ISSN 2515-8260 Volume 10, Issue 1, 2023

TO STUDY THE EFFECT OF ALLOPURINOL AND PROBENECID IN GOUT ARTHRITIS WITH CVD IN TERTIARY CARE HOSPITAL

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Abstract

Background: Gout is a type of arthritic disease correlated with several pains, stiffness and swelling of one or more joints. This disease can be diagnosed by testing synovial fluid, uric acid levels etc. the most commonly prescribed drug were probenecid, allopurinol, feburostat and NSAIDs. The main aim of the study is to detect whether allopurinol and probenecid shows efficiency in treating CVD patients with gout.

Aim: to study the effect of allopurinol and probenecid in gouty arthritis with CVD in tertiary care hospital.

Material and Method: The present study was conducted on 100 gout patients. All the patients were equally divided into two groups; group -1, 50 patients were treated with allopurinol and group 2, 50 patients treated with probenecid. All this patients monitored with symptoms and also tested with blood pressure, serum creatinine, blood urea, and blood uric acid.

Results: In our study male are more compared with female with a age group of 66 – 70 year in both group 1 & 2. Gout is mostly seen at ankle with swelling as a symptom followed by pain in both the groups. After 3 months of treatment in group 1 significant was observed in uric acid values, but in group 2 both uric acid and urea are shown significant. On comparing both the groups after 3 months uric acid levels shows significant difference between group 1 and 2 respectively.

Conclusion: probenecid is the better drug of choice when compared with that of allopurinol in controlling uric acid levels in gouty arthritis.

Keywords: gout, uric acid levels, CVD.

Introduction

Gout is a disease of kings (Hippocrates) that can occur due to high intake of food rich of dietary pure consumption such as meat, seafood, ethanol etc[1]. The peak incidence of gout can be observed in the age of 30 and 50 years, but at age 60 years, it can be observed both equally in male and female [2]. After the age of 80 years gout can be observed more in female than in males [2]. According to uric acid levels in blood the incidence of gout can be noted, were in the patient's serum uric acid levels greater than 9.0%, the annual incidence of gout was 4.9% [3]. In men and post menopausal women, hyperuricaemia is defined as a serum uric acid levels more that 7.0 mg/dl [3]. In pre menopausal women, hyperuricaemia, uric acid more than 6.0 mg/dl[1]. Gene polymorphism can also cause hyperuricaemia leading to gout. Gene such as SLC22A12, SLC2A9, ABCG2, SLC17A1, SLC17A3, SLC22A11, GCKR, LRRC16A, and

ISSN 2515-8260 Volume 10, Issue 1, 2023

PDZK. SLC22A12 encodes transporter of URT1 and SLC2A9 regulates uric acid excretion, if this gene polymorphism occur leading to increase in uric acid levels that may cause gouty arthritis [4.5]. The increased Uric acid levels can be calculated by fraction excretion of urate compared with creatinine clearance. For the calculation both the blood and urine samples as to be taken and tested at a time. The formula is [urine UA × serum Cr/serum UA x urine Cr]. The normal fraction excretion is 7.0% [6]. As per the diagnostic criteria, if a S.UA levels are between 7 to 7.9 mg/dl only 0.09 % development of gout can be seen every year. But if S.UA between 8 to 8.9 mg/dl, 0.4 % development of gout. If a uric acid level more than 9 mg/dl, only 0.5 % patients may get gout [7]. For the management of gout drugs such as Colchicine, NSAIDs, and steroids can be used but to control uric acid there are uric acid lowering drug such as allopurinol, xanthine oxidase inhibitor, inhibit formation of uric acid and uricosuric drug such as probenecid, causing uric acid excretion form the body through urine [8]. The main motto of the study is to know which is the better drug of choice in controlling gout after 3 months of treatment

Materials and Methods

Study Place

This study was carried out in the Department of orthopedic; Rama Medical College, Hospital & Research Centre, Kanpur, U.P. from June 2021 to November 2021 The study was approved after taking permission from Institute Ethics Committee.

Inclusion Criteria

1. Age between: 50 – 70 years.
2. Cardiovascular disease with gout patients.
3. Patient ready to give inform consent form.

Exclusion Criteria

1. Patient taking anti-gout drugs.
2. Age less than 50 years
3. Patient not ready to give inform consent form
4. Patient with cardiovascular surgery.
5. Patient with renal diseases.

