"COMPARATIVE STUDY ON EFFICACY OF LOSARTAN VERSUS TELMISARTAN IN HYPERTENSIVE PATIENTS"

Dissertation

Submitted to

The Tamil Nadu Dr. M.G. R. Medical University, Chennai.

In partial fulfillment for the award of the degree of

Master of Pharmacy

In

PHARMACY PRACTICE

By

Reg. No: 26113481

DEPARTMENT OF PHARMACY PRACTICE

ULTRA COLLEGE OF PHARMACY

4/235, COLLEGE ROAD, THASILDAR NAGAR,

MADURAI – 625020.

OCTOBER 2013

DECLARATION

I hereby declare that this thesis work entitled**" COMPARATIVE STUDY ON EFFICACY OF LOSARTAN VERSUS TELMISARTAN IN HYPERTENSIVE PATIENTS "**submitted to The Tamil Nadu Dr. M.G.R Medical University, Chennai was carried out by me in the Department of Pharmacy Practice ,Ultra College of Pharmacy, Madurai under the valuable and efficient guidance of **Mr.T.REGUPATHI, M.PHARM,MLM,MBA.,**Prof&Head, Department of Pharmacy Practice, Ultra College of Pharmacy, Madurai during the academic year Nov 2012-sept 2013. I also declare that the matter embodied in it is a genuine work and the same has not to formed the basis for the award of any degree, diploma, associateship, fellowship of any other university or institution.

PLACE: MADURAI (**Reg. No: 26113481)**

DATE:

ULTRA COLLEGE OF PHARMACY
4/235, COLLEGE ROAD,
THASILDAR NAGAR,
MADURAI.

CERTIFICATE

This is to certify that, this thesis work entitled**" COMPARATIVE STUDY ON EFFICACY OF LOSARTAN VERSUS TELMISARTAN IN HYPERTENSIVE PATIENTS "** submitted in partial fulfilment of the requirements for the award of degree of Master of Pharmacy in Pharmacy Practiceof The Tamil Nadu Dr. M.G.R Medical University, Chennai is a bonafide work carried out by **Reg.No: 26113481**and was guided and supervised by me during the academic year Nov 2012-Sept 2013.

PLACE: MADURAI

DATE:

Mr.T.REGUPATHI,M.PHARM,MLM,MBA

Prof&Head,

Department of pharmacy practice,

Ultra college of pharmacy,

Madurai.

ULTRA COLLEGE OF PHARMACY
4/235, COLLEGE ROAD,
THASILDAR NAGAR,
MADURAI.

CERTIFICATE

This is to certify that, this thesis work entitled **" COMPARATIVE STUDY ON EFFICACY OF LOSARTAN VERSUS TELMISARTAN IN HYPERTENSIVE PATIENTS "** submitted in partial fulfilment of the requirements for the award of degree of Master of Pharmacy in Pharmaceutical Chemistry of The Tamil Nadu Dr. M.G.R Medical University, Chennai is a bonafide work carried out by **Reg.No:26113481**and was guided and supervised by **Mr.T.REGUPATHI, M.PHARM,MLM,MBA.,**Prof&Head,Department of Pharmacy Practice, Ultra College of Pharmacy, Madurai during the academic year Nov 2012-sept 2013.

Dr.C.VIJAYA,
Dean (P.G Programme),
Ultra College of Pharmacy,
Madurai.

Prof.A.BABU THANDAPANI
Principal,
Ultra College of Pharmacy,
Madurai.

PLACE: MADURAI

DATE:

ULTRA COLLEGE OF PHARMACY
4/235, COLLEGE ROAD,
THASILDAR NAGAR,
MADURAI.

CERTIFICATE

This is certify that, this thesis work entitled**" COMPARATIVE STUDY ON EFFICACY OF LOSARTAN VERSUS TELMISARTAN IN HYPERTENSIVE PATIENTS "s**ubmitted in partial fulfilment of the requirements for the award of degree of Master of Pharmacy in Pharmacy Practice of the Tamil Nadu Dr. M.G.R Medical University, Chennai is a bonafide work carried out by **Reg.No:26113481** guided by **Mr.T.REGUPATHI, M.PHARM, MLM, MBA.**, Prof&Head, Department of Pharmacy Practice, Ultra College of Pharmacy Madurai during the academic year Nov 2012-Sept 2012 was evaluated by us.

