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COMPARATIVE EVALUATION OF EFFECT OF LOSARTAN AND AMLODIPINE AS MONOTHERAPY ON SERUM URIC ACID LEVELS IN PATIENTS OF HYPERTENSION WITH HYPERURICAEMIA

Pharmacology

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ABSTRACT

Randomised, prospective, comparative study was conducted in Government Medical College, Amritsar. 60 patients of hypertension with hyperuricaemia were assigned into two groups of 30 patients each. Group A was treated with Losartan 50mg and group B received Amlodipine 5mg, once daily orally. BP was recorded every 2 weeks for 12 weeks and serum uric acid was monitored every 4 weeks for 12 weeks. Systolic /diastolic blood pressure decreased by14.80/10.13 mm Hg respectively in group A and by 14.20/11.53 mm Hg respectively in group B which was highly significant ($p < 0.001$). Intergroup difference was non-significant. SUA reduction with losartan (22.69%) was more as compared to amlodipine (4.45%) and difference was statistically significant ($p<0.05$). Both the drugs were well tolerated in both the groups. Losartan was more efficacious in hypertensive patients with concomitant hyperuricaemia than amlodipine.

KEYWORDS

Angiotensin II receptor antagonist, Calcium channel blocker, adverse effects

INTRODUCTION

Hyperuricaemia is frequently associated with hypertension. 25 to 40% of adult patients with untreated hypertension have hyperuricemia (>6.5 mg/dl).[1] High blood pressure levels are associated with hyperuricaemia due to reduced renal blood flow causing decreased excretion of urate. Patients with hypertension and hyperuricaemia have 3-5 fold increased incidence of experiencing cardiovascular disease compared with normal uric acid levels.[2] Thus serum uric acid represents a new target for reduction of morbidity and mortality associated with hypertension. Since hyperuricaemia often coexist with hypertension, antihypertensives with favorable effect on hyperuricaemia will be a newer treatment strategy.

Losartan is a non-peptide competitive Angiotensin-II AT-I receptor antagonist that lowers BP by blocking angiotensin receptors, antagonize the effects of angiotensin II thereby promote vasodilatation, increase renal salt and water excretion and is an effective antihypertensive drug. Losartan is recently shown to target urate anion exchange {URATI} and inhibit urate uptake by this transporter thus reducing urate reabsorption from the proximal convoluted tubule of the kidney.[3]Amlodipine is a dihydropyridine calcium channel blocker that lowers BP by decreasing peripheral resistance without compromising cardiac output by inhibiting influx of calcium through voltage sensitive calcium channels.

The present study is envisaged to benefit hypertensive patients with concomitant hyperuricemia receiving antihypertensive monotherapy. Antihypertensive agents namely losartan and amlodipine were compared for their effect on serum uric acid levels, if any, in concomitant hyperuricaemia.

MATERIAL AND METHODS

A randomized, parallel, prospective, open label, comparative study between losartan and amlodipine in patients of hypertension with hyperuricaemia was conducted in the Department of Pharmacology in collaboration with Department of Medicine, Guru Nanak Dev Hospital attached to Government Medical College, Amritsar. Before starting the study, approval of Institutional Ethics Committee was taken. Sixty patients of either sex and age > 18 years and <70 years of age with hypertension having systolic BP>140 mm Hg and diastolic BP>90 mm Hg [JNC VIII guidelines] and with serum uric acid levels more than or equal to 6mg/dl were recruited in the study after taking their written informed consent. Patients with comorbidities like coronary heart disease, myocardial infarction, angina, peptic ulcer disease, pregnant and lactating females were excluded from the study. Patients were randomly divided into 2 groups- A and B consisting of 30 patients each. Group A received losartan 50 mg once daily and Group B was given amlodipine 5 mg once daily orally for 12 weeks. BP was recorded every 2 weeks for 12 weeks and serum uric acid was monitored every 4 weeks for 12 weeks. All the parameters were recorded, tabulated and analysed using 't' test; paired `t`-test for intragroup comparison and unpaired `t` test for intergroup comparison.

OBSERVATION AND RESULTS

At the end of 12 weeks, a highly significant ($p < 0.001$) reduction in Systolic /Diastolic blood pressure was observed in both the groups. Both systolic and diastolic BP were markedly decreased at 2 weeks showing highly significant difference ($p<0.001$) from 0 week values in both the groups (Table:I). The intergroup difference was observed to be non-significant. In group A, there was a highly significant decrease ($p<0.001$) in serum uric acid levels from initial value of 8.09± 0.62 mg/dl at baseline to 6.24±0.33mg/dl after 12 weeks.

In group B, there was a significant decrease ($p<0.05$) in serum uric acid levels from initial value of 8.01±0.79mg/dl at baseline to 7.41±0.75mg/dl after 12 weeks (Table:II). Serum uric acid reduction was more in group A(22.69%) as compared to 4.45% in group B and the difference was statistically significant (p=0.03) (Table III).

There was no significant change in ESR, total cholesterol, blood urea and serum creatinine in both the groups at the end of 12 weeks. Most common adverse effects observed in group A were headache (13.33%) and dizziness (6.7%) whereas in group B, edema (10%) was seen. The therapy was well tolerated in both the groups.

