

Original article

Comparison between Allopurinol and Febuxostat in management of gout patients - a prospective study

Singal KK¹, Goyal S², Gupta P³, Aggawal BK⁴

Abstract

Aim: To assess the efficacy of a relatively new drug-Febuxostat in management of gout and its comparison with allopurinol. **Method:** A comparative study of both Allopurinol and Febuxostat was done on 100 patients of gout. Both were studied for efficacy, side effects and for gout flare up. **Results:** Primary efficacy end point (baseline values) - a serum urate concentration of less than 6.0mg per deciliter at the last three measurements was reached by 54 % (27/50) of group A patients taking 80mgs of febuxostat and 25 % (12/50) of group B patients taking allopurinol 300mgs per day (P<0.001). Secondary efficacy end point (follow up values) - At first visit (after 2 weeks of onset of study), the proportions of subjects with serum urate concentration of less than 6.0mg/dl was significantly higher in the group A receiving febuxostat than the group B receiving allopurinol (P<0.001) [T able no-1]. **Conclusion:** Febuxostat, at a daily dose was more effective than allopurinol at the commonly used fixed daily dose of 300 mg in lowering serum urate. Results of side effects and gout flare up were similar in both groups.

Key words: Allopurinol, febuxostat, uric acid, gout

Introduction

Supersaturation of the extracellular fluid with urate along with serum urate concentration exceeding the 6.8 per deciliter is defined as hyperuricemia and it results in gout which manifest as acute gouty arthritis, gouty arthropathy, chronic tophaceous gout, uric acid urolithiasis and gouty nephropathy. There is deposition of monosodium urate or uric acid crystals in this disease¹. Gout is one of the most common forms of inflammatory arthritis. It is a common disease in elderly people and is increasing due to increased life span. The main stay of the treatment is reduction of serum urate concentration and its long term maintenance at the same low level to prevent or reverse the formation and deposition of urate crystals^{2,3}. There are two methods to lower urate level. One by reducing production (with a xanthine oxidase inhibitor) and 2ndly by increasing urinary excretion of uric acid (with the help of uricosuric agent). Until recently, xanthine oxidase inhibitor, allopurinol was a drug of choice used in average dose of 300 mg per day (range 100 to 800mg/day). But it has got severe life threatening side effects more often in patients with renal insuffi-

ciency^{4,5}. More recently, a novel drug febuxostat has been introduced. Febuxostat is a potent xanthine oxidase inhibitor with minimum effects on enzymes involved in purine and pyrimidine metabolism^{6,7}. Febuxostat is metabolized by glucuronide formation and oxidation in the liver^{8,9}. Absorption of febuxostat is rapid and can be administered regardless of food intake. Its elimination half-life is approximately 12 hours. Usually, no dose adjustments are recommended in patients with mild to moderate renal insufficiency.

Clinical Trail

We did a study of total 100 patients of hyperuricemia with gout at MM Institute of Medical Sciences & Research for duration of 6 months starting between months of March to August 2010. Patients were divided in two groups of fifty patients each. Group A was treated with febuxostat at daily dose of 80mg and group B was treated with allopurinol at daily dose of 300mg. Selection criteria was American College of Rheumatology for acute arthritis of gout[10] and exclusion criteria included patients with renal, hepatic insufficiency, pregnant or lactating

1. *Dr. Kiran Kumar Singal, Assistant Professor, Dept. of Medicine,
2. Dr Sunder Goyal, Associate Professor, Dept. of Surgery,
3. Dr. Parveen Gupta, Associate Professor, Dept. of Medicine,
4. Dr. Bimal Kumar Gupta, Professor & Head, Dept. of Medicine,
M.M. Institute of Medical Sciences & Research, Mullana (Ambala) India.

***Corresponds to:** Dr Kiran Kumar Singal, Kiran Hospital, Bal Bhavan Road, Ambala City-134002, India.
Email: drkirankumar@yahoo.co.in.

women, patients using azathiapurine, 6 mercaptopurine, thiazide diuretics, prednisolone more than 10 mg, oral-contraceptive therapy, aspirin or other salicylates and excessive alcohol.