EXAMINERS:

1.

2.

PLACE: MADURAI

DATE:

ACKNOWLEDGEMENT

Apart from my efforts, the success of this project depends largely on the encouragement and guidelines of many others. I take the privilege and pleasure to express my gratitude to the people who have been instrumental in the successful completion of this project.

First and foremost, I express my extreme sense of gratitude and profound thanks to my guide **Mr.T.REGUPATHI,M.pharm,MLM,MBA,** Prof&Head, Department of Pharmacy Practice, Ultra college of pharmacy, Madurai for his precious guidance, encouragement, abundant help, inspiring discussions and timely suggestions which proved for the success of this work.

I express my special thanks to **Dr.S.MOHAN SUNDARAM,MD,DPM.**and to other staffs, **MANOHAR HOSPITAL**,Kallai road, Calicut, Kerala, who had taken the pain to provide me with all the essential facilities for the completion of my project and has been a constant source of inspiration.

I do feel highly elated in manifesting a sense of gratitude to my honourable Chairman **Prof. K.R ARUMUGAM,M.pharm,** who permitted me to do this project and showered his blessings and guidance whole heartily in every walk of our successful careers.

I wish to thank with pleasure and gratitude **prof. BABUTHANDAPANI, M.pharm**, Principal, Ultra college of pharmacy,Madurai for his valuable suggestions and support for the fulfilment of my dissertation.

It is my privilege and honour to extend my profound gratitude and express my indebtedness to our Dean **Dr.C.VIJAYA.M.Pharm, Ph.D**, Ultra College of pharmacy,Madurai for her constant inspiration, valuable advice, help, encouragement and innovative ideas throughout the course of the project.

I wish to thank with pleasure and gratitude **Mr.S.KSathish, M.Pharm**, Department of pharmacy practice, Ultra college of pharmacy, Madurai for his valuable suggestions and support for the fulfilment of my dissertation.

I sincerely extend my thanks to the Librarian **Mr.P. Sankar, BA (Lit), M.L.I.Sc.,** Library Assistant **Mis.Sundharavalli, M.L.I.Sc.,** and all the Laboratory staffs in Ultra College of Pharmacy.

I extend my sincere thanks to my M.Pharmbatchmates**Mr.DalvinPoulose, Mr.jobukuruvilla, Mr.BinoBabu, Mr.Jacob Varghese, Mrs.SuryaSurendran, Mr.Menge Dennis Mengate, Ms. Sonia C.George.**who helped me throughout this project.

I am very much grateful to friends in Pharmaceutics Department especially **Mr.Deepu Thomas kurien, Mr.Ratheesh G, and Mr.Vishnu Prasad, Ms.Geethususan gorgy, Ms.preethafrancis** and grateful to all my seniors.

I am very much grateful to my friends**Ms.RinishaRasak, Ms.Moliniya Baby**who helped me throughout this project.

I am extremely debtful to the shadow of Lord i.e**My Parents(Mr.Sasidaran.k and Mrs.Ranjini.p) and my Brother Arun.k, all my beloved family members** for always standing behind me throughout the crests and troughs in journey of me and provoked me to successfully reach the destination of my project.

Last but not least, once more I express my heartfelt gratitude to the Almighty of God, without whose grave all those effects would not have achieves the goal.

I whole heartedly thank all those who have stretched their helping hands towards me directly and indirectly for successful completion of this dissertation.

Thank you one and all.....

ABBREVIATIONS

S.NO	ABBREVIATIONS	DESCRIPTION
1	ACE	Angiotensin-converting enzyme
2	ARBs	Angiotensin receptor blockers
3	AUC	Area under curve
4	BP	Blood pressure
5	BMI	Body mass index
6	CA^{2+}	Calcium ion
7	CCBs	Calcium channel blockers
8	CHD	Coronary heart disease
9	CHF	Congestive heart failure
10	CNS	Central Nervous System
11	CI	Cardiac index
12	CV	Cardiovascular
13	CVD	Cardiovascular Disease
14	CYP 450	Cytochrome p 450
15	DASH	Dietary approaches to stop hypertension
16	DBP	Diastolic blood pressure
17	DM	Diabetes Mellitus
18	ECG	Electrocardiogram

