CASE REPORT

Effective uric acid reduction with probenecid and febuxostat in a patient with chronic kidney disease

Robert Case,¹ Brian Wentworth,² Grant Jester¹¹Department of Internal Medicine, University of Florida, Gainesville, Florida, USA²University of Virginia, Charlottesville, Virginia, USA

Correspondence to

Dr Robert Case, racase42@gmail.com

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SUMMARY

A 33-year-old male with poorly controlled chronic tophaceous gout and chronic kidney disease (CKD) with estimated glomerular filtration rate (GFR) of 37 cc/min. His uric acid was 11 mg/dL despite maximal dosing of febuxostat. He had previously failed pegloticase infusions as well. This patient had a reduction in his uric acid level to less than 6 mg/dL following addition of probenecid to his febuxostat regimen. Most guidelines recommend against utilisation of probenecid therapy in patients with GFR <50, but there is no obvious contraindication to its use, provided renal calculi do not develop. Our case illustrates the synergistic effect probenecid can add to maximal xanthine oxidase inhibitor therapy for patients with refractory hyperuricaemia in a patient with CKD stage IIIb. With the approval of a new uricosuric medication, lesinurad, probenecid may remain a suitable alternative for patients with financial limitations to achieve target uric acid levels.

BACKGROUND

Current guidelines do not provide the clinician with a framework to manage refractory patients who have reached maximal febuxostat dosing. On PubMed review, we found no trials detailing the combination of febuxostat with probenecid. Despite a recommendation against using probenecid in chronic kidney disease (CKD), we found prior studies showing safe and effective use of this drug in patients with CKD.

CASE PRESENTATION

A 33-year-old white male who first presented with gout flare at age 17 years with uric acid level greater than 14 mg/dL. He was lost to follow-up on and off for several years, but by the time this paper was authored, he had failed allopurinol, pegloticase infusions and continued to have uric acid level >10 mg/dL with febuxostat 80 mg twice daily. He had CKD stage IIIb with glomerular filtration rate (GFR) of 37 cc/min. He had been admitted to our hospital over a dozen times in the past year with severe pain from gout flares and was on prednisone 40 mg daily and 0.6 mg colchicine daily. Imaging of his hands and feet revealed diffuse degenerative changes due to crystalline arthropathy as shown in images. He had innumerable tophi on his hands and feet.

This patient had limited financial resources and was physically disabled by his chronic tophaceous gout. He had a maternal family history of gout, but

those family members had presented at a later age than he had.

INVESTIGATIONS

An X-ray of his left foot revealed degenerative changes to the midfoot and first metatarsophalangeal (MTP) joint with erosion and pencil-in-cup deformity. An X-ray of his left hand demonstrated a crystalline arthropathy in the first metacarpophalangeal (MCP) joint with erosion of the lateral edge. Additionally, dual energy CT of the right radius/ulna showed extensive uric acid deposition within joints and soft tissues in the forearm, wrist and elbow joints. His hands and feet were diffusely covered with tophi, some of which were ulcerated.

Serum uric acid 11.2 mg/dL at presentation. Twenty-four-hour urine uric acid excretion was measured on two occasions and revealed profound underexcretion at 187 mg and 127 mg (normal levels are >700 mg), respectively.

TREATMENT

Febuxostat 80 mg twice daily was continued, and probenecid was added. He was started on 250 mg twice daily and titrated up to 500 mg twice daily.

OUTCOME AND FOLLOW-UP

He tolerated 1 g probenecid daily without development of renal calculi or worsening renal function. His uric acid was reduced to <6 mg/dL after 4 months combined febuxostat and probenecid treatment.

DISCUSSION

The American College of Rheumatology guidelines recommend against using probenecid in cases where the GFR is <50 cc/min.¹ The manufacturer of probenecid does not indicate increased risk of toxicity in CKD but suggests the drug may not be effective when GFR is <30 cc/min.² Probenecid has been shown to enhance the hypouricaemic effect of allopurinol but noted to be less effective in patients with renal impairment.³ We found no literature evaluating combined probenecid and febuxostat use.

Lesinurad is a new uricosuric drug, recently approved by the Food and Drug Administration in 2015, that blocks uric acid reabsorption by blocking the URAT-1 transporter.⁴ This drug is approved for use in combination with allopurinol and has also been shown to be effective in patients with CKD.⁵ Lesinurad is a promising new

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option for patients who fail to achieve target uric acid levels with xanthine oxidase monotherapy. Our findings will be most relevant in refractory gout cases where physicians are seeking a second agent to add on with xanthine oxidase inhibitors. Using the GoodRx website as a reference, lesinurad is approximately 10× more expensive than probenecid on average. Given the high cost, clinicians may look at probenecid as a less expensive alternative to achieve synergistic reductions in uric acid levels.

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Learning points

- ▶ Probenecid therapy may continue to provide uric acid-lowering effects for refractory gout patients with glomerular filtration rate <50 cc/min.
- ▶ The combination of febuxostat and probenecid led to marked reduction in uric acid levels in a patient with CKD stage IIIb who had failed xanthine oxidase monotherapy.
- ▶ For patients who are considered for lesinurad therapy, probenecid may continue to represent a less expensive option to achieve synergistic reduction in uric acid levels in combination with xanthine oxidase inhibitors.

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