PrescQIPP Community Interest Company

Acute Kidney Injury (AKI) – Sick Day Guidance

Acute Kidney Injury or AKI is defined as a sudden decline in kidney function.[1] The rates of AKI in the UK are similar across different regions and time periods: approximately 150 events per 10,000 people per annum (1.5% of the population).[2] AKI is seen in 13 - 18% of all people admitted to hospital, with older adults being particularly affected.[3]

Acute kidney injury is associated with an increased risk of death, length of hospital stay, risk of chronic kidney disease (CKD) and cost to the NHS.[1]

Particular prescribed medicines have the potential to impair renal function under certain circumstances. Most cases of AKI occur in conjunction with co-existing acute illness and are a result of infection, hypovolaemia, hypotension or medication effects.[1,4]

Costs to the NHS related to AKI are between £434 million and £620 million per year.[3] Prevention or amelioration of just 20% of cases of AKI would prevent a large number of deaths and substantially reduce complications and their associated costs.[3]

This bulletin provides information on offering individualised sick day guidance to patients when they are well, so that they are able to proactively manage medication known to impair renal function during a period of acute illness and reduce the risk of AKI. This bulletin also provides support material for organisations considering a review of this topic.

Recommendations

- For patients taking medication known to increase the risk of AKI or medication that can accumulate as a result of reduced renal function in AKI, ensure that the risk of AKI has been communicated with patients and carers. This should include a discussion about the possible causes, including the need to maintain fluid balance during episodes of acute illness.
- Provide sick day guidance about temporary cessation of medicines during periods of acute illness, to patients deemed at high risk of AKI, based on an individual risk assessment.
- All advice should be tailored to the individual patient.

National Guidance

NICE guideline 148 on AKI prevention, detection and management advises to consider temporarily stopping angiotensin converting enzyme (ACE) inhibitors and angiotensin receptor blockers (ARBs) in adults, children and young people suffering with diarrhoea, vomiting or sepsis until their clinical condition has improved and stabilised.[3]

Further to this, NHS Scotland and the Scottish Patient Safety Programme produced a 'Medicine Sick Day Rules' card that lists medicines that should be temporarily stopped during illness that can result in dehydration (vomiting, diarrhoea and fever).[5] These medicines generally include ACE inhibitors, ARBs, diuretics, metformin, NSAIDs with the provision to select those medicines that are appropriate and add others if required.[5] Electronic versions of the Medicine Sick Day Rules card and leaflets for patients and professionals can be found at: https://ihub.scot/improvement-programmes/scottish-patient-safety-programme-spsp/spsp-medicines-collaborative/high-risk-situations-involving-medicines/medicines-sick-day-rules-card/

The individual risk-benefit profile of temporarily discontinuing certain medication during periods of acute illness needs to be carefully weighed up for each patient. Other groups of medicines that warrant consideration include other blood pressure lowering drugs, some sulfonylurea drugs which can accumulate and increase the risk of hypoglycaemia and trimethoprim and aminoglycoside antibiotics.[4,6]

'Think Kidneys' is a national awareness raising campaign supported by NHS England and the UK Renal Registry. They have produced a number of resources to support healthcare professionals, including 'Guidelines for Medicines Optimisation in Patients with Acute Kidney Injury'[4] and a position statement relating to guidance given to patients when they are well, about how to manage their own medication should they become unwell.[6]

Current recommendations are that "the NHS England Think Kidneys Programme Board recommends that healthcare professionals communicate the risk of AKI with patients and carers. This should include discussion about possible causes of AKI 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 guidance on temporary cessation of medicines to patients deemed at high risk of AKI based on an individual risk assessment".[6]

Evidence

The NHS England Think Kidneys Programme Board have highlighted that the current evidence that the provision of sick day guidance reduced net harm is weak. At present, the major evidence base comes from observational studies and case series with limitations.[6] A systematic review and meta analysis showed that there is no evidence of the impact of drug cessation interventions on AKI incidence during intercurrent illness in primary or secondary care and there is low-quality evidence that withdrawal of ACEI/ARBs prior to coronary angiography and cardiac surgery may reduce the incidence of AKI.[7]

Consequently, the current advice surrounding the management of medicines during episodes of acute illness is that an individual risk assessment should be undertaken to determine whether a patient is at high risk of AKI and sick day guidance on the temporary cessation of medicines should be targeted at those patients.[6]

Medication known to cause or exacerbate AKI during periods of acute illness are included below with additional explanation of the potential problems that can arise:[6]

