BRITISH JOURNAL OF HOSPITAL MEDICINE

Optimising patient care: comprehensive evaluation of inpatient hypokalaemia

Gokul Prasanna Muthaluraj[1]
Abinivesh Sathyanarayanan[2]
Niels Larsen[3]
Cornelius Fernandez[4]

Author details can be found at the end of this article

Correspondence to:
Gokul Prasanna Muthaluraj
(gokul.m.1992@gmail.com)

Abstract

Hypokalaemia is a common electrolyte disorder affecting hospitalised patients. It is associated with adverse outcomes including increased mortality. Inpatients with hypokalaemia need a different approach to workup and management as the aetiologies and progression of the hypokalaemia are distinct to outpatients. Potassium homeostasis is predominantly maintained by renal potassium handling. The clinical manifestations of hypokalaemia depend on the severity of hypokalaemia, however, most of the findings are non-specific. The approach to management is guided by the severity of the hypokalaemia and the underlying aetiology. Oral potassium replacement can be used in many cases of mild hypokalaemia. Intravenous replacement of potassium is necessary for many inpatients. Close monitoring is essential to ensure adequacy and to prevent adverse outcomes. An interdisciplinary approach with critical care input is needed in severe cases, and in patients where routine intravenous replacement may not be feasible (e.g., patients with heart failure). In addition to replacement, the cornerstone of management is a comprehensive review of the patient to identify the underlying cause of the hypokalaemia and the factors sustaining it. In patients in whom the cause is not apparent, or the potassium does not improve as anticipated, a referral to nephrology or endocrinology should be considered. This paper reviews the assessment of hypokalaemia in a hospital setting. It is aimed at early career doctors on the wards to help carry out a thorough evaluation. It also provides a useful framework for management.

Key words: Administration; Hyperaldosteronism; Hypokalaemia; Inpatients; Oral; Potassium; Standard of care

Submitted: 4 May 2024; Revised: 8 June 2024; Accepted: 18 June 2024

Introduction

Hypokalaemia affects approximately 20% of hospitalised patients. Iatrogenic causes including intravenous fluid therapy and medications account for 56% of these cases. Factors increasing the risk of hypokalaemia include elderly patients, female sex, and comorbidities such as heart failure, nephrotic syndrome, haematological malignancies and gastrointestinal tumours (Jordan and Caesar, 2015; Clase et al, 2020). A quarter of these patients receive inadequate monitoring, and treatment, and are discharged with hypokalaemia. The mortality is tenfold increase in those with cardiovascular disease when compared to general inpatients with hypokalaemia (Jordan and Caesar, 2015).

Although institutional guidelines for hypokalaemia treatment exist, the underlying pathophysiological principles may not be addressed comprehensively. Here we discuss common causes of hypokalaemia among inpatients and provide a general approach to management, aimed at medical students and early-career doctors on the ward.

How to cite this article:
Muthaluraj GP, Sathyanarayanan A, Larsen N, Fernandez C. Optimising patient care: comprehensive evaluation of inpatient hypokalaemia. Br J Hosp Med. 2024. https://doi.org/10.12968/hmed.2024.0242

Regulation of potassium homeostasis

The kidneys play the most important role in potassium homeostasis as they are responsible for the excretion of about 90% of the daily oral potassium intake (Agarwal et al, 1994). Kidneys limit potassium excretion when there is a reduced intake, making hypokalaemia rare from intake reduction alone.

Potassium is mainly reabsorbed in the proximal convoluted tubule (PCT) after glomerular filtration. Only a small portion reaches the distal convoluted tubule (DCT), passively carried

by sodium and water movement. Potassium levels in the late DCT and collecting duct are regulated by principal cells and alpha-intercalated cells. Principal cells reabsorb sodium via the epithelial sodium channel (ENaC) and secrete potassium into the lumen through the renal outer medullary potassium channel (ROMK). Aldosterone enhances this process, while hypokalaemia inhibits it. Alpha-intercalated cells regulate acid-base balance by secreting H^+ ions. Hypokalaemia causes the activity of luminal H^+-K^+-adenosine triphosphatase (ATPase) on the alpha-intercalated cells to increase, leading to more reabsorption of potassium (Palmer, 2015; Patil and Patil, 2022).