TABLE I COMPARISON OF CHANGE IN BLOOD PRESSURE BETWEEN 0 AND 12 WEEKS

BP (mm Hg)	GROUP A			
	0 week (Mean ± SD)	12 weeks (Mean ± SD)	% change	p- value
SBP	149.46±3.10	134.66±2.94	9.86	**<0.001**
DBP	95.00±8.03	84.87±4.25	10.31	**<0.001**
	GROUP B			
SBP	148.40±4.93	134.20±6.11	9.56	**<0.001**
DBP	96.20±3.53	84.66±4.17	12.00	**<0.001**

FIGURE I

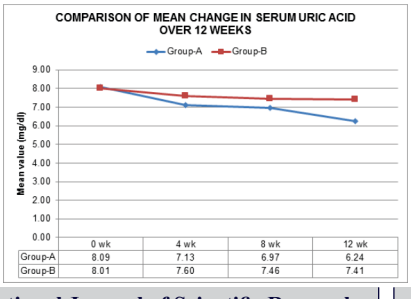

TABLE III COMPARISON OF SERUM URIC ACID LEVELS IN GROUP A vs GROUP B AT 12 WEEKS

	Group A (Mean ± SD)	Group B (Mean ± SD)	p – value
Serum uric acid (mg/dl)	6.24±0.33	7.60±0.78	**0.03**

DISCUSSION

Affecting 1 billion population world over, hypertension remains one of the leading causes of death worldwide making it a public health problem. Moreover, hypertension is also associated with various comorbid conditions and one of them is hyperuricaemia. In the present study, two commonly used antihypertensives (losartan and amlodipine) were considered for comparative evaluation on blood pressure and serum uric acid levels.

In the present study, on evaluation of demographic profile, the mean age of the two groups at baseline was found to be comparable which was 57.50 ± 6.35 years in group A and 58.00 ± 8.18 years in group B. Age distribution was comparative with a study by Podpalov et al. (2006).[4] In the present study, no significant effect was observed on ESR, total cholesterol, blood urea and serum creatinine after 12 weeks of treatment in Group A. Burnier et al (1996) also observed no effect on laboratory values with losartan which was comparable to the present study.[5]

In group B, no significant effect was observed on ESR, total cholesterol, blood urea and serum creatinine after 12 weeks of treatment. The study by Ahmed et al (2009) supports our result with a mean change of 1.4mg/dl in total cholesterol which was insignificant.[6] Iram Shaifali et al (2014) found that mean serum creatinine increased from 0.674±0.01 to 0.732±0.01 mg/dl ($p<0.05$) over 24 weeks and mean blood urea raised insignificantly over 24 weeks ($p>0.05$) after treatment with amlodipine.[7]

In group A (losartan), net fall in SBP was 14.80±0.78 mm Hg which was statistically significant ($p<0.001$). Similar observations were recorded by Giles et al(2007) who reported a fall in SBP of 13 mm Hg.[8] Net fall in DBP was 10.13±1.65 mm Hg which was statistically significant($p<0.001$). Giles et al (2007) noted a fall of 12 mm Hg in DBP after 12 weeks of treatment[8] and Lee et al(2004) observed fall of 9 mm Hg in DBP after 4 weeks of treatment with losartan.[9]

In group B (amlodipine), mean change in SBP and DBP at the end of the study was a fall of 14.20±1.43 mm Hg (9.56%) and 11.53±0.99 mm Hg (12.00%) respectively which was statistically significant ($p<0.001$). In a study by Verma et al (2004), a fall of 20/14 mm Hg in SBP and DBP was observed after 12 weeks of therapy.[10] However, the intragroup comparison between BP lowering effect in group A and B was non-significant with p value of 0.71 and 0.86 respectively for SBP and DBP.

In group A, losartan produced a significant decrease in SUA levels. The SUA levels dropped from a mean of 8.09±0.62 mg/dl at baseline to 6.24±0.33 mg/dl at week 12($P<0.0001$) which is in agreement with the results reported by Khan et al.[11] who observed a decrease in serum uric acid levels from 8.21 mg/dl ±0.17 at baseline to 6.19 mg/dl ± 0.11 ($p < 0.001$) in losartan group. In group B, the mean SUA levels decreased from mean of 8.01±0.79 mg/dl at baseline to 7.60±0.78 mg/dl at week 12. The reduction was statistically significant ($p<0.05$). Salve S et al (2012) observed that the mean SUA levels were 4.33±0.93 mg/dl before the start of the study and were 3.92 ± 0.68 mg/dl at the end of six months and the difference was statistically significant ($p<0.003$).[12] Target SUA levels were achieved by 4 and 0 patients in group A and group B respectively in 12 weeks. In the present study, both losartan and amlodipine decreased the SUA levels but losartan showed greater reduction in lowering SUA levels as compared to amlodipine and the difference was significant ($p=0.03$).

CONCLUSION

It can be concluded that both the drugs were well tolerated with comparable antihypertensive effect. Losartan was more efficacious in reducing SUA levels as compared to amlodipine. Hence losartan is more suitable for hypertensive patients with concomitant hyperuricaemia. Longer duration studies can be carried out to achieve normal serum uric acid levels in all patients.

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