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To Establish The Role Of Febuxostat In Pyrazinamide Induced Hyperuricaemia: A Prospective Study

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Abstract

Hyperuricemia is an abnormally high level of uric acid in the blood. Hyperuricemia can result from overproduction or under excretion of uric acid in the body. It can also be induced by certain medications.
Pyrizinamide causes hyperuricaemia by decreasing uric acid clearance. febuxostat decreases uric acid synthesis by inhibiting xanthine oxidase and is commonly used for treating hyperuricemia.

MATERIAL AND METHOD

This is a observational study , carried out on patients of Department of Respiratory Medicine in a tertiary care hospital North India. Total 100 patients (both male and females) of all aged diagnosed with pulmonary tuberculosis were taken for in this study. Baseline serum uric acid of enrolled patients was assessed at enrolment. Serum uric acid levels were re- assessed during treatment, on completion of week 1,2,3 and 4 of ATT i.e during intensive phase, Serum uric acid levels of the all patients was measured in the laboratory . Patients were treated by febuxostat (40 mg) twice a day daily for hyperuricaemia control.

RESULTS

In our study, in first week 80(80%) patients had uric acid level within the normal level i.e. 7.3 and 20(20%) patients had uric level >7.3. In second week 64(64%) patients had UA level <= 7.3 and 36 (36%) patients had UA level > 7.3 In third week 48(48%) patients had UA level <=7.3 and 52 (52%) patients had UA level > 7.3 in fourth week 58(58%) patients had UA level <= 7.3 and 42(42%) patients had uric acid level >= 7.3 so we saw that uric acid level gradually increased till third week and then decreased in forth weeks
Before treatment serum uric acid level was 8.25□2.70 and after treatment 6.25□2.75. The difference between groups was statistically significant (p value<0.05).

CONCLUSION

Uric acid level raised after 2 weeks of administration of pyrazinamide but it gradually increased in 4th week. Anti-tuberculous therapy with pyrazinamide affects the uric acid levels early. This change is reversible after the withdrawal of the agent.

Keywords: hyperuraecemia, febuxostat, pyrazinamide, gout.

Introduction

Hyperuricemia is an abnormally high level of uric acid in the blood. In the pH conditions of body fluid, uric acid exists largely as urate, the ion form. , The amount of urate in the body depends on the balance between the amount of purines eaten in food, the amount of urate synthesized within the body (e.g., through cell turnover), and the amount of urate that is excreted in urine or through the gastrointestinal tract. In humans, the upper end of the normal range is 360 µmol/ L (6 mg/dL) for women and 400 µmol/L (6.8 mg/dL) for men. . In the majority of individuals, hyperuricemia will be asymptomatic, but as UA tends to precipitate in tissues and in other body fluids, persistent hyperuricemia may eventually lead to the

accumulation of urate crystals in many places, resulting in either acute painful conditions, like gout/tophaceous gout/gouty arthritis, urolithiasis, or, in severe cases, like tumor lysis syndrome, in acute UA nephropathy.

Hyperuricemia can result from overproduction or under excretion of uric acid in the body. It can also be induced by certain medications. Xanthine oxidase inhibitors, such as allopurinol (Zyloprim, Prometheus Labs) or febuxostat (Uloric, Takeda), are commonly used to lower the body's uric acid production. Rasburicase (Elitek, Sanofi-Aventis), a urate-oxidase approved for tumor lysis syndrome, has been used off-label to lower uric acid levels quickly in situations of severe nephropathy.

Causes of hyperuricemia can be classified into three functional types: increased production of uric acid, decreased excretion of uric acid, and mixed type. Causes of increased production include high levels of purine in the diet and increased purine metabolism. Causes of decreased excretion include kidney disease, certain drugs (Like Diuretics, pyrazinamide, nicotinamide etc.) and competition for excretion between uric acid and other molecules. Mixed causes include high levels of alcohol and/or fructose in the diet, and starvation.

