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Research Article

Effect of losartan and amlodipine on insulin sensitivity in non-diabetic hypertensive patients

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ABSTRACT

Background: Hypertensive patients show higher insulin levels than normotensive controls. Hypertension is linked to impaired glucose tolerance and resistance to the action of insulin. Untreated hypertensive patients are at risk of developing new onset diabetes mellitus. Different antihypertensive drugs affect the insulin sensitivity distinctly. Few studies have demonstrated the beneficial effects of losartan, an angiotensin receptor blocker on the glucose insulin metabolism, but other studies have failed to demonstrate the insulin resistance lowering effect of losartan. Amlodipine, a long acting calcium channel blocker is considered to have neutral effects on the glucose-insulin metabolism.
Methods: In a prospective, open-label, parallel group study, non-diabetic patients with mild to moderate hypertension were randomized to either losartan (titrated from 50 to 100 mg /day, n=20) or amlodipine (titrated from 5 to 10 mg/ day, n=20) for period of 24 weeks. At baseline, 12 weeks and 24 weeks fasting plasma glucose, fasting plasma insulin, homeostasis model assessment for insulin resistance (HOMA-IR) apart from lipid parameters, mean systolic and diastolic blood pressures levels were determined.
Results: Intragroup comparison shows that both losartan and amlodipine significantly reduced the HOMA-IR index ($P < 0.05$, 24 weeks vs. baseline). Losartan reduced HOMA-IR more than amlodipine but this reduction was not statistically significant.
Conclusions: Losartan and amlodipine lowered insulin resistance in patients of mild to moderate hypertension.

Keywords: Hypertension, Insulin resistance, Losartan, Amlodipine

INTRODUCTION

Many studies have shown that lowering the blood pressure levels in hypertensive patients decreases the risk of cardiovascular mortality no matter which antihypertensive drug is chosen for the treatment.[1] Antihypertensive drug classes used for the treatment broadly include angiotensin converting enzyme inhibitors (ACEIs), angiotensin receptor blockers (ARBs), β-blockers (BBs), thiazide diuretics and calcium channel blockers (CCBs).[2] Antihypertensive drugs offer similar cardiovascular mortality lowering benefits but differ in terms of their adverse effect profile. Especially these drugs differ in how they affect the metabolic parameters including glucose insulin metabolic parameters and lipid levels.[1] Hypertension tends to impair glucose tolerance and induce a state of insulin resistance rendering hypertensive patients at a risk of developing diabetes mellitus.[3] Diabetes occurring with hypertension increases the risk of cardiovascular diseases by manifold.[4] So it is important that antihypertensive drugs are chosen such that they do not adversely affect the metabolic parameters and worsen the already insulin resistant state in hypertensive patients and rather prevent the new onset of diabetes mellitus in hypertensive patients. [5]

Various studies have illustrated the insulin sensitizing effects of ARBs especially telmisartan. Telmisartan is a mono-carboxylic acid, non-tetrozole ARB with thiazolidinedione like agonistic activity at peroxisome proliferator-activated receptor, gamma (PPAR-γ) which explains its effects on glucose- insulin metabolism.[6] But it

is not known if this favourable effect on insulin sensitivity is shared by whole ARB class or not. EXP-3174, a metabolite of losartan also has partial agonistic activity at PPAR- γ receptor.[7] Results of the studies showing the effect of losartan on glucose insulin metabolism have been conflicting.[8,9]

CCBs are considered to be metabolically neutral. Short acting nifedipine is associated with impaired insulin sensitivity.[10] Recent clinical studies have demonstrated that long acting calcium channel blockers such as amlodipine improve glucose tolerance and lower insulin resistance.[11]

The present study was carried out with the aim of studying the influence of commonly used first line anti-hypertensive drugs losartan and amlodipine on glucometabolic parameters in non-diabetic hypertensive patients.

