

Guidelines for Medicines Optimisation in Patients with Acute Kidney Injury

Drug	Effects on renal/fluid/electrolyte physiology	Change in the side effect profile when renal function is reduced	Direct action on the kidneys	Action in presence of AKI
Analgesics				
NSAIDs / COX II inhibitors	Altered haemodynamics within the kidney leading to underperfusion and reduced glomerular filtration		Acute interstitial nephritis (rare)	Avoid
Opioid analgesics		Accumulation of active metabolites (especially morphine, pethidine and codeine) – increased incidence of CNS side effects & respiratory depression		Avoid XL / SR preparations. Reduce dose and use short acting preparations wherever possible. Use opiates with minimal renal excretion e.g. fentanyl, oxycodone, hydromorphone
Tramadol		May accumulate leading to increased sedation, mental confusion and respiratory depression		Reduce dose Avoid XL preparations
Benzodiazepines		Accumulation of drug & active metabolites leading to increased sedation & mental confusion		Reduce dose & monitor for excessive sedation
Antibiotics / Antifungals / Antivirals				
Aciclovir		Accumulation leading to mental confusion, seizures.	Crystal nephropathy.	Reduce dose Beware if patient is at risk of dehydration - Encourage patient to drink plenty

Drug	Effects on renal/fluid/electrolyte physiology	Change in the side effect profile when renal function is reduced	Direct action on the kidneys	Action in presence of AKI
Aminoglycosides		Ototoxicity	Tubular cell toxicity	Avoid if possible. If use is unavoidable, reduce dose &/or increase dosing interval Monitor drug levels and renal function 2 – 3 times per week
Amphotericin IV – Fungizone®	Hypokalaemia		Tubular cell toxicity	Avoid rapid infusion Consider Ambisome® preparation
Co-trimoxazole	Hyperkalaemia		Crystal nephropathy	Reduce dose. Beware if patient is at risk of dehydration - Encourage patient to drink plenty
Fluconazole		Accumulation leading to acute mental confusion, coma, seizures		Reduce dose. Check for drug interactions that may be contributing to AKI, eg. consider withholding statins due to risk of rhabdomyolysis
Ganciclovir IV		Accumulation leading to neutropenia, anaemia and thrombocytopenia	Crystal nephropathy	Reduce dose Monitor renal function and full blood count Avoid rapid infusions
Penicillins		Accumulation leading to CNS side effects including seizures	Acute interstitial nephritis (rare) Glomerulonephritis	Reduce dose
Teicoplanin		Accumulation leading to CNS excitation, seizures, & blood dyscrasias		Reduce dose Monitor levels

Drug	Effects on renal/fluid/electrolyte physiology	Change in the side effect profile when renal function is reduced	Direct action on the kidneys	Action in presence of AKI
Tetracycline		Accumulation leading to renal dysfunction, benign cranial hypertension, jaundice, hepatitis	Acute interstitial nephritis (rare)	Avoid
Trimethoprim	Increased risk of hyperkalaemia. Interferes with tubular secretion of creatinine leading to a rise in serum creatinine (without affecting actual GFR), which can make the diagnosis of AKI more difficult.	Accumulation leading to hyperkalaemia (particularly with high doses), nausea and vomiting	Acute interstitial nephritis (rare)	Avoid or reduce dose (particularly if patient is already taking an ACEI, ARB or spironolactone) Studies have shown that elderly patients prescribed trimethoprim have a 12 x greater risk of developing life-threatening hyperkalaemia if already taking spironolactone, and a 7-fold increased risk of life-threatening hyperkalaemia, and a 1.5 x increased risk of sudden death if already taking an ACEI or ARB.
Valganciclovir		Accumulation leading to neutropenia, anaemia and thrombocytopenia		Reduce dose Monitor renal function and full blood count
Vancomycin		Accumulation leading to renal toxicity, ototoxicity	Acute interstitial nephritis (rare)	Reduce dose/increase dose interval Monitor levels
Antiepileptics (including drugs used for neuropathic pain)				
Phenytoin		Risk of phenytoin toxicity if patient has low serum albumin levels	Acute interstitial nephritis (rare)	Monitor levels Correct phenytoin levels for uraemia and low serum albumin or measure salivary phenytoin (if assay available)

