

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

A position statement from Think Kidneys, the
Renal Association, and the British Society for Heart
Failure

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Table of Contents

Subject	Page No
1. First principles	3
2. Kidney function: ACEI and ARB (including sacubitril valsartan)	3
3. Kidney function: Diuretics including MRAs*	4
4. Serum potassium	4

Disclaimer

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1. First principles

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 containing an ACEI or ARB, e.g. sacubitril valsartan), 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 eplerenone (Mineralocorticoid Receptor Antagonists, MRAs), then monthly for the first 3 months, and 3-monthly for 1 year, and 4-monthly thereafter.

The risk of death is higher in acute hyperkalaemia than in chronic hyperkalaemia.

ACEI/ARB/MRA/sacubitril valsartan are disease modifying drugs in patients with heart failure with reduced ejection fraction which improve patient outcomes. The risk of stopping or reducing dose is, in general, likely to be of greater detriment to a patient’s prognosis than a modest increase in serum creatinine, or mild hyperkalaemia.

Amongst patients with heart failure and normal ejection fraction (HeFPEF, HeFNEF, diastolic heart failure), there is no convincing evidence that ACEI/ARB/MRA alter prognosis. If renal function deteriorates significantly with their use, consider stopping them altogether and using an alternative agent.

2. Kidney function: ACEI and ARB (including sacubitril valsartan)

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
 - o try to continue ACEI/ARB treatment if there is a strong indication, e.g. heart failure with reduced ejection fraction, albuminuric CKD, history of myocardial infarction
 - o reduce or stop other BP-lowering drugs (calcium channel blockers, alpha blockers) if SBP <120 mmHg
 - o reduce concurrent diuretics if there is clinical evidence of hypovolaemia/overdiuresis

If serum creatinine increases at any point by \geq 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 with reduced ejection fraction, 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 serum creatinine remains >30% from initial baseline with these measures,
 - stop the ACEI or ARB, or
 - reduce the dose to a previously tolerated dose and re-check renal function in 5-7 days; add an alternative antihypertensive medication if required
 - obtain advice from local heart failure specialist team if the indication for treatment was heart failure with reduced ejection fraction: continuing an ACEI/ARB in HFREF may be beneficial even if serum creatinine rises by >30%
- consider obtaining advice from nephrology, even if serum creatinine returns to baseline

3. 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.

*MRAs are prescribed for prognostic benefit in patients with heart failure with reduced ejection fraction. They have adjunctive diuretic benefit in a patient who is volume overloaded.

4. 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 \geq 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), in patients with heart failure, and within 1-2 weeks of initiation or an increase in dose of an ACEI, ARB, or MRA.

NB Hyperkalaemia may be artefactual 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 \geq 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 artefactual hyperkalaemia.
 - Look for and remove other contributors to hyperkalaemia, including
 - Trimethoprim/co-trimoxazole
 - 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 with reduced ejection fraction

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 as soon as practicable. 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/co-trimoxazole
 - 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, consider halving 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 with reduced ejection fraction

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](#)