Study Sample

Total of 100 patients with cardiovascular disease with gout.

Study Design

Total of 100 patients were equally divided into two groups

- **Group –1** 50 patients prescribed with allopurinol
- **Group – 2** 50 patients prescribed with probenecid

Methodology

A total of 100 cardiovascular patients with gout were selected for the study. All the patient symptoms, region of arthritis and biochemical investigation of serum creatinine, blood urea and uric acid was estimated and noted.

ISSN 2515-8260 Volume 10, Issue 1, 2023

Statistical Analysis

Statical analysis was done by using SPSS software. For comparing within the group (before and after treatment) paired t test was conducted. On comparing different groups unpaired t test was done. Significance levels for tests were determined as 95% (P< 0.05)

Results

The study was carried out in 100 patients and divided into two group and equally divided into two group in group – 1, there were 32 male and 18 female and group – 2, there were 31 male and 19 females showing insignificant (p >0.642). (Table No 1). Majority of the patients were under the age group of 66 – 70 in group 1 & 2. (Table No 2).

Table No: 1 Tabular column represent the gender in group – 1 and 2.

Group – 1		Total Number of patients	Group – 2		Total Number of patients	P value
Male	Female		Male	Female		
32	18	50	31	19	50	0.642

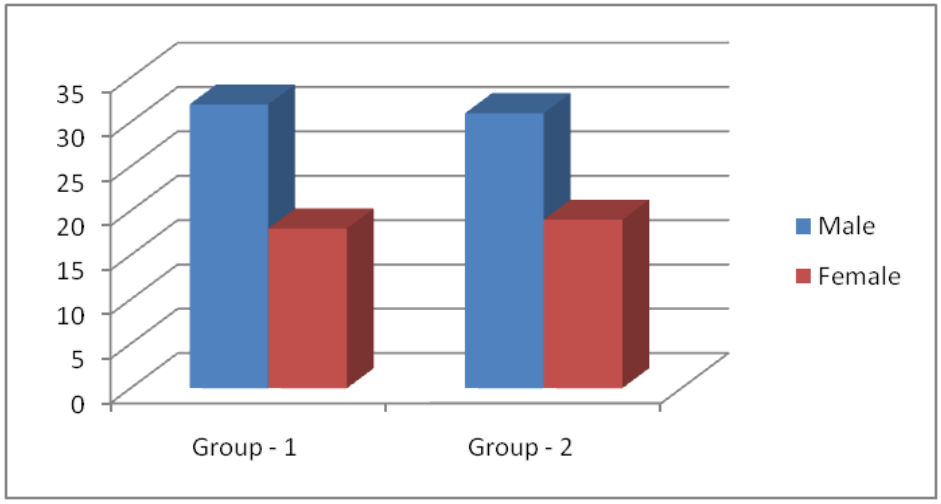


Figure No 01: Graphical representation of gender in group - 1 & 2.

Table No 02 : Tabular column represents the age groups of patients in groups 1 and 2.

Age Groups	Group – 1	Group – 2	Total Number of patients
50 – 55	04	06	10
56 – 60	08	10	18
61 – 65	15	14	29
66 – 70	23	20	43

ISSN 2515-8260 Volume 10, Issue 1, 2023

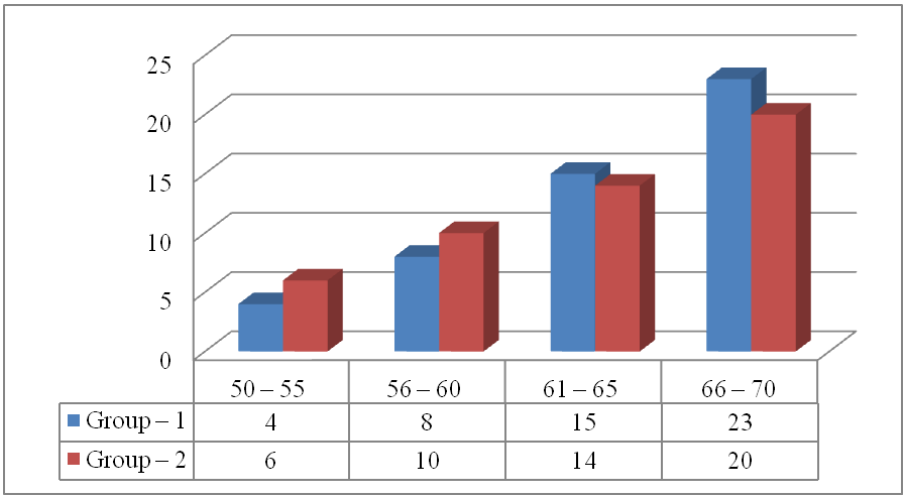


Figure No 02: Graphical representation of age groups of patients in groups 1 and 2.

