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Comparative Study On the Efficacy of Losartan and Amlodipine in Reducing Microalbuminuria in Patients with Primary Hypertension, A Randomized Open Labelparallel Group Study

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Majority of the cardiovascular and renal diseases has been associated withHypertension Primary hypertension also called as essential or idiopathic hypertension tends to be familial and the prevalence increases with age. Microalbuminuria has been correlated with microvascular damage in hypertension patients. To Compare the Efficacy of Losartan and Amlodipine in reducing microalbuminuria in patients with primary hypertension". An open labeled parellelgroup cross sectioned study was conducted in SreeBalaji medical college and hospital,Department of General Medicine Chrompet during the period of March 2015 to December 2015.In our research study suggested that there are major differences between Angiotensin receptor blockers and calcium chaneel blockers in reducing microalbuminuria in essential hypertension. After 6-month of losartan treatment, thereduction in urine albumin level is statistically highly significant ($p<0.01$) 71.17±66.04.compared with baseline101.95±94.70. After 6 months of Amlodipine treatment group resulted in statistically not significant($p>0.05$) in urine albumin excretion level 99.85±96.35compared with baseline 101.11±95.28 in essential hypertensive patients .Hence this study shows that losartan after administration for 6 months ,conferred significant advantages over amlodipine in terms of reduction of urinary albumin levelslevels in hypertensionpatients.**

Keywords: Primary hypertension ,Microalbuminuria,ARBs and CCBs.

Hypertension affects almost one billion individual worldwide (1). Hypertension accounts for 13.5 % of mortality annually. 90-95% of the patients are considered as primary hypertension in which etiology is due to life style changes and genetic factors(2).

Albuminuria is one of the best indicators of poor renal outcomes of essential hypertension and type 2 diabetes(3). It is also approved as a recent indicator of cardiovascular outcomes (4). Renal and Cardiovascular adverse effects are reduced by reducing albumin levels in the urine

Losartan is the first orally available drug, selective, competitive Angiotensin II receptor type 1 antagonist, its active metabolite is 5 –carboxylic acid which is a very long acting and 30 -40 times more potent. It has a prominent effect in urinary albumin excretion (5).Amlodipine is the dihydropyridine type calcium channel blocker .It is peripheral arterial vasodilator which causes reduction in peripheral arterial resistance and blood pressure.

The anti-hypertensive drugs used now are mostly designed to effect pathophysiological, cellular and biochemical mechanism involved in hypertension and not to address the disorders involved in urine albumin excretion. Several animal and human studies suggested that AT II receptor blocker and CCB have remarkable reduction in microalbuminuria(6). Hence this study was conducted in primary hypertension patients to reduce microalbuminuria bycomparing the efficacy ofLosartan (AT II Receptor Antagonist) with Amlodipine (CCB).

Objective

"To Compare the Efficacy of Losartan and Amlodipine in reducing microalbuminuria in patients with primary hypertension**"**.

MATERIALS AND METHODS

"An open labeled parellel cross sectioned study was conducted in the General Medicine, Department atSreeBalaji medical college and hospital, Chrompet during March 2015 to December 2015**"**. The study was approved by institutional ethics committee and written consent obtained from the patient.The study subjects were assigned randomly using a computer generated randomization chart to either of the two groups group A and group B ,each group consists of 50 patients of primary hypertension .The **"**inclusion criteria are Adult patients of age >18 years. Newly diagnosed Hypertensive patients with e"140/90 mm Hg of blood pressure ,or <1 year period of hypertension patients without taking any antihypertensive medications.and hypertensive patients with a blood pressure e"140/90 mm Hg, for more than 1 year period and taking 2 or more anti-hypertensive medications but still BP is not controlled).The exclusion criteria arepatient with sensitivity to ARB or CCB ,breast-feeding,pregnant .Patient with clinical cardiovascular disease , renal and hepatic disease (creatinine>2.2mg/dl). Patient with >180/110mm Hg ofblood pressure systolic.Type II Diabetes Mellitus and patients with secondary hypertension

Procedure

Urine microalbumin will be analyzed using immunoturbidimetry method by collecting spot urine samples done during initiation of study, after 3 months, and after 6 months of treatment.