Results: Total 100 patients of gout were treated over a period of 6 months starting between March 2010 to August 2010. Group A of 50 patients, received 80 mgs of febuxostat per day and Group B of 50 patients received 300 mgs of allopurinol per day. The mean age, sex ratio and mean baseline serum urate concentration, were similar in both the groups. The patients had gout for an average of 6-8 years. 10% had urolithiasis, 60% had previous history of treatment with allopurinol, 50% had hypertension, and 50% were obese. The mean baseline serum urate concentration ranged from 9.80 to 9.90mg/dl. Patients with renal impairment were not included in the study.

Primary efficacy end point (base line values)- a serum urate concentration of less than 6.0mg per deciliter at the last three measurements was reached by 54%(27/50) of group A patients taking 80mgs of febuxostat and 25%(12/50) of group B patients taking allopurinol 300mgs per day (P<0.001) [Table -1].

Secondary efficacy end point (follow up values)- At first visit(after 2 weeks of onset of study), the proportions of subjects with serum urate concentration of less than 6.0mg/dl was significantly higher in the group A receiving febuxostat than the group B receiving allopurinol(P<0.001)[Table-1].These differences were maintained at all visits during the study. The mean percentage reduction from the baseline serum urate concentration at the final visit was also greater in group A than group B.

Table no-1

	Febuxostat 80mg/day	Allopurinol 300mg/d
<u>End Point</u>		
<u>Primary End Point</u>		
Serum Urate <6.0mg/dl at last 3 monthly visits No./total no	27/50(54%)	12/50(25%)
P value	<0.001	
<u>Secondary End Point</u>		
Serum Urate <6.0mg/dl at final visit No./total no	37/50(74%)	18/50(36%)
P value	<0.001	

Gout flares-It was almost similar in both the groups. It was 8% among group A and 9% in group B.

Adverse Reactions- The most common adverse effect of allopurinol were rash (2%), hypersensitivity reactions (1%-mild in nature) and hepatotoxicity (4.5%). There was no case of severe hypersensitivity reaction during this small study. The most common adverse reaction of febuxostat was liver function abnormalities (3.5%), diarrhea (2%), headache (2%), nausea (2%), and rash (1.5%). Comparing rash and hepatotoxicity, incidence of adverse events were almost similar in both groups.

Discussion

The small controlled clinical trial was done on gout patients with hyperuricemia. Febuxostat and allopurinol were compared with regard to urate lowering efficacy, incidence of gout flares and safety. Administration of febuxostat or allopurinol resulted in prompt (within two weeks) and persistent reduction in serum urate concentration; however, all urate-lowering end points requiring serum urate concentration of less than 6.0mg /dl were reached by significantly greater proportions of patients receiving febuxostat 80mg/day than patients receiving allopurinol(300mg/day). The clinical outcome of reduction in gout flares and safety of these drugs, were almost similar. Incidence of treatment related adverse events were similar for both treatment groups.

Our study was designed to compare the efficacy of febuxostat and to test that febuxostat is not inferior to allopurinol with respect to urate-lowering efficacy. In our study in group B(patients receiving allopurinol 300mg/day), only 20% reached the end point where as in various studies it is upto 50-60%^{11,3,12,13}.

Various retrospective studies on the efficacy of febuxostat, have revealed that attainment and maintenance of serum urate concentration of less than 6.0mg/dl is associated with long term benefits in patients with gout including reduction in frequency of gout flare^{2,3}. Now doubt, it is a small study but results are the same.

Conclusion

Certainly, there is a need of a drug which can treat gout safely and effectively. Febuxostat is a great addition to the armamentarium for gout management particularly in patients in whom allopurinol therapy has failed because of either lack of efficacy or due to

adverse events. Febuxostat is a useful, non-purine, selective and potent inhibitor of xanthine oxidase. Other area of interest will be to study the role of febuxostat in management of gout patients with renal insufficiency as these patients were not included in this study

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