Management of acute kidney injury depends on the underlying cause and whether the condition is the result of pre-renal, intrinsic or post-renal dysfunction. All patients should have their medicines reviewed.

Acute kidney injury management

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There is no specific drug therapy for the treatment of acute kidney injury (AKI). Ideally, the condition should have been prevented but, once it has developed, management involves identifying and treating potential causes and optimising medicine choice and dosing.

Because any patient can develop AKI the condition is often managed outside the specialist setting. Therefore, the wider pharmacy team will be able to have input into the management of AKI.

Identifying and treating the cause

AKI is the result of underlying pathology, which should be identified and corrected so that renal function can recover. For example, sepsis causes a reduction in circulating blood volume, increasing the risk of AKI. In this case, treating the sepsis is essential for managing the AKI.

Management will also depend on the type of AKI. For patients with pre-renal AKI (including acute tubular necrosis) circulating blood volume should be restored and blood pressure managed (see Box 1, p104).

Patients thought to have intrinsic AKI should be referred to a nephrologist for investigation and management.

Post-renal AKI is diagnosed on ultrasound and patients suffering from the condition are often referred to a urologist for urgent treatment of urinary tract obstruction. This can include catheterisation or nephrostomy.

Medication review

All patients with AKI should have their medicines reviewed, including those that are used to treat comorbidities. The review should involve:
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Box 1: Managing fluid balance for patients with AKI

Acute kidney injury (AKI) is usually pre-renal in cause, which will respond to fluid administration. The use of intravenous fluids must take into account the need to balance fluid replacement with the risk of fluid overload (see Clinical Pharmacist 2011;3:274).

It is important to administer fluids to patients with dehydration and hypovolaemia. If a patient is dehydrated then fluid should be replaced slowly because excessive administration of fluid is associated with increased mortality. However, rapid and repeated administration of small volumes (250ml) of crystalloid or colloid should be given to patients who are hypotensive or in shock. Care should be taken when prescribing potassium-containing fluids because hyperkalaemia is often a complication of AKI.

No specific pharmacological therapy has been proven effectively to treat AKI caused by hypoperfusion.1 The routine use of loop diuretics to drive urine output is not advocated and high-dose therapy is associated with an increased risk of ototoxicity. Dopamine is not beneficial in AKI and its use is associated with side effects such as cardiac arrhythmias.2 Administration of fluid also assists in the management of hypotension and should be used to increase systolic blood pressure to above 110mmHg. For these patients, antihypertensive medication should also be reviewed. If these measures are ineffective, treatment with vasopressors or inotropes may be required — this treatment should occur in a high-dependency or intensive care unit.

Some patients with AKI will present with fluid overload. This occurs if a patient’s kidneys are unable to excrete sodium and water effectively. In this scenario fluid resuscitation is inappropriate and, instead, loop diuretics are given, often in high doses. Oral furosemide or bumetanide can be effective but, because gut oedema can reduce absorption of loop diuretics, intravenous therapy is often used first line. If a trial of high-dose diuretic does not induce diuresis it should be discontinued — this indicates that the kidneys are incapable of producing urine and further diuretic use will lead to toxicity.

Avoiding the need for renal replacement therapy is an aim of AKI management

- Temporarily or permanently withdrawing medicines that affect kidney haemodynamics
- Stopping nephrotoxic medicines that could have caused the AKI and ensuring that other nephrotoxic treatments are not started
- Reviewing the side effect profile of all medicines
- Ensuring a medicine, and its dose, is appropriate for use by patients with reduced renal function

Pharmacists should remember than some medicines can be nephrotoxic in some situations but be renoprotective in others; for example, the active metabolite of allopurinol can accumulate in renal impairment, but the drug can also be used prophylactically (with adequate fluid intake) to reduce the risk of chemotherapy-induced renal obstruction.

Medicines affecting renal haemodynamics Some medicines (see Box 2, p105) can exacerbate hypoperfusion of the kidneys and so should be withheld in patients with AKI until their condition has stabilised.