Pyrazinamide:

The occurrence of hyperuricaemia and acute gouty arthritis has also been reported with the use of some antituberculosis (anti-TBC) drugs such as ethambutol and pyrazinamide (PZA), both of which decrease uric acid clearance. Hyperuricaemia was reported in 42%–66% of patients treated with ethambutol , and in 43%–100% of patients treated with PZA (alone or combined with other drugs). , , Pyrazinoic acid, a major metabolite of PZA, can inhibit the renal tubular secretion of uric acid, which may cause hyperuricaemia. The hyperuricaemic effect of PZA is also acknowledged in the European Respiratory Society (ERS) Task Force's report on the management of tuberculosis in Europe. According to ERS guidelines, uric acid monitoring in patients receiving PZA treatment is generally not recommended, except in cases where hyperuricaemia was previously documented.

Management Of Hyperuricemia:

Acute gouty attacks are treated with indomethacin or other nonsteroidal anti-inflammatory drugs (NSAIDs), colchicine, and/or intra-articular corticosteroids. Oral NSAIDs are generally prescribed for a seven- to 10-day course or until a few days after inflammatory symptoms have diminished. Colchicine (Colcrys, Takeda) is used to manage intercritical gout. Urate-lowering drugs may be used for prevention in patients with recurrent gout. Probenecid and sulfinpyrazone are uricosuric agents used for patients who under-secrete uric acid. Rasburicase is a recombinant urate-oxidase indicated for initial management of plasma uric acid levels in cancer patients receiving chemotherapy likely to result in tumor lysis syndrome and subsequent elevation of plasma uric acid.

Management Of Drug Induced Hyperuricemea:

Drug induced hyperuricemea treated by using xanthine oxidase inhibitors. Allopurinol and febuxostat decrease uric acid synthesis by inhibiting xanthine oxidase and are commonly used for treating hyperuricemia. The usual adult daily maintenance dose is 200 to 300 mg and 40 to 80 mg orally for allopurinol and febuxostat, respectively. Pyrazinamide and ethambutol-induced hyperuricemia can normally be controlled by xanthine oxidase inhibitors (allopurinol and febuxostat).

Febuxostat:

Febuxostat is a non-purine inhibitor of xanthine oxidase. Because it is dissimilar from the structure of purines, it does not interfere with purine and pyrimidine metabolism. Furthermore, it is degraded by glucuronide formation and oxidation in the liver, with half of all febuxostat and its active metabolites excreted in the stool, with the other half in the urine. Unlike allopurinol, febuxostat does not require renal dose adjustment. , The major reservation is its use in patients with underlying liver disease, current alcohol use, or history of alcohol abuse, but short term use of febuxostat 80mg daily for seven days was demonstrated to be safe in 8 patients with Child-Pugh A liver disease and 8 patients with Child-Pugh B disease.

The registration labels for febuxostat in the United States and Europe are slightly different. The Food and Drug Administration has approved a dose of 40 and 80 mg per day respectively while the European

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Medicines Agency has approved a daily dose of 80 and 120 mg. The European Medicines Agency has advised to avoid the drug in patients diagnosed with coronary artery disease (CAD) and congestive heart failure (CHF). Adjustment of the dose in patients with renal impairment is not needed. There is no warning for cardiac failure. Febuxostat is not considered cost-effective in comparison to allopurinol as first-line therapy but is generally considered equi- valently tolerated and at least similarly effective. , , ,

Mechanism of Action: Febuxostat, a xanthine oxidase inhibitor, achieves its therapeutic effect by decreasing serum uric acid. Febuxostat is not expected to inhibit other enzymes involved in purine and pyrimidine synthesis and metabolism at therapeutic concentrations.

Tuberculosis is a disease of public health importance and as such treatment with anti-tuberculosis drugs is also important. However in patients with comorbidities such as renal insufficiency, renal calculi, transplantation or allopurinol allergy, treatment options are narrow and could complicate the management of symptomatic hyperuricemia or gout. Advance approaches for the treatment of drug induced (pyrazinamide) hyperuricemia by Fabuxastat, studied worldwide, but not many in India.

Aims And Objectives

1. To know the incidence of hyperuricemia in patient who were taking pyrazinamide for treatment of pulmonary tuberculosis.
2. The effect hyperuricemia may produce on the body systems renal stone, gouty arthritis, renal failure etc.
3. To establish the role of febuxastat in treatment of pyrazinamide induced hyperuricemia

Material And Method

This is a observational study was carried out on patients of Department of Respiratory Medicine in a tertiary care hospital North India. Total 100 patients (both male and females) of all aged diagnosed with pulmonary tuberculosis were taken for in this study.

