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RESEARCH ARTICLE

COMPARISON OF THE EFFECTIVENESS OF AMLODIPINE AND TELMISARTAN IN MACROVASCULAR AND MICROVASCULAR COMPLICATIONS IN TYPE2 DIABETES MELLITUS PATIENTS WITH HYPERTENSION

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ABSTRACT

Back ground and Objectives: Antihypertensive drugs Amlodipine and Telmisartan are used to control blood pressure and reduce macro and microvascular complications in diabetic patients with hypertension. Telmisartan is an angiotensin II receptor antagonist used in the management of hypertension. Telmisartan is a partial agonist of peroxisome proliferator –activated receptor. So this lower the risk of acute myocardial infarction, stroke, or heart failure in diabetic patients. Amlodipine is a calcium channel blocker. It works to control blood pressure and reduce the number of angina attacks by widening and relaxing blood vessels. The main objective of the study is to evaluate effectiveness of amlodipine and telmisartan in macrovascular (cardiovascular) and microvascular (nephropathic) complications in type 2 diabetes mellitus patients with hypertension.

Methods: A prospective, cross sectional study conducted in type 2 diabetes patients with hypertension at general medicine inpatients and outpatients department in a 500 bed tertiary care teaching hospital. After obtaining the consent Patients were categorised into 2 groups, one group treated with Amlodipine (5mg\day) and other group treated with Telmisartan 40(mg\day). Patients are evaluated for the parameter like blood pressure and echocardiograph to detect cardiovascular complication microalbumin and serum creatinine to detect nephropathic complications at baseline and follow up after 6 week.

Results and Discussion: A total of 60 patients were evaluated (30 patients in each group), with a predominance of male (51%) in both groups. After 6 weeks of treatment, the Amlodipine and Telmisartan group no significant difference in SBP (131mmHg and 127mmHgrespectively.P=0.206), and DBP (86.67mmHg and 82.67mmHg respectively, p=0.076), although the values were slightly lower in Telmisartan group. In the case of serum creatinine, in amlodipine group it about 1.28 and 1.23 in Telmisartan group. Serum creatinine value lower in Telmisartan group, but there is no significant difference (p value about 0.656). After 6 weeks of treatment with Amlodipine microalbumine present in 20% of patients and it present but decreased in 26.7% and it not present in 53.3%patients.in Telmisartan group it not present in 63.3%patients,present but it decreased in 16.7% and present in 20% patients. Telmisartan group has higher reduction in microalbumine compared to that of Amlodipine group. When comparing ECHO of the two groups after 6 weeks of treatment, in Amlodipine group 70% of the patients have complication present but decreased. Complication not present in 30% of patients.in the case Telmisartan group complication not present in 56.7% patients and complication present but decreased in 43.3% patients.

Conclusion: The result of the study shows that after 6 weeks of treatment, there is no significant difference between laboratorical parameters in two groups. The result shows the effectiveness of Amlodipine and telmisartan in macrovascular (cardiovascular complication detected from ECHO) and microvascular complication (nephropathy detected by checking microalbuminuria and serum creatinine) are almost same. Telmisartan shows higher reduction in parameters like SBP, DBP, SC and microalbumine compared to Amlodipine group. Amlodipine show higher reduction in uric acid and fasting blood sugar compared to Telmisartan group.

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INTRODUCTION

Diabetes is a metabolic disorder characterised by resistance to the action of insulin, insufficient insulin secretion or both. Hypertension and diabetes mellitus represent an important health problem as combination of the two disorders is common and carries significant morbidity and mortality. (Beckman *et al*., 2002; Libby *et al*., 2005; Duan *et al*., 2008; Kurtz, 2005) Tight control of hypertension prevents or retards microvascular and macrovascular complications, while only tight control of hyperglycaemia prevents or retard, the macrovascular complications such as myocardial infarction, stroke, neglecated gangrene of the limbs due to peripheral vascular disease, and

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all these risk can be prevented by tight control of hypertension along with optimal control of hyperglycaemia. Hyperglycaemia along with dyslipidemia, and cigarette smoking, hypertension is a major contributor to the development and progression of macrovascular and microvascular complications in people with diabetes (Beckman *et al*., 2002; Libby *et al*., 2005; Duan *et al*., 2008; Kurtz, 2005; Juurlink *et al*., 2006). Compared to the general population, people with diabetes face a two to four fold increased risk of cardiovascular disease. It significantly accelerate the progression of diabetic nephropathy, retinopathy and neuropathy (Duan *et al*., 2008; Juurlink *et al*., 2006). Telmisartan is an angiotensin II receptor antagonist used in the management of hypertension. Telmisartan is a partial agonist of peroxisome proliferator –activated receptor. So this lower the risk of acute myocardial infarction, stroke or heart failure in diabetic patients. (Hansson *et al*., 1999; Lewis *et al*., 1993) Amlodipine is a Calcium channel blocker and have an important role in reducing microalbuminuria in patient with hypertension and diabetes, which can be explained by their antihypertensive efficacy. (American Diabetes Association, 2008; KDOQI, 2007; http://www.nhlbi.nih.gov/ health/public/ heart/hbp/dash/new_dash.pdf, Rosendorff *et al*., 2007) Untreated or poorly controlled hypertension can significantly accelerate the development and progression of both the macrovascular and microvascular complication of diabetes. Aggresive blood pressure control improves patient outcomes.

Hypertension

Hypertension (defined as a blood pressure ≥140/90 mmHg) is an extremely common condi- tion in diabetes, affecting ~20-60% of patients with diabetes, depending on obesity, ethnicity, and age. Hypertension is a condition in which blood pressure is high. It can be caused by genetics, diet as well as stress. It is associated with significant health problems such as stroke and heart attack. The following clinical levels of hypertension have been described by The National Heart, Lung, and Blood Institute:

Stage one hypertension: Consistent (i.e., two or more consecutive) readings of 140-159/90-99 mmHg.

Stage two hypertension: Consistent readings of 160/100 mmHg or higher.

