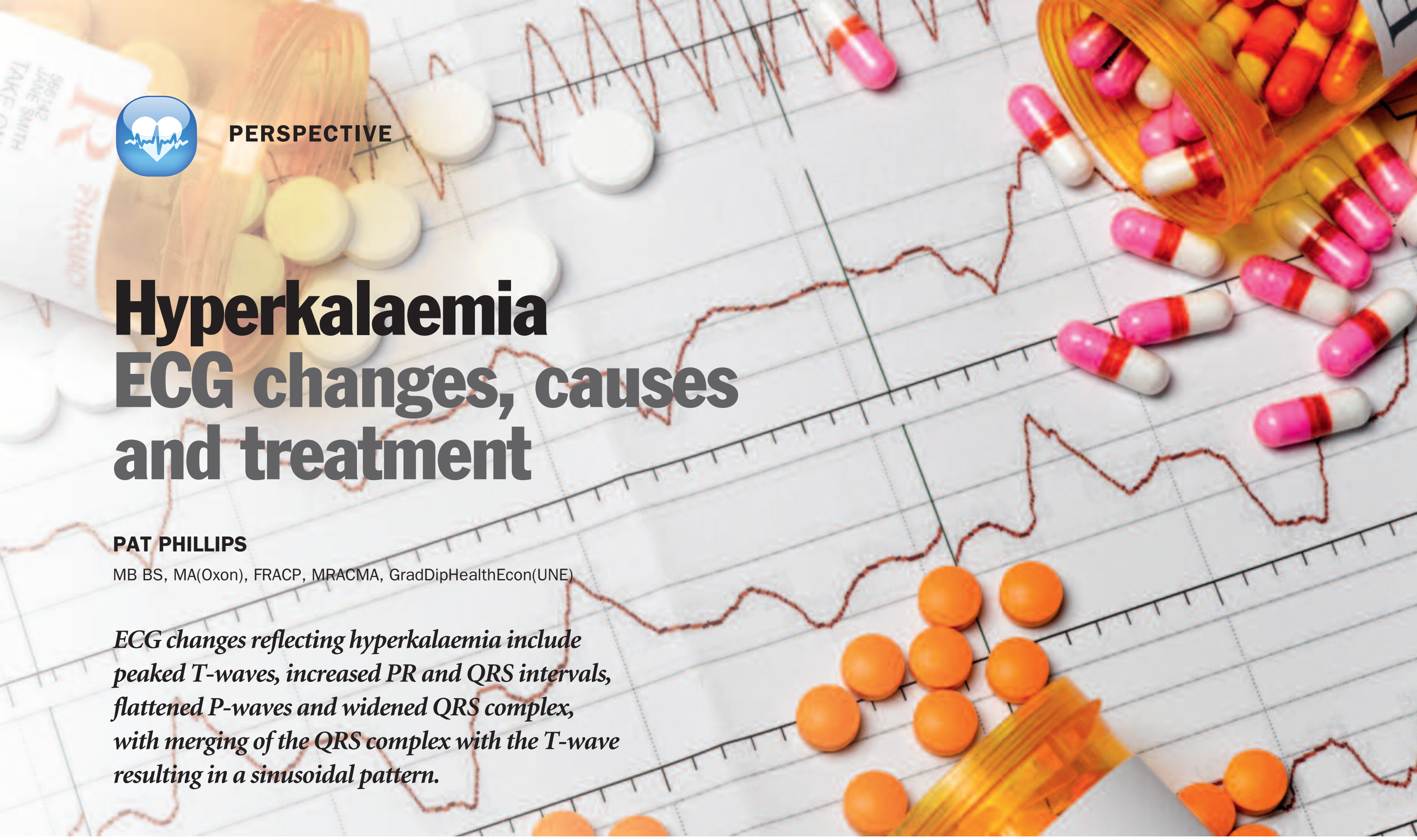

PERSPECTIVE

Hyperkalaemia ECG changes, causes and treatment

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ECG changes reflecting hyperkalaemia include peaked T-waves, increased PR and QRS intervals, flattened P-waves and widened QRS complex, with merging of the QRS complex with the T-wave resulting in a sinusoidal pattern.