METHODS

Study population

Forty non-diabetic patients of mild (SBP: 140-159 mmHg &/or DBP: 90-99 mmHg) to moderate hypertension (SBP: 160-179 mmHg &/or DBP: 100-109 mmHg) between 18 to 75 years, male or female subjects attending Medicine OPD of a tertiary care hospital and consenting to participate were enrolled in the study. The exclusion criteria were as follows: Type 1 or type 2 diabetes mellitus, secondary hypertension, history of hypersensitivity to ARBs/ β-blockers, one or both sided renal artery stenosis, acute or chronic renal failure, serum creatinine ≥ 2.5 mg/dl, serum potassium > 5.5 mEq/l, patients who are known case of COPD or bronchial asthma, smokers, patients with significant ECG abnormality, significant cardiovascular disease, history of hypertensive encephalopathy/ stroke/ transient ischemic attack (TIA) within last six months, pregnant/ lactating women, or women intending for pregnancy.

Participants of the study were made aware of the nature and purpose of this study and written informed consent was obtained. The study was conducted after obtaining approval from the Institutional Ethical Committee. This study was done in accordance with the Declaration of Helsinki.

Study design

This was a prospective, randomized controlled, open-label, parallel group study conducted in a tertiary care teaching hospital. The patients included in the study were randomized, using lottery method into two groups of 20 each to receive following treatments orally: Group I: losartan titrated from 50 mg to 100 mg daily, Group II: Amlodipine titrated from 5 mg to 10 mg daily. Treatment was initiated with 50 mg Losartan or 5 mg amlodipine with regular BP monitoring at follow-up visits every 4 weeks. At each of these visits BP was measured. The dose was doubled if the DBP was >90 mm Hg. A rescue therapy of indapamide was given to patients in whom the blood pressure was not controlled on titration to the highest possible doses of individual drugs. Patients received the medicines for 24 weeks and were followed at 12 weeks and 24 weeks to study the effects on systolic blood pressure (SBP), diastolic blood pressure (DBP) and heart rate (HR) and following metabolic parameters:

1. Fasting plasma glucose (FPG), fasting plasma insulin (FPI) were measured using standard techniques on samples obtained from the subjects after overnight fasting. Insulin was estimated by enzyme-linked immunosorbent assay (ELISA) technique. The homeostasis model assessment for insulin resistance (HOMA-IR) was computed as:

$$\text{HOMA} - \text{IR} = \frac{FPI\ (\mu\, U/ml)\ x\ FPG\ (mmol/L)}{22.5}$$

   HOMA-IR: It is a computer model of glucose-insulin interactions proposed by Matthews et al based on the supposition that averagely weighing healthy persons under 35 years have 100% β-cell function and labeled having insulin resistance of one.[12] Various studies have correlated the insulin resistance obtained from HOMA-IR with that from the gold standard hyperinsulinemic euglycemic glucose clamp (HEC) technique.[13]

2. Lipid parameters namely serum HDL cholesterol (HDL-C), serum triglycerides (TG), total cholesterol (total-C) were measured using standard methods. Low density lipoprotein cholesterol (LDL-C) levels were calculated using Friedewald's formula.

Blood pressure measurement

Mercury sphygmomanometer with appropriate sized cuff i.e. to encircle at least 80 % of the arm was used to record the blood pressure. Each patient was made to sit for at least five minutes in a chair with feet touching the floor and arm supported at heart level in a private, quiet setting with a comfortable room temperature. The auscultatory method of blood pressure measurement was used. Mean of the two recordings was noted.

Body mass index

Also called as Quetelet index was calculated using formula: BMI = Weight in Kg/ (Height in m)^2

Statistical analysis

Data was analysed using Graphpad Instat® ver 3.10, 32 bit for Windows. Data are stated as means ± SD for data following normal distribution and expressed as median (range) for the skewed data. After testing the data for normality (Kolmogorov–Smirnov test), inter-group

analyses between losartan and amlodipine groups for the data at baseline, at 12 weeks, 24 weeks and percent change from baseline till 24 weeks were assessed using the unpaired Student's t-test for Gaussian data with or without Welch correction and using Mann Whitney test for non-Gaussian data.