Clinical presentation

Inpatients with hypokalaemia are often asymptomatic. Only a quarter of patients with hypokalaemia have clearly attributable symptoms of low potassium. Patients can exhibit a wide range of symptoms reflecting the critical role of potassium in many physiological functions. However, almost all of these symptoms are non-specific (Kardalas et al, 2018). The severity of the symptoms depends on the degree of potassium reduction and the duration of hypokalaemia.

Early signs of hypokalaemia include weakness, fatigue, muscle cramps, and myalgias (from the impact on the neuromuscular system). As hypokalaemia progresses, cardiovascular changes occur, leading to electrocardiogram (ECG) abnormalities that increase arrhythmia risk. Both bradyarrhythmias and tachyarrhythmias have been reported (Kardalas et al, 2018). Gastrointestinal symptoms such as nausea, bloating and constipation can occur, and in severe cases, hypokalaemia can cause paralytic ileus. Renal complications manifest as polyuria due to impaired urine concentrating ability (transient nephrogenic diabetes insipidus). Severe hypokalaemia may lead to paresthesias and even paralysis (Zacchia et al, 2016).

In clinical practice, the disease process and its associated symptoms predominate and most cases of hypokalaemia are only detected incidentally on routine testing.

Approach to management

Initial assessment

Once hypokalaemia is confirmed with a blood gas and a serum sample, the focus should be on identifying the cause (pertinent history and examination) and the severity of the hypokalaemia (based on the potassium value and any associated features). Hypokalaemia is classified as mild (3–3.5 mmol/L), moderate (2.5–3 mmol/L) and severe (if <2.5 mmol/L).

Preliminary workup should include an urgent ECG, and blood tests for renal function and electrolytes including magnesium, bicarbonate and calcium. The main ECG changes seen with hypokalaemia are decreased T wave amplitude, T wave inversion, prolongation of the QT interval, and prominent U wave formation. In severe cases, it can lead to ventricular tachycardia and torsades de pointes (Khan et al, 2024).

It is important to note that there can be an underestimation of potassium on the blood gas analyser, compared to an optimal serum sample (Gupta et al, 2016). Hence, the treatment should always be reviewed based on subsequent laboratory values.

Treatment strategies

There are three main principles in the treatment of hypokalaemia-replenishing potassium stores, monitoring for complications, and correcting the underlying causes of hypokalaemia. Consideration should also be given to the location of care as guided by clinical signs and symptoms, and other investigative findings used to determine the true severity and requirements for higher levels of care (Grams et al, 2021).

Replenishing potassium stores

Oral and intravenous routes are primary for replacement, each with unique pros and cons. Selection depends on the case and the patient.

Oral replacement

Oral potassium supplements are effective in mild cases (if K >3 mmol/L). This can be in the form of potassium chloride/phosphate/bicarbonate or gluconate. Phosphate forms can be used in concurrent hypophosphataemia, and bicarbonate forms in metabolic acidosis, however, the rate of correction is slower in both these forms. Potassium chloride is hence the preferred choice for rapid potassium level elevation. Alkalotic patients with hypokalaemia are chloride depleted more frequently, hence potassium chloride serves well in this regard and it corrects hypokalaemia faster than the other forms. It is available in various forms-crystalline, liquid, slow-release forms. Liquid potassium, though unpalatable, suits patients with feeding tubes or swallowing issues. Oral potassium supplements are mostly well tolerated, but in some patients, they cause gastrointestinal irritations, abdominal cramps and vomiting, hence, advised to take them after a meal. Slow-release tablets, while generally well-tolerated, also carry a slight risk of gastrointestinal issues. Therefore, the tolerance to oral replacement must be reviewed periodically (Kim and Han, 2002).

Intravenous therapy

Potassium chloride can be given intravenously in moderate to severe hypokalaemia (if K <3 mmol/L) or when oral administration is impractical. Initially, potassium should be infused in saline to prevent dextrose-induced insulin release, which can exacerbate hypokalaemia. Aggressive intravenous potassium is essential in conditions like diabetic ketoacidosis where insulin and dextrose therapy may worsen hypokalaemia. It is recommended to infuse potassium at a rate no more than 10 mmol/hour in a ward setting. Intravenous potassium may cause pain or phlebitis when infused at rates more than 10–20 mmol/hour. Therefore, higher rates than 10 mmol/hour should usually be administered via a central line (Clase et al, 2020).