Case scenario

Ken has come to see you because he 'feels weak, flat and a bit tingly'. He is worried this might be due to nerve or muscle damage related to his statin therapy.

Ken is 75 years old and mildly overweight (170 cm, 79 kg, BMI 27.3 kg/m^2). He is usually a happy vigorous man, active in his garden and at the local bowls club – both interests shared with his wife, Carla, aged 72 years.

He has had type 2 diabetes for 15 or so years with moderate control (glycosylated haemoglobin [HbA$_{1c}$] 7.5 to 8.3% over the past two years) and is using intermediate-acting insulin (isophane) 42 units at bedtime, metformin 500 mg and propranolol 80 mg twice daily and once-daily simvastatin 40 mg, ramipril 10 mg and amiloride/hydrochlorothiazide 5/50 mg. He also takes celecoxib 200 mg if his arthritis flares up after gardening or at bowls.

Examination confirms mild weakness in his lower and upper limbs (power approximately 4/5) and some loss of sensation in his feet up to his ankles. His reflexes are decreased but present, and other examination is noncontributory.

You arrange some investigations (biochemistry, blood picture, thyroid function and HbA$_{1c}$) and arrange to see him two days later.

Later that day the laboratory phones you about the results of his electrolytes tests:

- *sodium 136 mmol/L (normal range, 137 to 145 mmol/L)*
- *potassium 6.7 mmol/L (3.5 to 4.9 mmol/L)*
- *chloride 106 mmol/L (100 to 109 mmol/L)*
- *bicarbonate 22 mmol/L (22 to 32 mmol/L)*
- *urea 8.3 mmol/L (2.7 to 8.0 mmol/L)*
- *creatinine 114 µmol/L (50 to 120 µmol/L)*

Key points

- **Hyperkalaemia may be caused by errors in collection or specimen processing, increased total body potassium or a compartmental shift of potassium from the cells to the extracellular fluid (ECF).**
- **Several medications are associated with hyperkalaemia, particularly NSAIDs, ACE inhibitors, angiotensin receptor blockers, aldosterone antagonists and potassium-sparing diuretics. These cause hyperkalaemia by decreasing output and/or affecting the potassium balance between the intracellular fluid (ICF) and ECF.**
- **ECG changes reflecting hyperkalaemia include peaked T-waves and slowing of conduction that increases the PR and QRS intervals, flattens the P-waves and widens the QRS complex so that it merges with the T-wave causing a sinusoidal pattern.**
- **Treatment of hyperkalaemia includes emergency measures to correct the electrophysiological effects, measures to shift potassium from the ECF to the ICF, and measures to reduce total potassium.**

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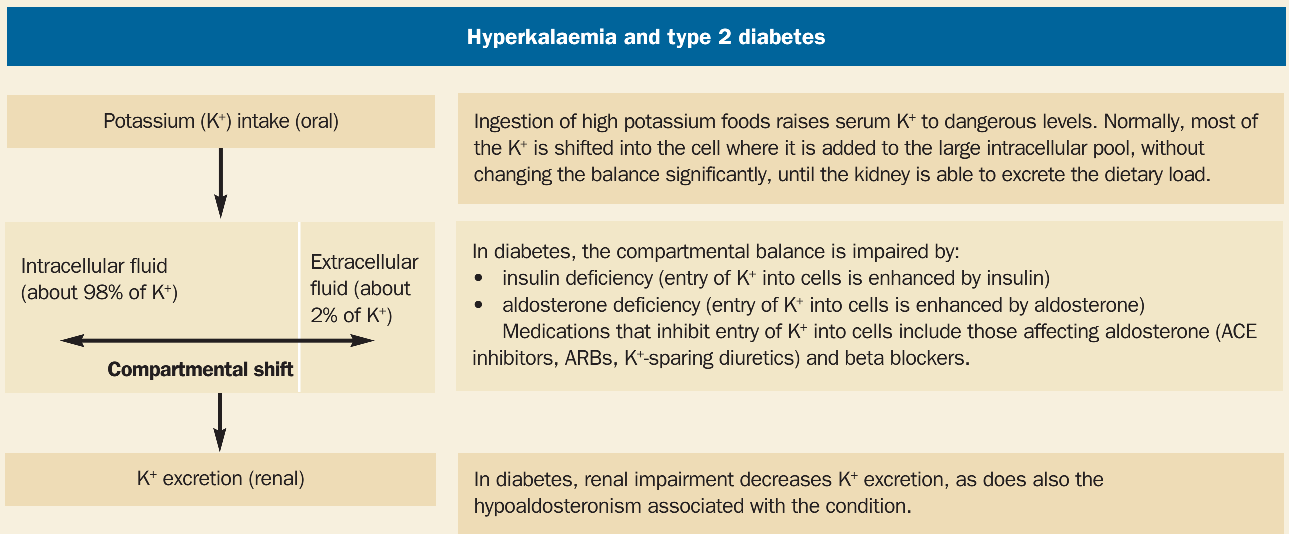

