Original Article

Efficacy of Febuxostat Compared to Allopurinol in reducing Hyperuricemia

Febuxostat VS Allopurinol for Uric Acid Treatment

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ABSTRACT

Objective: Evaluating the efficacy of Febuxostat in reducing hyperuricemia compared to Allopurinol in adult male.
Study Design: Cross sectional study
Place and Duration of Study: This study was conducted at the Department of Medicine, Isra University Hospital Hyderabad January 2019 – February 2020.
Materials and Methods: A sample of 200 adult healthy male diagnosed cases of systemic hypertension was selected according to the inclusion and exclusion criteria. Subjects were examined physically. Volunteers were asked for blood sampling. Serum Uric acid was estimated at baseline and after 12 weeks of febuxostat and allopurinol therapy. Data was analyzed in SPSS v 21.0 (IBM, Incor, USA) at 95% confidence interval ($P \leq 0.05$).
Results: Serum uric acid at baseline was 8.14±1.4 mg/dl. After 12 weeks of Febuxostat and Allopurinol therapy, it was reduced to 2.91±0.75 and 4.2±0.55 mg/dl respectively (F=745.1, P=0.0001). Febuxostat reduced serum uric acid by 64% compared to 48.4% by the Allopurinol
Conclusion: Serum uric acid was reduced by both febuxostat and allopurinol, however, the former was more effective in alleviating hyperuricemia.

Key Words: Uric acid, Febuxostat, Allopurinol, Adult Male

Citation of article: Munir A, Akbar M. Efficacy of Febuxostat Compared to Allopurinol in reducing Hyperuricemia. Med Forum 2020;31(11): 184-187.

INTRODUCTION

Hyperuricemia is a common problem of current era characterized by raised blood uric acid (UA) levels. Hyperuricemia is a disorder of purine metabolism. UA induces joint inflammation causing gout and has been associated with kidney disease, systemic hypertenison, metabolic syndrome, etc. Kidneys are commonly affected by raised uric acid levels. Urat renal stones and interstitial nephritis are caused by uric acid.[1] Hyperuricemia is observed commonly in the middle age adults and elderly persons. United States reported incidence of hyperuricemia approximates 18%.[2]
Hyperuricemia may be primary – caused by genetic enzyme defects and secondary – caused by dietary factors however, exact etiology and pathogenesis is not clear. Blood leukemias and lymphomas often induced hyperuricemia. Chronic diseases such as diabetes mellitus (DM), chronic kidney diseases (CKD) and atherosclerosis is often accompanied by hyperuricemia.[3] During early stages, hyperuricemia shows no obvious symptoms, however, it may develop extremely fast. It may induce threat to patient health in comorbid conditions for example CKD.[4] It is conlcuded that hyperuricemia once complicated, then chances of mortality show linear increase.[5] Previously, most commonly used drug was the allopurinol and still used in clinical practice.[6] Allopurinol is xanthine inhibitor of purine analogue, traditionally used for hyperuricemia with established clinical efficacy.[7,8] Major drawback of allopurinol is inhibition of purine metabolism resulting in serious side effects as other active enzymes involved in purine metabolism are negatively affected.[7,8] In cases of kidney disease, its toxic side effects have been perplexed.[9] Another drug of new class is the febuxostat that is now widely used in clinical practice and has replaced the allopurinol. Febuxostat is a non-purine xanthine oxidase inhibitors hence adverse drug reactions are less compared to allopurinol. It is strong inhibitor of uric acid synthesis with little side effects.[10] Febuxostat shows excellent therapeutic effect on hyperuricemia.[11] Exact mechanisms of Febuxostat is not well elucidated and there is little research compared to allopurinol. The present study was conducted to analyze serum uric acid in hyperuricemia patients before and after febuxostat and allopurinol therapy and results were compared among healthy adult male population.

