CODEN [USA]: IAJPBB ISSN: 2349-7750

INDO AMERICAN JOURNAL OF
PHARMACEUTICAL SCIENCES

http://doi.org/10.5281/zenodo.1248874

Available online at: http://www.iajps.com Research Article

STUDY IN HYPERURICEMIC PATIENTS TO KNOW THE FENOFIBRATE SAFETY AND ITS EFFICACY

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Abstract:

Background: *Allopurinol is commonly used as antihypertensive medicine. Fenofibrate, a fibric acid derivative, is widely used in hyperlipidemia treatment. Fenofibrate reduce serum uric acid levels effectively.*

Objective: *This study was performed to evaluate the safety and efficacy of fenofibrate in patients with hyperuricemia.*

Study Design: *Interventional Study*

Place and Duration: *The study was performed in the Out Patient Department of Nephrology Unit of Nishter Hospital, Multan for the period of six months from January 2017 to July 2017.*

Materials and methods: *Sixty hyperuricemic patients with serum uric acid levels of desil- lary or higher of 7.0 mg were enrolled and assigned to receive 300 mg allofurinol or 200 mg fenofibrate for 12 weeks. The efficacy of the drug was measured in percentage of patients successfully controlling serum uric acid levels of less than 6 mg P. Dl at 90 days. The efficacy of the drug was also checked by measuring the percentage of serum uric acid levels changes at day 1 to 90 days. Safety was checked by observing side effects (AE) and laboratory investigations.*

Findings: *The percentage comparison of cases in which uric acid level in serum was lower than 6.5 mg at 90th day in both groups was statically significant (P = 0.14). However, the percentage difference in uric acid level between 0 and 90 days was significantly highly among the two groups (p = 0.001). Although the proportion of individuals experiencing any side effects was greater in the fenofibrate group, the side effects that caused the allopurinol group to discontinue treatment were found to be higher.* ***Conclusion:*** *Fenofibrate 200 mg is an effective antihypertensive agent once a day.*

Key words: *Uric acid, Fenofibrate, hyperuricemia.*

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Please cite this article in press Awais ur Rehman et al., ***Study in Hyperuricemic Patients to Know the Fenofibrate Safety and Its Efficacy,*** *Indo Am. J. P. Sci, 2018; 05(05).*

INTRODUCTION:

The final result of purine nucleotide degradation is Uric acid . Serum uric acid levels in males are five ± two and 4.0 ± 2.0 mg / dl in females. It is in ionized form in plasma as urate. The concentration of uric acid in the plasma in which it is deposited is 6.8 mg P. Dl. Hyperuricemia is an abnormality biochemically presented with leavels of a serum uric acid level ranging from two to seven percent up to a maximum of 6.8 mg per decilit. Hyperuricemia in 90 % of cases is because of low urinary kidneys excretion, while in other cases (10%) the concentration of uric acid increases as the acid production increases in the uric acid crystals. The resulting urate crystals can cause nephrolithiasis or gout to develop hyperlipidemia, hypertension, cardiovascular disease, diabetes and renal disease probably also linked with plasma levels 7-9 uric acid dl.10 (6.8 mg / dl), which is used as a medication for lowering the uric acid in plasma, contains a plasma uric acid lowering agent below 6 mg / dl of hyperuricemia therapy, which is a new inhibitor of the production of allopurinol uricostatics Febuxostat substances and uric acid and uricosuric substance probenecid medication, hyperuricemia, not allopurinol, is the most commonly used drug in acid excretion therapy. However, about half of all patients who have developed allopurinol and adverse side effects which limit uso.8, 12, s of ineffective serum uric acid have decreased. pruritus and skin inflammation, 2% 1, not common as allopurinol-dependent drugs, but in this case the mortality rate is 20%. a fibric acid derivative fenofibrate, the use of fenofibrate used in the treatment of common hyperlipidemia. 14, has been shown to reduce renal15-16 increase in serum uric acid excretion. This study was performed to evaluate the safety and efficacy of fenofibrate with hyperuricemia in patients.

MATERIALS AND METHODS:

This is an open interventionist work approved by the ethical committee of institution. From all patients written patient consent was obtained. Patients were admitted to the rheumatology and nephrology polyclinic from OPD, Nishter Hospital, Multan. The criteria for inclusion were male to female patients between 41 and 72 and a mean serum uric acid deciliter or higher was 7.0 mg. Exclusion criteria were lactating women and pregnant, active liver disease, chronic kidney disease, coliliasis, myopathy, hypersensitivity and urolithiasis to examine any use of drugs and other medicines that changes serum uric acid levels. Sixty patients were enrolled for study and two equal groups were allocated. Allopurinol group asked to take tab. (allopurinol) 300 Zyloric is an allotment group to receive mg fenofibrate Cap once daily for twelve weeks. Fenoget (fenofibrate) 200 mg once daily for 12 weeks. All individuals were monitored remotely. Biochemical and Clinical evaluations (serum alanine aminotransferase, serum uric acid and creatine kinase) at day 0 were analyzed in an automatic analyzer from the Main Laboratory of Nishter Hospital, Multan for 30 days 60 days and 90 days was measured. The efficacy of the drug was checked by measuring the number of subjects successfully controlling serum uric acid levels of less than 6 mg per deciliter at 90 days. The efficacy of the drug was also checked by measuring the change in serum uric acid levels in percentage at day 0 to 90 days. Safety was assessed by observing side effects (AE) and laboratory values. These include dizziness, headache, acute gout, vomiting, nausea, diarrhea, deep redness, muscle cramps, increased area of aminotransferase (ALT) increased more than 3 times upper limit of normal (UNL), and more than 5 times upper limit of creatine kinase (normal UNL).

