
Dosing of Anti-Gout Drugs in Renal Disease and Dialysis

Allopurinol:

- xanthine oxidase inhibitor
- prevents production of uric acid
- useful in both patients with increased synthesis and decreased clearance of uric acid
- no 24 hour urine needed
- can be used in renal failure
- rarely associated with bone marrow suppression, hepatotoxicity, and hypersensitivity reactions

Allopurinol is well absorbed orally and, within 2 to 4 hours, extensively catabolized to oxypurinol, an analogue of xanthine. Oxypurinol binds to xanthine oxidase and inhibits this enzyme, preventing conversion of hypoxanthine and xanthine to uric acid. Oxypurinol is slowly cleared by the kidneys, with a serum half-life of 14 to 26 hours in patients with normal renal function. There is a direct relation between the renal clearances of creatinine and oxypurinol over a creatinine clearance range of 10 to 140 mL per minute.

Allopurinol can cause severe life-threatening toxicity in 0.1% to 0.4% of patients. Eighty percent of these patients have been shown to have some degree of renal dysfunction. It has been attributed to accumulation of oxypurinol in patients with decreased creatinine clearance.

CrCl (ml/min)	Maintenance Dose of Allopurinol
10	100 mg q 3 days
20	100 mg q 2 days
30	100 mg daily
40	150 mg daily
60	200 mg daily
80	250 mg daily
100	300 mg daily
120	350 mg daily
>140	400 mg daily

Colchicine

Colchicine has been widely used for several diseases including gout, psuedogout, and Behçet disease, prophylaxis of recurrent familial Mediterranean fever (FMF) and prevention of amyloidosis in patients with FMF.

Colchicine clearance is significantly reduced in patients with renal and hepatic insufficiency. The T half-life of colchicine in patients with severe renal failure was 2-fold to 3-fold longer when compared with patients with normal kidney function.

Colchicine-induced toxicity has been observed when it has been used for acute treatment, as well as for prophylaxis of gout in patients with impaired renal function.

They recommended using a dose of less than 0.6 mg daily in patients with elevated serum creatinine levels (>1.6 mg/dL), or with creatinine clearances of 50 mL/min or less.

The prolonged use of colchicine should be avoided if the GFR is below 50 mL/min, though acute therapy need not be altered for GFR above 10 mL/min, but should be halved below this level.

In general, colchicine should not be given to patients requiring hemodialysis for management of renal failure. It can neither be removed by dialysis nor by exchange transfusion. The risk of toxicity under these circumstances may be very high.

Probenecid

- uricosuric
- decreases uric acid reabsorption at the proximal renal tubules
- useful in patients with decreased renal clearance of uric acid
- can only be used if creatinine clearance >40 cc/min
- must have 24 hour urine for uric acid <800 mg/dl
- can be used in renal failure
- increased risk of renal stones

Probenecid may be given to patients with decreased clearance of uric acid by the kidney and normal renal function. In general its use should be limited to patients under the age of 60.

Probenecid acts by inhibiting reabsorption of uric acid in the proximal tubules of the kidney. Starting dose is at 500 mg to 1000 mg daily and increased to 1500 mg to 2000 mg as needed. Occasionally higher doses are needed. Probenecid may precipitate renal stone formation and good oral hydration should be encouraged. Probenecid is contraindicated in patients with renal stones (including calcium and uric acid stones) and in patients with urate nephropathy.

Probenecid given inappropriately to patients with hyperuricemia due to overproduction of uric acid can cause renal stones and urate nephropathy.