Pre-hypertension: Consistent readings of 120- 139/80-89 mmHg.

Diabetes mellitus

Diabetes mellitus often simply referred to as diabetes is a condition in which a person has a high blood sugar level, either because the body doesn't produce enough insulin, or because body cells don't properly respond to the insulin that is produced (Hypertension in diabetes study (HDS), 1993). There are many types of diabetes, the most common of which are:

Type 1 diabetes: Results from the body's failure to produce insulin, and presently requires the person to inject insulin.

Type 2 diabetes: Results from insulin resistance, a condition in which cells fail to use insulin properly, sometimes combined with an absolute insulin deficiency. Gestational diabetes: it is when pregnant women, who have never had diabetes before and have high blood glucose level during pregnancy. It may precede development of type 2 diabetes mellitus.

Other forms of diabetes mellitus include con- genital diabetes, which is due to genetic defects of insulin secretion, cystic fibrosis-related diabetes, steroid diabetes induced by high doses of glucocorticoids, and several forms of monogenic diabetes.

How are Diabetes and Hypertension Related?

Diabetes and high blood pressure tend to occur together because they share certain physiological traits. High blood pressure is a dangerous disease that becomes even more problematic in the setting of diabetes. Unfortunately, many people with diabetes are also affected by high blood pressure, and the two diseases commonly occur together (Kumar, 2000). Diabetes and high blood pressure occur together so frequently that they are officially considered to be "comorbidities" (diseases likely to be present in the same patient). In the case of diabetes and high blood pressure, these effects include:

Increased Fluid Volume – Diabetes increases the total amount of fluid in the body, which tends to raise blood pressure.

Increased Arterial Stiffness – Diabetes can decrease the ability of the blood vessels to stretch, increasing average blood pressure.

Impaired Insulin Handling – Changes in the way the body produces and handles insulin can directly cause increases in blood pressure.

Apart from above factors the two diseases are likely to occur together simply because they share a common set of risk factors. Some important shared risk factors are:

Body Mass – Being overweight significantly increases the risk of both diabetes and high blood pressure.

Diet – High fat diets rich in salt and processed sugars are known to contribute to the develop- ment of organ problems that can lead to both diabetes and high blood pressure.

Activity Level – A low level of physical activity makes insulin less effective (which can lead to diabetes) and can contribute to the development of stiff blood vessels, increasing the risk of high blood pressure.

The well-studied example of the self-reinforcing relationship between diabetes and high blood pressure takes place in the kidneys. The kidneys are the body's most important long-term blood pressure regulator. By balancing the amount of salt and potassium in the body, the kidneys ultimately control how much fluid is excreted as urine. This fluid regulating function helps to modulate long-term blood pressure by physically controlling how much liquid is present in the blood vessels.

Relationship between diabetes and hypertension

The interrelationship between the hyperglycemia and the hypertension through the intervention of insulin resistance, a common link between the two diseases. Statistical Relationship Individuals with diabetes are at a much greater risk for

developing. Hypertension is twice as common in those with diabetes as in non diabetic individuals. Physical Relationship Diabetes causes hyperinsulinemia and raises the risk of hypertension. This condition increases the amount of sodium that the body absorbs. It also promotes the stimulation of the sympathetic nervous system. This is thought to cause changes in blood vessel structure, which affects the function of the heart and blood pressure (Tierney *et al*., 2000; Epstein and Sowers, 1992; Hypertension in diabetes study (HDS), 1993).

Guidelines for the management of hypertension in diabetics

Effective blood pressure control is an important goal for diabetic patients. The patients who suffer from both diabetes and hypertension have greater chances of developing cardiovascular disorder (Geleijnse *et al*., 1994). The following guidelines must be considered for the management of hypertension in dia- betic patients:

Measurement of Arterial Blood Pressure: The object of identifying and treating high blood pressure is to reduce the risk of cardiovascular disorder and associated morbidity and mortali- ty. It is, therefore, necessary to provide a classification of blood pressure in adults so as to identify the high risk individuals and to provide guidelines for treatment and follow up. Arterial blood pressure measured in the sitting position should be considered as ideal (Moore and Mcknight, 1995).

Systolic and Diastolic Pressure Target Values: The level to which blood pressure should be reduced in a diabetic hypertensive patient has not been known (Morris and Reusser, 1995). There are no specific guide- lines on the exact values for hypertension control in diabetes. A number of epidemiological studies suggest an inverse relationship exist between calcium, magnesium, potassium in- take and blood pressure level (Cutler *et al*., 1997; Midgley *et al*., 1996; Staessen *et al*., 1989). Most of these studies are cross-sectional, but none of these studies has analyzed diabetic patients separately from the general hypertension population. There are no randomized clinical trials on magnesium supplementation in diabetic subjects with hypertension. Screening and Initial Evaluation: All patients with diabetes should have blood pressure mea- sured at the time of diagnosis and at each scheduled diabetes visit$_{38}$. Initial assessment of a hypertensive diabetic patient should include a complete medical history with special em-phasis on cardiovascular risk factors and the presence of diabetes complication. The physi- cal exam should include height, weight, and careful evaluation of arterial circulation. Initial laboratory examination should include serum creatinine, electrolytes, fasting lipid profile, and urinary albumin excretion (Chobanian *et al*., 1997). Behavioral Treatments of Hypertension: Dietary management with moderate sodium re- striction has been effective in reducing blood pressure in individuals with essential hyper- tension (Chobanian *et al*., 1997; Hairejoshu *et al*., 2002). Weight reduction can reduce blood pressure independent of sodium intake and can also improve blood glucose and lipid levels (Hairejoshu *et al*., 1999). Sodium restriction has not been tested in the diabetic population in controlled clinical trials. Reductions in daily sodium intake to levels of 10-20 mmol (230-460 mg) per day have resulted in decreases in systolic blood pressure of 10-12 mmHg (Allhat officers and coordinators for the all- hat collaborative research group, 2002). Smoking cessation and moderation of alcohol intake are also recommended to reduce blood pressure (Buse *et al*., 2007; Parving *et al*., 2001).

