



Important New Evidence Service In Partnership with The Centre for Medicines Optimisation at Keele University

ScriptSwitch[™] Rapid Update 1 – July 2017

Acute Kidney Injury (AKI): What are the effects of temporarily discontinuing medications to prevent AKI?

To help reduce the risk of Acute Kidney Injury (AKI), patients may be advised to temporarily stop some medicines ahead of surgical or radiologic procedures. Patients may also be given advice - commonly referred to as “sick day rules” - to stop taking certain medicines during bouts of illness that can cause dehydration. A new [systematic review](#) found low-quality evidence that AKI incidence was reduced by the withdrawal of some medicines prior to coronary angiography and cardiac surgery. There was no evidence available on the impact of stopping medicines during intercurrent illness in either secondary or primary care.

Reference: Whiting P, Morden A, Tomlinson LA et al. [What are the risks and benefits of temporarily discontinuing medications to prevent acute kidney injury? A systematic review and meta-analysis.](#) BMJ Open 2017;7:e012674. doi:10.1136/bmjopen-2016-012674

What do we know already?

- [Estimates](#) suggest that up to 100,000 deaths a year in hospital are associated with AKI. AKI is also increasingly seen in primary care, with approximately 65% of cases starting in the community. The ‘Think Kidneys’ NHS campaign hosts a wealth of information on AKI, including resources for [primary care](#) and [medicines optimisation guidance](#).
- AKI may be caused or exacerbated by some medicines including non-steroidal anti-inflammatory drugs (NSAIDs), angiotensin converting enzyme inhibitors (ACEI), angiotensin receptor blockers (ARBs), diuretics, metformin and aminoglycosides. To reduce the risk of AKI, such medicines may be temporarily stopped ahead of surgery and prior to radiological procedures involving the use of contrast materials. Patients may also be advised to stop taking some medicines during episodes of intercurrent illnesses that can result in dehydration (e.g. bouts of vomiting, diarrhoea or fever) and which may raise the risk of AKI. Recommendations on assessing AKI risk and stopping medicines are available in the [NICE guideline on AKI](#).
- Guidance on stopping medicines during periods of illness may be provided to patients via sick day rules cards, an intervention that has been widely rolled out in [Scotland](#), where the cards are predominantly issued via community pharmacies, and also in some local initiatives in the UK.
- However, the investment into such initiatives has been questioned. In 2015, the Think Kidneys Programme Board issued an [interim position statement](#) suggesting that although there is a strong professional consensus that advice on sick day ‘guidance’ should be given, which is based on an individual risk assessment of a patient, the evidence that the advice reduces net harm was very weak and investment to increase uptake of sick day rules should only be undertaken in the context of a formal evaluation.

What does this evidence add?

- This is the first systematic review to summarise the available evidence on the temporary cessation of medicines with the aim of preventing AKI – an important topic in light of the current interest in AKI prevention.
- Based on the six eligible studies that were identified, all of which were carried out within secondary care, there was only low quality evidence that the withdrawal of ACEI or ARBs prior to coronary angiography and cardiac surgery may reduce the incidence of AKI.
- There was no evidence on the impact of drug cessation on AKI incidence during intercurrent illness in either primary or secondary care. There was also no evidence on the cessation of other medications (NSAIDs, diuretics, sulphonylureas, metformin or combinations of medicines).

- In 2013, the [NICE guideline development group](#) noted the limited evidence in this area, and whilst this latest review includes new studies, the evidence of benefit remains weak.
- An [evaluation](#) of Salford CCG's sick card guidance project has recently been published. It indicated that educational sessions on the cards had resulted in new learning in health practitioners, and that conversations were taking place with patients about AKI prevention. However, communicating temporary cessation of medicines to patients was identified as a challenge and issues with coding impeded a quantitative evaluation of the project. The reports suggests that sick day guidance cards that focus solely on medicines management may be of limited benefit without either adequate resourcing, or if delivered as a standalone intervention.

Study details

This systematic review and meta-analysis aimed to summarise the evidence on the temporary discontinuation of medications to prevent AKI.

Eligibility criteria for studies:

- Eligible studies were randomised or non-randomised studies that evaluated adult patients who were taking a specified medicine (*see below*) and experiencing an intercurrent illness, or undergoing a radiological/surgical procedure and in whom the medicine was temporarily discontinued for any reason.
- Studies had to report a measure of kidney function and include a comparator group consisting of placebo, no treatment or usual care.
- The medicines of interest were diuretics, ACEI, ARBs, direct rennin inhibitors, NSAIDs, metformin or sulphonylurea drugs.

Identified studies:

- Six eligible studies were identified, which had a combined population of 1663 adults. Where reported, the mean age of participants in these studies ranged from 65 to 73 years and the proportion of women ranged from 31% to 52%. Three were randomised controlled studies and three were prospective cohort studies.
- All studies were carried out within hospital settings. No studies evaluated the discontinuation of medication in the community following an acute illness.
- Of the six studies, five evaluated the discontinuation of medication prior to coronary angiography and one prior to cardiac surgery. All but one study restricted inclusion to patients deemed at high risk of AKI (e.g. who had chronic kidney disease, diabetes or other criteria that defined a patient as at high risk).
- Five studies evaluated the discontinuation of ACEI or ARBs; one study evaluated NSAIDs. However the NSAID study had only a very small number of patients discontinuing the medications and it was not possible to draw conclusions with regards to discontinuing NSAIDs.
- Definitions of AKI varied across the identified studies, with the currently accepted AKI definition used in only one study. Four studies may have used a definition that could overestimate AKI incidence.
- The likelihood of publication bias in this therapeutic area was considered to be high.

Meta-analysis:

- The primary outcome for the meta-analysis of eligible studies was the incidence of AKI. Secondary outcomes included urinary biomarkers, clinical outcomes, creatinine, eGFR, urea and blood pressure.
- Based on the five studies that provided numerical data on patient outcomes, there was an increased risk of AKI of around 15% in those patients in whom ACEI or ARBs were continued compared with those in whom they were discontinued ([relative risk \[RR\]](#) 1.17, 95% [Confidence Interval \[CI\]](#): 0.99 to 1.38).
- When the results from randomised controlled trials only (three studies) were pooled, the increase in risk was almost 50% (RR 1.48, 95% CI: 0.84 to 2.60), but the CIs were wider.
- For secondary outcomes, there was no difference between the groups.

Level of evidence:

Level 2 (limited quality patient-orientated evidence) according to the SORT criteria.

Study funding:

National Institute for Health Research (NIHR)