ABBREVIATIONS: ACE = angiotensin-converting enzyme; ARB = angiotensin II receptor blocker.
SOURCE: Phillips P. Medication-induced diabetes urgencies. Medicine Today 2011; 12(12): 66-74.

Figure 1. Potassium balance and the effect of diabetes.

The body compartments and potassium balance

The general assumption is that 60% of body weight is water, with two-thirds intracellular and one-third extracellular. Younger people have proportionately more water and women and older people proportionately less. The normal distribution of potassium between the two compartments is about 98% in the intracellular fluid (ICF) and about 2% in the extracellular fluid (ECF), normal levels being approximately 145 and 4.5 mmol/L, respectively.

Because of the greater proportion of water and the much higher normal concentration of potassium in the ICF compared with the ECF, the ICF has a large capacity to accommodate extra potassium without the intracellular concentration being significantly affected.

Taking as an example a 70 kg man. His body would contain 42 L of water, with 28 L in the intracellular space and 14 L in the extracellular space. Assuming his potassium levels are in the normal range, he would have a body potassium content of 145 x 28 (4060) mmol in the ECF and 14 x 4.5 (63) mmol in the ICF, giving a total of 4123 mmol potassium.

An extra potassium load of 100 mmol in the ECF would increase this man's extracellular potassium content from 63 to 163 mmol (that is, by 159%) but the same 100 mmol load in the intracellular compartment would increase the intracellular potassium content from 4060 to 4160 (that is, by only 2.5%). The extracellular concentration increases (by 159%) from 4.5 to 11.6 mmol/L whereas the intracellular concentration increases (by 2.5%) from 145 to 149 mmol/L.

What are likely causes of Ken's hyperkalaemia?

When confronted with an unexpected laboratory value, a misleading result should always be considered. Apparent hyperkalaemia is commonly caused by delay or error in collection or specimen processing, either of which can cause red blood cell potassium to move from the high concentration inside red cells to the lower concentration in plasma/serum.

Truly pathological causes of hyperkalaemia can reflect increases in total body potassium (increased intake or decreased output) or a compartmental shift from cells (intracellular fluid; ICF) to the extracellular fluid (ECF). Figure 1 shows how the compartmental balance is affected by diabetes.[1]

Excess potassium intake is rarely a direct cause of hyperkalaemia because the kidney has a large capacity to eliminate potassium (filtering nearly 1000 mmol/day) and the ICF has a large capacity to accommodate extra potassium without significantly affecting the intracellular concentration. For example, and as shown in detail in the box on this page, a potassium load of 100 mmol in the ECF would increase the potassium concentration there from 4.5 mmol/L to 11.6 mmol/L but the same 100 mmol load would only increase the intracellular potassium concentration from 145 mmol/L to 149 mmol/L.

Ken's creatinine level of 114 µmol/L is in the normal range (50 to 120 µmol/L) but his calculated glomerular filtration rate (GFR) of 50 mL/min is low (over 90 mL/min is normal; see the box on page 29). Also, he may well have some degree of metabolic acidosis (his bicarbonate is slightly low) but, again, this is minor whereas his potassium abnormality is highly significant.