Treatment goals

In the setting of diabetes, the target blood pressure is <130/80. Significant improvements in long term cardiovascular and kidney health do not become apparent until blood pressure is re- duced to this level. Because it is difficult to reduce blood pressure to this level, it is a recom- mendation usually reserved only for specific patients. Drug Therapy Drug therapy is a necessary step for most patients during treatment. Vast amounts of research have been done in an effort to determine which drug or drug combination is the "best" for treating high blood pressure in patients with diabetes. The best drugs to use in the setting of diabetes are:

Angiotensin Converting Enzyme (ACE) Inhibitors: ACE inhibitors have proved benefi- cial in patients who have myocardial infarc- tion or congestive heart failure, or who have diabetic renal disease10. ACE inhibitor therapy results in 20 to 30 percent decrease in the risk of stroke, coronary heart disease, and major cardiovascular events (American Diabetes Association, 2002; Tight blood pressure control and risk of macrovascular and microvascular complications in type 2 diabetes, 1999). ACE in- hibitors are found to be more beneficial when compared with other antihypertensives in the reduction of acute myocardial infarction, cardiovascular events, and mortality. Captopril and atenolol are similar in terms of reduction in microvascular and macrovascular complications (American Diabetes Association, 2008).

Diuretics: Thiazide diuretics have been shown to benefit patients with diabetes and systolic hypertension. Chlorthalidone therapy is effective in preventing major cerebrovascular and cardiovascular events in older non-insulin-treated patients with diabetes and isolated systolic hypertension. Lower dosages of thiazides (e.g., hydrochlorothiazide) are generally well toler- ated and not associated with adverse metabolic effects. Thiazide diuretics are not as effective in patients with renal insufficiency; in such patients, loop diuretics are preferred.

Calcium Channel Blockers (CCB): Controver- sy exists regarding the use of CCBs, particu- larly the dihydropyridines (e.g., amlodipine, nifedipine) in treating hypertension in patients with diabetes. The combination of an ACE in- hibitor and a dihydropyridine CCB has been shown to reduce proteinuria$_2$. The nondihy- dropyridine CCBs (e.g., verapamil) demonstrate reductions in cardiovascular risk when used as monotherapy. Combining a nondihy- dropyridine CCB with an ACE inhibitor in hypertensive patients with diabetes is associated with greater reductions in proteinuria than if either agent was used individually (Hansson *et al*., 1999).

Angiotensin II Receptor Blockers (ARB): Candesartan and lisinopril are used to treat patients with type 2 diabetes, hypertension, and microalbuminuria (Bakris and Weir, 2000). Candesartan is as ef- fective as lisinopril in blood pressure reduction and minimization of microalbuminuria (Hansson *et al*., 1998; Tuomilehto *et al*., 1999). Losartan therapy produced a renoprotective effect independent of its blood-pressure-lower- ing effect in patients with type 2 diabetes and nephropathy (Hansson *et al*., 1998; Tuomilehto *et al*., 1999). Irbesartan is found to be renoprotective in patients with type 2

diabetes who have microalbuminuria. Valsartan lowers urine albumin excretion to a greater degree than amlodipine in type 2 diabetic patients with microalbuminuria (Wang *et al*., 2000).

Beta Blockers: Traditionally, the use of beta blockers in patients with diabetes has been dis- couraged because of adverse metabolic effects and the masking of hypoglycemic symptoms. There is no difference in hypoglycemic episodes in patients treated with atenolol compared with captopril, but the mean weight gain in the atenolol group was greater. Cardio selective beta blockers are preferred over the non-selective type because they are associated with less blunting of hypoglycemic awareness and less elevation of lipid and glucose levels. The alpha beta blocker carvedilol causes fewer alterations in lipid and glucose levels com- pared with traditional beta blockers. Beta- blocker therapy can be advantageous in many patients with diabetes because of its proven ability to decrease cardiovascular morbidity and mortality in persons with atherosclerotic heart disease.

Hypertension management in diabetic patients

Renin Inhibitors: A new and promising approach in rennin angiotensin aldosterone system blockade has been started with the de- velopment of first direct renin inhibitor, aliskiren, recently approved by US Food and Drug Administration (FDA) for the treatment of hypertension in diabetic patients. Aliskiren is generally well tolerated and, in contrast to ACE inhibitors, it does not induce accumulation of substance P or bradykinin. Therefore, side effects such as cough and angioedema are very rare. It has demonstrated a favorable safety and tolerability profile alone or in combination with other drugs (Neutel and Smith, 1998). Aliskiren monotherapy demonstrated significant, dose-dependent antihypertensive effects in several placebo-controlled clinical trials[51]. Renin inhibition seems an interesting new approach for preventing the progression of chronic kidney disease[52].

Benefits of telmisartan used in type 2 diabetes mellitus patients with hypertension (Vasan *et al*., 2001; Lewis *et al*., 2001; Hansson *et al*., 1999; Lewis *et al*., 1993)

Telmisartan is an angiotensin 2 receptor antagonist used in the management of hypertension.it shows high affinity for the angiotensin 2 receptor type (AT1). (Chalmers *et al*., 1999) In addition to blocking the RAS, Telmisartan acts as a selective modulator of peroxisome proliferator activated receptor gamma, a central regulator of insulin and glucose metabolism. It is believed that Telmisartans dual mode of action may provide protective benefits against the vascular and renal damage caused by diabetes and cardiovascular disease.So the person with cardiovascular or kidney disease including microalbuminuria,or with cardiovascular risk factors in addition to diabetes and hypertension angiotensin should be started.

Pharmacological properties of telmisartan[24]

Angiotensin 2 receptor blockers are highly effective antihypertensive agents and are widely regarded as having tolerability profiles similar to that of placebo of the commercially available ARB'S. Telmisartan has the longest half life of about 24 hours.this suggest that Telmisartan should have a long duration of action. Another feature distinguishing Telmisartan from other ARB'S is it's higher lipophilicity. This enhance tissue penetration, intracellular absorption and bioavailability. High lipophilicity is reflected in the high volume of distribution of approximately 500h. Another feature that distinguishes Telmisartan from other ARB'S that it's not a prodrug thus antihypertensive potency is related to the activity of the parent drug.