The use of intravenous potassium may cause volume overload. This is of particular concern in patients who have heart failure with diuretic-induced hypokalaemia and in patients with anuria and hypokalaemia. Involvement of critical care early is important in such cases. In cases of redistributive losses, intravenous administration should be very closely monitored as even low rates of potassium correction can lead to hyperkalemia once the redistributed potassium returns to the extracellular compartment. Also, to avoid inadvertent errors in potassium administration, an infusion pump is generally advised to be used (May et al, 2016).

Monitoring for complications

Continuous cardiac monitoring is needed for patients at risk of arrhythmias, especially if other electrolytes are replaced concomitantly. Serum potassium should be checked every 2–4 hours until stable, to avoid hyperkalemia, then less frequently. Once hypokalaemia improves, the rate of potassium administration can be reduced or replacement can be switched to oral therapy. Intravenous replacement can be repeated if the potassium is not improving with initial infusions. Refractory cases need a careful re-evaluation of the causes (Kardalas et al, 2018). Gastrointestinal irritation could be prevented/treated by a proton pump inhibitor cover. Pain and phlebitis during intravenous replacement can occur, and need to be monitored for.

Correcting the underlying cause

In hospitalised patients, particularly those without hypokalaemia upon admission, the cause often stems from their illness or treatment. Typically, a thorough review of presentation, symptoms, medication history, and blood results reveals the underlying cause.

The main causes and their management are listed below in the descending frequency of their occurrence.

Gastrointestinal losses

This is either due to vomiting or diarrhoea in most cases. Patients on nasogastric suction as part of their treatment can also develop profound hypokalaemia. Typically, loss of gastric fluid through vomiting leads to a hypochloremic metabolic alkalosis and can be a useful clinical clue to the aetiology. Lower gastrointestinal losses of fluid can lead to acidosis in some cases depending on the duration and the cause.

Where appropriate an antiemetic could be considered. Antidiarrheals such as loperamide may also be used with caution after the exclusion of infective causes of diarrhoea (Kardalas et al, 2018; Palmer and Clegg, 2019).

Medications

Correcting hypokalaemia induced by essential therapy presents challenges, as discontinuing treatment may not be feasible for severe conditions. Balancing risks and benefits are vital; if risks outweigh benefits, discontinuation should be considered, otherwise, monitoring and replacement are warranted.

Common agents causing hypokalaemia include

1. Both loop and thiazide diuretics cause hypokalaemia by enhancing distal sodium delivery, and increasing urinary potassium excretion. Hypokalaemia severity is higher when a combination of diuretics is used (e.g., heart failure). Hypokalaemia due to diuretics is also typically accompanied by hypochloremic metabolic alkalosis. Therefore, it is important to monitor the potassium levels every 24–48 hours in patients on intravenous diuretics therapy.
2. Corticosteroids (such as prednisone or dexamethasone) and fludrocortisone can increase urinary potassium excretion and decrease potassium absorption from the gastrointestinal tract, leading to hypokalaemia, especially with prolonged therapy.
3. Beta-2 Agonists (e.g., salbutamol) can stimulate cellular uptake of potassium, leading to hypokalaemia, particularly with high doses or frequent use ('back to back' treatment). This is important to recognise in patients with chronic obstructive pulmonary disease as the standard of care for an exacerbation includes steroids, and a significant proportion of them are on diuretics for cor pulmonale-related symptoms.
4. Insulin stimulates cellular uptake of potassium, leading to hypokalaemia. This is seen in patients on intravenous insulin therapy especially when used for the management of a hyperglycaemic emergency. These patients should receive a potassium-containing intravenous solution alongside their insulin where required and monitored with at least daily potassium checks to assess levels. This is even more vital where patients are started on a variable rate infusion for vomiting (vomiting itself can cause hypokalaemia).
5. Laxatives, particularly stimulant laxatives like bisacodyl, can cause hypokalaemia by increasing intestinal motility and secretion, leading to excessive potassium loss through the stool.
6. Certain antibiotics such as aminoglycosides like gentamicin or antifungals like amphotericin B, can cause tubular dysfunction, leading to renal potassium wasting and subsequent hypokalaemia.