For intra-group (or within-group) comparison, repeated measure- analysis of variance (RM-ANOVA) was applied for comparing different parameters with normal distribution in the same group at different time points. For non-Gaussian data, Kruskal-wallis test was used. Tukey Kramer test and Dunn's test was used as a post-test with multiple comparisons to detect the group responsible for the difference for the Gaussian and non-Gaussian data respectively. The results were evaluated at a significance level of P-value < 0.05 and with 95% confidence intervals.

RESULTS

Baseline parameters

Forty patients enrolled in the study were randomized to each treatment group: amlodipine or losartan. Table 1 shows that study subjects were comparable with each other for different demographic and clinical variables.

SBP, DBP & HR

Intergroup comparison (Table 2) between amlodipine & losartan groups at 12 & 24 week follow up showed no statistically significant difference in SBP, DBP and HR. While intragroup analysis confirms significant systolic and diastolic blood pressure lowering actions of the two antihypertensive drugs at 12 & 24 week follow up (P <0.0001, vs. baseline).

Table 1: Baseline characteristics of patients in the study groups.

		Amlodipine (n= 20)	Losartan (n=20)	P-value
Age (Year)	mean ± SD	51 ± 8.75	50.3 ± 9.09	0.8054 NS
Age- Range		32 - 64	40 - 68	
Gender	(Male/ Female)	12:8	13: 7	
BMI (Kg/m^2)	mean ± SD	23.49 ± 5.10	23.64 ± 4.34	0.9203 NS
HR (per min)	mean ± SD	73.6 ± 7.53	74.3 ± 7.77	0.7738 NS
SBP (mm Hg)	mean ± SD	162.2 ± 10.09	163.4 ± 10.52	0.7149 NS
DBP (mm Hg)	mean ± SD	96 ± 9.86	96.9 ± 8.11	0.7544 NS
Fasting plasma glucose (mg/dl)	mean ± SD	100.9 ± 13.59	101.35 ± 8.13	0.8996 NS
Fasting plasma insulin (µIU/ml)	mean ± SD	11.11 ± 4.09	11.53 ± 3.61	0.7314 NS
HOMA-IR	mean ± SD	2.72 ± 0.94	2.88 ± 0.92	0.5906 NS
LDL-cholesterol (mg/dl)	mean ± SD	115.1 ± 23.47	115.95 ± 27.66	0.9171 NS
HDL-cholesterol (mg/dl)	mean ± SD	39.55 ± 11.56	37.8 ± 11.64	0.6362 NS
Triglycerides (mg/dl)	median (range) **$**	126 (65 to 310)	155.5(65 to 256)	0.9892 NS
Total-cholesterol (mg/dl)	mean ± SD	184.88 ± 33.78	184.29 ± 31.74	0.9549 NS

Data expressed as mean ± SD except for non-Gaussian data where data is expressed as median (range); $: Mann-Whitney Test; NS: Not significant.

FPG, FPI & HOMA-IR

Intergroup analysis (Table 2) shows no difference between the two groups with respect to the levels of FPG, FPI & HOMA-IR at 12 and 24 week follow up. However intragroup analysis (Table 3) shows that both drugs improve the glucometabolic variables. In amlodipine group, changes in FPG are not significant, while changes in FPI and HOMA-IR are statistically significant at the end of study (P <0.05 vs. baseline). In losartan group, at the end of 24 weeks FPG, FPI & HOMA-IR levels compared to baseline are respectively statistically significant (P <0.05), very significant (P <0.001) and extremely significant (P < 0.0001).

