PERSPECTIVE

Hypokalaemia Common and commonly underestimated

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Hypokalaemia is common but often unrecognised and can have serious metabolic and functional effects in many organ systems. Characteristic changes appear on the ECG as hypokalaemia becomes severe.

Key points

- **Hypokalaemia is common in clinical practice and can lead to cardiac, neuromuscular and gastrointestinal abnormalities.**
- **Hypokalaemia is usually associated with total body potassium depletion caused by inadequate intake and/or excess gastrointestinal or renal loss.**
- **Occasionally, significant hypokalaemia is caused by a compartmental shift of potassium from the extracellular to the intracellular fluid caused by alkalosis, insulin or aldosterone excess.**
- **Severe potassium depletion (below 2.5 mmol/L) can cause ECG abnormalities, arrhythmias, weakness, rhabdomyolysis and renal tubular dysfunction.**
- **Hypokalaemia is often associated with other electrolyte abnormalities including alkalosis, hypomagnesaemia and hypophosphataemia, which can have other adverse effects.**

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Hypokalaemia – a potassium level below 3.5 mmol/L – is common in clinical practice but often unrecognised. However, when severe (K^+ below 2.5 mmol/L), it can have serious adverse metabolic and functional effects in many organ systems, including ECG abnormalities, arrhythmias, weakness, rhabdomyolysis and renal tubular dysfunction. The condition, which usually occurs as a complication of certain illnesses or medications, can be of particular concern in cardiac patients because these patients have an inherent risk for arrhythmias and often take medications that increase the risk of hypokalaemia and/or arrhythmia.

This article uses a case study to illustrate the main causes and consequences of hypokalaemia (other management of the patient is outside the scope of this short article).

Case scenario

Robert retired from his plumbing business two years ago and moved to the family coastal holiday house with his wife, Maxine. Robert is 62 years old, overweight (height, 182 cm; weight, 91.4 kg) and has had hypertension for 12 years, type 2 diabetes for seven years and multiple musculoskeletal aches and pains he attributes to his years of accessing various plumbing 'nooks and crannies'.

Robert takes amlodipine/valsartan/hydrochlorothiazide 5/160/12.5 mg/day, modified release gliclazide 60 mg/day, metformin 1 g three times a day, pantoprazole 80 mg/day and paracetamol 'fairly often'. He says he has been well except for a 'gastro bug' that has given him some loose bowel actions over the past week. General examination is noncontributory and his blood pressure is 134/74 mmHg. He has not had any problems with his medications. You arrange some laboratory investigations. The next day you note he has hypokalaemia (see Table). You arrange for him to collect a prescription for a potassium supplement (potassium chloride, 600 mg/day).

Two days later his wife rings because Robert's 'gastro bug' has got worse – he has been vomiting and is now so weak he cannot get out of bed. You arrange for Robert to be admitted to the local hospital. Robert

looks very unwell and dehydrated. His blood pressure is 117/66 mmHg and he is tachycardic (115 beats per minute). His abdomen is nontender and rectal examination is unremarkable with liquid stool. He is weak and has trouble sitting up in bed. Investigations and an ECG are organised. The results of the ECG are shown in Figure 1.

What are the significant abnormalities in Robert's ECG?

Robert's ECG shows prominent U waves following the T wave, ST depression, T-wave inversion and a long QU interval (Figure 1). These changes, particularly the prominent U waves, are consistent with hypokalaemia, and may result in life-threatening ventricular arrhythmias. PR prolongation may also occur in hypokalaemia, but is not showing in this ECG.