Drug	Effects on renal/fluid/electrolyte physiology	Change in the side effect profile when renal function is reduced	Direct action on the kidneys	Action in presence of AKI
Pregabalin & Gabapentin		Accumulation leading to increase in CNS side effects		Reduce dose
Levetiracetam		Accumulation leading to increase in CNS side effects		Reduce dose
Antihypertensives				
Antihypertensives (including Ca-channel blockers, α -blockers, β -blockers, etc)		Hypotension. May exacerbate renal hypoperfusion		Consider withholding / reduce dose depending on clinical signs Some patients who continue taking β -blockers during an episode of AKI have developed complete heart block and required temporary pacing.
ACEI / ARBs / Aliskiren	Hyperkalaemia		Altered haemodynamics. Can impair the kidneys' ability to maintain GFR when perfusion is compromised.	In some situations, e.g. heart failure with a decent blood pressure, continuing these agents might actually be helpful. If patient is hypertensive, consider alternative antihypertensive agents, eg, calcium channel blockers, thiazide-type diuretics, alfa-blockers, beta-blockers if appropriate

Drug	Effects on renal/fluid/electrolyte physiology	Change in the side effect profile when renal function is reduced	Direct action on the kidneys	Action in presence of AKI
Thiazide & Loop Diuretics	Hypokalaemia, hypocalcaemia, hypomagnesaemia, hyponatraemia, hyperuricaemia (rare)	Tinnitus & deafness (usually with high doses and rapid IV administration),	Overdiuresis leading to hypoperfusion of the kidneys can cause or exacerbate AKI.	Loop diuretics (furosemide & bumetanide) preferred as thiazides less effective if GFR < 25ml/min. However thiazides can potentiate the effects of loop diuretics. Higher doses may be needed to achieve a diuresis in patients with fluid overload. Monitor and adjust dose as necessary
Potassium sparing Diuretics	Hyperkalaemia		Hypoperfusion of the kidneys	Avoid
Hypoglycaemic agents		Accumulation leading to hypoglycaemia		Avoid MR preparations. Monitor blood glucose levels & Reduce dose if necessary
Metformin		Lactic acidosis. Accumulation leading to hypoglycaemia		Avoid if GFR < 30 ml/min Seek nephrologist advice if undergoing contrast procedure or at risk of AKI
Contrast Media			Direct tubular toxic effect. Incidence of CIN higher with high- & isosmolar contrast media, and lower with low-osmolar, non-ionic contrast media	Ensure patient is well hydrated pre-exposure to contrast, PROVIDED the patient is able to tolerate IV fluids. This is NOT recommended for patients with congestive heart failure pre-coronary angiogram. IV sodium chloride or sodium bicarbonate are most effective

Drug	Effects on renal/fluid/electrolyte physiology	Change in the side effect profile when renal function is reduced	Direct action on the kidneys	Action in presence of AKI
Immunosuppressants (DMARDs, chemotherapy)				
Calcineurin inhibitors e.g. ciclosporin, tacrolimus	Increased risk of hyperkalaemia	Increased risk of neurotoxicity	Increased risk of nephrotoxicity	Seek advice of transplant centre regarding monitoring levels and dose adjustment
Methotrexate		Accumulation leading to e.g. excessive bone marrow suppression, mucositis, acute hepatic toxicity, acute interstitial pneumonitis	Crystal nephropathy	Avoid especially if patient at risk of hyperkalaemia Monitor levels and consider folinic acid rescue Correct fluid balance
Others				
Allopurinol		Accumulation of allopurinol and its metabolites leading to agranulocytosis, aplastic anaemia, thrombocytopenia	Acute interstitial nephritis (rare)	Start at a low dose to avoid severe rash, but can then usually safely be titrated up against serum urate
5 – aminosalicylates			Tubular and glomerular damage.	Avoid
Antihistamines, Anti-psychotics, Antispasmodics		Anticholinergic side effects. Urinary retention.	Acute interstitial nephritis (rare)	Reduce dose Avoid XL preparations
Ayurvedic medicines		Some ayurvedic medicines also contain heavy metals	Cases of renal impairment have been reported	Avoid Check drug history thoroughly Patients may not consider herbal preparations / teas as medicines