Subjects & selection method: All patients admitted with active pulmonary Koch's as part of ATT (CAT 1 DOTS OR NON DOTS) Presenting to the IPD as well as OPD to the Department of Respiratory Medicine, will be selected purely on voluntary basis.

Inclusion Criteria:

1. Newly diagnosed cases of pulmonary Koch's disease.
2. Patients who were having pyrazinamide containing regimen of ATT.
3. Patients who were having S. uric acid more than 6mg/dl.
4. Patients who were willing to take part in the study.

Exclusion Criteria:

1. Patients with diagnosis other than pulmonary Koch's disease.
2. Patients suffering with renal disease, gout or any kind of arthopathies (Osteoarthritis/Rheumatoid disease).
3. Patients with known heptic disorder or at revised risk heptic involvement.
4. Patients where pyrazinamide had discounted due to non-resolution or persistant hyperuricaemia despite adequate measures.
5. Patients who were had other causes of hyperuricaemia leading to gout.

Study Tool:

Predesigned Proforma for data collection (Annex I)

Procedure Methodology

In this study we took newly diagnosed cases of pulmonary Koch's from both out patient and in patient department. All patients were investigated before starting the ATT as advocated by the Revised National Tuberculosis Control program (RNTCP) of India to rule any other diseases like renal, Hepatic or cardiac etc.

Baseline serum uric acid of enrolled patients was assessed at enrolment. Serum uric acid levels were re- assessed during treatment, on completion of week 1,2,3 and 4 of ATT i.e during intensive phase, Serum uric acid levels of the all patients was measured in the laboratory . Patients were treated by febuxostat (40 mg) twice a day daily for hyperuricaemia control.

Patient's demographic details such as age, sex, educational status, marital status, occupational status, and family support were collected from the patients

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Serum Uric Acid Determination

Uric acid (UA) was quantified in all serum samples using the uricase method in the Hitachi 916 automated chemistry analyzer (Hitachi, Japan). The reference range for this assay is 2.5 to 6.2 mg/dL for females and 3.5 to 8.5 mg/dL for males. The author's defined hyperuricemia as a serum uric acid concentration greater than the highest mean uric acid level (6.5 mg/dL) observed after 4 weeks of combination therapy.

Statistical Analysis

Data was analyzed using SPSS version 20 (SPSS Inc., Chicago, IL). Continuous variable are presented as mean±SD. Categorical variables are expressed as frequencies and percentages. The comparison of normally distributed continuous variable within the group at 1st week 2nd week, 3rd week and 4th week from the baseline was performed using paired t test. Nominal categorical data between the groups was compared using Chi- squared test or fisher's test as appropriate. For all statistical tests, a p value less than 0.05 was taken too indicate a significant difference.

Observation And Results:

AGE: When age was analyzed in age group of 0-20 years, 21-40 years, 41-60 years and 61-80 years: it was observed that most of the cases were in the age group of 41-60 years and 61-80 years (31% each). Twenty - seven (27%) were in the age group of 21-40 years and only 11 eases (11%) were in the age group of 0-20 years. This was depicted in bar graph figure number 1.

Table no 1 showing no. of patients according to age group of studied patients

Age Groups	**No of Patients**	**%**
0-20	11	11%
21-40	27	27%
41-60	31	31%
61-80	31	31%
Total	100	100%
Mean ± SD	**45.18 ±19.04**	

The study group consisted of 49% (49/100) females and 51% (51/100) males; The male; female ratio was calculated to be 1.04.

In our study group 73 (73%) patients were non - smoker and 27 (27%) patients was smoker.

In our study 62(62%) patients were non-vegetarian and 38(38%) patients were vegetarians.

Table no 2 showing mean serum uric acid level over the observation period.In our study, the mean serum uric acid level was observed to be within the normal limit of 7.3mg during the first 2 weeks after the initiation of ATT. This is depicted in stock figure number 7.

Table no 2 showing mean serum uric acid level over the observation period of studied patients

Serum Uric Acid	**Mean± SD**	**Min-Max**	**P Value**
Baseline	4.89±1.18	3.1-7.0	NS*
1stWeek	5.88±1.60	3.0-8.9	<0.001
2ndWeek	6.67±2.11	3.2-11.0	<0.001
3rdWeek	7.55±2.71	4.0-12.0	<0.001
4thWeek	7.34±2.78	3.5-12.7	<0.001

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SD= standard deviation, min= minimum, max= maximum.