- Non-steroidal anti-inflammatory drugs (NSAIDs) impair renal autoregulation by inhibiting prostaglandin-mediated vasodilatation of the afferent arteriole and may increase the risk of AKI.
- Drugs that lower blood pressure, or cause volume contraction, might increase the risk of AKI by reducing glomerular perfusion. ACE inhibitors and ARBs reduce systemic blood pressure and also cause vasodilatation of the efferent arteriole, further reducing glomerular perfusion pressure. Diuretics (including the mineralocorticoid receptor antagonists spironolactone and eplerenone) can cause a reduction in GFR if their use results in hypovolaemia. Other blood-pressure-lowering drugs can increase the risk of AKI by lowering systemic blood pressure.
- Metformin can accumulate, which may be associated with an increased risk of type A lactic acidosis in high risk patients.
- Some sulfonylurea drugs can also accumulate, which can increase the risk of hypoglycaemia.
- Trimethoprim increases the risk of hyperkalaemia and also interferes with tubular creatinine secretion. Therefore, it causes a rise in creatinine levels and may result in a 'false positive' diagnosis of AKI.

Safety

There are concerns around the 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.[6]

These include:[6]

1. Decompensated heart failure when drugs blocking the renin-angiotensin-aldosterone system (RAAS) and diuretics are discontinued.
2. AKI caused by right-sided congestion complicating withdrawal of diuretics, particularly in right-sided heart failure.
3. Development of poorly controlled hypertension with cessation of antihypertensive medication.
4. 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 permanently, even in the absence of, or after recovery from, an acute illness.
5. Patients may over-interpret the advice and stop their drug treatment during even minor illnesses.
6. Patients may not re-start their drug treatment on recovery.
7. The drugs may not be titrated back to the previous evidence-based levels even when there has been no evidence of AKI.
8. People may self-manage inappropriately and not seek professional help at an appropriate stage.
9. Making changes to regular medication in patients reliant on monitored dosage systems (e.g. dosette boxes) is complex and can have unintended consequences.
10. Diabetes control may be adversely affected by inappropriate cessation of glucose lowering treatment.

It is also a theoretical possibility that ACEi and ARB treatments 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.[6]

The concept of temporary cessation is not always a straightforward concept to communicate, particularly with patients deemed at higher risk of AKI and with less capacity to self-manage.[6]

Patient factors

It is important that the above safety factors are accounted for when determining the risk of AKI versus the risk of temporary treatment cessation during periods of acute illness and weighing up the individualised advice for patients.

Individual risks factors for AKI during periods of acute illness include:[3]

- Chronic kidney disease - adults with an estimated glomerular filtration rate (eGFR) less than 60ml/min/1.73m^2 are at particular risk
- Heart failure
- Liver disease
- Diabetes
- History of AKI
- Oliguria (urine output less than 0.5ml/kg/hour)
- Young age, neurological or cognitive impairment or disability, which may mean limited access to fluids because of reliance on a carer
- Hypovolaemia

- Use of drugs with nephrotoxic potential such as NSAIDs, aminoglycosides, ACE inhibitors, ARBs and diuretics within the past week, especially if hypovolaemic
- Use of iodinated contrast agents within the past week
- Symptoms or history of urological obstruction, or conditions that may lead to obstruction
- Sepsis
- Deteriorating early warning scores
- Age 65 years or over
- Severe diarrhoea (children and young people with bloody diarrhoea are at particular risk)
- Symptoms or signs of nephritis (such as oedema or haematuria)
- Haematological malignancy
- Hypotension

Environmental temperatures can also have an effect on hydration status and subsequent risk of AKI, particularly for vulnerable patients and those with other risk factors.[8] Heatwaves, with average temperatures of around 30°C by day and 15°C overnight can have a significant effect on people's health if they last for at least two days and the night in between.[8] It is important to encourage at risk patients to maintain adequate fluid balance during heatwaves, as well as periods of acute illness, and to be aware of the increased risk of urinary tract infection (UTI) that may also be associated with dehydration.

Medicine Sick Day Guidance

Medicine sick day guidance is provided to patients (or their carers) proactively when they are well, to provide advice on managing their medicines during periods of acute illness that may cause dehydration and increase the risk of acute kidney injury.

In this context, acute illness is defined as vomiting, diarrhoea or fever. Medicines should be stopped during this time, with the exception of minor sickness and diarrhoea (i.e. just a single episode).

Medicine sick day guidance should be provided to patients deemed to be at high risk of AKI after individualised risk assessment.