Nephrotoxic medicines For all patients with AKI, pharmacists should check for medicines that could have caused the condition. The causative medicine can often be identified by exploring a patient’s medication history, paying particular attention to what medicines have been started or stopped recently (although AKI can develop after short- or long-term use of certain medicines). Non-essential medicines can be discontinued until the cause of a patient’s AKI has been identified.

Acute tubular necrosis, the most common manifestation of drug-induced AKI, can occur with normal doses of particular medicines but more often results from high-dose treatment or accumulation of a drug due to pre-existing renal impairment.1 Risk factors include:

- Dose and formulation
- Impaired baseline renal function
- Concurrent diuretic use
- Dehydration

For example, amphotericin can cause acute tubular necrosis, but the risk of nephrotoxicity can be minimised by administering fluids concomitantly and using the liposomal preparation.

Acute interstitial nephritis is a hypersensitivity reaction that can cause AKI hours, days or months after starting a medicine. Patients with drug-induced acute interstitial nephritis can present without the classic
Drug doses

AKI can affect drug pharmacokinetics — the most significant of these changes is reduction in the excretion of renally cleared drugs and their metabolites. Accordingly, pharmacists should review the use and doses of all medicines when a patient has an acute deterioration in renal function. For example, gabapentin and pregabalin are entirely renally cleared and can accumulate when renal function declines.

The duration of action of some drugs will be increased in AKI, such as renally cleared opioid analgesics (eg, morphine). Modified-release preparations of these drugs should be avoided.

Box 3: Medicines to monitor and avoid in AKI

The UK Renal Pharmacy Group has developed a medication optimisation toolkit (soon to be published) to help pharmacists and other healthcare professionals review the medicines of patients with acute kidney injury (AKI). The toolkit recommends the following medicines should be stopped or avoided for patients with AKI:

- Angiotensin-converting enzyme inhibitors and angiotensin-II receptor blockers
- Non-steroidal anti-inflammatory drugs
- Cyclo-oxygenase-2 inhibitors
- Metformin
- Anticoagulants
- Anticonvulsants (eg, phenytoin, gabapentin)
- Antivirals (eg, aciclovir, ganciclovir)
- Digoxin
- Immunosuppressants (eg, cyclosporin)
- Disease-modifying antirheumatic drugs (eg, methotrexate)

The toolkit also lists “red flag” drugs — those that require dose adjustment or additional monitoring, or that may need to be withheld temporarily for patients with AKI. Examples of such medicines are:

- Aminoglycosides
- Anticoagulants
- Anticonvulsants (eg, phenytoin, gabapentin)
- Antivirals (eg, aciclovir, ganciclovir)
- Digoxin
- Immunosuppressants (eg, cyclosporin)
- Hypoglycaemic medicines

Drug distribution can change in AKI. One reason for this is the accumulation of urea, which can bind competitively to albumin. This increases the free concentration of highly protein-bound drugs such as phenytoin and warfarin. Another change is in the distribution of water-soluble drugs for patients with fluid retention (eg, the volume of distribution of aminoglycoside antibiotics is increased in such patients).

The modification of diet in renal disease (MDRD) and Cockcroft and Gault formulae can be used to estimate renal function, and outputs from these equations are often used to recommend drug doses for patients with CKD. However, it should be borne in mind that in AKI using these formulae can be unreliable because serum creatinine levels can change rapidly. Pharmacists should be recalculating renal function daily if using these equations to guide drug dosing (for more practice points for pharmacists see Box 4, p106).

Rather than dose-adjusting, in certain circumstances it may be possible to avoid a particular medicine altogether and switch to an alternative. For example, aminoglycosides are the cause of half of all cases of drug-induced AKI in hospitals and alternative antibiotics should be used if possible for patients with, or at risk of, AKI. If aminoglycosides are required, once-daily dosing is believed to cause less nephrotoxicity than traditional multiple-daily dosing (due to reduced tissue accumulation). Drug levels and renal function should be monitored during therapy and the dose interval may need to be increased further, or the dose reduced, depending on the results.

