Management of Gout in patients with CKD (GFR < 30)

In patients with CKD there are significant concerns about common drugs used in the management of gout.

NSAIDS can potentiate acute renal failure and should be avoided in all patients with a GFR of 30 and patients with a GFR of 30-60 who are taking an ACE or ARB. NSAIDS can be used in stable patients with a GFR > 30 provided they are told to maintain a liberal fluid intake, have close monitoring of their U+E and stop the NSAID if they note a reduction in urine output.

Colchicine clearance is significantly reduced in patients with renal (and liver) disease. With prolonged use colchicine can accumulate causing bone marrow suppression (neutropenia) and progressive myopathy. This is characterised by myalgia, proximal muscle weakness and numbness. Patients on prolonged colchicine therapy should have regular (2 – 4 weekly) monitoring of WCC, CK and AST.

Colchicine and Calcineurin Inhibitors

Cyclosporin (Neoral) : Colchicine should be used with great caution due to the increased risks of nephrotoxicity and myotoxicity. It should be avoided in such patients with a GFR < 60

Tacrolimus (Prograft): Concomitant administration of Colchicine can increase Tacrolimus levels. Tacrolimus levels and GFR should be monitored more frequently.

Colchicine and GFR < 10

Dialysis patients: Colchicine should not be prescribed as it cannot be removed by dialysis.

Colchicine should not be prescribed in patients with a GFR < 10

Colchicine, CKD and other medications which are CYP3A4 inhibitors or P-Glycoprotein inhibitors

CYP3A4 inhibitors

Clarithromycin, Ritonavir, atazanavir, indinavir, telithromycin, itraconazole or ketaconazole

P-Glycoprotein inhibitors

Verapamil, Quinidine

Colchicine should not be co-prescribed with the drugs listed above in patients with a GFR < 60

Colchicine and Statins

Statin therapy can potentiate colchicine toxicity in patients with CKD causing an acute myopathy. Patients should be warned to report any muscle pains or weakness.

ACUTE ATTACK. 3 options available:

1. Colchicine 0.5mg bd for 2 days– followed by Prevention dose (see below). If multiple joint involvement or side-effects develop (eg diarrhoea or abdominal pain) then use prednisolone (as below).
2. Prednisolone 20 – 30mg/day for 3 days and reduced by 5mg every 3 to 5 days according to response.
3. Intra-articular steroid injection can be used where only 1 – 2 joints are involved and systemic steroids are a concern.

PREVENTATIVE THERAPY

Uricoscuric agents are ineffective in patients with a GFR of < 50 and should not be used.

Colchicine

Colchicine will prevent recurrent episodes of gouty arthritis but does not prevent continued urate deposition.

Colchicine should be continued at the doses listed below for at least 6 months

eGFR	Colchicine Dose
➢ 50	0.5mg bd
35 - 49	0.5mg daily
10 - 35	0.5mg alt days
< 10	Caution, 0.5mg x 3 week – close monitoring of WCC/CK/AST

Lowering serum urate

In order to prevent acute attacks and avoid urate deposition, the serum urate should be reduced to 0.3.

Dietary treatment

All patients should be referred to a dietician for advice on a low salt, reduced protein, reduced fructose (sugar-sweetened soft drinks) diet. Weight loss and low fat dairy product can help. In patients taking diuretics – an increase in dose can often precipitate an attack – a low salt diet can reduce diuretic requirement. Alcohol consumption should be restricted.

Decreasing urate synthesis

Uric acid lowering drug therapy should be commenced following a second attack. In patients with CKD or in patients needing high dose diuretic therapy, this can be considered after the first attack. Patients with chronic gouty arthritis or with tophi should be treated.

Wait 4 weeks after an acute episode before starting treatment. However, if an acute attack is settled with prednisolone then it can be introduced earlier. Treatment should be continued indefinitely.

Prophylaxis against acute gout (with colchicine or prednisolone) must be given usually for 6 months when introducing uric acid lowering drug therapy. It should be continued for 2-3 months after the serum urate is down to 0.3 or below. The prevention dose of colchicine (as above) can be used if tolerated and effective. Prednisolone 5mg – 7.5mg is an alternative.

Allopurinol

Allopurinol's half-life is increased in patients with CKD and can result in potential toxicity.

Allopurinol is commenced at 100mg/day and can be titrated up in 4 weekly intervals to a dose of

300mg – if GFR 20 – 50

200mg if GFR < 20

Target serum urate is 0.3. It should be titrated at monthly intervals according to the serum urate.

Febuxostat

No dose adjustment is necessary in patients with mild – moderate renal impairment. Caution should be used when it is prescribed in patients with a GFR < 30 – as there are no data available.

Febuxostat is indicated:

1. For patients intolerant of allopurinol or for whom it is contraindicated
2. In whom serum urate remains above 0.3 and attacks of gout persist despite 200mg of Allopurinol.

Dose of Febuxostat is initially 80mg/day which can be increased to 120mg/day after 2 – 4 weeks aiming to lower the serum urate to 0.3.

Currently, Febuxostat is not recommended in ischaemic heart disease and congestive heart failure.

Allopurinol and febuxostat interact with azathioprine and should not be prescribed along with azathioprine.