Benefits of amlodipine used in type 2 diabetes mellitus patients with hypertension[19-22]

Amlodipine belongs to the family of medication known as calcium channel blockers. Amlodipine is used to treat high blood pressure and angina (chest pain). It works to control blood pressure and reduce the number of angina attacks by widening and relaxing blood vessels. Amlodipine is used with or without with other medications to treat high blood pressure. Lowering high blood pressure helps prevent strokes, heart attack and kidney problems. Amlodipine also used to prevent certain types of chest pain (angina). It may help to improve your ability to excersise and decrease the frequency of angina attacks. It should not be used to treat attacks of chest pain when they occur. (American Diabetes Association, 2008; KDOQI, 2007) The mechanism of the antihypertensive action of amlodipine is due to a direct relaxant effect on vascular smooth muscle. The precise mechanism by which amlodipine relieves angina has not been fully determined but amlodipine reduces total ischaemic burden by the following two actions.

1) Amlodipine dilates peripheral arterioles and thus,reduce the total peripheral resistance (after load) against which the heart works. Since the heart rate remain stable, this unloading the heart reduce myocardial energy consumption and oxygen requirements.
2) The mechanism of action of amlodipine also probably involves the dilation of the main coronary arteries and coronary arterioles, bothin normal and ischaemic regions. This dilation increasing myocardial oxygen delivery in patients with coronary artery spasm (prinzmental or variant angina).

Amlodipine has not been associated with any adverse metabolic effect or changes in plasma lipids and is suitable for use in patients with asthma, diabetes, and gout.

Pharmacologic properties of amlodipine

Amlodipine is an intrinsically long acting, vasoselective calcium antagonist. Structurally related to Nifidipine, but with unique binding and pharmacologic properties that distinguish it from other agents of this class. Pharmacokinetic studies in animal models demonstrate a more prolonged half life, high volume of distribution and gradual elimination of Amlodipine compared with that of other calcium antagonists. The presence of a basic side chain at the two position of the dihydropyridine ring renders the molecules>90% ionised at physiologic pH and is believed to be primarly responsible for it's markedly different pharmacologic and pharmacokinetic properties. Amlodipine has slow receptor binding kinetics that result in gradual onset of action and may allow for less dependence on instantaneous plasma levels. Although Amlodipine appears to bind to additional calcium channel recognition sites blocked by Dilthiazem and Verapamil, does not significantly depress heart rate nor does it produce significant negative inotropic effects or electrophysiologic disturbances. Preclinical studies indicate that Amlodipine is a potent antihypertensive agents with

natriuretic and diuretic properties that may enhance it ability to reduce blood pressure without affecting fluid retension.

Hypertension treatment in diabetes: efficacy and goal blood pressure

Reducing blood pressure in people with hypertension and diabetes decreases both macrovascular and microvascular complications. Clinical trials using a variety of antihypertensive agents have demonstrated that modest reductions in blood pressure of just 9–11 mmHg systolic and 2–9 mmHg diastolic decrease CVD events by 34–69% and microvascular complications (retinopathy and nephropathy) by 26–46% within just 2-5yrs. Untreated or poorly controlled hypertension can significantly accelerate the development and progression of both the micro and macrovascular complications of diabetes. Aggressive blood pressure control improves patient outcomes and reduces health care costs. Unfortunately nearly two-thirds of people with diabetes do not have blood pressure readings within the, target range. Effective antihypertensive regimens maximize nonpharmacological therapies, minimize adverse effects on glucose control, lessen the risk of medication- related side-effects, and provide adequate cardiac and renal protection.

Methodology

Study design

Prospective cross sectional study.

Study site

Department of General medicine.

Study duration

The duration of the study was 9 months.

Study population

60 samples

Ethical approval

Ethical clearance was obtained from institutional ethical committee.

Study criteria

Inclusion criteria

- Patients who are willing to participate in the study
- Patients ≥30 years old
- Type 2 diabetes patients with hypertension
- Patients prescribed with Amlodipine or Telmisartan more than 1month
- Patients prescribed with oral hypoglycaemic or insulin or both

Exclusion criteria

- Patients with co-morbidities other than cardiovascular and nephropathy complications
- Pregnant and lactating women
- Mentally and physically disabled

Study procedure

It is a prospective, cross sectional study conducted in type 2 diabetes patients with hypertension at general medicine inpatients and outpatients department in a 500 bed tertiary care teaching hospital. After obtaining the consent Patients were categorised into 2 groups, one group treated with Amlodipine (5mg\day) and other group treated with Telmisartan 40(mg\day). Patients are evaluated for the parameter like blood pressure and echocardiograph to detect cardiovascular complication microalbumin and serum creatinine to detect Nephropathic complications at baseline and follow up after 6 week.

RESULTS AND DISCUSSION

A prospective cross sectional study was conducted among those patients diagnosed with diabetes mellitus with hypertension in the department of general medicine for a period of 6 months. 60 patients were selected for the study. In this study, we aimed to compare the effectiveness of Amlodipine and Telmisartan in Macrovascular (cardiovascular) and Microvascular (nephropathy) complication in type 2 diabetes mellitus patients with hypertension. For this purpose, 60 diabetic patients with hypertension were recruited from the department of general medicine as per the selection criteria. The patients were categorized into two groups, one group having Amlodipine and other group taking Telmisartan. Effectiveness of the drug determined based on laboratorical values at base line and during follow up after 6 weeks. Laboratorical values like systolic and diastolic blood pressure, fasting blood sugar, serum creatinine, microalbumin, uric acid and ECHO. Serum creatinine and micro albumin is used to check nephropathic complication and ECHO used to check cardiovascular complication.