Additionally, antipsychotics, verapamil overdose, and xanthines are other medications linked to hypokalaemia (Kardalas et al, 2018; Palmer and Clegg, 2019).

Renal losses

In the normal state, distal nephron sodium delivery and aldosterone secretion are inversely related, i.e., conditions that cause decreased sodium delivery (e.g., dehydration/volume depletion) cause a compensatory rise in aldosterone levels. This usually does not lead to hypokalaemia. Renal potassium wasting occurs in pathology that affects this balance-resulting in increased sodium delivery or increased aldosterone/mineralocorticoid action without a compensatory reduction in the other. This is a useful way to think about the underlying causes.

Any cause of polyuria (e.g., primary polydipsia, diabetes insipidus) leads to a 'high flow' state where there is an increase in the glomerular filtration rate and the filtered load of Na^+ exceeds the transport maximum (re-absorptive capacity) of the PCT. This leads

to increased distal nephron sodium delivery and can cause hypokalaemia. In addition, polyuria following resolution of an acute kidney injury, including after resolution of urinary retention, can also lead to hypokalaemia (Clase et al, 2020).

Primary hyperaldosteronism can cause profound chronic hypokalaemia, metabolic alkalosis and hypertension. In some cases, primary hyperaldosteronism can be 'unmasked' in patients when they are commenced on a diuretic as an inpatient. Suspected cases should be referred to the endocrinology team for assessment (Palmer and Clegg, 2019).

Hypomagnesemia can also lead to hypokalaemia due to the inability of the kidneys to reabsorb potassium adequately. More than 50% of patients with hypokalaemia have associated hypomagnesemia. Without correcting the magnesium, the hypokalaemia can be difficult to correct due to the ongoing renal losses (Gragossian et al, 2024).

Intracellular shifts

In addition to insulin therapy and beta-agonists discussed previously, there are a few rarer causes of intracellular shift in potassium that can be seen in inpatients (Palmer and Clegg, 2019). In anabolic states, newly formed cells can sequester potassium. This is commonly seen in the treatment of megaloblastic anaemia with vitamin B12. It can also occur with use of granulocyte-macrophage colony-stimulating factor for neutropenia (Ringelstein et al, 2013). In the treatment of both these conditions, there is production of new blood cells, a process that requires potassium-a major intracellular ion.

Both metabolic and respiratory alkalosis can cause hypokalaemia. As hydrogen ions move out of the cells to correct for the alkalosis, to maintain electroneutrality, potassium enters into the cell. Where possible the underlying cause of this alkalosis should be managed to improve the hypokalaemia.

Conclusion

Hypokalaemia is a common electrolyte abnormality incidentally detected in many inpatients and it is associated with increased morbidity and mortality (Jordan and Caesar, 2015). We have discussed a brief overview of common aetiologies seen among hospital inpatients and an approach to the management of these patients.

While rarer causes of hypokalaemia such as renal tubular acidosis, genetic syndromes and salt wasting nephropathies exist, they are beyond the scope of this review. Where they are suspected or a diagnosis is unclear, a referral to nephrology and/or endocrinology is recommended to guide further investigation.

Key points

- Potassium homeostasis relies predominantly on renal function, with kidneys handling 90% of potassium excretion.
- Hospitalised patients, especially the frail elderly, are at risk of hypokalaemia, often exacerbated by iatrogenic causes.
- Medications, gastrointestinal losses, renal disorders, and intracellular shifts are common contributors to inpatient hypokalaemia.
- Clinical presentation varies widely, from neuromuscular symptoms to cardiovascular complications, emphasising the need for routine monitoring of high-risk patients.
- Diagnostic approach involves review of the patient's underlying illness, blood and urine studies, including ECG monitoring, to identify severity and underlying causes.
- Treatment strategies include oral and intravenous potassium replacement tailored to severity and addressing contributing factors for effective management.

Curriculum checklist

This article addresses the following competencies outlined in the internal medicine curriculum.

- Generic CiP 3—Communicates effectively and is able to share decision-making, while maintaining appropriate situational awareness, professional behaviour and professional judgement.
- Clinical CiP 3—Providing continuity of care to medical in-patients, including management of comorbidities and cognitive impairment.
- Clinical CiP 5—Managing medical problems in patients in other specialties and special cases.

