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Original Research Article

A Comparative Study between Febuxostat and Allopurinol in the Treatment of Chronic Gout Patients

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Abstract

Introduction: Gout is a common and complex form of Arthritis. It is caused by excess uric acid levels in the bloodstream. The symptoms of Gout are due to the formation of uric acid crystals in the joints.Gout most classically affects the joint in the base of the bigtoe. During an acute attack, Anti-inflammatory drugs (NSAIDs) help to relieve pain and shorten the duration of the attack. Patients with Chronic Gout are used drugs to reduce uric acid levels. Now a days Febuxostat is more effective than Allopurinol for lowering the levels of serum uric acid in Chronic Gout Patients.

Objective: To compare the effectiveness and Tolerability of Febuxostat and Allopurinol in gout patients.

Materials and methods: It was an observational study on 35 patients each in Febuxostat Group A and Allopurinol Group B. After enrollment in study follow up was done at 8 weeks of therapy.

Results: The Change in serum uric acid level in Group A was from 9.24±0.84 to 5.79+0.79 mg/dl and in Group B was from 8.9±0.93 to 6.32±0.60mg/dl. Change in both the groups were highly statistically significant with P-value <0.001. The reduction in uric acid level in Group A was more than in Group B.

Conclusion: The present study clearly indicates Febuxostat 80 mg was responsible for lowering the level of serum uric acid much more effectively than Allopurinol 300mg.

Keywords: Febuxostat, Allopurinol, Gout, Uric Acid.

Introduction

Göut is one of the most common forms of inflammatory arthritis. Greek Physician Hippocrates (400 BCE), The father of modern medicine, who referred to it as podagra, or "the unwalkable disease". Gout represents the most frequent inflammatory joint disease in the general population, and it largely contributes to healthcare burden[1]. Monosodium urate deposition due to longstanding hyperuricemia leading to urate Crystal formation in tissues represents the pathophysiological mechanism of gout[2]. Recent evidence suggests that the mean serum urate (SUA) levels in the general population are increasing worldwide due to a number of factors such as the "epidemic" of overweight and obesity in developed countries as well as the shift in diet with overconsumption of foods rich in purines, alcohol, fructose sweetned soft drinks [3], in addition to the use of diuretic drugs to treat comorbid condition[(4)]. Patients with Gout often present comorbid condition in addition to obesity, such as Cardiovascular Disease, Arterial Hypertension, Diabetes Mellitus and Chronic Kidney Disease (CKD)[4].There is evidence suggesting that increased SUA may be a risk factor also in these condition[5]. A number of guidelines are available to improve Gout management and reduce hyperuricemia [6].

Incidence of gout in India is not clearly documented. The prevalence is 0.12%. as per international League of Nations as compared to Rheumatism, community oriented program for control of Rheumatic Disease (ILAR COPCORD) Study in Bhigwan village of India. Vellore revealed that 15.8% of the affected patients are less than 30 years of age, urban Indian population is involved more than the rural population due to increased prevalence of metabolic syndrome in younger population[7].

There are four stages of gout.

1. First is Asymptomatic Hyperuricemia. Elevated levels of urate are present within the body but the individual does not display symptoms clinically.
2. Stage 2, an Acute Gout attack or flare, comprises of the build up and small deposits of monosodium urate crystals in and around specific joint spaces. Characteristically, the Patient may suffer pain, redness, swelling and warmth.
3. Intercritical gout occurs in a patient who had prior gout flares,which have successfully subsided and who has no current expression of gout symptoms. A patient may report normal joint function, though hyperuricemia continues to occur with an increasingly greater possibility for damage in tissues due to continued deposition of urate crystals.
4. Final stage of progression, Chronic Gout, is typified by a resulting destructive and disabling inflammatory process causing ongoing pain and aching of the joints. Chronic tophaceous arthritis is a product of the continuous deposition of urate crystals around and within the joints space. The main therapeutic agents for the treatment of acute attacks are Colchicine, NSAIDS and Corticosteroids.

The American college of Rheumatology guidelines recommend either Allopurinol or Febuxostat as first line therapy. Allopurinol is a non-selective Xanthine oxidase (xo) inhibitor that decrease acute gout attack incidence by decreasing the amount of serum uric acid through the inhibition of Xanthine oxidase enzyme, which is involved in uric acid synthesis. Febuxostat, is a nonpurine analogue XO inhibitor. It inhibits both the reduced and oxidized forms of the enzyme in contrast to allopurinol. Febuxostat as a non-purine analogue does not block the other

metabolites of purine and has no effect on pyrimidine metabolism. All these help to alleviate allopurinol toxicities. Another advantage is its effectiveness in mild to moderate renal failure. There is lesser drug interaction with azathioprine, 6 mercaptopurine and theophylline. The present study aimed to compare the efficacy of two urate lowering drugs (Febuxostat and Allopurinol) for providing symptomatic pain relief and improving the functional state of the patients having gout.

Aim and Objective

Gout is a form of Arthritis characterized by severe pain, redness and swelling in joints,often at night.Earlier many studies have been done with different drugs for their comparative safety and efficacy in the management of Chronic Gout.Through our study, We aim to compare the efficacy and safety of Febuxostat and Allopurinol.