a) Categorisation of study population based on age range

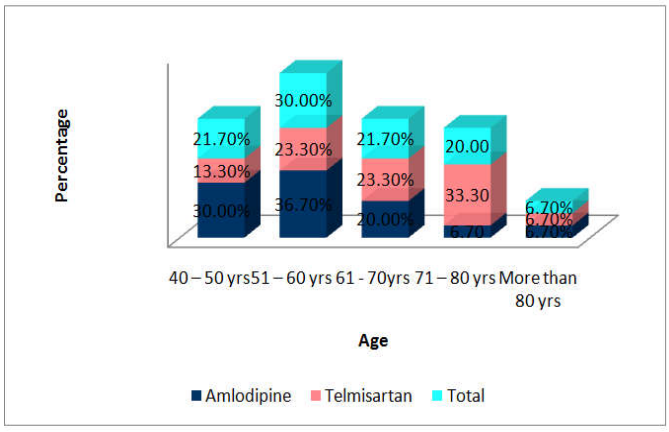

Figure 1. Categorisation of study population based on age range (years) (N=60)

In a total population of 60 patients, a higher percentage of patients comes under the age range of 51-60yrs (30%) and 21% in the age range of 40-50 yrs, 61-70yrs followed by other age groups (71-80, more than 80 respectively). While considering Amlodipine and Telmisartan group separately, in Amlodipine group most patients comes under the age of 51-60yrs (36.7%), followed by other age groups (40-50, 61-70,71-80 and more than 80). In Telmisartan group most patients

comes under the age of 71-80yrs (33.3%), followed by other age groups (51-60,61-70,40-50 and more than 80 respectively). In total population higher incidence of diabetes mellitus patients with hypertension was seen in the age range of 51-60yrs (30.3%). In Amlodipine group most patients comes under the age of 51-60yrs (38.7%), in Telmisartan group most patients comes under the age of 71-80yrs (33.3%). Higher incidence of diabetes mellitus with hypertension found in elderly patients. In this more elderly patient taking Telmisartan than the Amlodipine.

b) Based on gender

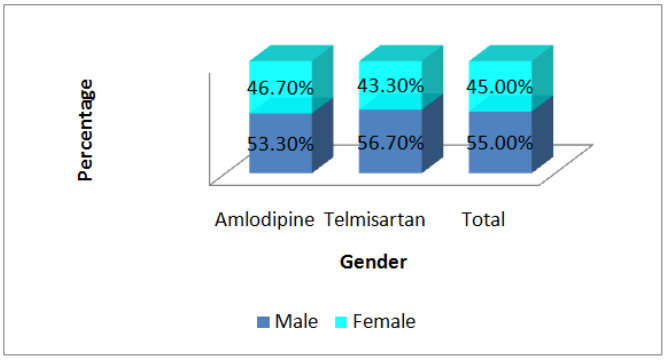

Figure 2. Categorisation of study population based on gender

In Amlodipine and Telmisartan groups males (Amlodipine 53.3%, Telmisartan 56.7%) are predominated over females (Amlodipine-46.7%, Telmisartan-43.3%). Male patients constituted the majority in the total study population (51%). In Amlodipine group 53.3% were males and 46.7% females. In Telmisartan group there were 56.7% were males and 43.3% females. The total number patients in two groups were selected as per the selection criteria.

c)Based on educational status

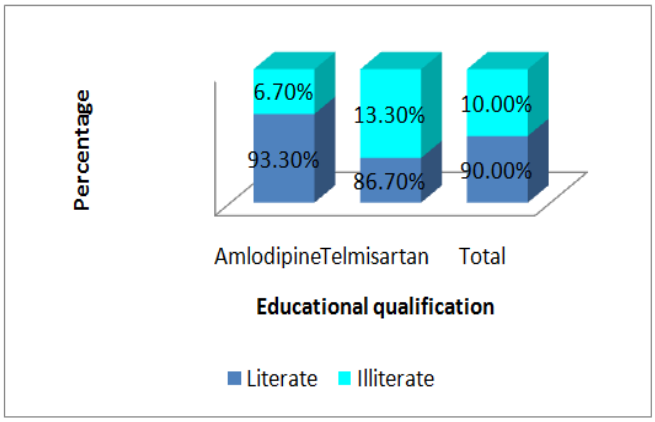

Figure 3. Categorization of study population based on educational status

In a total of study population majority of the patients are literate(90%) and group wise in Amlodipine group most patients are literate (93.3%) and illiterate (6.7%) and in Telmisartan group most patients are literate (86.7%). In group wise comparison patient taking Amlodipine are more literate (60%) than Telmisartan (46.7%). This can be correlated with age, as there are more elderly patients in which literacy rate is found to be less.

d) Based on occupation

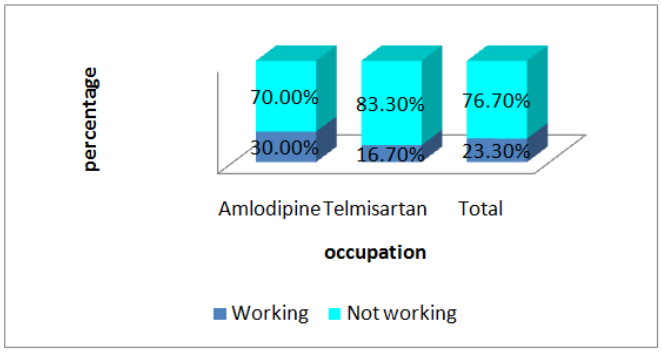

Figure 4. Categorisation of study population based on occupation

Out of the total population studied, 23.3% were working and 76.7% of patients were not working. In Amlodipine group 70% are not working and 30% are working, in Telmisartan group 83.3% are not working and 16.7% are working. In the total population, 23.3% were working and 76.7% were not working. This may have a clear connection with the age range, gender and physiological condition. As there is more number of elderly patients, they may not be able to work. Most of the female patients with a non working status.

