

Treatment of UTIs in patients with renal failure

What is the treatment of choice for a urinary tract infection (UTI) in a patient with renal failure?

Bacterial sensitivities provide initial guidelines on drug choice.

Normal renal function

For the treatment of a UTI in a patient with normal renal function, it is recommended to use a drug that is cleared extensively by the kidneys such as nitrofurantoin, trimethoprim, ciprofloxacin, or gentamicin. This ensures that sufficiently high concentrations of antibiotic are at the site of infection.

Chronic renal failure

Patients with chronic renal failure (CRF) (creatinine clearance < 0.3mL/sec) have reduced filtering ability. For drugs that are eliminated by filtration this may lead to low drug concentrations at the site of infection. This may lead to therapeutic failure, and drug accumulation resulting in toxicity.

- ◇ *Acute pyelonephritis:* Patients with CRF have reduced kidney perfusion due to their underlying condition and possibly inflammation associated with the infection. Antibiotics are required which have good tissue penetration as well as being filtered and secreted by the kidney eg. ciprofloxacin.
- ◇ *Cystitis:* In comparison, antibiotics with increased tissue penetration are not required in patients with cystitis although these antibiotics must be highly filtered eg. trimethoprim. In theory, antibiotics which are filtered and secreted unchanged in the urine should achieve the required concentrations at the site of infection, even in CRF.

Fluoroquinolones

A fluoroquinolone appears to be a drug of choice for the treatment of pyelonephritis in patients with renal dysfunction unless bacterial sensitivities indicate otherwise. Fluoroquinolones are also appropriate for the treatment of cystitis.

Compared to norfloxacin, ciprofloxacin is eliminated in the urine to a greater extent (fraction excreted unchanged, fu=0.7). It is secreted as well as filtered, and has good tissue penetration. Norfloxacin is mainly eliminated by hepatic metabolism (fu=0.3) and has lower tissue penetration. Theoretically, ciprofloxacin would appear to be the preferred fluoroquinolone in CRF.

Cephalosporins

A broad spectrum cephalosporin such as ceftriaxone may also be considered as an alternative to ciprofloxacin in CRF. Local guidelines suggest that empiric treatment of acute pyelonephritis for patients with severe renal failure could constitute intravenous ceftriaxone, followed by oral ciprofloxacin or trimethoprim (see the Preferred Medicines List, 6th ed, p129).

Trimethoprim

Trimethoprim can be used for treatment of a UTI in a patient with CRF. No dose reduction is necessary if a patient with CRF is being treated for cystitis.

Nitrofurantoin

Nitrofurantoin should not be used in patients with significant renal dysfunction. In CRF, insufficient drug is filtered to be effective in the treatment of cystitis. Prolonged use of nitrofurantoin in CRF is associated with increased risk of neuropathies due to systemic drug accumulation.

Gentamicin

Although aminoglycosides are concentrated in the kidneys and urine, the use of gentamicin is not recommended in patients with CRF due to an increased risk of nephro- and ototoxicity. Furthermore, gentamicin may not be effective with very low filtration rates. If this is the only alternative, a nephrology consult is recommended.

Metformin-Induced Lactic-Acidosis

It has been noted that some diabetic patients on metformin who have been admitted to hospital for acute illnesses have not had their metformin stopped on admission. A rare but potentially fatal side effect of biguanide antihyperglycaemic agents eg. metformin, is lactic acidosis. Many diabetic patients have abnormal lactate metabolism even in the absence of metformin therapy. Metformin also interferes with the production and clearance of lactate. If lactic acidosis occurs in a patient on metformin, there is significant mortality (up to 50%).

Chronic conditions such as renal, cardiovascular, hepatic and pulmonary dysfunction, and alcoholism can further predispose patients to developing metformin-induced lactic acidosis. However, acute conditions such as infections, a sudden decline in renal function, myocardial infarction and hypovolaemia, *greatly* increase the risk.

If a patient is admitted on metformin and is acutely ill - STOP metformin.