



The NHS campaign to improve the care of people at risk of, or with, acute kidney injury
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“Sick day rules” in patients at risk of Acute Kidney Injury: an Interim Position Statement from the Think Kidneys Board

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As health professionals one of our key aims is to reduce the risk of avoidable harm to our patients. Some people are at increased risk of Acute Kidney Injury (AKI), for example those with Chronic Kidney Disease (CKD), heart failure, or those taking particular medications (1). Many health care professionals provide advice to such patients that certain drugs should be temporarily discontinued during acute intercurrent illnesses, particularly where there is disturbed fluid balance. This advice is commonly described as ‘sick day rules’ or to take a ‘drug holiday’.

This Interim Position Statement refers to such advice given to patients when they are well, about how to manage their own medication should they become unwell. It does not relate to clinical management of known or suspected AKI by health care professionals.

The definition of ‘acute illness’ in this context has to be simple enough to be understood by patients at risk. The NHS Highland definition (2) is a good example:

‘when you are unwell with any of the following;

- vomiting or diarrhoea (unless minor)
- fevers, sweats and shaking’

There are three main reasons for providing such advice:

1. Non-steroidal anti-inflammatory drugs impair renal autoregulation by inhibiting prostaglandin-mediated vasodilatation of the afferent arteriole and may increase the risk of AKI.
2. Drugs that lower blood pressure, or cause volume contraction, might increase the risk of AKI by reducing glomerular perfusion. These drugs include:
 - a. ACE inhibitors (ACEI) and Angiotensin Receptor Blockers (ARBs), which reduce systemic blood pressure and also cause vasodilatation of the efferent arteriole. This impairs renal autoregulation and reduces glomerular perfusion pressure.



- b. Diuretics, which can exacerbate hypovolaemia and electrolyte disturbance. This group also includes the mineralocorticoid receptor antagonists spironolactone and eplerenone, used frequently in heart failure.
 - c. Other blood-pressure-lowering drugs, which will lower systemic blood pressure.
3. Drugs might accumulate as a result of reduced kidney function in AKI, increasing the risks of adverse effects.

These drugs include:

- a. Metformin which is associated with an increased risk of lactic acidosis in high risk patients.
- b. Sulfonylurea drugs which may have an increased risk of hypoglycaemia, as the drug is renally cleared.
- c. Trimethoprim, which increases the risk of hyperkalaemia. This drug also interferes with tubular creatinine secretion, and therefore causes a rise in creatinine levels and may result in a 'false positive' diagnosis of AKI.

Although there is strong professional consensus that advice on sick day rules should be given, and this approach is advocated in the NICE AKI guideline (3), the evidence that provision of such advice reduces net harm is very weak. The major evidence comes from observational studies and case series that demonstrate an association between receipt of ACEI, ARBs and NSAIDs, and a risk of AKI during acute illness (4, 5, 6). However, these studies may be confounded by indication. For example patients receive ACEIs or ARBs because they have a pre-existing condition - for example, heart failure with a poor cardiac output - that is independently associated with an increased risk of AKI.

It is possible that there are potential harms associated with widespread provision of 'sick day rules,' particularly when the patients have not been clinically assessed and where it is unclear at what level of ill health the medication should be discontinued. These include:

1. Decompensated heart failure when drugs blocking the RAAS system and diuretics are discontinued.
2. Development of poorly controlled hypertension with cessation of antihypertensive medication.
3. Reduced adherence to drug treatment which may have been incorrectly described as 'nephrotoxic'. Patients may consider that the potential harm outweighs the potential benefit and decide to stop taking the drug despite the absence of an acute illness.
4. Patients may over-interpret the advice and stop their drug treatment during even minor illnesses.
5. Patients may not re-start their drug treatment on recovery.
6. The drugs may not be titrated back to the previous evidence based levels even when there has been no evidence of AKI.
7. People may self-manage inappropriately and not seek professional help at an appropriate stage.
8. Issues related to removing medication from dosette boxes, requesting new dosette boxes and up titrating medication in dosette boxes.
9. Diabetes control may be adversely affected by inappropriate cessation of glucose lowering treatment.

It is also a theoretical possibility that ACEI and ARB treatment might **reduce** the severity or duration of AKI, at least in a subset of patients. These drugs, by causing efferent arteriolar vasodilatation, increase blood flow to the renal tubules: and it is tubular injury that causes persistent AKI and the increased risk of subsequent chronic kidney disease.

A systematic review of the published evidence on this topic is under way. This position statement is provided as a temporary measure until that review is completed. It has been agreed by specialists in kidney medicine and also by representatives from primary care. Aligned with NICE Quality Standard 76, the NHS England Think Kidneys Programme Board recommend that health professionals communicate risk of AKI with patients and carers (1). This should include discussion about possible causes including the need to maintain fluid balance during episodes of acute illness. In terms of medicines management, advice from the Think Kidneys Programme Board is that it is reasonable for clinicians to provide “sick day rules” guidance on temporary cessation of medicines to patients deemed at high risk of AKI based on an individual risk assessment. However, we consider that investment in a systematic approach to increase uptake of ‘sick day rules’ by patients should only be undertaken in the context of a formal evaluation.

We welcome comment and debate on this issue, and contact with those people who have already rolled out local programmes, or who have evidence on the implementation and effectiveness of this approach to add to the review.

Please respond to thinkkidneys@renalregistry.nhs.uk

1. Acute Kidney Injury: NICE Quality Standard 76: <http://www.nice.org.uk/guidance/qs76>
2. NICE NHS Highland interim report.
<http://www.knowledge.scot.nhs.uk/media/CLT/ResourceUploads/4061736/NHSH%20updated%20evaluation%20medicine%20sick%20day%20rules%20April%202015.pdf>
3. NICE CG169: Prevention, detection and management of acute kidney injury up to the point of renal replacement therapy. <http://www.nice.org.uk/guidance/cg169>
4. Lobo K.K. & Shenfield G.M.(2011). Drug combinations and impaired renal function- the triple whammy. Br J Pharmacol, 59.2, 239-243
5. Plataki, M,et al (2011). Predictors of Acute Kidney Injury in Septic Shock Patients: An observational Cohort Study. Clin J Am Soc Nephrol 6: 1744-1751
6. Adhyanan, V., Asghar, M., Oke, A. and Shah, I.U. (2001) Nephrotoxicity in the elderly due to co-prescription of angiotensin converting enzyme inhibitors and nonsteroidal anti-inflammatory drugs. J R Soc Med, 94: 512-514