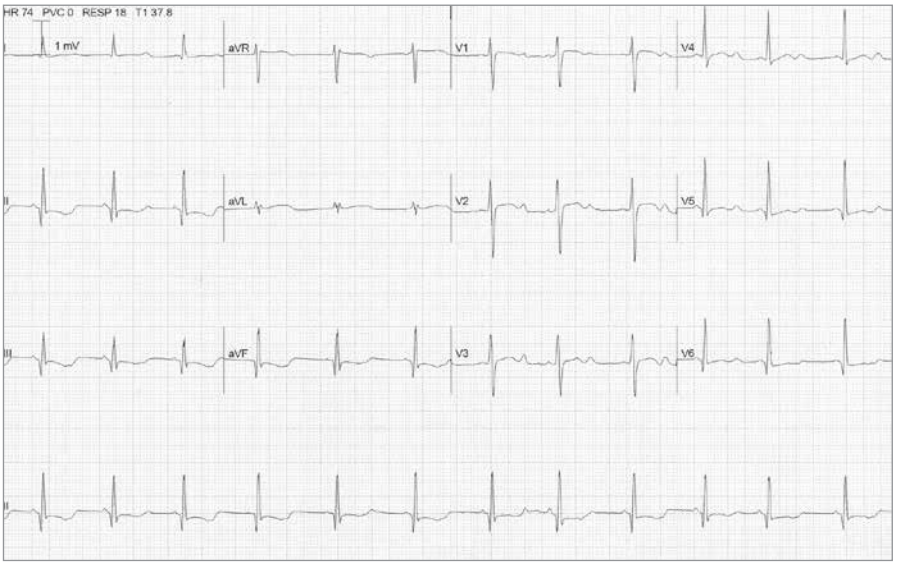

Figure 1. Robert's ECG. Note the bradycardia, ST depression (especially in the inferior leads), T-wave inversion, prominent U waves (especially in the precordial leads, where they resemble p waves) and the apparent long QT interval due to fusion of the T and U waves (long QU interval).

Case scenario continued

Robert's electrolyte levels are significantly abnormal (see Table).

What are the potential contributors to Robert's hypokalaemia?

The main features of potassium balance are outlined in Figure 2. Hypokalaemia can be caused by:

- total body potassium (TBK) depletion because of decreased intake and/or excess gastrointestinal (GI) or renal loss
- compartmental shift of potassium from the extracellular fluid (ECF) to the intracellular fluid (ICF).

Robert's hypokalaemia is likely to reflect TBK depletion because of GI loss of potassium associated with his diarrhoea and renal loss because of the alkalosis caused by vomiting acidic gastric contents. Other potential contributors include magnesium depletion associated with his diarrhoea and increased renal potassium loss associated with his diuretic therapy. A compartmental shift of potassium from the ECF to the ICF might be a minor contributor because of the metabolic alkalosis causing an exchange of ICF hydrogen ions and ECF potassium ions.

It is important to identify significant TBK depletion because it can, as in Robert's case, adversely affect several organ systems (see Box). It is also important to remember that other electrolyte abnormalities, particularly magnesium and phosphate depletions, can be associated with TBK depletion and also cause significant clinical problems:

- magnesium depletion (<0.5 mmol/L) – renal tubular dysfunction with potassium loss; parathyroid dysfunction with hypocalcaemia
- phosphorus depletion (<0.3 mmol/L) – abnormal cognition; weakness, rhabdomyolysis; thrombocytopenia, haemolysis.

In retrospect, should you have responded differently to his initial electrolyte abnormalities?

At the time of Robert's initial presentation, his diarrhoea had caused significant hypokalaemia associated with a metabolic alkalosis (increased plasma bicarbonate). Both his diarrhoea and hypokalaemia would have been amplified by his medication:

- diarrhoea by his metformin
- hypokalaemia by his diuretic (hydrochlorothiazide).

Robert may not have previously had GI side effects from his metformin but metformin could still amplify the effects of an incidental GI problem (diarrhoea and/or nausea and vomiting). It is recommended that metformin be stopped in such a situation and any resulting hyperglycaemia controlled by other hypoglycaemic agents.

Table. Robert's electrolyte results

Analyte	Initial level	Three days later	Reference range
Sodium (mmol/L)	137	133	137 to 145
Potassium (mmol/L)	3.3	2.0	3.5 to 4.9
Chloride (mmol/L)	91	79	100 to 109
Bicarbonate (mmol/L)	32	38	22 to 32
Urea (mmol/L)	8.4	11.5	2.7 to 8.0
Creatinine (µmol/L)	105	122	50 to 120