Just as the intracellular compartment can buffer swings in potassium content, shifts of potassium between the intracellular

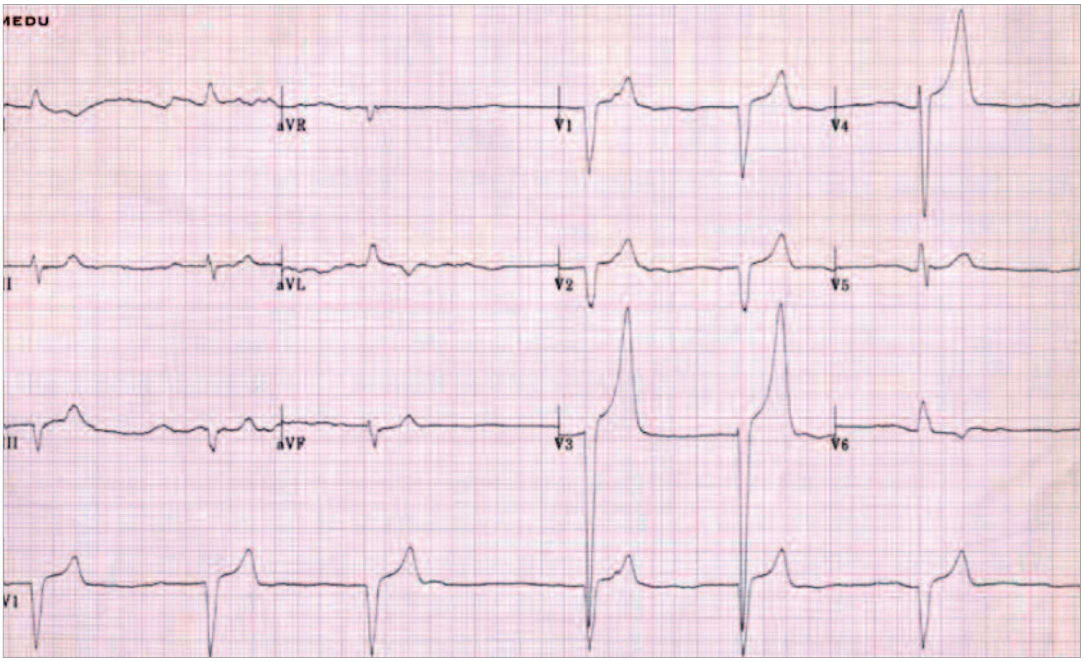

Figure 2. Ken's ECG. Note the peaked (tented) T-waves typical of hyperkalaemia (see the anterior leads). Courtesy of Dr Vivienne Miller, Sydney.

and extracellular compartments can greatly increase or decrease extracellular, and thus plasma, potassium concentrations. Several pathological processes and medications have the potential to affect renal potassium excretion and potassium balance within the body and one or more of these may be responsible in Ken's case.

The case continued

You arrange to see Ken later that day and ask your nurse to perform an electrocardiograph. The ECG is shown in Figure 2.

What does Ken's ECG show?

The T-waves in Ken's ECG are peaked or tented, which reflects the increased membrane repolarisation associated with mild to moderate hyperkalaemia (e.g. 5 to 6 mmol/L).

As potassium levels further increase, conduction slows, having the effect of initially increasing the PR and QRS intervals and then flattening the P-waves and further widening the QRS complex so it eventually merges with the T-wave, providing a sinusoidal pattern. Further potassium increases are associated with ventricular fibrillation or asystole.

Which of Ken's medications could be causing his hyperkalemia?

Commonly used medications that increase potassium and the mechanism by which they do so are listed in the box on page 30. The most commonly used are probably NSAIDs, ACE inhibitors, angiotensin receptor blockers, aldosterone antagonists and potassium-sparing diuretics. Ken is taking three of these medication classes and also a nonselective β-blocker.

The combination of Ken's relative insulin deficiency due to his long-standing type 2 diabetes (which reduces any compensating insulin secretion to counteract any hyperkalaemia), his renal impairment, renal tubular acidosis and use of these medications were responsible for his hyperkalaemia.

How would you manage Ken's hyperkalaemia?