e) Based on duration of diabetes mellitus

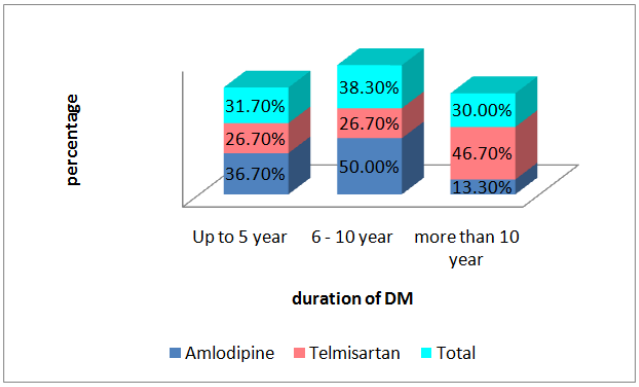

Figure 5. Categorisation of study population based on duration of diabetes mellitus

50% of patients in Amlodipine group were having diabetic history of 6-10yrs, 36.7% upto 5 yrs and 13.3% more than 10 yrs. In Telmisartan group 46.7% were having diabetic history of more than 10yrs and upto 5yr, 6-10yrs having 26.7%. In total of the study population 38.3% of patients having diabetic history of 6-10yrs. In total of the study population 38.3% of patients having diabetic history of 6-10yrs.in Amlodipine group 56.5%of patients having diabetic history of 6-10yrs. While in Telmisartan group more number of (46.7%) of patient having diabetic history of more than 10yrs. It indicates that Telmisartan is preferred in more aged patients.

f) Based on duration of hypertension

In total of the study population 50% of patients were having hypertension history of 4-6yrs followed by 20% having 1-3yrs and 13.3% having 7-9yrs. Majority of the patients in Amlodipine(60%) and Telmisartan(40%) group having hypertension history of 4-6yrs.

Table 1. Baseline comparisons of Amlodipine and Telmisartan

Variables	Group	Mean	Std. Deviation	Mean Difference	Standard Error Difference	T value	P value
SBP1	Amlodipine	166.00	26.47	8.67	6.42	1.349	0.183
	Telmisartan	157.33	23.18				
DBP1	Amlodipine	96.00	8.94	1.00	2.68	0.372	0.711
	Telmisartan	95.00	11.67				
FBS1	Amlodipine	227.60	83.64	15.80	19.41	0.814	0.419
	Telmisartan	211.80	65.60				
SC1	Amlodipine	1.51	0.58	0.03	0.12	0.251	0.803
	Telmisartan	1.48	0.26				
UA1	Amlodipine	4.57	1.49	0.41	0.34	1.196	0.236
	Telmisartan	4.17	1.13				

Table 2. Post comparisons of Amlodipine and Telmisartan

Variables	Group	Mean	Std. Deviation	Mean Difference	Standard Error Difference	T	P value
SBP2	Amlodipine	131.00	13.98	4.00	3.13	1.280	0.206
	Telmisartan	127.00	9.88				
DBP2	Amlodipine	86.67	8.44	4.00	2.21	1.809	0.076
	Telmisartan	82.67	8.68				
FBS2	Amlodipine	115.57	24.96	-0.50	5.58	0.090	0.929
	Telmisartan	116.07	17.62				
SC2	Amlodipine	1.28	0.52	0.05	0.10	0.447	0.656
	Telmisartan	1.23	0.22				
UA2	Amlodipine	3.99	0.94	-0.20	0.29	0.702	0.485
	Telmisartan	4.19	1.25				

Table 3. Comparison of laboratorical parameters at baseline and after 6week of treatment-Amlodipine group

S.No.	Variables	Test	Mean	Std. Deviation	Mean Difference	Standard Error Difference	T value	P value
1	SBP	Base line	166.00	26.47	35.00	3.61	9.690	0.001
		After	131.00	13.98				
2	DBP	Before	96.00	8.94	9.33	1.91	4.877	0.001
		After	86.67	8.44				
3	FBS	Before	227 .60	83.64	112.03	13.21	8.481	0.001
		After	115.57	24.96				
4	SC	Before	1.51	0.58	0.24	0.05	4.688	0.001
		After	1.28	0.52				
5	UA	Before	4.57	1.49	0.58	0.14	4.098	0.001
		After	3.99	0.94				

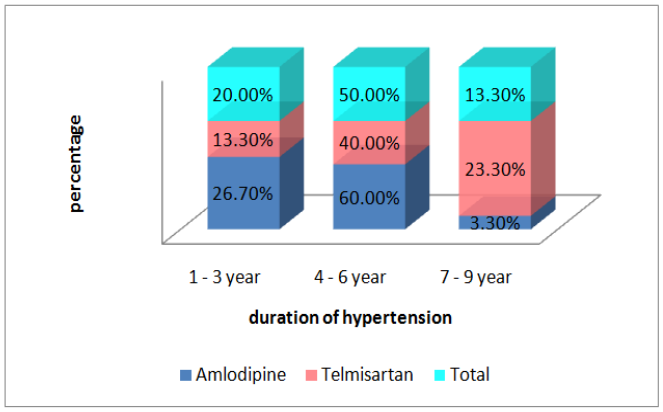

Figure 6. Categorization of study population based on duration of hypertension

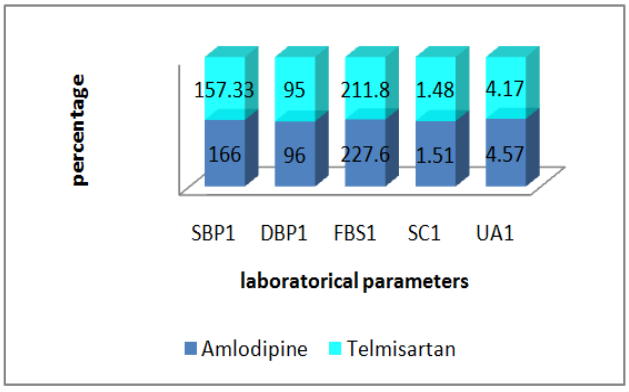

Figure 7. Baseline comparisons of Amlodipine and Telmisartan

g) Baseline comparison of Amlodipine and Telmisartan

When comparing the two drug at base line no significant change. In the case of SBP and DBP Amlodipine group has high blood pressure compared to that of Telmisartan group. In case of FBS, serum creatinine and uric acid Amlodipine group have high value compared to that of Telmisartan group.

h) Post comparisons of Amlodipine and Telmisartan

Comparing the two drugs after 6weeks of treatment no significant changes in the laboratical values. In the case of SBP, DBP, serum creatinine and uric acid Amlodipine group have high value than Telmisartan but in case of FBS Telmisartan group has high value than Amlodipine group.