46	UTI	Urinary tract infection
47	VLDL	Very low density lipoprotein
48	VS	Versus
49	WHO	World health organization
50	2HPG	2Hour Post Prandial Plasma Glucose Level
31	LVH	Left ventricular hypertrophy
32	met S	Metabolic syndrome
33	MI	Myocardial infraction
34	mm Hg	Millimeter of mercury
35	Na- Cl	Sodium chloride
36	NCEP-ATP III	National cholesterol education program adult treatment panel
37	NSAID	Non Steroidal Anti Inflammatory Drug
38	OD	Once daily
39	OGTT	Oral glucose tolerance test
40	PPAR	Peroxisome proliferator activated receptor
41	SBP	Systolic blood pressure
42	SD	Standard deviation
43	SI	Insulin sensitivity index
44	TC	Total cholesterol
45	TG	Triglycerides

CONTENTS

1. HYPERTENSION

Hypertension is a silent killer, currently affects approximately one billion adults globally. Hypertension is an important risk factor for cardiovascular diseases and stroke and is associated with metabolic syndromes including insulin resistance and lipid abnormalities. At a defining cut of 140/90 mmHg, 28-44% of world population has hypertension[1]. Estimated prevalence of hypertension is about 25% among urban adults and 10% in the rural areas[2]. The life time risk for developing hypertension is estimated to be up to 90%. It's a condition, the blood pressure is elevated to an extend; where clinical benefit can be obtained from blood pressure lowering. Components used for determination are systolic and diastolic blood pressure. There is no clear cut off point between hypertensive and normotensive subject.

The blood pressure is a product of cardiac output and the total resistance of peripheral system, of that high blood pressure arises as a result of increased resistance of peripheral system due to constriction of small arterioles. Hypertension is a condition, the pressure that's put on the walls of the arteries as blood is pumped through the circulatory system. The circulation of blood through the veins and arteries is at certain pressure. In natural limit it is not harmful. But with this pressure increase, heart is over worked and an abnormal interior tissue growth can be developed in arteries. This cause further blocked in passage of blood, leading to blood pressure increasing.

In many cases, genetic susceptibility to hypertension is observed. Hypertension is twice common in subjects with hypertensive parents. Essential hypertension occurs four times more frequently in blacks than whites. And in middle aged population males are more frequent with hypertension than the females.

Many drugs which are commonly using can cause high blood pressure as side effect. Some of the drugs belongs to the above category includes non-steroidal anti-inflammatory drugs, contraceptives, steroids. Obesity causes high blood pressure due to increased body weight and additional pressure that it exerts on the heart and arterial system. An unhealthy diet which is rich with salt and fats lack of dietary fibers along with

a secondary life style devoid of proper exercise ,excessive use of alcohol , cigarette smoking is an another culprit for hypertension.

Advanced medical researchers are developing new methods to lower the high blood pressure and it has gone to great lengths. Even the arterial hypertension is almost never a serious health treat; doctors attempt to lower high blood pressure because it can have serious long term consequences.

It's was also shown that more than 64% of patients with hypertension also have dyslipidemia and 47% of patients with dyslipidemia have hypertension[3]. Highly elevated TGL levels are found in hypertensives on comparing with normotesives[4]. Patients with hypertension frequently have additional cardiovascular risk[5]. Conversely hypertension is a significant risk factor in patients with elevated cholesterol and diabetes[6].

Strategies that reduce BP and lipid levels simultaneously are likely to lead to a greater reduction in the incidence of CVD related events than treating either factor in isolation.

A.1 DEFENITION

Hypertension is defined as a sustained diastolic blood pressure greater than 90 mm Hg accompanied by an elevated systolic blood pressure greater than 140 mm Hg[7]. Blood pressure is the force by which blood drives through blood vessels to supply oxygen and nutrients to the body organs and carry away metabolites and waste materials. The blood pressure is optimal if it is less than 120/80 mm Hg.

A.2 ETIOLOGY

More than 90% of the patients having essential hypertension, it is a disorder of unknown origin effect the BP regulating mechanism. A subject with family history of hypertension is likelihood to develop hypertensive disease. Primary hypertension is four times more frequently in blacks than in whites. Likely it observed more often in middle aged male subjects than middle aged females. Many environmental factors like stressful

life style , un-healthy diet , obesity , smoking and alcoholism, lack of proper exercise and usage of drugs such as NSAID are predisposing factors to develop hypertension[8].

