

CASE REPORT

Oral allopurinol desensitization

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ABSTRACT

Allopurinol, a xanthine oxidase inhibitor, is an effective urate-lowering drug. Unlike majority of patients tolerate allopurinol well, in 2% of patients receiving allopurinol, hypersensitivity reactions have been reported. In this case a 71-year-old woman with tophaceous gout since 10 years ago, presented to our rheumatology clinic. Because of occurring hypersensitivity reactions, allopurinol was discontinued and disease worsened despite administration of colchicine. She was admitted several times due to flare up of gout. Other forms of allopurinol are not available in Iran, so we decided to conduct an allopurinol desensitization protocol with tablets form. Side effects have not been reported yet.

Key words: allopurinol, desensitization, gout

INTRODUCTION

Allopurinol, a xanthine oxidase inhibitor, is an effective urate-lowering drug. Unlike majority of patients tolerate allopurinol well, in 2% of patients receiving allopurinol, hypersensitivity reactions have been reported.^{1,2}

Since there are limited alternative treatments in gout, one of them is febuxostat, another xanthine oxidase inhibitor.⁴ It is expensive and unavailable in Iran so we must desensitize hypersensitive patients to allopurinol.³ About 78% of patients experience successful desensitization.²

CASE REPORT

A 71-year-old woman with tophaceous gout since 10 years ago presented to our rheumatology clinic. She had been treated with allopurinol for years, but because of occurring hypersensitivity reactions like facial rashes, swelling of lips and rashes in her wrists, drug use was stopped. Despite administration of colchicine, her disease worsened and she had renal dysfunction. She was admitted several times due to flare-up of gout. Multiple tophaceous deposits on both wrists, and left forth metatarsophalangeal and right second metatarsophalangeal joints, and arthritis in left elbow, and right first metatarsophalangeal joint were revealed in physical examinations. Laboratory findings are shown in Table 1.

We decided to start on an allopurinol desensitization protocol. We dissolved 200 mg of allopurinol in 100 ml of normal saline (N/S) to make a concentration of 2mg/ml. Then we diluted 10 ml of this suspension in 100 ml of N/S to achieve a concentration of 200 µg /

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ml (1 mg/5 ml). Oral desensitization was started according to Fam et al. Protocol.² She was desensitized to allopurinol successfully in 30 days. Next, 100 mg tablet of allopurinol was prescribed daily to the patient for one year. After one year we increased dose of allopurinol to 150 mg daily. No side effects have been reported in follow up for two years and her renal function get normal and last serum uric acid was 5 mg/dL.

DISCUSSION

Allopurinol is the most widely prescribed urate-lowering drug.⁵ About 2 percent of patients using allopurinol experience hypersensitivity reactions such as pruritic maculopapular rash, fever, facial swelling, or eosinophilia. Moreover, 0.4% of patients, with a mortality rate of 20%, experience more serious reaction such as erythema multiform, toxic epidermal necrolysis (TEN), acute hepatitis, interstitial nephritis, Stevens-Johnson syndrome (SJS), and vasculitis.¹

² The mechanism of hypersensitivity to allopurinol is not determined completely.⁶ Some studies noted that there are at least three main patterns of hypersensitivity: 1) Nonspecific skin rash, 2) IgE-mediated hypersensitivity reactions, and 3) Cell-mediated hypersensitivity syndrome.^{7,8} Allopurinol hypersensitivity occurrence risk increases with aging and renal impairment.⁹ In patients with history of vesiculobullous

Blood measurements	24-hour urine measurements
Uric acid: 10 mg/dL	Creatinine: 1100 mg
Hemoglobin: 10 g/dL	Protein: 47 mg
Creatinine: 1.3 mg/dL	Uric acid: 272 mg
Urea: 52 mg/dL	Volume: 1600 cc

Daily dose	Preparation	Days (approximate)
50 µg	0.25 ml suspension (1 mg/5 ml)	1-3
100 µg	0.5 ml suspension (1 mg/5 ml)	4-6
200 µg	1 ml suspension (1 mg/5 ml)	7-9
500 µg	2.5 ml suspension (1 mg/5 ml)	10-12
1 mg	5 ml suspension (1 mg/5 ml)	13-15
5 mg	2.5 ml suspension (10 mg/5 ml)	16-18
10 mg	5 ml suspension (10 mg/5 ml)	19-21
25 mg	12.5 ml suspension (10 mg/5 ml)	22-24
50 mg	One-half a 100 mg tablet	25-27
100 mg	One 100 mg tablet	28 +

lesions, exfoliate dermatitis, Stevens - Johnson syndrome, or toxic or other life threatening conditions, desensitization is not recommended.^{2, 10}

When a patient experience hypersensitivity reactions by considering few alternative treatments, starting desensitization protocols is preferred.

Fam *et al.* made a suspension with two 100 mg tablets of allopurinol in 33ml of 1 % methylcellulose, simple sugar, and 4 ml cherry flavor.² Schumacher *et al.* did IV desensitization to allopurinol in a heart transplant patient.¹⁰ Damadoğlu *et al.* prepared a suspension by dissolving 50mg allopurinol powder in 500ml of distilled water with 14% NaHCO₃.¹¹ Owlia *et al.* did oral desensitization in a patient with Lesch-Nyhan syndrome with a suspension made by dissolving one 100 mg tablet of allopurinol in 1000 ml of N/s.¹² As other forms of allopurinol such as powder form and other alternative treatments like febuxostat, are not available in our country, we decided to prepare a suspension by dissolving tablets of allopurinol in 100 ml of N/S that is isotonic and iso-osmolar. This method of allopurinol desensitization like other studies is effective and cost effective. However, more research is need

CONCLUSION

Allopurinol is an effective drug in lowering uric acid level. Unlike most of the drugs, if a patient experiences hypersensitivity reactions to allopurinol, we should consider desensitization to the drug instead of not using allopurinol. Oral allopurinol desensitization is an effective, available and cost beneficial method.

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