Statistical analysis

The analysis of the Data was assessed by SPSS software for Windows (version 10).The results were convey as mean±SD. ANOVA test of

Table 1. Matching of the two groups according to their baseline characteristics and metabolic parameters

Variable	Group A Losartan (50) Mean ± S.D	Group B Amlodipine (50) Mean ± S.D
Age (years)	49.46 ± 9.58	50.28 ± 10.5
No.ofyrs in Hypertension	5.96±3.78	5.48±3.61
SBP(mmHg)	152.18±8.04	151.54±7.83
DBP(mmHg)	95.56±4.78	95.38±4.12
UAE(mg/dl)	101.95±94.71	101.11±95.28
Uric acid (mg/dl)	5.66±0.88	5.67±0.84
Serum Creatinine (mg/dl)	1.43±0.52	1.44±0.49
Serum Urea(mg/dl)	25.89±2.19	25.18±2.29
AST (U/L)	27.06 ± 7.5	26.8 ± 7.7
ALT (U/L)	28.56 ± 6.5	28.6± 7.0
Haemoglobin (gm/dl)	12.82 ± 3.2	12.78 ± 2.8

Table 2. Gender Distribution

Gender	Group-A (Losartan)		Group-B(Amlodipine)		Pearsonchi-square test
	Number	%	Number	%	
Male	26	52%	27	54%	X^2= 0.00
Female	24	48%	23	46%	
Total	50	100%	50	100%	

·Statistical analysis was done by using ÷ ² .p value was not significant.
·There was a male preponderance in both the groups.

Table 3. Effect of Losartan on Urine Albumin Excretion

Urine albuminexcretion	Baseline	3 months	6 months
Mean ±S.D	101.95±94.70	84.65±79.12**	71.17±66.04**

Table 4. Effect Of Amlodipine On Urine Albumin Excretion

Urine albumin excretion	Baseline	3 months	6 months
Mean ±S.D	101.11±95.28	100.51±96.99NS	99.85±96.35NS

Table 5. Incidence of Adverse Effects

S. No	Adverse effect no (%)	Losartan group (50)	Amlodipine group (50)
1	Nausea	-	2(4%)
2	Fatigue	1(2%)	-
3	Dizziness	2(4%)	1(2%)
4	Head ache	3(6%)	4(8%)
5	Abdominal pain	-	1(2%)
	Total	6	8

One-wayanalysis was used to measure the baseline data . The end result values was calculatedat the end of 24-Week treatment minus the value obtained at baseline. The significance differencesbetween and within groups wasanalysed byANOVA. Student's *t*-testare assessed to compare Before and after treatment values. At the end of the duration of the studylosartan and amlodipineeffect on microalbumin levels were compared in terms oftherapeutic efficacy and adverse effects. p -values