Materials and Methods:

This prospective, randomized, open, comparative observational study was conducted in department of Pharmacology, PMCH, Patna. This was 8 weeks study between 2 March 2021 to 27 April 2021 in 70 gout patients (male 52 and - female18). With Age ranging between 37 to 79 years visiting outdoor of Medicine department PMCH, Patna.

The following categories of patients were enrolled in the study.

Inclusion Criteria

1. Patients who are allowed to be on urate lowering therapy and
2. Patients without any co-morbidity.
3. Patients who agreed to sign the informed consent form.A Written and informed consent form was taken from each patients before the start of study.

The following categories of Patients were, excluded from the study.

Exclusion Criteria

1) Patients with secondary hyperuricemia, xanthinuria, previous history of hypersensitivity to NSAIDS, Allopurinol and febuxostat, uncontrolled diabetes, pregnancy, lactation, pepticulcer.
2) Patients not willing to give consent.

Patients were randomly distributed in to two groups of 35 each (Group A and Group B).

Group A - Comprised of patients receiving Febuxostat at daily dose of 80mg.

Group B - Comprised of patients receiving Allopurinol at daily dose of 300mg. Baseline serum uric acid levels were measured. Follow-up was done at 8 weeks of therapy. At 8 week serum uric acid levels and safety of drugs were measured.

Results :

Table 1: Age and Gender distribution of patients in the 2 groups.

Characteristics	Group A	Group B
Age (Years, mean)	59.2	53.7
Gender (numbers)		
Male	25	27
Female	10	8

Table 2: Comparison of Changes in uric acid levels in mg/dl at 0 week and 8 weeks in Group A and Group B

Group	Baseline (Mean±SD) 0 weeks	(Mean±SD) 12 weeks	Reduction in uric acid level (Mean±SD)	P. Value
Group A Febuxostat 80mg (n=35)	9.24± 0.84	5.79 ± 0.79	3.45 ± 0.05	P<0.001
Group B Allopurinol 300mg(n=35)	8.9 ± 0.93	6.32 ± 0.60	2.58 ± 0.33	P<0.001

The change in serum uric acid in Group A was from 9.24± 0.84 to 5.79 ±0.79 mg/dl and in Group B was from 8.9 ±0.93 to 6.32 ±0.60 mg/dl. Changes in both the groups were highly statistically significant with p-value <0.001. The reduction in uric acid level in Group A was more than Group B. The safety analysis was performed on all patients who completed the study. Gout flares - It was almost similar in both the groups. It was 10% among Group A and 12% in group B.

Adverse Reaction:

The most common adverse effect of Allopurinol were rash (4%), hypersensitivity reaction (1% mild in nature) and hepatotoxicity (3%). The most common adverse reaction of Febuxostat was liver function abnormalities (2%), diarrhea (2%), headache (3%), nausea (1%.) and rash (1%).

Disscussion:

Gout is the commonest crystal arthropathy seen in clinical practics primarily affecting the joints and kidneys: The development of gout depends on factors like age of the patient and degree of hyperuricemia.

Diet and lifestyle management are some important steps in its management. Protein intake restriction should be an important factor. Patients of gout should be encouraged to abstain from alcohol. Pharmacological management consists of xanthine oxidase inhibitors like Febuxostat and Allopurinol. Febuxostat is indicated in case of

1. Allopurinol hypersensitivity or intolerance.
2. Failure of allopurinol to normalize SUA.
3. CKD where the reduced allopurinol dose suboptimally controls SUA levels.

In this study, it was found that a significant proportion of patients receiving Febuxostat had achieved a target serum uric acid level of about <6.0 mg/dl as compared to those receiving Allopurinol[8].

Becker el al, showed that febuxostat was more effective than allopurinol in terms of reduction of gout flares[9].

Jackson et al, showed that Febuxostat. 80 mg was significantly more efficacious than allopurinol in achieving the serum uric acid <6.0 mg/dl in gout patients >65 years. of age[10]. In this study total of 75 patients were selected out of which 35 patients were provided Febuxostat and 35 patients were provided Allopurinol. Average age group for Febuxostat group and Allopurinol group were 59.2 yrs and 53.7 yrs respectively whereas the pre-treatment levels of uric acid for Febuxostat and Allopurinol group were 9.24± 0.84 and 8.9 + 0.93 mg/dl respectively. Febuxostat was provided at a dose of 80 mg and Allopurinol was provided at a dose of 300 mg. On keeping the duration of dose administration of both febuxostat and

allopurinol same, it was found that Febuxostat lead to more efficacious lowering of serum uric acid as compared to Allopurinol.

Conclusion:

In our study, it was found that Febuxostat was responsible for lowering the level of serum uric acid much more efficiently than Allopurinol. It was found that Febuxostat showed a better outcome in Chronic Gout patients over allopurinol, as the mean level of uric acid was found to be 5.79 ± 0.79 mg/dl in Febuxostat group as compared to that of Allopurinol group which was about 6.32 ±0.60mg /dl. So Febuxostat was more effective compared to Allopurinol in the overall management of Chronic Gout patients.

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