Effect of losartan vs. amlodipine on percent change in FPG, FPI and HOMA-IR at the end of study is shown in Figure 1. The percent decrease in FPG levels in amlodipine and losartan groups are 2.85% and 5.99% respectively. While, the percent decrease in FPI levels are 10.37% and 23.59% .And that of HOMA-IR levels are 13.52% and 26.86%.

Lipid metabolic parameters: There was no significant difference between the losartan and amlodipine groups at 12 week and 24 week follow up in the lipid metabolic parameters (Table 2). Intragroup analysis (Table 3) showed no difference in the levels of different lipid metabolic variables at 12 and 24 week follow up compared to baseline.

DISCUSSION

The present study is an effort to study the glucometabolic effects of commonly used first line antihypertensive drugs losartan and amlodipine in non-diabetic hypertensive patients. Our study demonstrated that in non-diabetic hypertensive patients, both study drugs exhibited favourable effects on the glucometabolic variables. Though not statistically significant, losartan lowered the insulin resistance index, HOMA-IR more than amlodipine.

Table 2: Effect of amlodipine vs. losartan on different variables: intergroup analysis.

Variable	Time Points	Treatment groups		P value
		Amlodipine (n= 20)	Losartan (n=20)	
HR (per min)	Baseline	73.6 ± 7.52	74.3 ± 7.76	0.7738 NS
	12 weeks	72.9 ± 5.78	74.8 ± 6.06	0.3171 NS
	24 weeks	73.7 ± 5.16	74 ± 5.23	0.8561 NS
SBP (mm Hg)	Baseline	162.2 ± 10.09	163.4 ± 10.52	0.7149 NS
	12 weeks	150.5 ± 7.81	151.4 ± 11.33	0.7716 NS
	24 weeks	146.4 ± 7.15	146.1 ± 9.18	0.9089 NS
DBP (mm Hg)	Baseline	96 ± 9.86	96.9 ± 8.11	0.7544 NS
	12 weeks	86.4 ± 6.41	87.6 ± 5.67	0.5347 NS
	24 weeks	83.8 ± 4.89	83.4 ± 4.59	0.7913 NS
FPG (mg/dl)	Baseline	100.9 ± 13.59	101.35 ± 8.13	0.8996 NS
	12 weeks	97.4 ± 8.89	95.45 ± 5.68	0.414 NS
	24 weeks #	96.4 ± 6.16	94.7 ± 3.38	0.2889 NS
FPI (µIU/ml	Baseline	11.11 ± 4.09	11.53 ± 3.61	0.7314 NS
	12 weeks	10.26 ± 3.30	9.49 ± 4.68	0.5485 NS
	24 weeks	8.42 ± 2.56	7.65 ± 2.12	0.3084 NS
HOMA-IR	Baseline	2.72 ± 0.93	2.88 ± 0.917	0.5906 NS
	12 weeks **$**	2.32 (1.18 to 3.94)	2.01 (1.11 to 5.74)	0.2287 NS
	24 weeks	2.01 ± 0.634	1.79 ± 0.515	0.2462 NS
LDL-C (mg/dl)	Baseline	115.1 ± 23.47	115.95 ± 27.67	0.9171 NS
	12 weeks	116.3 ± 21.23	114.45 ± 20.68	0.7817 NS
	24 weeks **$**	118 (84 to 158)	120 (80 to 144)	0.6848 NS
HDL-C (mg/dl)	Baseline	39.55 ± 11.56	37.8 ± 11.64	0.6362 NS
	12 weeks	39.8 ± 9.65	38.2 ± 8.67	0.5848 NS
	24 weeks	40.6 ± 9.47	40.6 ± 7.71	> 0.9999 NS
TG (mg/dl)	Baseline **$**	126 (65 to 310)	155.5 (65 to 256)	0.9892 NS
	12 weeks **$**	127 (78 to 354)	141 (78 to 258)	0.5608 NS
	24 weeks	138.45 ± 54.69	144.5 ± 50.25	0.7177 NS
Total-cholesterol (mg/dl)	Baseline	184.88 ± 33.78	184.29 ± 31.74	0.9549 NS
	12 weeks	184.89 ± 33.52	181.89 ± 23.95	0.7465 NS
	24 weeks	185.34 ± 31.23	181.95 ± 22.04	0.6939 NS

Data expressed as mean ± SD except for non-Gaussian data where data is expressed as median (range); #: Unpaired t-test with welch correction, **$:** Mann-Whitney Test; NS: Not significant.

