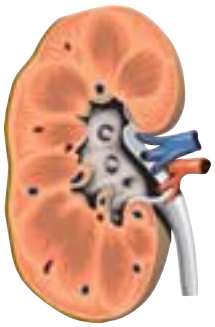
Acute-on-Chronic Renal Failure

:avoidable drug errors and insults



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Many usually well-tolerated medications and procedures pose a threat to the patient with underlying moderate chronic renal failure (CRF) i.e. GFR < 60mls/min. When combined with volume depletion (eg. diuretics) and blockade of renal autoregulation (eg. NSAIDs or renin-angiotensin axis blockade), this can precipitate an episode of hypoperfusion acute-on-CRF - the so-called "triple whammy" drug insult. Direct drug nephrotoxicity is also common. Patients with diabetic nephropathy, vascular diseases or heart failure are at especial risk.

Systematic approach to causes

Most medical cases of acute-on-CRF are due to **pre-renal insults** proceeding to reversible "ischaemic" acute tubular necrosis, and most urological cases are due to **post-renal obstruction** (eg calculi or tumour). Nevertheless, four **renal differential diagnoses** need to be remembered: drug nephrotoxicity, acute interstitial nephritis, acute vascular injury and acute glomerulonephritis (AGN).

Drug nephrotoxicity can be due to direct tubular cell toxicity (aminoglycosides, amphotericin, cidofovir and pamidronate), intratubular crystal deposition (sulfadiazine, acyclovir, uric acid post-chemotherapy, indinavir) or hyperosmotic injury (immunoglobulin, Haemaccel). Non-prescription items (such as aristolochic acid in some Chinese herbs) have caused cases of irreversible renal failure and cancer.

Thankfully, most acute episodes are avoidable with advance knowledge, dose modification and hydration.

The individual hypersensitivity reaction of **interstitial nephritis** can occur with many agents, especially antibiotics (penicillins and sulphurs), NSAIDs and proton pump inhibitors, as well as some viruses or beestings. The onset may be subtle and delayed for up to months, or abrupt with severe loin pain and/or rash.

Acute renal **vascular injury** can occur from vessels outside or inside the kidney. No amount of saline or NAC will prevent the atheroembolic form of post-arteriography renal failure. Consider AGN and urgent referral when the urine sediment shows haematuria and/or proteinuria.

Prevention the key

For example, does this "renal" patient's pain need NSAIDs or will paracetamol suffice? Is a contrast study required or is adequate information provided by ultrasound? Is fasting necessary before this procedure? Can a non-aminoglycoside antibiotic be used?

In moderate CRF (ie GFR < 60mls/min), an imminent operation or X-ray contrast procedure should be accompanied by simple **preventative measures**:

- Saline infusion whilst fasting
- Withholding of diuretics, NSAIDs, ACE inhibitors/angiotensin receptor blockers and metformin* pre- and post-procedure
- Maintenance of usual BP
- Monitoring of fluid balance and serum creatinine

N-Acetyl Cysteine (NAC, 600mg bd orally the day before and the day of the procedure) has been shown to reduce the incidence of mild acute-on-CRF following X-ray contrast, by its anti-oxidant action.

***Metformin** is a very useful drug for obese Type 2 diabetic patients, but is renally excreted and blocks lactic acid hepatic metabolism. An otherwise "routine" episode of acute renal failure (ARF) and tissue hypoxia (eg. myocardial infarct, infected PVD) can precipitate profound and fatal lactic acidosis if metformin is not ceased immediately the patient becomes unwell. With careful dose reduction however, it can generally be used relatively safely in CRF. To avoid the chronic nausea and diarrhoea of excess dosing, my personal daily maximum dosages are 2g for any GFR > 60, 1g for GFR < 60, 500mg for GFR < 30 and 250mg for GFR < 15 (ie dialysis-requiring).

Several controlled trials have now shown low-dose dopamine or frusemide infusions to have no benefit in preventing or treating ARF or acute-on-CRF.

Treatment of **gout** is a common thorny problem in CRF (and especially renal transplant patients): NSAIDs (including all COX-2 inhibitors), colchicine and allopurinol all can cause problems in certain circumstances. I advise vigorous hydration and short-term use of either an NSAID or colchicine in the lowest doses necessary, with b.p. and electrolyte monitoring.

Further Reading references available on request (see: www.rph.wa.gov.au/nephrol under /Teaching/Tutorial)

Take-home messages

- Recognise the at-risk patient (raised creatinine, diabetic or vasculopath, small elderly female, sepsis)
- Avoid the insult if possible (volume depletion, NSAID, XRay contrast)
- Dose reduce or avoid renally-excreted drugs (metformin, digoxin, and aminoglycosides)
- On the day of a procedure, hydrate and withhold "triple whammy" drugs (diuretics, NSAIDs, ACE inhibitors/angiotensin receptor blockers) and metformin
- If affected, monitor BP, body weight, serum creatinine and electrolytes until recovered

Footnote. Kidney Health Australia (formerly Australian Kidney Foundation) has initiated a nation-wide education project, Kidney Check Australia Taskforce (KCAT), to reduce endstage renal disease through earlier detection and management of mild chronic renal failure. The key elements are investigation of high risk groups, initiation of appropriate therapy and timely referral. Opinions expressed in this article are those of the author and not necessarily endorsed by KCAT.