum bicarbonate level in the blood, †PCO_2- Partial pressure of carbon dioxide in arterial blood, ‡ IV access-Intravenous access, § GI- gastrointestinal tract, ‖ NSVT- Non-sustained ventricular tachycardia, ¶PVC- Premature ventricular contractions, *DKA- Diabetic Keto acidosis, †† HIV Human immunodeficiency virus

Table-2 IV KCL infusion rates at different serum potassium retest hours

Patient	**Time of potassium retest (hours)**				**Rate of potassium infusion before retest (meq/l/hr.)**			
	1st retest	2nd retest	3rd retest	4th retest	1st rate	2nd rate	3rd rate	4th rate
1	4	9	ND*	ND	30	20	ND	ND
2	12	13	12	ND	10	10	10	ND
3	12	ND	ND	ND	20	ND	ND	ND
4	6	ND	ND	ND	20	ND	ND	ND
5	15	6	3	14	20	30	30	30
6	6	8	ND	ND	20	20	ND	ND

*ND-Not done

Patient	Total IV KCL* required (meq)	Total time of infusion (Hours)	Starting potassium (meq/L)	Last potassium (meq/L)	ΔK† (meq/L)
1	300	13	1	3.43	2.43
2	370	37	1.8	3.67	1.87
3	240	12	1.5	4.48	2.98
4	120	6	1.5	4	2.5
5	990	38	1.13	4.26	3.13
6	280	14	1.4	3.9	2.5

IV KCL- Intravenous potassium chloride, †ΔK- change in potassium

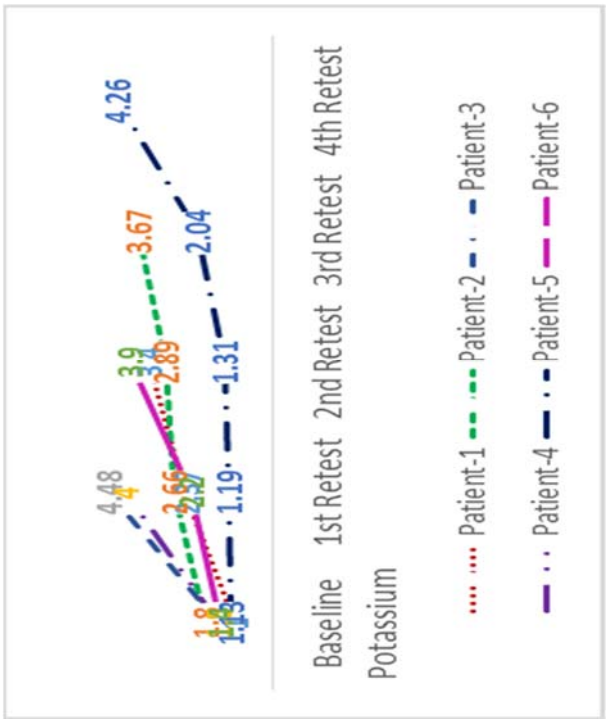

Figure-1 Serum potassium level at different retest hours

We have demonstrated in this case series that the total amount of IV KCl required to treat severe hypokalemia in our institution is at least 50% lower than that recommended in the literature. We have also shown that when the recommended infusion rate of ≥20meq/l/hr., via a central line, was used to replace serum potassium, the patients either reached their target in a short duration or required less amount of IV KCl. This effect was uniformly seen even when the patient's acid-base and hydration status was taken into account.

Discussion:

A computerized administrative and laboratory database review in Israel found that among hypokalemic patients, 54% were males with most of the patients having diabetes, kidney, and cardiovascular disease(1). A case series of patients with hypokalemic periodic paralysis found that the median age of patients was 34 (20-50) years (10), while others had patients aged between 58 to 72 years(5) and a mean age of 54.4± 16.3 years(2). A review of hypokalemic critically ill medical patients showed that 12% had renal dysfunction, and 34% had metabolic alkalosis with the commonest comorbidities being sepsis, respiratory failure, and cardiac arrest(4). These background clinical characteristics are similar to our patients with some variances arising likely due to sampling size and some of the studies including mild and moderate hypokalemia in their study.

In a series of hypokalemic patients with periodic paralysis, the presenting serum potassium was 1.9±0.4mmol/l with all patients achieving normokalemia within 6 hours(10). In a computerized review of hypokalemic patients, the mean and median time from diagnosis of hypokalemia to its correction were 50 and 25 hours respectively(1). A retrospective chart review of trauma patients with mild hypokalemia showed that the infusion of 95meq of KCl induced a 0.4meq/l change in the serum potassium(7), while a hypokalemia update review estimates that

the serum potassium will drop by 0.27meq for a 100meq drop in the total serum potassium level(8). Our patients had more severe hypokalemia but required the same amount of time and a lesser dose of IV KCL. This might have arisen from a potentially low total body water of our patients, early alkalosis correction, and rehydration that might cause transcellular shifts.

A hypokalemia review update shows that a low serum magnesium level worsens hypokalemia response while an impaired renal function decreases the IV KCL requirement of patients(8).

This was shown in our series with patient four having the worst renal dysfunction requiring a shorter duration and a lower dose of IV KCL to reach normokalemia, while it was difficult to see the effect of hypomagnesemia because of concurrent replacement of IV KCL with IV magnesium sulfate during the management of patients three and six.

Based on our results we recommend caution during the infusion of KCL to hypokalemic patients. We also recommend a larger and multicenter study to assess the effect of KCl infusion on serum potassium levels.

Conflict of interest-
The authors have no conflict of interest to declare.

Ethical clearance

was taken from Addis Ababa health bureau as part of a large ICU registry being run in the hospital's ICU (BIRD project) (A/A/H/2464/227).

Author contribution
ZM did diagnosis, treatment and follow up of the patients, inception of the study, data collection, data analysis, manuscript write up, manuscript revision
DK did diagnosis, treatment and follow up of the patients, manuscript revision and data interpretation.
SG did diagnosis, treatment and follow up of the patients, manuscript revision and data interpretation.

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