Chart no 1 bar graph showing mean serum uric acid level over the observation period of studied patients

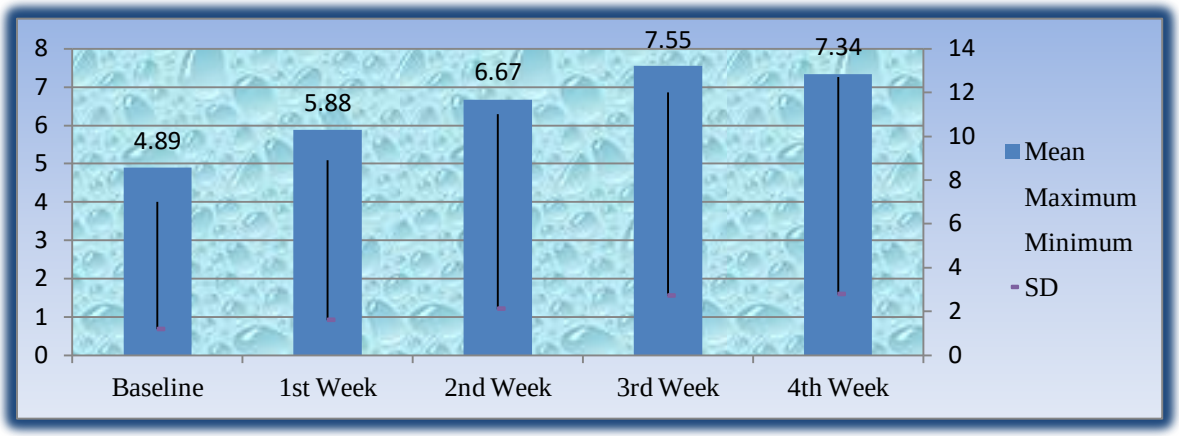

Table no 3 showing Uric Acid Levels from Week 1 to Week 4.In our study, in first week 80(80%) patients had acid level within the normal level i.e. 7.3 and 20(20%) patients had uric level >7.3. In second week 64(64%) patients had uric acid level <= 7.3 and 36 (36%) patients had uric acid level > 7.3 In third week 48(48%) patients had uric acid level <=7.3 and 52 (52%) patients had uric acid level > 7.3 in fourth week 58(58%) patients had uric acid level <= 7.3 and 42(42%) patients had uric acid level >= 7.3 so we saw that uric acid level gradually increased till third week and then decreased in forth weeks this is depicted in bar graph figure number 8.

Table no 3 showing Uric Acid Levels from Week 1 to Week 4of studied patients.

Uric acid level	Week 1		Week 2		Week 3		Week 4	
	No of Patients	%	No of Patients	%	No of Patients	%	No of Patients	%
<=7.3	80	80.0%	64	64.0%	48	48.0%	58	58.0%
>7.3	20	20.0%	36	36.0%	52	520.0%	42	42.0%
Total	**100**	**100%**	**100**	**100%**	**100**	**100%**	**100**	**100%**

Chart no 2 bar graph showing Uric Acid Levels from Week 1 to Week 4 of studied patients.