A.3 CAUSES OF HYPERTENSION

90-95% of hypertension is essential hypertension and 5-10% of hypertension belongs to Secondary hypertension. Causes of primary hypertension are not clearly unknown. Secondary hypertension is renal or endocrine diseases, vascular diseases. And the same may be arising due to the drugs.

` Endocrine diseases which can produce secondary hypertension are Acromegaly**,**Conn's syndrome**,** Cushing's syndrome**,** Phaeochromocytoma**,** Pre eclampsia**.** Vascular causes includes Fibro muscular hyperplasia**,** renal artery atheroma etc. Many drugs can also be leading factors for secondary hypertension. Adrenal steroids, Antidepressants Appetite suppressants,Cocaine,Cyclosporine, Erythropoietin, Nasal decongestants, NSAIDs, Oral contraceptives**,** Sympathomimeticsarethere in the category of drugs which can induce hypertension[9].

A.4COMPLICATIONS OF HYPERTENSION

MI

Stroke

Malignant hypertension

Dissecting aortic aneurysm

Hypertensive nephrosclerosis

Peripheral vascular disease[10]

A.4 a) MYOCARDIAL INFRACTION[12]

A heart attack occurs when blood flow to a part of heart is blocked for a long enough time that part of the heart muscle is damaged or dies. The medical term for this is

myocardial infarction. Most heart attacks are caused by a blood clot that blocks one of the coronary arteries. The coronary arteries bring blood and oxygen to the heart. If the blood flow is blocked, the heart is starved of oxygen and heart cells die .A hard substance called plaque can build up in the walls of coronary arteries. This plaque is made up of cholesterol and other cells. Chest pain is the most common symptom of a heart attack. One may feel the pain in only one part of your body, or it may move from your chest to arms, shoulder, neck, teeth, jaw, belly area, or back. Other symptoms of a heart attack can include anxiety, cough, fainting, light headedness, dizziness, nausea, vomiting, and shortness of breath, sweating, palpitation[11].

A.4 b) STROKE

A stroke happens when blood flow to a part of the brain stops. A stroke is sometimes called a **"brain attack."**If blood flow is stopped for longer than a few seconds, the brain cannot get blood and oxygen. Brain cells can die, causing permanent damage. There are two major types of stroke, ischemic stroke and hemorrhagic stroke. Ischemic stroke occurs when a blood vessel that supplies blood to the brain is blocked by a blood clot. This may happen in two ways, thrombotic stroke or embolic stroke. Ischemic strokes may be caused by clogged arteries. Fat, cholesterol, and other substances collect on the artery walls, forming a sticky substance called plaque. A hemorrhagic stroke occurs when a blood vessel in part of the brain becomes weak and bursts open, causing blood to leak into the brain. Some people have defects in the blood vessels of the brain that make this more likely.

A.4 c) MALIGNANT HYPERTENSION

Malignant hypertension is very high blood pressure that comes on suddenly and quickly. The lower (diastolic) blood pressure reading, which is normally around 80 mmHg, is often above 130 mmHg.The disorder affects about 1% of people with high blood pressure, including both children and adults. It is more common in younger adults.It also occurs in people with collagen vascular disorders, kidney problems, toxemia

of pregnancy. High risk for malignant hypertension includes kidney failure, renal hypertension.

A.4 d) DISSECTING AORTIC ANEURYSM

Aortic dissection occurs when a tear in the inner wall of the aorta causes blood to flow between the layers of the wall of the aorta, forcing the layers apart. In most cases this is associated with severe characteristic chest or abdominal pain described as "tearing" in character, and often with other symptoms that result from decreased blood supply to other organs. Aortic dissection is a medical emergency and can quickly lead to death, even with optimal treatment, as a result of decreased blood supply to other organs, cardiac failure, and sometimes rupture of the aorta. Aortic dissection is more common in those with a history of high blood pressure, a known thoracic aortic aneurysm, and in a number of conditions that affect blood vessel wall integrity such as Marfan syndrome and the vascular subtype of Ehlers–Danlos syndrome. The treatment of aortic dissection depends on the part of the aorta involved. Surgery is usually required for dissections that involve the aortic arch, while dissections of the part further away from the heart may be treated with blood pressure lowering only.Aortic dissection is relatively rare, occurring at an estimated rate of 2–3.5 per 100,000 people every year. It is more common in males. Mean age at diagnosis is 63, although all age groups may be affected. Many cases of aortic dissection (40%) lead to death so rapidly that the person doesn't make it to hospital in time.