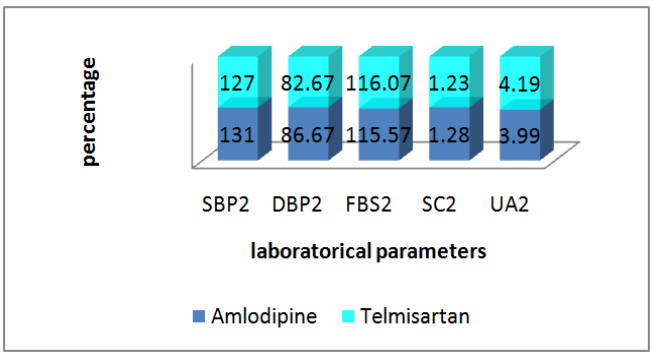

Figure 8. Post comparisons of Amlodipine and Telmisartan

i) Comparison of laboratorical parameters at baseline and after 6week of treatment-Amlodipine group

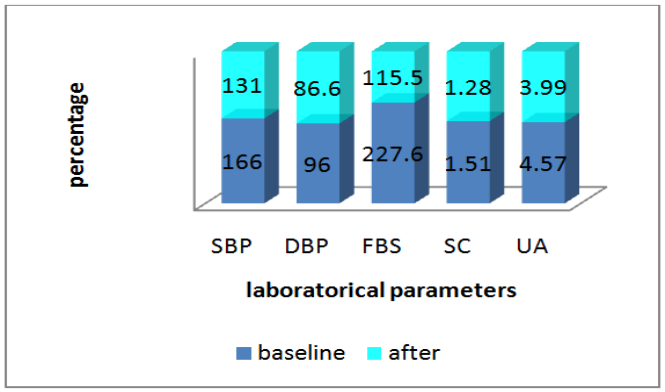

Figure 9. Comparison of laboratical parameters at baseline and after 6week of treatment-Amlodipine group

When comparing Amlodipine group there is a significant changes in laboratical parameters like FBS, SBP, DBP, SC and UA. At baseline SBP is 166mmHg after 6 weeks of treatment it reduced to 133mmHg.DBP changes from 96mmHg to 86.67mmHg.FBS from 227 to 115, SC from 1.5 to 1.28, uric acid from 4.5 to 3.9. After 6 weeks of treatment, the Amlodipine and Telmisartan group no significant difference in SBP (131mmHg and 127mmHg respectively. p=0.206), and DBP (86.67mmHg and 82.67mmHg respectively. p=0.076), although the values were slightly lower in Telmisartan group. The same result of the study was shown in the study conducted by Pozzobon *et al*.

j) Comparison of laboratorical parameters at baseline and after 6week of treatment- Telmisartan group

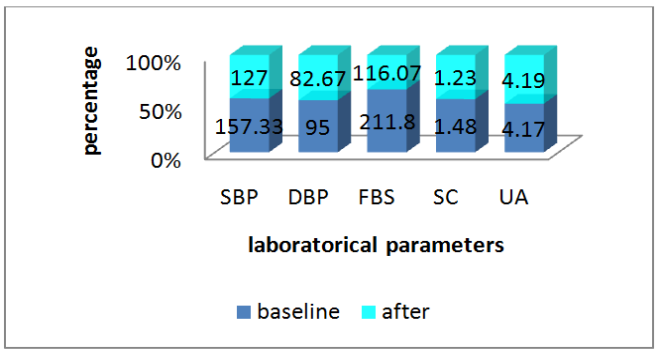

Figure 10. Comparison of laboratorical parameters at baseline and after 6week of treatment- Telmisartan group

When comparing the Telmisartan group there is a significant changes in the laboratical parameters like SBP, DBP, FBS and SC but there is no significant changes in serum uric acid value. It little increased after 6 weeks of treatment with Telmisartan.

k) Comparison of ECHO of Amlodipine and Telmisartan group

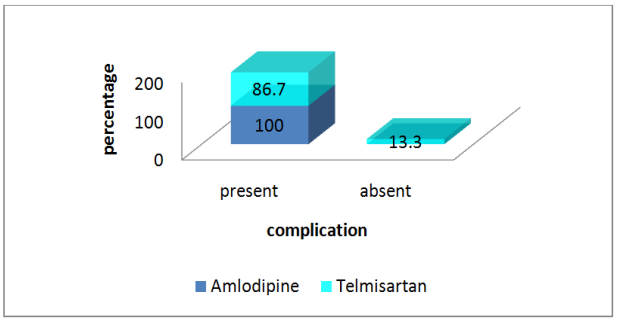

Figure 11. Baseline comparison of ECHO of Amlodipine and Telmisartan group

When comparing ECHO of the two groups at baseline to detect cardiovascular complications, Amlodipine group have higher cardiovascular complication than Telmisartan group. When comparing the ECHO of two groups, 100% of patients in Amlodipine group have abnormal ECHO (cardiovascular complication present) and in Telmisartan group 86.7% of patients with abnormal ECHO.