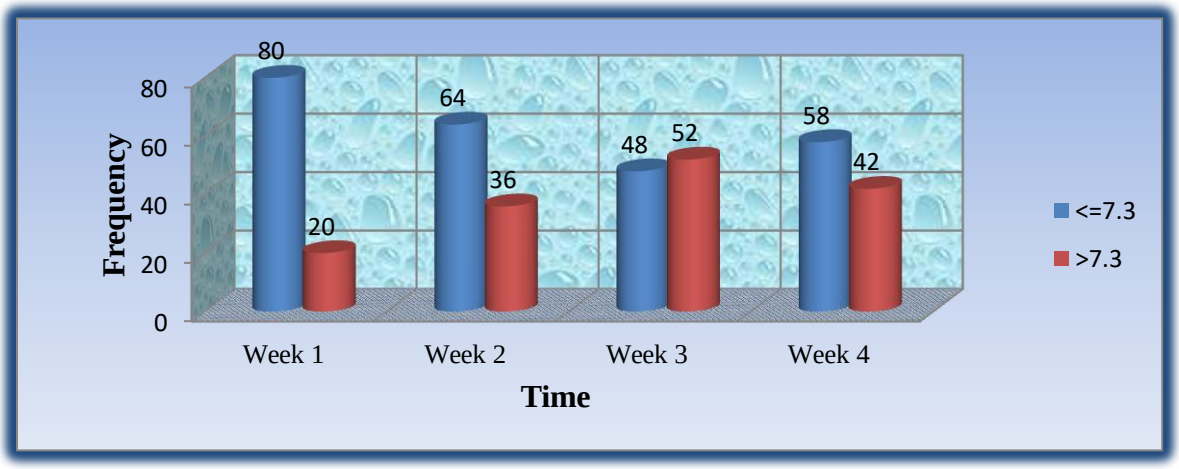

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Table no 4 showing patients who required febuxostat among those who developed hyperuricemia. In our study group out total 52(52%) patients who developed hyperuricemia till 3rd week, only 36(36%) patients required Febuxostat because they were symptomatic because of raised uric acid level. Remaining 16(16%) patients were asymptonatic in spite of having hyperuricemia and so they not require febuxostat. This is depicted in pie chart figure number 9.

Table no 4 showing patients who required febuxostat among those who developed hyperuricemia of studied patients.

Febuxostat Requirement among Hyperuricemics	**No of Patients**	**%**
No	16	16%
Yes	36	36%
Total	**52**	**52%**

Table no 5 showing febuxostat requirement as per age groups.In our study in the age group of 0-20 years none of the patients required febuxostat. In the age group of 21-40 years 5 (13.9%) patients required Febuxostat and in the age group of 61-80 Years 14 (38.9%) patients required Febuxostat. This is depicted in bar graph figure number 10.

Table no 5 showing febuxostat requirement as per age groups among study group.

Age Groups	**Febuxostat Requirement**			
	No		**Yes**	
	No. of Patients	**%**	**No. of Patients**	**%**
0-20	11	17.2%	0	0.0%
21-40	22	34.4%	5	13.9%
41-60	14	21.9%	17	47.2%
61-80	17	26.6%	14	38.9%
Total	**64**	**100.0%**	**36**	**100.0%**

Table no 6 showing sex distribution as per Febuxostat requirement. In our study group of the patients who required febuxostat dose 10(27.8%) patients were females and 26(72.2%) patients were males. This depicted in bar graph figure number 11.

Table no 6 showing sex distribution among study group as per Febuxostat requirement.

Sex	**Febuxostat Requirement**				**P value**
	No		**Yes**		
	No. of Patients	**%**	**No. of Patients**	**%**	
Female	39	60.9%	10	27.8%	0.002
Male	25	39.1%	26	72.2%	
Total	**64**	**100.0%**	**36**	**100.0%**	

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Table no 7 showing smoking status group as per Febuxostat requirement.In our study of the patients who required Febuxostat, 19(52.8%) patients were non- smokers and 17(47.2%) patients were smokers. This is depicted in bar graph figure number 12.

Table no 7 showing smoking status among the study group as per Febuxostat requirement.

Smoker	**Febuxostat Requirement**				**P value**
	No		**Yes**		
	No. of Patients	**%**	**No. of Patients**	**%**	
No	54	84.3%	19	52.8%	<0.001
Yes	10	15.7%	17	47.2%	
Total	**64**	**100.0%**	**36**	**100.0%**	

Table no 8 showing alcohol drinkers as per Febuxostat requirement.In our study group among the patients worequired Febuxostat 12(33.3%) were alcohol drinkers and 24 (66.7%) patients were non-alcoholics. This is depicted bar graph figure number 13.

Table no 8 showing alcohol drinkers among study group as per Febuxostat requirement.

Alcoholic	**Febuxostat Requirement**				**P value**
	No		**Yes**		
	No. of Patients	**%**	**No. of Patients**	**%**	
No	51	79.7%	24	66.7%	0.159
Yes	13	20.3%	12	33.3%	
Total	**64**	**100.0%**	**36**	**100.0%**	

Table no 9 showing dietary habits as per Febuxostat requirement.In our study group among the patients worequired Febuxostat 12(33.3%) were alcohol drinkers and 24 (66.7%) patients were non-alcoholics. This is depicted bar graph figure number 13.

Table no 9 showing dietary habits among the study group as per Febuxostat requirement.