Table No 03: Tabular column represents gouty arthritis in different regions in group 1 and group 2 patients.

Gout in different places	Group – 1 (50 patients)	% in gout in different places	Group – 2 (50 patients)	% in gout in different places	Total
Toes	15	30%	13	26%	28
Mid foot	05	10%	04	08%	09
Ankles	10	20%	11	22%	21
Knees	08	16%	07	14%	15
Fingers	04	08%	05	10%	09
Wrists	06	12%	08	16%	14
Elbows	02	04%	02	04%	04

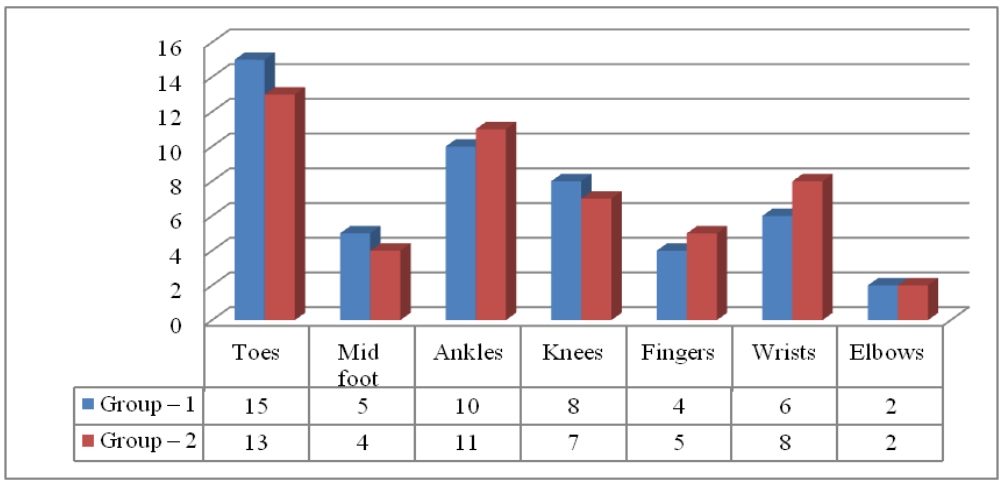


Figure No 03: Graphical representation gouty arthritis in different regions in group 1 and group 2

Table No 04: Tabular column represents the symptoms of gouty in group – 1 and 2

Symptoms	Group – 1	Group – 2	Total no of symptoms
Pain	38	32	70
Discoloration or	26	30	56

ISSN 2515-8260 Volume 10, Issue 1, 2023

Redness			
Stiffness	34	38	72
Swelling	46	43	89
Tenderness	24	20	44
Itching	08	06	14
Total	176	169	345