Author details

[1]Internal Medicine, Nottingham University Hospitals NHS Trust, Nottingham, UK

[2]Aston Medical School, Birmingham, UK

[3]Diabetes and Endocrinology, Nottingham University Hospitals NHS Trust, Nottingham, UK

[4]Department of Diabetes and Endocrinology, United Lincolnshire Hospitals NHS Trust, Nottingham, UK

Availability of data and materials

All the data of this study are included in this article.

Author contributions

GPM, AS, NL, and CF contributed to the article's conception and the important editorial changes. GPM drafted the manuscript. All authors read and approved the final manuscript and have participated sufficiently in the work and agreed to be accountable for all aspects of the work.

Ethics approval and consent to participate

Not applicable.

Acknowledgement

Not applicable.

Funding

This research received no external funding.

Conflict of interest

The authors declare that there are no conflicts of interest.

References

Agarwal R, Afzalpurkar R, Fordtran JS. Pathophysiology of potassium absorption and secretion by the human intestine. Gastroenterology. 1994;107(2):548–571. https://doi.org/10.1016/0016-5085(94)90184-8

Clase CM, Carrero JJ, Ellison DH et al. Potassium homeostasis and management of dyskalemia in kidney diseases: conclusions from a kidney disease: improving global outcomes (KDIGO) controversies conference. Kidney Int. 2020;97(1):42–61. https://doi.org/10.1016/j.kint.2019.09.018

Gragossian A, Bashir K, Bhutta BS et al. Hypomagnesemia. StatPearls Publishing: Treasure Island, FL, USA. 2024.

Grams ME, Hoenig MP, Hoorn EJ. Evaluation of hypokalemia. JAMA. 2021;325(12):1216–1217. https://doi.org/10.1001/jama.2020.17672

Gupta S, Gupta AK, Singh K, Verma M. Are sodium and potassium results on arterial blood gas analyzer equivalent to those on electrolyte analyzer? Indian J Crit Care Med. 2016;20(4):233–237. https://doi.org/10.4103/0972-5229.180044

Jordan M, Caesar J. Hypokalaemia: improving the investigation, management and therapeutic monitoring of hypokalaemic medical inpatients at a district general hospital. BMJ Qual Improv Report. 2015;4(1):u209049.w3670. https://doi.org/10.1136/bmjquality.u209049.w3670

Kardalas E, Paschou SA, Anagnostis P et al. Hypokalemia: a clinical update. Endocr Connect. 2018;7(4):R135–R146. https://doi.org/10.1530/EC-18-0109

Khan U, Afzal U, Kask L et al. Ion-flux: the natural course of ECG changes in severe hypokalemia. Curr Probl Cardiol. 2024;9(1):102158. https://doi.org/10.1016/j.cpcardiol.2023.102158

Kim GH, Han JS. Therapeutic approach to hypokalemia. Nephron. 2002;92(Suppl 1):28–32. https://doi.org/10.1159/000065374

May S, Dodge J, Stock T. 892: evaluation of intravenous potassium replacement in the critically ill patient. Crit Care Med. 2016;44(12):299. https://doi.org/10.1097/01.ccm.0000509568.65676.d5

Palmer BF. Regulation of potassium homeostasis. Clin J Am Soc Nephrol. 2015;10(6):1050–1060. https://doi.org/10.2215/CJN.08580813

Palmer BF, Clegg DJ. Physiology and pathophysiology of potassium homeostasis: core curriculum. Am J Kidney Dis. 2019;74(5):682-695. https://doi.org/10.1053/j.ajkd.2019.03.427

Patil S, Patil M. Potassium homeostasis. IntechOpen: London, UK. 2022.

Ringelstein EB, Thijs V, Norrving B et al. Granulocyte colony-stimulating factor in patients with acute ischemic stroke: results of the AX200 for Ischemic Stroke trial. Stroke. 2013;44(10):2681–2687. https://doi.org/10.1161/STROKEAHA.113.001531

Zacchia M, Abategiovanni ML, Stratigis S, Capasso G. Potassium: from physiology to clinical implications. Kidney Dis. 2016;2(2):72–79. https://doi.org/10.1159/000446268