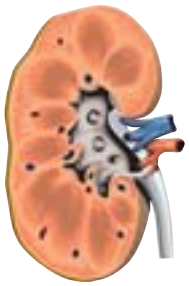

Hyperkalaemia and rising creatinine

how to keep the ACE inhibitor going

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Hyperkalaemia may limit the ability of a patient to receive the full vascular and renal benefits of ACE inhibition (ACEIs) or angiotensin receptor blockade (ARBs). Patients most at risk of hyperkalaemia are those with moderate to severely impaired renal function, where moderate chronic renal failure (CRF) is defined as a glomerulofiltration rate (GFR) < 60mls/min. Mild elevations are usually well-tolerated, especially if associated with stable CRF. Exacerbating factors are usually present, including excess dietary intake, transcellular redistribution from acidosis, or impaired excretion from concurrent drugs. Reversal of these factors, addition of a diuretic, or modification of ACEI/ARB dose according to GFR, can permit safe and beneficial renin-angiotensin axis blockade.

Pharmacology

ACEIs and ARB's inhibit the aldosterone-mediated distal tubular secretion of potassium, producing an average 0.5mmol/L rise in serum potassium. The extent of the potassium rise depends in part on the intensity of renin:angiotensin axis blockade. ACEIs mediate their actions via their active "-prilat" metabolite, which is renally-excreted (fosinopril is 50% hepatically-metabolised).

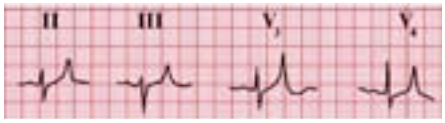
Of the currently available ARBs, telmisartan and eprosartan are also renally-excreted, whereas irbesartan and candesartan are hepatically-metabolised.

Use of renally-excreted ACEI/ARBs in the presence of moderate-severe CRF can produce much higher plasma drug levels and exacerbate hyperkalaemia. Dose-reduction according to GFR can minimise this problem.

Clinical significance

Elevations of serum potassium up to 6 mmol/L are usually asymptomatic in otherwise well people, and levels up to 8mmol/L are occasionally incidentally found in dialysis patients prone to dietary excess.

Weakness, areflexia and ileus may accompany the sequential ECG changes of tall peaked T waves, flattened P waves, broadened (sine wave) QRS complex, briefly followed by sustained ventricular arrhthymias and finally, intractable asystole. The Cardioplegia solution used to paralyse the heart during coronary bypass is potassium chloride.



Hyperkalaemia. A tall peaked and symmetrical T wave is the first change seen on the ECG.

Patients with underlying heart disease, or who develop hyperkalaemia during acute renal failure, are much more at risk of cardiac symptoms and arrhythmias.

Systematic diagnostic approach

A step-wise approach to hyperkalaemia in a patient receiving an ACEI or ARB involves:

1. Check clinical status of patient (act quickly if patient is weak or oliguric)
2. Calculate GFR (using stable serum creatinine and lean body weight)
3. Review dietary intake and drug history (including OTC medications)
4. Repeat sample (including serum HCO3), avoiding any delay in serum separation to prevent spurious elevations

The main sources of **excess intake** include:

- Diet: fruit, fruit juices, nuts, chocolate, Milo & Horlicks powder, unprocessed bran or cillium husks, salt substitute
- Medication: K supplements

The main causes of **transcellular K+ redistribution** include:

- Systemic acidosis (metabolic or respiratory)
- Beta-blockers, digoxin, insulin resistance (to a minor degree)

Case Study

Mrs Jones, aged 70, has improved remarkably on ramipril 10mg daily for mild CCF, with better energy, exercise tolerance and appetite. Routine electrolytes show a rise in **potassium** from 4.9 to **6.5 mmol/L**, and serum creatinine from 75 to 90 umol/L, compared to two months earlier. Serum bicarbonate has fallen from 23 to 19 mmol/L, with normal serum chloride. Her BP has improved to 135/85, she weighs 52 Kg, and is 155cm tall.

Calculated GFR, based on her stable previous creatinine is:

(140 – age) x weight/creatinine = (140 – 70) x 52 / 75 = **48 mls/min** (i.e. half normal, or moderate CRF).

Dietary review finds a generous intake of grapes over the last few days. You confirm her results, advise temporary cessation of ramipril and avoidance of fruits and fruit juices. Her K has fallen to 4.8 two days later, so you reintroduce **ramipril at reduced dose** of 5mg daily (equivalent to 10mg in someone with normal renal function), suggesting only **one serve of fruit or fruit juices daily**. Her serum potassium stays less than 6 mmol/L on follow-up, but you have a low threshold for converting her to the thiazide combination if her BP or exercise tolerance deteriorates in the future.

The main conditions causing **impaired renal excretion** are:

- ARF or CRF (with normal s. Chloride), or renal tubular acidosis (acidosis with raised s. Cl-)
- Medications: K+-sparing diuretics (spironolactone, amiloride, triamterene), ACEIs/ARBs, NSAIDs (both over-the-counter COX-1 and prescription COX-2 inhibitors), trimethoprim
- Adrenal insufficiency (esp. if low BP)

The main cause of **impaired gut excretion** of K+ is constipation.

Approach to asymptomatic hyperkalaemia

- Correct dietary excess
- Withdraw/review any recently-added K+-sparing medications, (esp. NSAIDs, spironolactone, trimethoprim)
- Dose-reduce renally-excreted ACEI/ARBs according to GFR (see case study below).
- Switch to ACEI/ARB combined with thiazide
- Correct constipation
- Add sodium bicarbonate 840mg to achieve serum HCO3 > 22 mmol/L
- If persistent, consider low-dose fludrocortisone (0.1mg 3 x weekly), where K+-lowering effect is usually greater than Na+-retaining effect.

Note: I usually avoid potassium-binding resins (e.g. Resonium) due to their expense, unpalatibility, constipating effect and delayed action, unless all other measures fail.

Acute symptomatic hyperkalaemia is a medical emergency, especially if associated with acute ECG changes and warrants referral to Emergency. Standard-dose salbutamol via nebuliser or inhaler is a quick effective way of reducing the serum potassium by 0.5 mmol/L within 15-30 minutes for 4-6 hours, acting by temporarily pushing potassium back within cells, but not removing it from the body.

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Further reading

www.rph.wa.gov.au/nephrol under /Teaching/Tutorial

Palmer BF. Angiotensin-converting enzyme inhibitors and angiotensin receptor blockers: what to do if the serum creatinine and/or serum potassium concentration rises. Nephrol Dial transplant (2003) 18:1973.