Drug	Effects on renal/fluid/electrolyte physiology	Change in the side effect profile when renal function is reduced	Direct action on the kidneys	Action in presence of AKI
Bisphosphonates IV			Can cause impaired renal function – especially when given in high doses and short duration infusions	Reduce dose and infuse at correct rate Advantages of correction of severe hypercalcaemia may outweigh risks: seek specialist advice
Colchicine		Diarrhoea / vomiting causing hypovolaemia	Exacerbates hypoperfusion if also taking a NSAID	Low doses e.g. 500mcg bd or tds are effective. Do not use NSAIDs for gout; if Colchicine causes unacceptable adverse effects, consider a short course of corticosteroids
Digoxin	Aggravates hyperkalaemia	May accumulate leading to bradycardia, visual disturbances, mental confusion		Reduce dose Monitor drug level
Herbal preparations		Cat's Claw has anti-inflammatory properties and has been implicated in causing AKI and hypotension with antihypertensives	The toxic effects of herbal remedies to the kidneys may be exacerbated when used with concomitant medicines which can affect kidney function. Chinese herbal medicines with aristocholic acid have been implicated in interstitial nephritis.	Some herbal medicines also interact with prescribed medicines, eg. St. John's Wort potentiates the effects of ciclosporin & tacrolimus. Check drug history thoroughly. Patients may not consider herbal preparations / teas as medicines

Drug	Effects on renal/fluid/electrolyte physiology	Change in the side effect profile when renal function is reduced	Direct action on the kidneys	Action in presence of AKI
Lipid-lowering agents e.g. fibrates, statins		Possible increased risk of rhabdomyolysis		Stop if AKI due to rhabdomyolysis. Otherwise, continue therapy but monitor. Stop if patient develops unexplained / persistent muscle pain
Lithium	Hypernatraemia. AKI exacerbated in hypovolaemia and in combination with ACE inhibitors/ARB/NSAIDs	Accumulation leading to nausea, diarrhoea, blurred vision, fine resting tremor, muscular weakness and drowsiness, increasing confusion, blackouts, fasciculation and increased deep tendon reflexes, myoclonic twitches and jerks, choreoathetoid movements, urinary or faecal incontinence, increasing restlessness followed by stupor.	Chronic interstitial nephropathy (rare)	Avoid where possible Monitor lithium levels Seek advice for alternative Encourage patient to drink plenty. Be aware that patients on long-term lithium nearly always have a degree of diabetes insipidus, and are therefore at serious risk of developing hypernatraemia due to true dehydration when unwell without ready access to adequate water intake. Monitor serum sodium concentration
Nitrates / Nicorandil		Hypotension	May exacerbate hypoperfusion	Consider withholding/reduce dose depending on clinical signs

Drug	Effects on renal/fluid/electrolyte physiology	Change in the side effect profile when renal function is reduced	Direct action on the kidneys	Action in presence of AKI
Anticoagulants				
Low molecular weight heparins		Risk of accumulation leading to increased risk of bleeding		Monitor anti-Xa levels and consider reducing dose or switching to an alternative agent as per local guidelines
Warfarin		INR may be raised due to acute rise in urea and warfarin displacement from binding sites		Monitor INR and consider reducing dose or withholding depending on indication for use