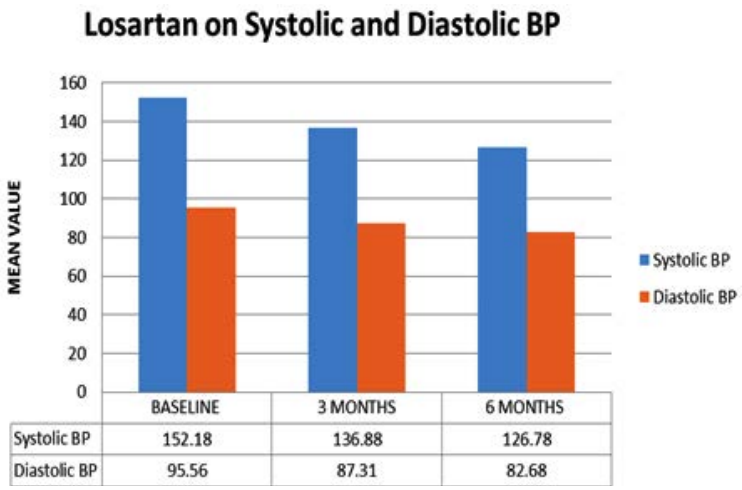

Fig. 1. Effect of losartan on SBP and DBP

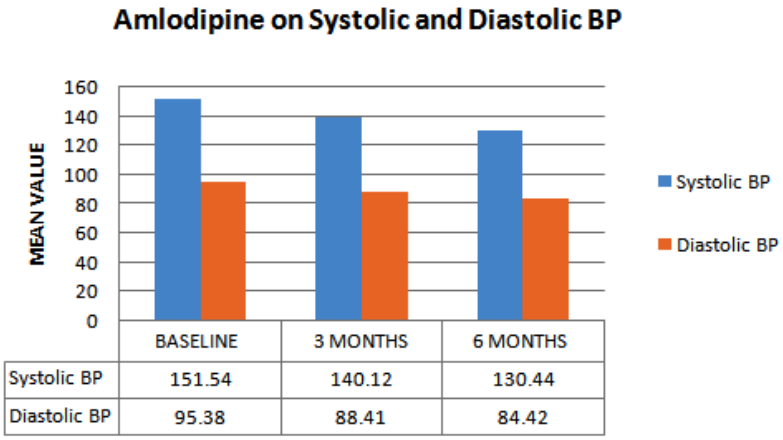

Fig. 2. Effect of Amlodipine on Systolic BP and Diastolic BP

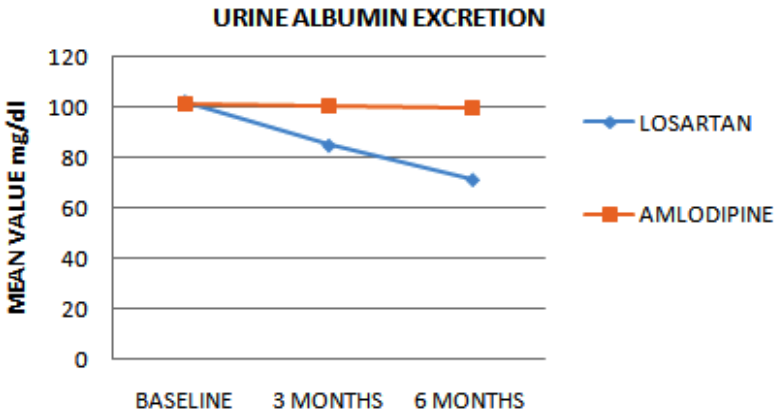

Fig. 3. Effect of Losartan and Amlodipine on Urine Albumin Excretion

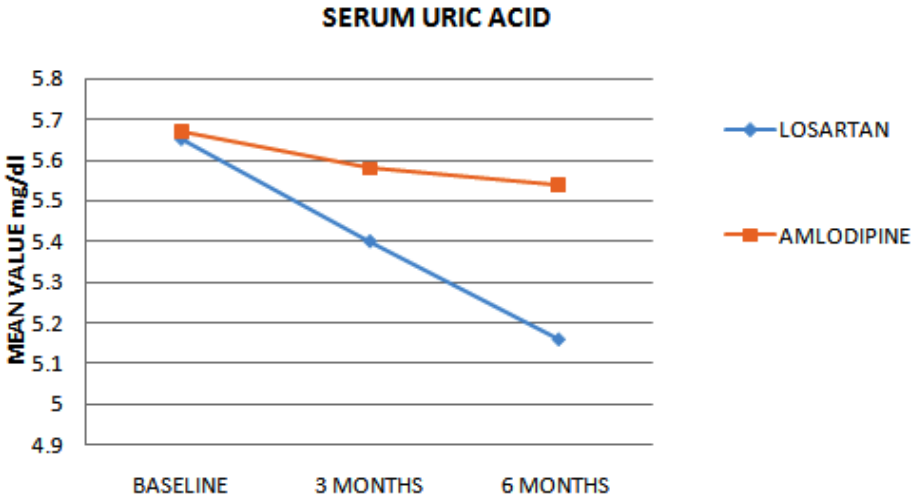

Fig. 4. Compare the effect of Losartan and Amlodipine on Uric Acid

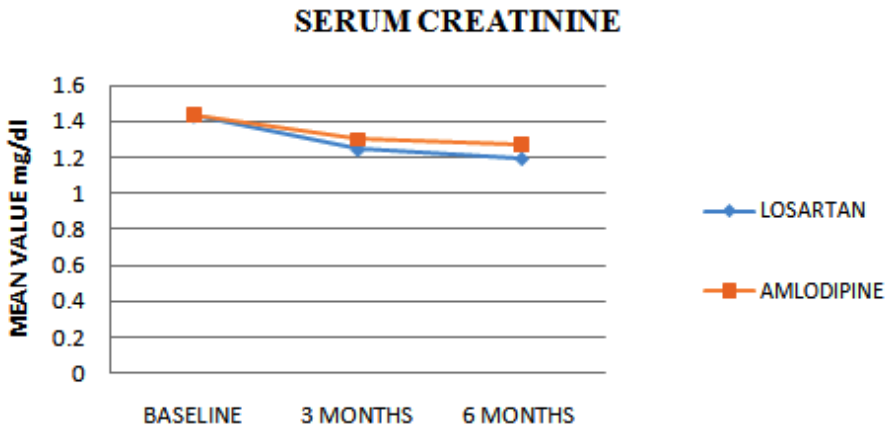

Fig. 5. Evaluate the Effect of Losartan and Amlodipine on Serum creatinine

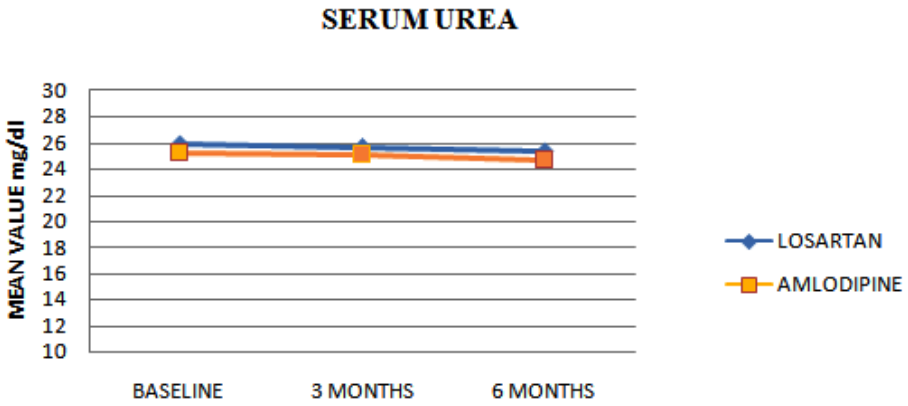

Fig. 6. The Effect of Losartan and Amlodipine on serum urea

($p<0.05$) were treated as statistically significant in two tailed test.

DISCUSSION

The current study shows that after 6 months of treatment, both losartan and amlodipine significantly ($p<0.01$) reduced SBP and DBP compared with baseline (figure 1 and 2).The blood pressure in hypertensive patients is controlled due to the blockade of RAS with ARBs i.e. Losartan has antihypertensive and conferring cerebral, cardiac and renal target-organ protection by exhibiting their pleiotropic effects(7).Ca^{2+}channel blocker (Amlodipine) is a very effective antihypertensive agent that lowers blood pressure primarily through arteriolar vasodilatation and decreasing peripheral vascular resistance.Ca^{2+}channel blocker may reduce the cardiovascular risk to a greater extent than BP lowering effect (8).