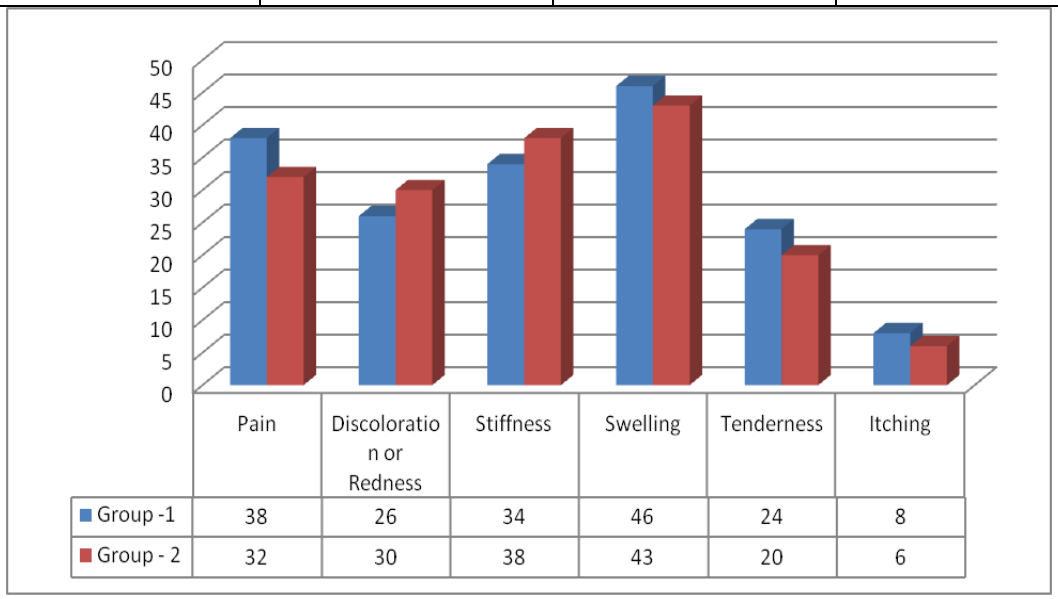


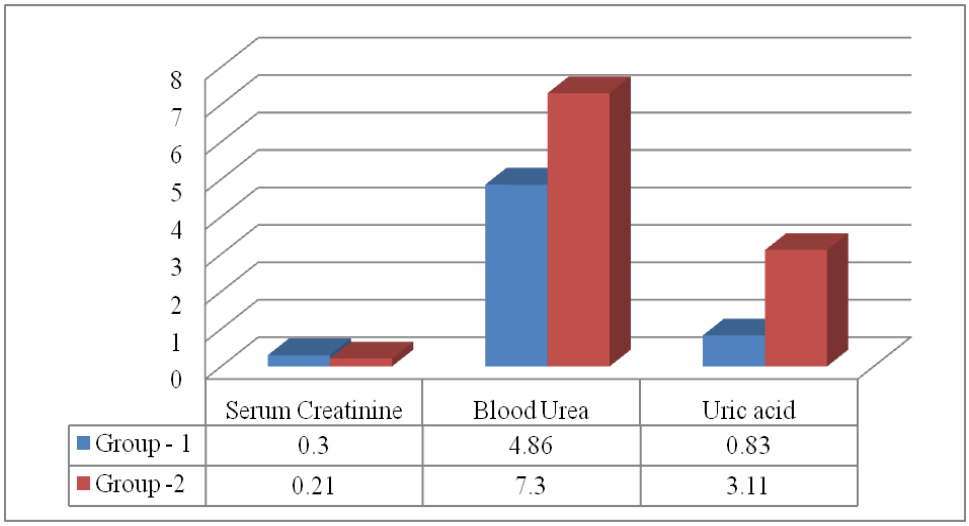
Figure No 04: Graphical representation of number of symptoms in gouty arthritis patients

Table No 05: Tabular column represents comparison of baseline values with 3months values of serum creatinine, blood urea, and uric acid in group - 1 and 2 after conducting paired t test.

Parameter Group – 1	(Baseline)	3 Months	MD ± SD	P value
Serum Creatinine	1.06 ± 0.35	0.76 ± 0.39	0.30 ± 0.04	0.146
Blood Urea	37.30 ± 4.50	32.44 ± 7.06	4.86 ± 2.56	0.055
Uric acid	8.67± 0.85	7.84 ± 0.94	0.83 ± 0.09	0.050*
Parameter Group – 2	(Baseline)	3 Months	MD ± SD	P value
Serum Creatinine	1.09 ± 0.37	0.88 ± 0.30	0.21 ± 0.07	0.114
Blood Urea	36.18 ± 4.16	28.88 ± 6.72	7.30 ± 0.56	0.042*
Uric acid	9.73 ± 0.79	6.62 ± 1.07	3.11 ± 0.28	0.014*

Paired t test; Significance levels for tests were determined by $p<0.05$.