ECG COURTESY OF DR ED BURNS, PERTH, WA, AND HTTP://LIFEINTHEFASTLANE.COM

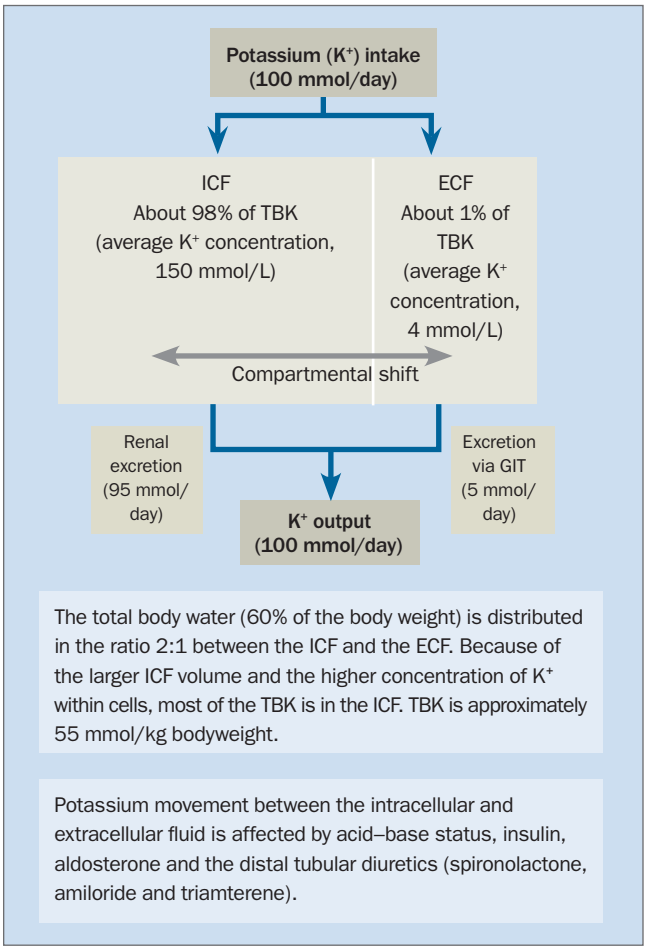

Figure 2. Potassium balance.
Abbreviations: ECF = extracellular fluid; GIT = gastrointestinal tract; ICF = intracellular fluid; TBK = total body potassium.

The hydrochlorothiazide in Robert's combined hypotensive therapy decreases sodium ion reabsorption in the ascending loop of Henlé and results in increased sodium ion reabsorption in exchange for potassium and/or hydrogen ion secretion. As with metformin, this may not have been a problem before his GI upset. However, the loss of body fluids and activation of the renin–angiotensin–aldosterone system would have also increased distal tubular sodium reabsorption and increased renal potassium and hydrogen ion loss. (Although Robert is also taking valsartan, this is a competitive rather than a complete angiotensin receptor blocker.)

The potassium supplement initially prescribed (one 600 mg tablet a day of potassium chloride, equivalent to K^+ 8 mmol/day) is a very small supplement given the usual K^+ intake of 100 mmol/day (mainly from fruit and vegetables) and Robert's TBK (about 5000 mmol, calculated using the average value for K^+ per kg of bodyweight of 55 mmol, i.e. 91.4 x 55). Moreover, Robert required replacement of his TBK depletion as well as replacement of ongoing losses. He should have been given more potassium supplementation (three to four 600 mg tablets a day; K^+, 24 to 32 mmol/day) and had his potassium levels monitored several days later to guide ongoing potassium therapy.

Effects of severe potassium depletion and associated abnormalities

Potassium <2.5 mmol
- Heart: ECG abnormalities, arrhythmias
- Muscle: weakness, rhabdomyolysis
- Kidney: tubular dysfunction with potassium loss

Magnesium <0.5 mmol/L
- Kidney: renal tubular dysfunction with potassium loss
- Parathyroid: hypocalcaemia

Phosphorus <0.3 mmol/L
- Central nervous system: abnormal consciousness, coma
- Muscle: weakness, rhabdomyolysis
- Heart: myocardial dysfunction
- Haematological: thrombocytopenia, haemolysis

Case scenario continued

Robert's metformin and hydrochlorothiazide were stopped, and he was given intravenous saline to replenish his extracellular fluid depletion and intravenous potassium chloride to replenish his potassium stores and correct his metabolic alkalosis. He did not require magnesium or phosphorus repletion. His muscle strength improved, his ECG returned to its previous status and he was discharged on the fourth day after his admission.

What should be done if the hypokalaemia recurs?

If the hypokalaemia recurs, further investigation for conditions such as primary hyperaldosteronism and Cushing's syndrome should be considered.

Conclusion

A common but often unrecognised condition in clinical practice, hypokalaemia can, when severe, cause ECG abnormalities, arrhythmias, weakness, rhabdomyolysis and renal tubular dysfunction. Hypokalaemia is often associated with other electrolyte abnormalities, including alkalosis, hypomagnesaemia and hypophosphataemia, which can have other adverse effects. It is usually caused by total body potassium depletion due to inadequate intake and/or excess gastrointestinal or renal loss but occasionally is caused by a compartmental shift of potassium from the extracellular to the intracellular fluid due to alkalosis or insulin or aldosterone excess. **CT**

Further reading

Mount BD, Zandi-Nejad K. Disorders of potassium balance. In: Brenner BM, ed. Brenner and Rector's the kidney. 8th ed. Philadelphia: Saunders; 2008. Ch 15; p 547-587.

COMPETING INTERESTS: Dr Phillips has received research and travel grants, acted on advisory boards and been involved with clinical trials and seminars sponsored by a range of pharmaceutical companies. He does not think these associations have influenced the content of this article.