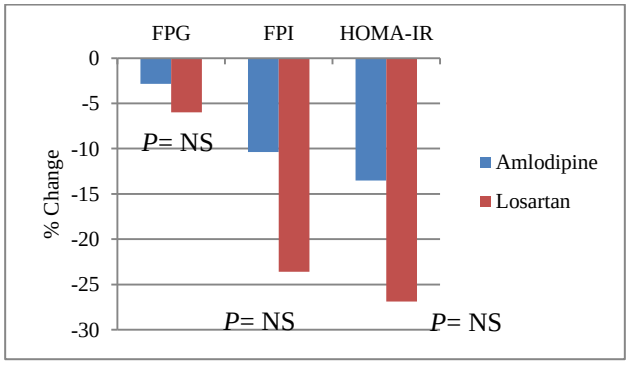
Results of this study are in unison with that of other studies investigating the effects of losartan and/or amlodipine on the insulin resistance.[14-16] Jin et al studied the effects on HOMA-IR of losartan (100 mg) and amlodipine (10 mg) administered daily for three months in type 2 diabetes patients associated with nephropathy. Losartan significantly decreased the HOMA-IR levels when compared to the baseline. But reductions were not statistically significant in comparison to the amlodipine group.[14] Aksnes et al investigated the effects of amlodipine versus losartan on adipokines, inflammatory markers, and whole blood viscosity in 24-week, double-masked, randomized crossover study in hypertensive patients. After 4-week run-in on amlodipine 5 mg, patients were randomized to receive additional losartan 100 mg or amlodipine 5 mg for 8 weeks. HOMA-IR was used as the marker of insulin resistance. There was a trend towards lower values of HOMA-IR after losartan treatment (2.8 versus 3.1, not significant), indicating improved insulin sensitivity after additional treatment

with losartan compared to amlodipine.[15] In a different study, the effects of losartan on serum adiponectin levels with regard to insulin sensitivity were studied. Prediabetic patients were randomized to receive losartan or a calcium channel blocker (amlodipine, azelnidipine, clinidipine, or benidipine) for three months. Insulin sensitivity was assessed by HOMA-IR. Insulin resistance defined as HOMA-IR >2.5. Losartan treatment resulted in a significant decrease in HOMA-IR (23.9%); percentage changes were greater than those induced by calcium channel blocker treatment (P <0.05).[16]

Table 3: Effects of amlodipine and losartan on different variables at different time points of follow-up: intra-group analysis.