MATERIALS AND METHODS

The present observational cross sectional study was conducted at the Department of Medicine, Isra University Hospital Hyderabad January 2019 –

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Received: April, 2020
Accepted: August, 2020
Printed: November, 2020

February 2020. A sample of 200 adult male diagnosed cases of systemic hypertension was selected. Sample size was estimated by Rao-software. Both in – and out – patient department subjects were included in the study. Study protocol observed strict inclusion and exclusion criteria. Inclusion criteria were; adult male of age 40- 60 years. Subjects suffering from secondary systemic hypertension, CKD, CLD, DM, Ischemic coronary artery disease (CAD) and alcoholics were excluded from study protocol. Subjects taking ACE-Inhibitors, thiazide and loop diuretics were also excluded. Study was approved by ERC. Volunteer adult male of fulfilling inclusion criteria were asked for physical examination. Age, body weight, blood pressure was noted in a pre – structured proforma. Systemic hypertension was as per criteria of JNC-VIII. BP was measured by a mercury sphygmomanometer. Volunteers were requested for blood sampling that was taken from ante cubital fossa after area was cleaned with spirit swab. A tourniquet was tightened above ante – cubital fossa. Blood was drawn from prominent vein in a 5 ml Disposable syringe. Blood was centrifuged for 15 minutes (x3000 rpm) for separating sera that were taken into sterilized Eppendorf tubes. Samples were stored at −20°C for analysis. Written participant consent was taken. Proforma were kept in lockers to maintain confidentiality of personal data. Serum uric acid and creatinine were estimated by colometric technique. All values were saved in proforma and typed in Microsoft Excel sheet. Data was analyzed on statistical software – SPSS v 21.0 (IBM, Incor, USA). Paired sample t – test analyzed the numerical data. Data was presented as mean +/- standard deviation (SD). Graphs were designed on Microsoft Excel sheet. % decrease in serum uric acid was calculated manually and graphed in Microsoft Excel sheet. Significance level of SPSS analysis was 95% CI ($P \leq 0.05$).

RESULTS

General information of study subjects is shown in table 1. Serum uric acid at baseline was 8.14±1.4 mg/dl. After 12 weeks febuxostat and allopurinol therapy, it was decreased to 2.91±0.75 and 4.2±0.55 mg/dl respectively (F=745.1, P=0.0001). Table 2 and graph 1 show the serum uric acid levels at baseline and after febuxostat and allopurinol therapy. Febuxostat decreased serum uric acid by 64% compared to 48.4% by the Allopurinol as in line graph 2.

Table No.1. General Information of study subjects

	Study subjects (n=200)
Age (years)	49.3±4.1
Body weight (kg)	77.2±17.8
BMI (kg/m^2)	28.5±2.3
Systolic BP (mmHg)	135.5±12.7
Diastolic BP (mmHg)	88.9±11.3
Creatinine (mg/dl)	0.92±0.01

Table 2. Serum Uric acid (mg/dl)

Baseline	Febuxostat	Allopurinol	t-value	P-value
8.14±1.4	2.91±0.75	4.2±0.55	745.1	0.0001