A.4 e) HYPERTENSIVE NEPHROSCLEROSIS

Hypertensive nephropathy or hypertensive nephrosclerosis, or Hypertensive renal disease is a medical condition referring to damage to the kidney due to chronic high blood pressure. It should be distinguished from renovascular hypertension which is a form of secondary hypertension.In the kidneys, as a result of benign arterial hypertension, hyaline (pink, amorphous, homogeneous material) accumulates in the wall of small arteries and arterioles, producing the thickening of their walls and the narrowing of the lumina hyaline arteriolosclerosis. Consequent ischemia will produce tubular atrophy,

interstitial fibrosis, glomerular alterations and periglomerular fibrosis. In advanced stages,renal failure will occur. Functional nephrons have dilated tubules, often with hyaline casts in the lumens. Additional complications often associated with hypertensive nephropathy include glomerular damage resulting in protenuria and hematuria[12].

A.4 f) PERIPHERAL VASCULAR DISEASE

Peripheral vascular disease is a narrowing of blood vessels that restricts blood flow. It mostly occurs in the legs, but is sometimes seen in the arms. Peripheral vascular disease includes a group of diseases in which blood vessels become restricted or blocked. Typically, the patient has peripheral vascular disease from atherosclerosis. Atherosclerosis is a disease in which fatty plaques form in the inside walls of blood vessels. Other processes, such as blood clots, further restrict blood flow in the blood vessels. Both veins and arteries may be affected, but the disease is usually arterial. All the symptoms and consequences of peripheral vascular disease are related to restricted blood flow. Peripheral vascular disease is a progressive disease that can lead to gangrene of the affected area. Peripheral vascular disease may also occur suddenly if an embolism occurs or when a blot clot rapidly develops in a blood vessel already restricted by an atherosclerotic plaque, and the blood flow is quickly cut off. There are many causes of peripheral vascular disease. One major risk factor is smoking cigarettes. Other diseases predispose patients to develop peripheral vascular disease. These include diabetes, Burger's disease, hypertension, and Reynaud's disease. The main symptom is pain in the affected area. Early symptoms include an achy, tired sensation in the affected muscles. Since this disease is seen mainly in the legs, these sensations usually occur when walking. The symptoms may disappear when resting. As the disease becomes worse, symptoms occur even during light exertion and, eventually, occur all the time, even at rest. In the severe stages of the disease the leg and foot may be cold to the touch and will feel numb. The skin may become dry and scaly. If the leg is even slightly injured, ulcers may form because, without a good blood supply, proper healing cannot take place. At the most severe stage of the disease, when the blood flow is greatly restricted, gangrene can develop in those areas lacking blood supply. In some cases, peripheral vascular disease

occurs suddenly. This happens when an embolism rapidly blocks blood flow to a blood vessel. The patient will experience a sharp pain, followed by a loss of sensation in the affected area. The limb will become cold and numb, and loose color or turn bluish.

The most common and important CV complication associated with hypertension are stroke and myocardial infarction, Increase of 5 mm Hg diastolic pressure from usual range shows 35- 40% increased risk of stroke and similar but less steep association for coronary heart disease . According to Framingham heart study subjects with BP values between 130 to 139 and 85 to 89 mm Hg are associated with more than two fold increase in relative risk from CVD when comparing subjects with a BP level less than 120/80 mm Hg.

A.5 RISK FACTORS OF CVD

- Hypertension
- Elevated LDL or low HDL
- Age
- Diabetes mellitus
- Renal disease
- Family history
- Obesity
- Life style [13]

Management of hypertension and other risk factors is essential to reduce the morbidity and mortality risks arise due to hypertension.

A.6 CLASSIFICATION OF BLOOD PRESSURE

Table1. [14]

Classification	Systolic (mm Hg)	Diastolic (mm Hg)
Normal	<120	<80
Prehypertension	120–139	80–89
Stage 1 hypertension	140–159	90–99
Stage 2 hypertension	≥160	≥100

Table2.