Development and distribution of trust guidance on the use of particular medicines in renal dysfunction can help
Renal function can recover quickly (eg, in cases of dehydration where fluids are given to correct the cause of AKI), which can result in clinically significant underdosing of some medicines. For example, patients with sepsis whose antibiotic doses were reduced during AKI could have subtherapeutic antibiotic blood levels once renal function recovers. Medicines review is critical for all patients with acute kidney injury (AKI). Pharmacists can:

- Help to identify potential drug causes of AKI
- Ensure medicines are appropriately withheld or stopped and suggest suitable alternatives
- Advise on the use of fluids, if required to manage AKI
- Provide recommendations around fluid restriction and minimum infusion volumes for drugs used in fluid-overloaded patients
- Advise prescribers about drug dosing in AKI
- Counsel patients regarding medication changes

Promote appropriate prescribing for patients with AKI. The UK Renal Pharmacy Group’s AKI working group recommends that such guidance should include recommendations for the use of analgesics, anti-infectives, contrast agents, immunosuppressants, low molecular weight heparins and oral bowel cleansing preparations. Box 3 (p105) lists some medicines that should be reviewed for patients with AKI. Electronic prescribing systems can help to disseminate such guidance.1  

As AKI resolves, medicine doses should be reviewed. Renal function can recover quickly (eg, in cases of dehydration where fluids are given to correct the cause of AKI), which can result in clinically significant underdosing of some medicines. For example, patients with sepsis whose antibiotic doses were reduced during AKI could have subtherapeutic antibiotic blood levels once renal function recovers.

Sharing information

Patients should receive education to ensure that they understand any changes to their medication before they are discharged. Patients should be given information about any medicines that should be avoided in future. Pharmacists should also advise patients at risk of AKI who are receiving ACE inhibitors, ARBs, diuretics or non-steroidal anti-inflammatory drugs to seek medical advice if they become acutely unwell or think they might be dehydrated.

To ensure that GPs are well informed, discharge prescriptions should include information about changes to medication, medicines to be restarted after discharge (and when this should occur) and the counselling provided.

Managing complications

Renal replacement therapy (RRT) may be required to support the kidneys to function until they recover from AKI. Patients who require RRT will be managed in a specialist renal or intensive care unit where renal or critical care pharmacists can provide advice relating to drug use.

RRT can also be used to remove potassium in patients with AKI and hyperkalaemia (this can be a factor that influences a clinician’s decision to start RRT). Other strategies for management of hyperkalaemia include administration of calcium gluconate, insulin plus dextrose infusions, or salbutamol.

Patients with AKI can develop metabolic acidosis because their kidneys are unable to secrete acid or produce bicarbonate, ammonia and other buffers. Oral or intravenous sodium bicarbonate 1.26% or 1.4% may be administered to correct the acidosis.

Monitoring

Electrolytes, urea and creatinine should be measured daily, paying particular attention to creatinine and potassium. For patients with suspected pre-renal AKI in whom renal function does not improve despite fluid challenge and correction of hypotension, consider referral to a nephrologist so that the possibility of an underlying intrinsic cause of AKI can be investigated.

Venous bicarbonate or arterial blood gases should be measured for signs of metabolic acidosis. Symptoms of the underlying medical condition causing AKI should be recorded (eg, temperature, full blood count, C-reactive protein, stool chart).

A patient’s fluid balance charts and daily weights and urine output should be monitored to ensure that fluids are administered appropriately and that he or she is not becoming overloaded (outside intensive care, daily weights should be used to track changes in hydration status, rather than relying on fluid charts). Pharmacists should consider fluid administration associated with drug therapy and be able to recommend suitable concentrations if fluid needs to be restricted. Regular blood pressure monitoring is essential.

References


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