Diet	**Febuxostat Requirement**				**P value**
	No		**Yes**		
	No. of Patients	**%**	**No. of Patients**	**%**	
Non-Veg	39	60.9%	23	63.9%	0.832
Veg	25	39.1%	13	36.1%	
Total	**64**	**100.0%**	**36**	**100.0%**	

Table no 10 showing Serum uric acid level of the study groups. Where before treatment serum uric acid level was 8.25±2.70 and after treatment 6.25±2.75. The difference between groups was statistically significant (p value<0.05).

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Table no 10 showing serum uric acid level of the study groups and treatment given by febuxostate.

Serum uric acid level	Mean±SD	P value
Before treatment	8.25±2.70	0.005
After treatment	6.25±2.75	

Discussion:

Pyrazinamide (PZA) has become an important component of short-term, multiple-drug therapy of tuberculosis (TB). It is a synthetic analogue of nicotinamide that is only weakly bactericidal against extracellular Mycobacterium tuberculosis organisms, but it has potent intracellular bactericidal activity, particularly in the relatively acidic intracellular environment of macrophages and areas of acute inflammation. This drug is highly effective during the initial 2 months of treatment, in which acute inflammatory changes persist, and its use has enabled shorter treatment regimens and has reduced the risk of relapse. It is mainly metabolized in the liver and is excreted largely in the urine.,

Pyrazinamide inhibits renal tubular excretion of urate by inhibiting its renal tubular secretion, resulting in some degree of hyperuricemia that is often asymptomatic. Occasionally, however, acute episodes of gout can occur in patients treated with PZA. In addition, arthralgia may occur in these patients, unrelated to their uric acid level, that is responsive to treatment with analgesics such as aspirin.

The current urate-lowering strategies include reducing the urate production with xanthine oxidase (XO) inhibitors and accelerating the urinary excretion of uric acid (UA) with uricosuric agents. , Uricosuric agents, such as probenecid and benzbromarone, may have limited effectiveness in patients with reduced renal function., The purine analog XO inhibitor, allopurinol, has remained widely prescribed for the treatment of hyperuricemia, but requires dose adjustment in subjects with renal impairment, which may lead to a reduced benefit. ,

Febuxostat, a newer XORI, is highly efficacious in reducing serum urate levels (sUAs). , , It also reduces UA levels in healthy volunteers and in individuals with hyperuricemic gout. Total 100 patients (both male and females) of all aged diagnosed with pulmonary tuberculosis were taken for in this study.

Demography Data

In this study the mean age of participants was 45.18 □19.04 years which indicate that adult with more than 40 year age vulnerable to uric acid. The male; female ratio was calculated to be 1.04. Similarly, Goldfarb DS et al reported mean age above 40 year and men are dominating than female. Few studies have reported men are affected more than women. Older age confers greater risk to both gender groups as reported by Weaver AL , Roddy E et al and Smith EUR et al.

Comparison Of Uric Acid Level Using Pyrazinamide To Other Comparative Studies

In our study, the mean serum uric acid level was observed to be within the normal limit of 7.3mg/dl during the first 2 weeks after the initiation of ATT. The trend of present study we observed between increasing serum UA levels and the number of weeks on therapy is consistent with the studies by Sharma and colleagues, Zierski and colleagures, Khana and colleagues, and Inoue and colleagues in which the incidence of hyperuricemia was 43.4%, 56.0%, 73.7%, and 86.3%, respectively, in patients treated with combination therapy or PZA alone. In similar studies by others, the incidence of hyperuricemia following PZA therapy alone was as high as 100%. , Iyer, K et al and Jenner, P.J et al also have been reported hyperuricemia in 100% of the subjects treated with pyrazinamide. , Such differences in the prevalence of hyperuricemia following combination therapy is probably attributable to rifampicin. Raghupati and colleagues have shown previously that rifampicin enhances the renal excretion of UA regardless of the presence or absence of PZA as a component of the combination therapy used in the treatment of patients with TB. In the present study, the relatively lower prevalence (52.0%) of hyperuricemia was probably related to the small sample size and small follow up duration. One of the causes of the difference between our study and other studies could be racial difference. Exclusion of ethambutol in the present study might also have been

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responsible for the lower frequency of hyperuricemia, since this drug is known to increase serum UA levels.