There are two general approaches to managing a patient with hyperkalaemia: emergency measures to address the electrophysiological effects of the hyperkalaemia, using calcium or sodium; and measures to shift potassium from the extracellular to the intracellular

Calculating the GFR

Laboratories provide the estimated GFR (eGFR) calculated from a formulation that uses the person's age and sex as provided on the request form. The eGFR provides a value based on body surface area (mL/min/1.73m^2). This may be misleadingly low/high in a large/small person.

The calculated GFR (which is technically creatinine clearance) gives the total GFR, takes account of body size and is based on the Cockroft Gault equation:

GFR (mL/min) = [(140 – age in years) x healthy weight in kg] divided by serum creatinine in μmol/L,

where healthy weight (kg) = height (cm) – 100

To allow for the greater muscle mass per kg of body weight in men, the value derived from the above formula is multiplied by 1.23 (or 1.25 for easier calculation) for men.

In Ken's case:

GFR = 1.25 x [(140 – 75) x (170 – 100)]/114
= 1.25 x 65 x 70/114
= 50 mL/min

Drugs causing hyperkalaemia

Mechanism: renal excretion
- NSAIDs
- ACE inhibitors/ARBs
- Lithium
- Cyclosporin

Mechanism: compartmental balance
- Beta-2 blockers*
- Succinyl choline

Mechanism: renal excretion and compartmental balance
- Aldosterone antagonists:
  - spironolactone
  - eplerenone
- Other potassium-sparing diuretics:
  - amiloride
  - triamterene
- Digitalis (overdose)

ABBREVIATIONS: ACE = angiotensin-converting enzyme; ARBs = angiotensin II receptor blockers; NSAIDs = nonsteroidal anti-inflammatory drugs.
* The adrenergic effect is through β_2-receptors; selective β_1-blockers have little effect.

compartment, using insulin, a short-acting β_2-agonist (e.g. salbutamol by aerosol) or sodium bicarbonate (which reduces acidosis).

At the same time, the potentially contributing medications would be stopped and measures started to reduce the total potassium load. Such measures would be removing potassium indirectly via the gut (using ion exchange resins) or the kidney (using loop diuretics or fludrocortisone) or directly from the blood (dialysis).

Ken's hyperkalaemia has probably taken some time to develop, which reduces the likelihood of a severe ventricular dysrhythmia such as fibrillation or asystole. Stopping use of the contributing medications, starting use of a potassium exchange resin and closely monitoring potassium levels would seem appropriate. Emergency measures are probably not called for, although telephone advice from a renal physician would be useful.

How will you reduce the risk of future hyperkalaemia?

Ken's relative insulin deficiency and his renal impairment will continue and the ACE inhibitor is providing renal and cardiovascular protection, as well as treating his hypertension. However, he could change from a nonselective β-blocker to a β_1-selective agent (e.g. metoprolol), stop his NSAID and use paracetamol and other measures for his osteoarthritis. Finally, he should stop the potassium-sparing diuretic (amiloride) and continue the thiazide or start a loop diuretic if necessary.

Ken and Carla should also be advised to limit their intake of foods with a particularly high potassium content, such as fruits (especially dried fruit and fruit juices) and vegetables (especially vegetable juices, pulses, soy beans, potato skin and spinach). If significant restriction of these foods is required, a dietitian could provide useful advice.

Conclusion

Several pathological processes and medications have the potential to affect renal potassium excretion and potassium balance within the body, causing hyperkalaemia, as illustrated in this case of an elderly man with type 2 diabetes who is taking, among other medications, an NSAID, a potassium-sparing diuretic, an ACE inhibitor and a nonselective β-blocker.

An ECG is often performed if hyperkalaemia is suspected because changes typical for hyperkalaemia may be shown. ECG changes reflecting hyperkalaemia include peaked T-waves and slowing of conduction that increases the PR and QRS intervals, flattens the P-waves and widens the QRS complex so that it merges with the T-wave causing a sinusoidal pattern. The ECG will also be able to identify cardiac arrhythmias that result from the hyperkalaemia. **CT**

Reference

1. Phillips P. Medication-induced diabetes urgencies. Medicine Today 2011; 12(12): 66-74.

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.