RESULTS:

Sixty cases with hyperuricemia were randomly assigned to study. Two patients in the allopurinol group and one patient in the fenofibrate group stopped treatment due to side effects. Initial values of all patients are shown in Table 1.

Table 1: Baseline Characteristics of Subjects

Variable	Allopurinol 300mg/day n = 30	Fenofibrate 200mg/day n = 30	All subjects n = 60	"P" value
Age in year mean (SD)	53.9 (6.73)	54.0 (5.39)	53.95 (6.04)	0.95
Male sex - No (%)	26 (86.7)	25 (83.3)	51 (85.0)	0.50
Baseline serum urate concentration in mg/dl mean (SD)	8.68 (1.13)	8.54 (0.99)	8.61 (1.05)	0.59
Body mass index mean (SD)	27.62 (2.36)	27.59 (2.17)	27.6 (2.25)	0.96
Hyperlipidemia No (%)	9 (30)	9 (30)	18 (30.0)	0.61
Hypertension No (%)	10 (33.3)	12 (40)	22 (36.6)	0.395
Tobacco use No (%)	9 (30)	8 (26.7)	17 (28.3)	0.50

At the beginning of the study, two groups were similar in terms of age, gender, serum uric acid concentration and body mass index. A similar proportion of patients in each treatment group showed hyperlipidemia, hypertension and tobacco use. 46.4% of the patients in the allopurinol group and 41.3% of the patients in the combination group were found to have serum uric acid levels less than 6 mg per deciliter at 90 days. Comparison of the percentages of the cases The two groups reaching a serum uric acid level below 6.0 mg / dl at 90 days (P = 0.14) were not significant (Table 2).

Table 2: Efficacy Parameters

Group	Subjects with serum uric acid <6mg/dl at day 90 (%)	P value	Percent change in serum uric acid from day 0 to day 90 (Mean ±SD)	P value
Allopurinol 300mg	46.4	0.14	-32.2 ± 2.35	0.001
Fenofibrate 200mg	41.3		-28.4 ± 2.52	

In the allopurinol group, the mean percentage reduction of the uric acid level between day 0 and day 90 was 32.2% while in the fenofibrate group it was 28.4% on average. %. The mean percentage reduction in serum uric acid level between two groups from 0 to 90 days was significant between the two groups (P = 0.001) (Table 3).

Table 3: Adverse Effects No. (%)

	Allopurinol 300mg/d n=28	Fenofibrate 200mg/d n=29
Headache	2 (6.66)	3 (10)
Dizziness	0 (0)	1 (3.3)
Nausea/vomiting	1 (3.3)	3 (10)
Diarrhea	1 (3.3)	1 (3.3)
Rashes	2 (6.66)	1 (3.3)
AHS	0 (0)	-
Muscle pain/weakness/cramps	0 (0)	2 (6.66)
Acute gout	2 (6.66)	1 (3.3)
AST > 3x UNL	0 (0)	1 (3.3)
CPK > 5x UNL	0 (0)	0 (0)
Any treatment related AE	8 (26.6)	13(43.3)

Key: AST=alanineaminotransferase, CPK=creatinephosphokinase UNL=upper normal limit

The proportion of subjects with any side effects was higher in the fenofibrate group (43.3%) than in the allopurinol group (26.6%) (Table 3). However, the proportion of patients who discontinued medication due to side effects was higher in the allofurinol group (6%) than in the fenofibrate group (3%). The main cause of the absence of allopurinol group was the development of scrapes, and in the fenofibrate group, the serum alanine aminotransferase (ALT) had more than three times the upper normal limit.

DISCUSSION:

Allopurinol is the most commonly used uric acid reducing agent. Limitations of treatment with allopurinol include infertility pacientes.17 outbreaks occur in up to 10% of patients in five percent of patients and significant reduction in plasma urate levels in the development of severe side effects is observed in allopurinol hypersensitivity syndrome alopurinol.18 Reduced serum levels of 11 fenofibrate serum albumin are approximately 20% widespread mortality occurs in patients with allopurinol hypersensitivity syndrome crónica.6 renal disease This three-month study was conducted to assess the efficacy and safety of uric acid in serum. This is the standard drug in the treatment of hyperuricemia when compared to 300 mg fenofibrate daily, 300 mg allopurinol per day. In our study, 46.4% of patients in the allopurinol group and 41.3% of patients in the fenofibrate group reached a serum uric acid level of 6 mg / dl less than 90 days. these values showed the same values for allopurinol and fenofibrate, respectively, to lower the serum uric acid levels, accepting various estudios20-21. The mean percentage reduction in patients receiving 300 mg allopurinol daily decreased by 2% and by 4% for fenofibrate users. Study Treatment was well tolerated by 6% of the patients and the side-effect-exclusion rate was tolled from the 3% fenofibrate group when compared to the allopurinol group. due to adverse effects. Serum transaminase elevation is the major side effect of up to 3 times the withdrawal in the group of fenofibrate, including ULN. The main side effects leading to withdrawal in the allopurinol group included the development of the rashes. These side effects are well documented effects of fenofibrate and allopurinol. Although fenofibrate reduced comparable serum uric acid levels compared to allopurin, no acute exacerbation of gout was seen when fenofibrate therapy was initiated. This may be due to the anti-inflammatory effect of fenofibrate and is observed in other studies.

CONCLUSION:

Fenofibrate has significant uric acid reduction properties. It can be used as an alternative drug to allopurin in patients who can not take allopurinol because of side effects. Fenofibrate can be used as a single agent in hyperuricemia patients with hyperlipidemia, thereby reducing the need for multiple drug treatments. Further work is needed to

assess the role of fenofibrate in the treatment of hyperuricemia.

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