		At different time points			P value	Post-test (Multiple comparison test)		
Variable	Treatment groups	Baseline	12 weeks	24 weeks		*P* (12 wks vs. baseline)	*P* (24 wks vs. baseline)	*P* (24 wks vs. 12 wks)
SBP (mmHg)	Amlodipine	162.2 ± 10.09	150.5 ±7.81	146.4 ± 7.15	<0.0001***	<0.0001***	<0.0001***	<0.05*
	Losartan	163.4 ± 10.52	151.4 ± 11.33	146.1 ± 9.18	<0.0001***	<0.0001***	<0.0001***	NS
DBP (mmHg)	Amlodipin@	98 (80 to 110)	88 (74 to 96)	84 (76 to 92)	0.0003**	<0.05*	<0.0001***	NS
	Losartan	96.9 ± 8.11	87.6 ± 5.67	83.4 ±4.59	<0.0001***	<0.0001***	<0.0001***	<0.05*
HR (/ min)	Amlodipine	73.6 ± 7.52	72.9 ±5.78	73.7 ± 5.16	0.8228	NS	NS	NS
	Losartan	74.3 ±7.76	74.8 ± 6.06	74 ± 5.23	0.7266	NS	NS	NS
FPG (mg/dl)	Amlodipin@	101(82to104)	95.5(89to123)	95.5(88to111)	0.6978	NS	NS	NS
	Losartan @	100.5(89to122)	94.5(89to112)	94.5(90to102)	0.0086 *	<0.05 *	<0.05 *	NS
FPI (µIU/ml)	Amlodipine	11.11 ± 4.09	10.26 ± 3.30	8.42 ± 2.56	0.044	NS	<0.05 *	NS
	Losartan @	12.09(5.2to16.6)	8.37(4.72to25.5)	7.55(4.9to11.5)	0.0029 *	NS	<0.01**	NS
HOMA-IR	Amlodipine	2.72 ± 0.94	2.47 ± 0.84	2.01 ± 0.63	0.0253	NS	<0.05*	NS
	Losartan @	2.84(1.30to4.4)	2.01(1.11 to 5.7)	1.78(1.10to2.5)	0.001 **	<0.05 *	<0.0001***	NS
LDL-C (mg/dl)	Amlodipine	115.1 ± 23.47	116.3 ± 21.23	117.05 ± 22.78	0.8611	NS	NS	NS
	Losartan	115.95 ± 27.66	114.45 ± 20.68	112.45 ± 20.06	0.7155	NS	NS	NS
HDL-C (mg/dl)	Amlodipine	39.55 ± 11.56	39.8 ± 9.65	40.6 ± 9.47	0.7764	NS	NS	NS
	Losartan	37.8 ± 11.64	38.2 ± 8.67	40.6 ± 7.71	0.2495	NS	NS	NS
TG (mg/dl)	Amlodipine	151.15 ± 59.88	143.95 ± 67.53	138.45 ± 54.69	0.2834	NS	NS	NS
	Losartan	152.7 ± 60.31	146.2 ± 48.97	144.5 ± 50.25	0.5258	NS	NS	NS
Total-C (mg/dl)	Amlodipine	184.88 ± 33.78	184.89 ± 33.51	185.34 ± 31.23	0.9949	NS	NS	NS
	Losartan	184.29 ± 31.74	181.89 ± 23.95	181.95 ± 22.04	0.847	NS	NS	NS

Data expressed as mean ± SD except for non-Gaussian data where data is expressed as median (range); @: Kruskal Wallis test; *** - extremely significant; ** - very significant; * - significant; NS- not significant



FPG: Fasting plasma glucose; FPI: Fasting plasma insulin; HOMA-IR: Homeostasis model assessment index- insulin resistance; NS: Not significant.

Figure 1: Percentage change in FPG, FPI and HOMA-IR in study groups at the end of study.

Renin angiotensin system (RAS) plays an important part in the promoting insulin resistance. Vasoconstriction induced by angiotensin II impairs the tissue blood flow further hampering utilization of glucose.[17] Angiotensin II is involved in phosphorylation of insulin receptor substrates (IRS)-1 via jannus kinase 2 (JAK2) linked to AT1 receptor which further decreases phosphatidylinositol (PI) 3-kinase activation. This disturbs insulin signalling and results in induction of an insulin resistant state.[18] Besides angiotensin II is linked with up regulation of oxidative stress which further hampers insulin sensitivity. RAS has a role in increasing skeletal muscle TNF-α levels consequentially affecting the translocation of glucose transporters (GLUT), thus hinders glucose utilization. Angiotensin II through its AT1 & AT2 receptors induces adipose tissue hypertrophy and preadipocyte differentiation respectively. Cytokines released from this hypertrophied adipose tissue promote

insulin resistance.[19] Hence, Angiotensin receptor blockers (ARBs) have their favourable effects on glycaemic control through a variety of mechanisms related to the inhibition of angiotensin-II.[10]