NICE considers patients with acute illness to be at risk of AKI if they have used drugs that can cause or exacerbate kidney injury, such as NSAIDs, aminoglycosides, ACE inhibitors, ARBs and diuretics, within the past week, especially if they are hypovolaemic.[3]

Common medicines to consider proactively advising patients to withhold on sick days include:[3,6]

- Diuretics
- ACE inhibitors (or 'prils')
- ARBs (or 'sartans')
- Metformin
- NSAIDs (prescribed and purchased over the counter, but not including low dose aspirin*)

*Low dose aspirin can be safely continued in patients with AKI.[9]

Additional consideration should be given to patients taking a combination of these medicines.

Generally, medicines that have been temporarily ceased during a period of acute illness should be restarted 24 to 48 hours after the patient is well and eating and drinking normally again.[5]

The individual risks versus benefits of stopping medicines during a period of acute illness should be evaluated for each patient.[6]

Identification of patients at risk

Diuretics, ACE inhibitors, ARBs, Metformin and NSAIDs are referred to as DAMN medicines in the NHSBSA polypharmacy dashboard.[10] Patients prescribed two or more DAMN medicines can be identified using the NHSBSA dashboard on Polypharmacy Prescribing Comparators. The following eight indicators are available:

- % patients prescribed two or more unique medicines likely to cause kidney injury (DAMN medicines)
- % patients prescribed two or more unique medicines likely to cause kidney injury (DAMN medicines) aged 65 and over
- % patients prescribed two or more unique medicines likely to cause kidney injury (DAMN medicines) aged 75 and over
- % patients prescribed two or more unique medicines likely to cause kidney injury (DAMN medicines) aged 85 and over
- % patients prescribed a NSAID and one or more unique medicines likely to cause kidney injury (DAMN medicines)
- % patients prescribed a NSAID and one or more unique medicines likely to cause kidney injury (DAMN medicines) aged 65 and over
- % patients prescribed a NSAID and one or more unique medicines likely to cause kidney injury (DAMN medicines) aged 75 and over
- % patients prescribed a NSAID and one or more unique medicines likely to cause kidney injury (DAMN medicines) aged 85 and over

These indicators allow for identification of the number of patients prescribed medicines that may put them at a higher risk of community acquired acute kidney injury if they develop an illness associated with hypovolaemia or hypotension. Prescribers are reminded that whilst this comparator focuses on two or more DAMN medicines it is important to emphasise that a single DAMN medicine may be a problem in some patients.[11]

Reviewing the indicators allows practices and CCGs to:[11]

- See the variation across practices within a CCG and across CCGs
- Identify whether this is an area to be investigated or to demonstrate the impact of initiatives addressing this topic
- Raise awareness amongst prescribers of the problems associated with certain medicines that increase risk of AKI

The PrescQIPP AKI GP clinical system searches may be used to search for patients at high risk of AKI.

The PrescQIPP AKI sick day audit may be used to audit patients identified in the PrescQIPP AKI searches prescribed diuretics, ACE inhibitors, ARBs, metformin, NSAIDs (excluding low dose aspirin) and injectable or nebulised gentamicin to determine whether individualised medicine sick day guidance is appropriate to reduce the risk of acute kidney injury (AKI) (Attachment 1).

Summary

Particular prescribed medicines have the potential to impair renal function under certain circumstances. Most cases of acute kidney injury (AKI) occur in conjunction with co-existing acute illness and are a result of infection, hypovolaemia, hypotension or medication effects.[1,4] Medicine sick day guidance can be provided to patients (or their carers) proactively when they are well, to provide advice on stopping medicines such as ACE inhibitors, ARBs, diuretics, metformin, aminoglycosides and NSAIDs (prescribed and purchased over the counter, but not including low dose aspirin) during periods of acute illness that may cause dehydration, with the aim of reducing the risk of AKI.[3,5] Individualised advice should be considered for patients deemed to be at high risk of AKI, after undertaking an individual risk assessment.[6] The need to maintain adequate fluid balance during periods of acute illness, extreme temperatures and other situations that may result in dehydration should be emphasised for all at risk patients.[6,8]

Additional Resources

Acute kidney injury (AKI): use of medicines in people with or at increased risk of AKI. Key Therapeutic Topic (KTT17). Published date: February 2016. Last updated September 2019. https://www.nice.org.uk/advice/ktt17/chapter/Key-points Last accessed 07/02/20.

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Briefing	https://www.prescqipp.info/our-resources/bulletins/bulletin-260-acute-kidney-injury-aki-sick-day-guidance/
Implementation tools	

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