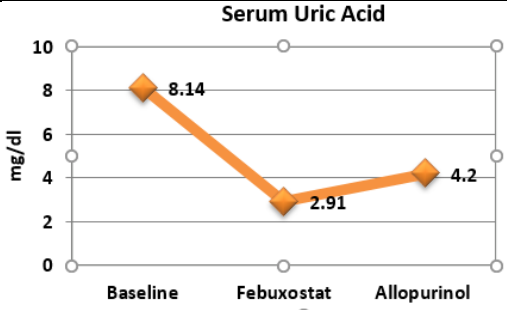

Figure No.1: Serum Uric acid distribution

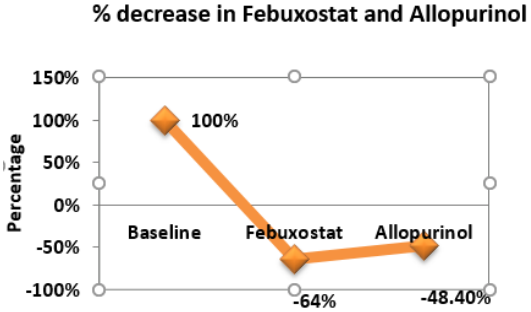

Figure No.2: % Reduction in Serum Uric acid

DISCUSSION

The present is the first study reporting on the efficacy of febuxostat and allopurinol in reducing serum uric acid level in adult male of systemic hypertension. Present study found 64% reduction of uric acid in febuxostat group compared to 48.4% in allopurinol group. Serum uric acid at baseline was 8.14±1.4 mg/dl. After 12 weeks febuxostat and allopurinol therapy, it was decreased to 2.91±0.75 and 4.2±0.55 mg/dl respectively. The findings are supported by previous studies.[12-15] Febuxostat is a new class of non – purine drug that selectively inhibits xanthine oxidase (XO).[12] Febuxostat was found superior in alleviating hyperuricemia in the present study. Now the Febuxostat is widely used drug in the country but the comparative studies with allopurinol are limited. The present study is worth in terms of inclusion and exclusion criteria for selecting the study protocol to be included. Results of present cross sectional study show Febuxostat had superior clinical efficacy compared to allopurinol (table – 1). Allopurinol was also effective in reducing uric acid level compared to baseline but less effective than Febuxostat. The finding is of utmost clinical importance in practice. Febuxostat had more effective clinical efficacy compared to allopurinol. The finding is consistent to a previous study[16] that showed similar results. Febuxostat was quite safe as regards adverse drug reactions that are similar to previous studies.[12-15] Renal function testing shows no significant difference in serum creatinine in two groups that is consistent with

previous studies.[12-15] Uric acid was improved and serum creatinine was found within normal limits in both drug groups. Febuxostat is suggested to reduce the reactive oxygen species (ROS) and inhibits XO, both mechanisms help in alleviating the hyperuricemia. ROS scavenging activity provides vascular protection.[12,17] It has been speculated that the allopurinol may be toxic to the liver and kidney. Allergic reactions are frequent with alllopurinol and were not observed with Febuxostat. XO is inhibited by the Febuxostat effectively compared to Allopurinol. Febuxostat is safe as it has no inhibitory effect on other enzyme systems of purine metabolism hence least side effects are complained it.[12] Febuxostat is excreted through both renal and hepatic routes[18] hence renal toxicity is minimized. Febuxostat has safe renal therapeutic effect for uric acid compared to Allopurinol because of its urate transport acceleration in the proximal renal tubule (PRT). Hence large volumes of uric acids are excreted in urine and are prevented from being deposited in the renal interstium, this improves the clinical efficacy. A previous study[19] reported Febuxostat does not affect the renal drug kinetic parameters. Febuxostat has an excellent bioavailability of 80% and has no significant limit on the drug dosage. Febuxostat has low use restriction and utilization rate is high compared to Allopurinol. In the present study, clinical value of Febuxostat was demonstrated in comparison to Allopurinol that is a known uric acid lowering agent of purine analogue. Allopurinol use is clinically unfavorable due to its adverse drug reactions.[20-23] Evidence based findings of present study supported by published literature shows Febuxostat is an excellent, clinically effective drug for alleviating hyperuricemia in systemic hypertension patients without renal toxicity. However, further clinical studies are recommended as the sample size of present study was small enough and findings are not generalizable to other settings.

CONCLUSION

In present study, the Febuxostat reduced serum uric acid by 64% compared to 48.4% by the Allopurinol. Serum uric acid was reduced by both febuxostat and allopurinol however the former was more effective in alleviating hyperuricemia.

Author's Contribution:

Concept & Design of Study:	Akram Munir
Drafting:	Muhammad Akbar
Data Analysis:	Muhammad Akbar
Revisiting Critically:	Akram Munir, Muhammad Akbar
Final Approval of version:	Akram Munir

Conflict of Interest: The study has no conflict of interest to declare by any author.

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