Our study differs from the studies which show that losartan fails to improve the insulin sensitivity.[20-23] Bahadir et al investigated effect of telmisartan (80 mg/day) vs. Losartan (50mg/day) given for 8 weeks on insulin resistance in hypertensive patients with metabolic syndrome where insulin resistance was evaluated by using HOMA-IR. Mean HOMA-IR levels at baseline and at the end of the study in losartan group were 1.8±0.6 and 1.8±0.6 ($P > 0.05$).[20] Yavuz et al investigated the effects of enalapril 5 to 40 mg versus losartan 50 to 100 mg administered daily for 6 months on insulin resistance and endothelial function. Losartan group showed no significant decrease in the HOMA-IR levels at the end of 6 months (2.3+0.6 to 1.5+0.7, $P > 0.05$).[21] In a study by Huang et al, telmisartan was compared against losartan both administered for 16 weeks for their effects on body fat distribution and insulin sensitivity in obese Chinese hypertensive patients. HOMA-IR levels did not show significant improvement in the losartan group.[22] Perl et al investigated the antihypertensive and metabolic effects of telmisartan and losartan administered for 12 weeks in hypertensive patients associated with impaired glucose tolerance. HOMA-IR was used to assess the insulin resistance. Losartan failed to show improvement in insulin sensitivity (Baseline: 3.04±0.60, after losartan treatment: 3.38 ± 0.84, $P >0.05$).[23] Moan et al studied the effects of losartan administered at dose of 50-100 mg daily for 4 weeks on the glucose insulin metabolism in patients with mild hypertension. Insulin sensitivity was assessed by euglycemic glucose clamp technique. Losartan did not significantly change insulin sensitivity.[8] Later same author demonstrated improvement in insulin sensitivity by losartan in patients with severe hypertension.[9] The incongruity between these studies and our study regarding effects of losartan on insulin resistance are possibly because of variation in the dose, duration of the losartan treatment, severity of hypertension, inclusion of non-diabetic patients or other unknown variables. With regards to the effects of amlodipine on the glucometabolic parameters, different studies support results of our study. In a study by Ersoy et al, amlodipine administered at doses 5-10 mg for 12 weeks to type 2 diabetic hypertensive patients has shown to decrease HOMA-IR from pre-treatment levels of 5.59 ± 1.0 to 3.61 ± 0.5 ($P <0.05$).[11]

CCBs are generally considered to be having neutral effects on insulin sensitivity. But they might do a little more than being metabolically neutral. CCBs may decrease insulin resistance by having vasodilator action especially in the insulin sensitive tissues with negligible increase in sympathetic activity. CCBs may help in the translocation of glucose transporters and prevent the inhibition of glycogen synthase by calcium. Improvement in insulin sensitivity by CCBs might be linked through their antioxidant effects.[24] Insulin resistance in obese patients is linked to the raised intracellular levels of calcium. Therefore long acting calcium channel blockers might be enhancing insulin sensitivity by limiting intracellular Ca2+. Further calcium channel blockers namely nicardipine, amlodipine and manidipine have shown to lower the levels of TNF-α in experimental and clinical studies. TNF-α is produced by the adipose tissue and is implicated in the development of obesity related insulin resistance.[25,26] One of the important limitations of this study is that the mechanisms responsible for the improvement in insulin resistance index by losartan and amlodipine were not determined. Since it is known from studies that about 50% of the hypertensive patients are insulin resistant, our study has an important part to contribute.[27] Our study is one of the very few studies which attempt to investigate the effect of antihypertensive drugs on insulin sensitivity in hypertensive patients before diabetes sets in.

CONCLUSION

Our study demonstrates that losartan and amlodipine equally lowered insulin resistance in patients of mild to moderate hypertension. Also, this study emphasizes the importance of choosing an antihypertensive drug that does not increase the risk of developing diabetes mellitus in patients of hypertension.

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