Compelling indications for use of antihypertensive drugs
1. Heart failure 2. high coronary artery disease risk 3. H/O MI in the past 4. H/O stroke in the past 5. Diabetes 6. Chronic renal disease

People with stage 1 and stage 2 are to be treated. The goal of treatment in individuals without Compelling indications for use of antihypertensive drugs is >140/90 mm hg , and the same in subjects with prehypertension is to lower the BP with life style changes to prevent it's further progression[15].

A.7 PREVENTION OF HYPERTENSION

By preventing the rise in BP, hypertensive risk like cardiovascular diseases, renal diseases, stoke, and the hypertension itself can be reduce or minimize. For that preventive measures to minimize or avoid the causing factors or risk factors of hypertension should be introduced to the specific population. The causing factors that are to be avoided or minimized for attaining the aim of prevention of hypertension includes smoking, intake of sodium rich and fatty diet, excess of alcohol intake, excess of body weight[18] etc. A diet which is rich with fruits and vegetables, with sufficient potassium is suggested with an improved physical activity to minimize the rise in BP. It is mainly meant for the population who belong to prehypertension. It is observed and estimated from studies that it can be attain a reduction of 8% in mortality rates with stroke, 5% reduction in mortality due to CAD, by reducing 3mm Hg of systolic BP[16].

1. Engage in regular aerobic physical activity such as brisk walking (at least 30 minutes per day, most days of the week).
2. Maintain normal body weight for adults (body mass index 18.5 – 24.9 kg/m2).
3. Limit alcohol consumption to no more than 1 oz (30 ml) ethanol (e.g., 24 oz [720 ml of beer, 10 oz [300 ml] of wine, or 2 oz [60 ml] 100-proof whiskey) per day in most men and to no more than 0.5 oz (15 ml) of ethanol per day in women and lighter weight persons.
4. Reduce dietary sodium intake to no more than 100 m mol per day (approximately 2.4 g of sodium or 6 g of sodium chloride).
5. Maintain adequate intake of dietary potassium (more than 90 m mol [3,500 mg] per day).
6. Consume a diet that is rich in fruits and vegetables and in low fat dairy products with a reduced content of saturated and total fat (Dietary Approaches to Stop Hypertension [DASH] eating plan).

A.8 DIAGNOSTIC PROCEDURES AND LABORATORY TESTS

The primary parameter for diagnosing of primary hypertension is physical examination of BP. The arteriolar narrowing, focal arteriolar narrowing, arteriovenous nicking, and retinal hemorrhages, exudates, and infarcts are examined for hypertensive emergency. Cardiopulmonary examination are done for identifying the abnormality in heart rate or rhythm, left ventricular (LV) hypertrophy, pericardial heave, third and fourth heart sounds. Peripheral vascular examinations are performed to evidence of atherosclerosis, aortic or abdominal bruits, distended veins, and edema[17]. Renal artery stenosis can be indicated by abdominal systolic-diastolic bruit. Hypokalemia may suggest mineralocorticoid-induced hypertension. The presence of protein, blood cells, and casts in the urine are examined for presence of renovascular disease.

Laboratory tests recommended prior to initiating drug therapy include urinalysis, serum chemistries (sodium, potassium, creatinine, fasting glucose, fasting lipid panel), and a 12-lead electrocardiogram (ECG).

These laboratory tests are recommended to identify the risk factors, and the metabolic changes that are produced due to treatment. More extensive testing for identifiable cause is not generally indicated unless Bp control is not achieved or the clinical and routine laboratory evaluation strongly suggests an identifiable secondary cause.

A.9 PATHOPYSIOLOGY OF HYPERTENSION

Hypertension is a heterogeneous disorder. The underlying mechanism for hypertensionthat may have specific cause which is known as secondary hypertension and may be a pathophysiologic mechanism of unknown etiology which is known as primary or essential hypertension.10% of total hypertension cases belong to the secondary hypertension, renovascular disease or chronic kidney disease is the major causing factor for secondary hypertension.The other underlying conditions are Cushing's syndrome, pheochromocytoma, hyperthyroidism, hyperparathyroidism, pregnancy, primary aldosteronism, obstructive sleep apnea, and coarctation of the aorta etc. Many drugs can also be a leading factor for secondary hypertension. Adrenal steroids**,** Antidepressants, Appetite suppressants, Cocaine, Cyclosporine, Erythropoietin, Nasal decongestants**,** NSAIDs**,** Oral contraceptives**,** Sympatho-mimetics are some drugs in above class.