ISSN 2515-8260 Volume 10, Issue 1, 2023

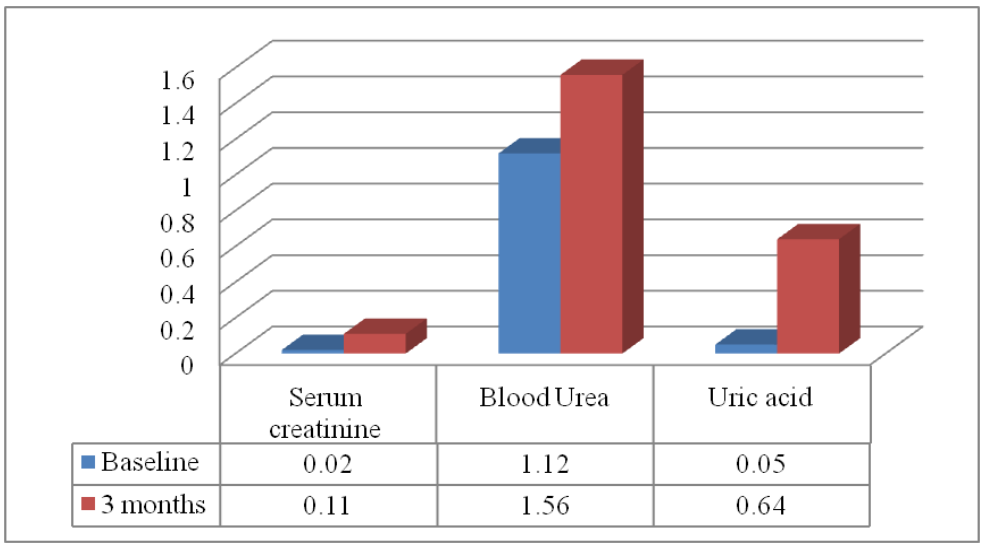


Graph No 05: Graphical representation mean difference after comparing baseline values with 3 months of serum creatinine, blood urea and uric acid in group – 1 and 2.

Table No 06: Tabular column represents comparison between the groups – 1 and 2 of serum creatinine, blood urea and uric acid.

Parameters	Duration of treatment	Group – 1	Group – 2	MD ± SD	P value
Serum Creatinine	Baseline	1.06 ± 0.35	1.09 ± 0.37	0.02 ± 0.02	0.722 (95% CI(-0.17to-0.11)
	3 Months	0.76 ± 0.39	0.89 ± 0.30	0.11 ± 0.09	0.095 (95% CI(-.025 to 0.02)
Blood Urea	Baseline	37.30 ± 4.50	36.18 ± 4.16	1.12 ± 0.34	0.200 (95% CI(-0.60 to 2.84)
	3 Months	32.44 ±7.06	30.88 ± 6.72	1.56 ± 0.34	0.261 (95% CI(-1.17 to 4.29)
Uric Acid	Baseline	8.67 ± 0.85	9.73 ± 0.79	1.06 ± 0.06	0.135 (95% CI(-0.38 to 0.27)
	3 Months	7.84 ± 0.94	6.62 ± 1.07	1.22 ± 0.13	0.002* (95% CI(0.24 to 1.04)

Unpaired t test ; Significance levels for tests were determined by $p<0.05$.



Graph No 06: Graphical representation mean difference between the groups – 1 and 2 of serum creatinine, blood urea and uric acid.

Discussion

The present study was carried out on 100 gouty arthritis patients and they were divided into two groups. In group 1 and 2 majority of the patients were male followed by female, showing