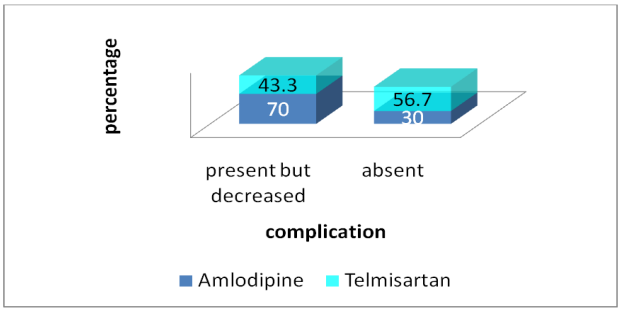

Figure 12. Post comparison of ECHO of Amlodipine and Telmisartan groups

When comparing ECHO of the two groups after 6 weeks of treatment, in Amlodipine group 70% of the patients have complication present but decreased. Complication not present in 30% of patients. In the case Telmisartan group complication not present in 56.7% patients and complication present but decreased in 43.3% patients. When comparing ECHO of the two groups after 6 weeks of treatment, in Amlodipine group 70% of the patients have complication present but decreased. Complication not present in 30% of patients. In the case Telmisartan group complication not present in 56.7% patients and complication present but decreased in 43.3% patients.

l) Comparison of Microalbumin of Amlodipine and Telmisartan group

In the case of Amlodipine group at baseline microalbumine present in 60% of patients and in Telmisartan group microalbumin present in 63.3%. At baseline, in the Amlodipine group 60% of patients present with microalbuminuria, in the Telmisartan group 73.3% of patients present with microalbuminuria.

Table 4. Comparison of laboratorical parameters at baseline and after 6week of treatment- Telmisartan group

S. No.	Variables	Test	Mean	Std. Deviation	Mean Difference	Standard Error Difference	T value	P value
1	SBP	Before After	157.33 127.00	23.18 9.88	30.33	3.23	9.381	0.001
2	DBP	Before After	95.00 82.67	11.67 8.68	12.33	1.90	6.495	0.001
3	FBS	Before After	211.80 116.07	65.60 17.62	95.73	11.52	8.313	0.001
4	SC	Before After	1.48 1.23	0.26 0.22	0.25	0.04	6.656	0.001
5	UA	Before After	4.17 4.19	1.14 1.25	0.03	0.06	0.477	0.637

Table 5. Comparison of ECHO of Amlodipine and Telmisartan group

Group			$ECHO_2$		Chi square	P value
			Complications not present	Complication present but decreased		
Amlodipine	ECHO1	Complications not present	0 0.0%	0 0.0%	---	---
		Complication present	9 30.0%	21 70.0%		
	Total		9 30.0%	21 70.0%		
Telmisartan	ECHO1	Complications not present	4 100.0%	0 0.0%	3.529	0.06
		Complication present	13 50.0%	13 50.0%		
	Total		17 56.7%	13 43.3%		
Total	ECHO1	Complications not present	4 100.0%	0 0.0%	5.604	0.018
		Complication present	22 39.3%	34 60.7%		
	Total		26 43.3%	34 56.7%		

Table 6. Comparison of Microalbumin of Amlodipine and Telmisartan group

Group			AL2			Chi square	P value
			Present	Not present	Present but decreased		
Amlodipine	AL1	Present	6 33.3%	4 22.2%	8 44.4%	17.5	0.0001
		Not present	0 0.0%	12 100.0%	0 0.0%		
	Total		6 20.0%	16 53.3%	8 26.7%		
Telmisartan	AL1	Present	6 27.3%	11 50.0%	5 22.7%	6.306	0.043
		Not present	0 0.0%	8 100.0%	0 0.0%		
	Total		6 20.0%	19 63.3%	5 16.7%		
Total	AL1	Present	12 30.0%	15 37.5%	13 32.5%	21.429	0.0001
		Not present	0 0.0%	20 100.0%	0 0.0%		
	Total		12 20.0%	35 58.3%	13 21.7%		

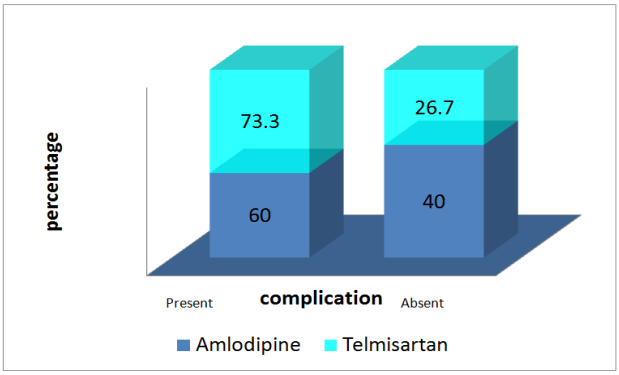

Figure 13. Baseline comparison of Microalbumin –Amlodipine and Telmisartan group

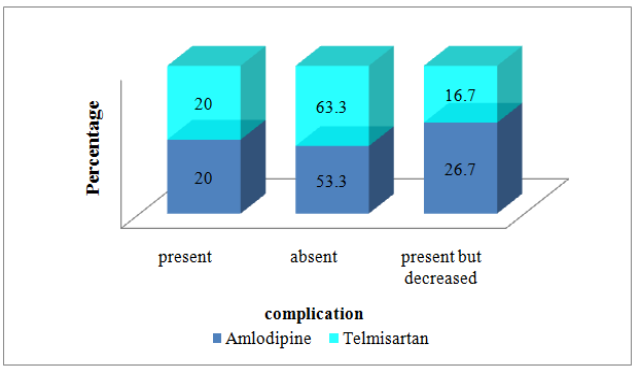

Figure 14. Post comparison of microalbumin-amlodipine and telmisartan group

After 6 weeks of treatment with Amlodipine microalbumin present in 20% of patients and it present but decreased in 26.7% and it not present in 53.3% patients.in Telmisartan group it not present in 63.3% patients, present but it decreased in 16.7% and present in 20% patients. Telmisartan group has higher reduction in microalbumin compared to that of Amlodipine group. After 6 weeks of treatment with Amlodipine microalbumin present in 20% of patients and it present but decreased in 26.7% and it not present in 53.3% patients. In Telmisartan group it not present in 63.3% patients, present but it decreased in 16.7% and present in 20% patients. Telmisartan group has higher reduction in microalbumin compared to that of Amlodipine group.

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