After 6-month of losartan treatment, the reduction in urine albumin level is significant ($p<0.01$) from a baseline value of 101.95±94.70 to 71.17±66.04(Table 3). Amlodipine treatment group urine albumin excretion level resulted in statistically not significant ($p>0.05$) compared with baseline101.11±95.28 to 99.85±96.35(Table 4). The reductions in urine albumin levels achieved with losartan were significantly greater ($p<0.05$) than those by Amlodipine (Figure 3).But the reduction in uric acid, serum creatinine and serum urea levels achieved with losartan group were not significant ($p>0.05$) than amlodipine groups (Figure 4,5,6).

The beneficial effects of an ARB have been demonstrated in mild to moderate hypertensive

patients with prevention of early kidney damage being independent of the antihypertensive activity(9).Losartan has been shown to reduce microalbuminuria by restoring the effect on renal hemodynamics, proximal tubular function, but calcium channel blockers like Amlodipine has no change in proximal tubular function(10).Theeffect of losartan on insulin resistance is found to be positive or neutral, thus producing a better effective controlon diabetes(11).

Amlodipine therapy has limited albumin sparing effect because the levels ofurinary albumin excretion is not reduced in this study implies statistically not significant even they are effective in reducing the blood pressure in essential hypertension. The amlodipine effect on albumin excretion might be prevented due to inhibition of reabsorption of albumin at theproximal tubules

Limitations

Small sample sizeandShort duration of study.

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