Changes in kidney function and serum potassium during ACEI/ARB/diuretic treatment in primary care

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Think Kidneys is a national programme led by
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This advice applies to monitoring of pharmacotherapy in clinically stable patients; **it does NOT apply to patients with intercurrent acute illness.**

Measure urea, creatinine, and electrolytes (U&Es) before initiation or up-titration and again within 2 weeks of initiation or up-titration of dose of ACEI, ARB (including compound preparations including an ACEI or ARB, e.g. Valsartan/Sacubitril), or diuretic.

Use the immediate pre-treatment serum creatinine concentration as the baseline. In patients with heart failure, measure U&Es within 1 week of initiation or up-titration of Spironolactone or Epleronone (Mineralocorticoid Receptor Antagonists, MRAs), then monthly for the first 3 months, and 3-monthly for 1 year, and 4-monthly thereafter.

1. Kidney function: ACEI and ARB

If serum creatinine rises by >15% but < 30% from initial baseline

- continue but repeat U&Es in a further 1 to 2 weeks
- arrange clinical review including assessment of fluid status and blood pressure
    - try to continue ACEI/ARB treatment if there is a strong indication, e.g. heart failure, albuminuric CKD, history of myocardial infarction
    - reduce or stop other BP-lowering drugs (calcium channel blockers, alpha blockers) if SBP <120 mmHg
    - reduce concurrent diuretics if there is clinical evidence of hypovolaemia/overdiuresis

If serum creatinine increases at any point by ≥ 30% from initial baseline

- arrange clinical review including assessment of fluid status and blood pressure
    - try to continue ACEI/ARB treatment if there is a strong indication, e.g. heart failure, albuminuric CKD, history of myocardial infarction
    - reduce or stop other BP-lowering drugs (calcium channel blockers, alpha blockers) if SBP <120 mm Hg
    - reduce concurrent diuretics if there is clinical evidence of hypovolaemia/overdiuresis
- re-check renal function within 5-7 days. If renal function does not return to baseline with these measures,
    - stop the ACEI or ARB, or
    - reduce the dose to a previously tolerated dose and recheck renal function in 5-7 days; add an alternative antihypertensive medication if required
- consider obtaining advice from nephrology, even if serum creatinine returns to baseline
- obtain advice from local heart failure specialist team if the indication for treatment was heart failure: continuing an ACEI/ARB in heart failure with reduced ejection fraction may be beneficial even if serum creatinine rises by > 30%

2. Kidney function: Diuretics including MRAs

Increases in serum creatinine and urea are an expected consequence of haemoconcentration caused by diuretic treatment, and do not necessarily mean that the drugs have caused kidney damage. **Treat the patient, not the blood test**: repeated clinical examination is key, paying attention to avoidance of hypovolaemia and hypotension. Disproportionate rises in blood urea may reflect effective hypovolaemia and should prompt clinical reassessment.
Stop blood-pressure-lowering drugs that are not specifically indicated, or contraindicated, in heart failure (e.g. calcium channel blockers, alpha blockers) if SBP < 120 mm Hg. Seek specialist advice from a heart failure team or nephrologist if concerned.

Serum potassium
Hyperkalaemia is common in patients with CKD, particularly if they are receiving treatment with ACEI, ARB, MRA (e.g. Spironolactone), or NSAIDs. Hyperkalaemia can cause cardiac arrest, often without warning symptoms, or muscle paralysis. Management in primary care depends on the severity of hyperkalaemia and on the clinical context. Hyperkalaemia is classified as follows:

- Severe hyperkalaemia = serum K ≥ 6.5 mmol/L
- Moderate hyperkalaemia = serum K 6.0-6.4 mmol/L
- Mild hyperkalaemia = serum K 5.5 – 5.9 mmol/L

Measurement of serum potassium
Serum K should be measured in patients with CKD (frequency depends on CKD stage, see table), in patients with heart failure, and within 1-2 weeks of initiation or an increase in dose of an ACEI, ARB, or MRAs.
NB Hyperkalaemia may be artifactual in samples sent from primary care: this can be caused by fist clenching during phlebotomy, use of small-gauge needles causing low-grade haemolysis, prolonged tourniquet use, and, most importantly, delays in sample processing, particularly in cold weather.