Treatment Given By Febuxostat

Following the >40-year period during which allopurinol (marketed in 1966) was available as the only XO inhibitor, febuxostat was approved in 2009 in the USA for the chronic management of hyperuricemia in patients with gout. Oxypurinol, the active metabolite of allopurinol, exerts the XO-inhibitory activity (the Kd value: 0.54 nmol/L) by binding to the reduced form of XO (Mo(IV)) through a strong covalent bond. However, the covalent bond disappears and oxypurinol is released because Mo (IV) is reoxidized with time and returns back to the oxidized form of XO (Mo (VI) whose half-life is 300 min at 25°C), and enzyme activity thus recovers. Febuxostat presents striking contrast to oxypurinol because of its strong binding to enzyme proteins through multiple interactions, e.g., ionic bond, multiple hydrogen bonds, and hydrophobic interactions. Therefore, febuxostat does not depend on the oxidized or reduced form of XO and is strongly bound to both the oxidized and reduced forms of XO, thus inhibiting the enzyme for a long period of time and translating into its obvious therapeutic advantages. Furthermore, febuxostat has high enzyme selectivity because of minimal effects on enzymes other than XO involved in the purine and pyrimidine metabolism. Moreover, rat models, in which oxonic acid is used to induce hyperuricemia , , indicate that hyperuricemia provokes a diversity of pathophysiological changes, e.g., activation of the renin-angiotensin system, decreased creatinine clearance, and severe arteriolopathy of the afferent arteriole. , Experimental studies afforded evidence that allopurinol and febuxostat, when used before the development of irreversible histological damage in the vasculature and glomeruli, can reverse these adverse changes, thereby preventing renal function reduction. ,

Present study showed significant decrease of uric acid after the treatment ($p<0.05$). Two large-scale RCTs published before the approval of febuxostat by the Food and Drug Administration as reported by Becker MAet al and Schumacher HR Jr et al demonstrated that febuxostat 80 mg daily more effectively lowered serum UA concentrations than did allopurinol 300 mg daily. In an 8-week, double-blind, randomized, allopurinol-controlled clinical trial in 244 patients with gout, febuxostat 40 mg daily showed a significantly more potent urate-lowering effect than allopurinol 200 mg daily. The treatment of patients with asymptomatic hyperuricemia (a serum UA level higher than 8 mg/dL) with urate-lowering agents has been recommended and applied in Japan, A 6-month, large-scale, RCT of febuxostat 40/80 mg or allopurinol 300 mg (200 mg in moderate renal impairment) was conducted in 2,269 patients with gout and SUA ≥8.0 mg/dL ; A phase II, multicenter, double-blind study was conducted to assess the efficacy and safety of doses of febuxostat in 128 patients with gout or hyperuricemia (serum urate levels ≥8.0 mg/dL). Participants were randomized to receive once-daily doses of placebo or febuxostat (10 mg, 20mg, or 40 mg; n = 32, per group). Patients assigned to the febuxostat groups were administered 10 mg febuxostat for the first 2 weeks, followed by 10 mg, 20 mg, or 40 mg for a subsequent 6-week treatment period, while individuals assigned to the placebo group received placebo throughout the 8-week trial. Serum urate levels of <6.0 mg/dL were achieved in 0%, 22%, 31.5%, and 41.9% of patients with placebo, 10 mg, 20 mg, and 40 mg febuxostat groups, respectively. There was no significant difference in response rate between gout and hyperuricemia patients or between urate overproducers or underexcreters. Febuxostat was safe and well tolerated at all doses (Kamatani et al).

Conclusion

1. In our study we took 100 patients from OPD and ward in a tertiary care hospital as per our inclusion criteria
2. In our study the mean age was 45.18 ± 19.04.
3. Greater number of patients was in the age group of 41-60 (31 %) and 61-80 (31 %) years and uric acid was also higher in these two age groups.
4. Uric acid level raised after 2 weeks of administration of pyrazinamide but it gradually increased in 4th week.
5. Anti-tuberculous therapy with pyrazinamide affects the uric acid levels early. This change is reversible after the withdrawal of the agent.
6. The equivalent UL efficacy and comparable safety for febuxostat 40 mg daily

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7. There is significantly greater efficacy of febuxostat 40 mg daily in lowering serum uric acid.
8. Although further observation on post-marketing safety and efficacy of long term treatment with febuxostat in patients with gout or hyperuricemia and with other complications is required**.**

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