The NHS campaign to improve the care of people at risk of, or with, acute kidney injury
www.thinkkidneys.nhs.uk

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Think Kidneys no longer wishes to use the term 'sick day rules' but will instead henceforth use the term 'sick day guidance'. The reason for this change is described in the update at the end of the position statement.

"Sick day" guidance 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 or guidance 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 guidance 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 – i.e. 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 or guidance, 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 dossette boxes, requesting new dossette boxes and up titrating medication in dossette 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 guidance 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. Loboz 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. Adhiyaman, 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

Update to the Position Statement on Sick Day Guidance – November 2015

The authors have reviewed the statement in response to recent evidence and comments and would like to thank those professionals who have contacted the Think Kidneys Programme offering opinions on the Statement.

Both the Think Kidneys team team and some of those who have commented, believe that the term 'Sick Day Rules' may be unhelpful since it suggests a dogmatic approach to management instead of providing individualised advice. We suggest that 'Sick Day Guidance' may be a more helpful term. In addition, there remains the need to characterise Sick Day Guidance, defining the target audience and how it is operationalised.

Although a time series analysis from NHS Highland appears to show a reduction in AKI at around the time of systematic roll-out of 'sick day rules', the fall in heart failure admissions at around the same time raises the possibility of a secular trend or data problem leading to both: it is difficult to explain how advice on temporary withdrawal of ACEIs and ARBs during intercurrent illness would cause a fall in heart failure admissions.

A literature review is at present being undertaken to assess the effectiveness of advice given to patients on the reduction of risk of AKI and this will be reported early in 2016.

At present it is recommended that professionals offer advice to individuals considered to be at higher risk of AKI should they become unwell and that the advice should include fluid and medicines management. It should also include advice about assessment of illness severity and when to seek professional help.

It is considered that all antihypertensive medication may increase the risk of AKI. The relative risk of blood pressure therapies is still uncertain and it may be unhelpful to single out ACEi and ARB. We would also encourage people to avoid using the term 'nephrotoxic' to describe them.

The Think Kidneys team will review their Interim Position Statement on sick day guidance again once we have the results of the full literature review.

Please continue to offer your opinions to help us to develop sick day guidance.

Please respond to thinkkidneys@renalregistry.nhs.uk