statically insignificant (p>0.642). As per the age group consent, most of the patients were less than 66 – 70 years in both group 1 &2 (Table & Figure No 2) respectively. In our study gouty arthritis was observed in different areas, such as toes, mid foot, ankles, knees, figures, wrists, & elbows, mostly gouty arthritis was observed at ankles 20 & 22% in group – 1 & 2 respectively (table & figure No 3). As per the Symptoms majority of the patients in group – 1 & 2 having Swelling, followed by pain, stiffness, discoloration or redness, tenderness, itching, almost the patients having more than one symptoms majority was swelling (89/100 patients). Mostly gout arthritis is caused due to accumulation of uric acid crystals in joint leading to severe pain and swelling. The treatment goal is to prevent the formation of uric acid and excretion uric acid through urine. Increasing in Uric acid levels in blood may also cause renal problem due to accumulation of urate crystals in kidney, as such it may cause cardiovascular complications. Our study coincides with the study of Manik K et al (2019) [9] mentioned that urate lowering therapy is the best to control the gout with CVD. The mechanism such as hyperuricaemia, inflammation, endothelial dysfunction, and oxidative stress can cause CVD, that can be lowered by using urate lowering therapy. As such in our study all the patients were tested with serum creatinine, urea and uric acid levels, there were treated with allopurinol (group – 1) and probenecid (group – 2) followed upto 3 months. In group – 1 patients, after 3 months of treatment there is no significant mean reduction in serum creatinine and blood urea in (p>0.05) but significant mean reduction was observed in uric acid levels. In group - 2, no significant was observed in serum creatinine (p>005), were as significant was observed in blood urea and uric acid levels (p<0.05) respectively (Table & figure No 5). Our study correlates with the study of Reinders, M.K et al (2007) [10], allopurinol dose of 200 – 300 mg/day shows a less potent in lowering serum uric acid levels, its success rate is 13%. Were as with probenecid is a better in lowering uric acid levels, its success rate is 86%. On comparing both the groups i.e group 1 and 2 no significance was observed at baseline & after 3month values of serum creatinine, blood urea, significance was observed after comparing 3 months values of uric acid in between group – 1 and 2 (Table & Figure No 6). Our study shows similarity with the study of Kim S et al (2018) [11] in his study he concluded that probenecid shows better decrease in MI, stroke, and mild heart failure compared with allopurinol. Another study by Stocker S.L et al (2011) [12] in his study he noted that combination of allopurinol with probenecid showing significant hypouricemic effect after comparing with single use of allopurinol.

Conclusion

Hyperuricaemia plays a major role in causing gout. Probenecid is the better drug of choice in lower urea and uric acid levels compared with allopurinol group. If a uric acid excretion is more that cannot accumulate in kidney's that may lead in bettering CVD.

References

1. Kim KY, Schumacher HR, Hunsche E, Wertheimer AI, Kong SX. A literature review of the epidemiology and treatment of acute gout. Clin Ther 2003;25(6):1593–617.
2. Kirby BS, McTigue JC, Edwards NL. Pain management in gout. Curr Pain Headache Rep 2008 December;12(6):418–22.
3. Gaffo AL, Saag KG. Management of hyperuricemia and gout in CKD. Am J Kidney Dis 2008;52(5):994–1009.
4. Phipps-Green A.J., Merriman M.E., Topless R., Altaf S., Montgomery G.W., Franklin C. Twenty-eight loci that influence serum urate levels: analysis of association with gout. Ann Rheum Dis. 2016;75(1):124–130

5. Kolz M., Johnson T., Sanna S., Teumer A., Vitart V., Perola M. Meta-analysis of 28,141 individuals identifies common variants within five new loci that influence uric acid concentrations. PLoS Genet. 2009;5(6):e1000504.
6. Kosmadakis G., Viskaduraki M., Michail S. The validity of fractional excretion of uric acid in the diagnosis of acute kidney injury due to decreased kidney perfusion. Am J Kidney Dis. 2009;54(6):1186–1187.
7. Dincer H.E., Dincer A.P., Levinson D.J. Asymptomatic hyperuricemia: to treat or not to treat. Clevel Clin J Med. 2002;69(8):594. 7, 600-2.
8. G. Ragab et al. Gout: An old disease in new perspective – A review. Journal of Advanced Research .2017; 8(1): 495–511
9. Manik K. Gupta & Jasvinder A. Singh. Cardiovascular Disease in Gout and the Protective Effect of TreatmentsIncluding Urate-Lowering Therapy. Drugs. 2019;79:531-541.
10. Reinders, M.K., van Roon, E.N., Houtman, P.M. et al. Biochemical effectiveness of allopurinol and allopurinol-probenecid in previously benzbromarone-treated gout patients. Clin Rheumatol 26, 1459–1465 (2007).
11. Kim S, Neogi T, Kang E, et al. Cardiovascular Risks of Probenecid Versus Allopurinol in Older Patients With Gout. J Am Coll Cardiol. 2018; 71 (9): 994–1004.
12. Stocker SL, Graham GG, McLachlan AJ, Williams KM, Day RO. Pharmacokinetic and pharmacodynamic interaction between allopurinol and probenecid in patients with gout. J Rheumatol. 2011 May;38(5):904-10. doi: 10.3899/jrheum.101160. Epub 2011 Feb 1. PMID: 21285173.