Severe hyperkalaemia
(K ≥ 6.5 mmol/L): refer to hospital (via A&E) for immediate assessment and treatment

Moderate hyperkalaemia
(K 6.0-6.4): management depends on clinical context:

- If the patient is acutely unwell, or has AKI, stop the ACEI, ARB or MRA and refer to hospital for immediate assessment and treatment.
- If the patient is clinically stable (i.e. the test was done as a routine check rather than for acute illness, and there is no AKI warning stage test result), undertake medication review within 1 working day of the result. If hyperkalaemia is unexpected, consider arranging a repeat test the following day taking steps to minimise any of the factors that can cause artifactual hyperkalaemia.
    - Look for and remove other contributors to hyperkalaemia, including
        - Trimethoprim/CoTrimoxazole
        - Potassium supplements
        - Potassium-sparing diuretics (beware combinations with Furosemide)

        - Use of salt substitutes e.g. 'LoSalt'
        - NSAIDs
        - Non-selective beta-blockers
        - Digoxin toxicity
    - Review the patient clinically: reduce/stop diuretics if evidence of over-diuresis.
    - If the patient is on ACEI, ARB or MRA, stop immediately, repeat serum K within 1 week, and review indications (NB patients should not be treated with combinations of ACEI and ARB):
        - If used for hypertension, consider an alternative antihypertensive drug.
        - If used for heart failure with reduced ejection fraction or kidney disease with albuminuria, re-start at a lower dose once serum K < 5.5 mmol/L and then continue to monitor: if the patient was on a combination of ACE or ARB and an MRA, only re-start one of these drugs at a time.
    - Provide patients with a diet advice sheet on reduction of potassium intake.
    - If problems with hyperkalaemia persist, refer to renal medicine for dietetic advice
    - Seek advice from local heart failure specialist team if the indication for treatment was heart failure

Mild hyperkalaemia (K 5.5-5.9): management depends on clinical context

- If the patient is acutely unwell, or has AKI, stop the ACEI, ARB or MRA and consider referral to hospital for immediate assessment and treatment.
- If the patient is clinically stable (i.e. the test was done as a routine check rather than for acute illness, and there is no AKI warning stage test result), undertake medication review within 1 working day of the result. If hyperkalaemia is unexpected, consider arranging a repeat test within 3 days, taking steps to minimise any of the factors that can cause artifactual hyperkalaemia
    - Look for and remove other contributors to hyperkalaemia, including
        - Trimethoprim/CoTrimoxazole
        - Potassium supplements
        - Potassium-sparing diuretics (beware combinations with Furosemide)
        - Use of salt substitutes e.g. 'LoSalt'
        - NSAIDs
        - Non-selective beta-blockers
        - Digoxin toxicity
    - Review the patient clinically: reduce/stop diuretics if evidence of over-diuresis.
    - If the patient is on ACEI, ARB or MRA, halve dose of one or both, and review indications (NB patients should not be treated with combinations of ACEI and ARB):
        - If used for hypertension, consider an alternative antihypertensive drug.
        - If used for heart failure with reduced ejection fraction or kidney disease with albuminuria, continue, but monitor carefully.
    - Provide patients with a diet advice sheet on reduction of potassium intake.
    - If problems with hyperkalaemia persist, refer to renal medicine for dietetic advice

- Consider seeking advice from local heart failure specialist team if the indication for treatment was heart failure

This advice is based on the Renal Association/Resuscitation Council guideline on hyperkalaemia section on primary care (p78), on Think Kidneys Acute Kidney Injury guidance, on ESC guidelines, on the British National Formulary, and on NICE Clinical Knowledge Summaries