A.10 Primary hypertension can result from multiple factors which includes

1. Abnormalities in rennin-angiotensin-aldosterone-system,natriuretic hormone
2. Pathological disturbance in nerves system (in CNS, nerve fibers of autonomic nerve system , adrenergic or baroreceptors)
3. Abnormalities in renal system or auto regulatory process for sodium excretion, plasma volume, arteriolar constriction.
4. Either because of increased production of angiotensin II and endothelin I (vasoconstrictors) or a decrease in synthesis of vasodilators like - prostacyclin, bradykinin, and nitric oxide.
5. Sodium intake: increased vascular reactivity and a rise in BP can be resulted from excessive sodium intake and inhibition of sodium transport.
6. Intracellular calcium concentration: a rise in intracellular calcium concentration may results in alteration of vascular smooth muscle function and elevation in peripheral vascular resistance.

The life threatening events in hypertensive patients is mainly associated with cerebrovascular events, CV events and renal failure.

A.11 TREATMENT

The overall aim of antihypertensive therapy is to reduce morbidity and mortality associated with elevated blood pressure[18]. A disproportionate rise in systolic blood pressure with respect to diastolic blood pressure is founded in elderly patients due to decreased compliance of blood vessels associated with aging and atherosclerosis. So it's founded that more difficulty is there with systolic pressure reduction than diastolic blood pressure reduction. Systolic blood pressure is used as primary clinical marker in hypertension, and the same is the better predictor of CV complication. In most of the population an achievement of blood pressure <140/90 mm Hg is considered as desirable. It is preferred to be <130/80 mm Hg in subjects with diabetes mellitus, chronic kidney disease, coronary artery disease (MI, angina) etc. And for patients with LV dysfunction a blood pressure lower than 120/80 mmHg is advised.

The primary focus is given to SBP reduction. Life style modifications, pharmacological treatment with single drug or combination are required to reduce blood pressure. And that must be prescribed according to patient condition and the other co-morbidities present.

A.12 NON PHARMACOLOGICAL THERAPY

Lifestyle modifications are advisable as initial approach to pharmacological treatment. Epidemiological data's supports its importance in hypertensive population. Minor alteration in normal physical activity and diet control can reduce blood pressure.Non pharmacological method helps the patients to participate actively in management of disease.

Body weight reduction[19], sodium restriction, increased physical activity, smoking cessation, moderate consumption of alcohol is the major consideration in life style modification.

A.12 a) BODY WEIGHT REDUCTION

Obesity and hypertension are closely associated and have positive degree of correlation[20]. Even the exact mechanism is not known with lowering of BP body can be attain regardless of salt consumption. Secretion of insulin is high in obese population that may cause an increase in insulin mediated renal tubular reabsorption of Na^+ and extra cellular volume expansion[21]. A combination of aerobic exercise with good dietary consideration is advised in hypertension.

A.12 b) SODIUM RESTRICTION

Restriction of salt intake up to 5g/day offers a significant reduction in pressure (12/6 mm Hg),the better response is observed in subjects with high blood pressure.When it come to the age consideration subjects over 40 years are more responsive to the moderate restriction of salt[22]. Improved responsiveness to some antihypertensive drug is an additional benefit of moderate salt intake. Reduced sodium intake to approximately

100 mmol /day can prevent hypertension. Lower intake of sodium approximately 60 mmol /day further reduce pressure in both hypertensive and normotensive subjects[24].

A.12 c) INCREASED PHYSICAL ACTIVITY

Lack of physical activity is highly correlated with hypertension. The cardiovascular disease is decreased with increased physical activity[25]. A regular isotonic exercise reduces the blood volume and plasma catecholamine's, with this atrial natriuretic peptide concentration in plasma is increased[26].Regular isotonic exercise offers a reduction of 10mm hg of blood pressure.

It also reduced plasma renin activity, norepineprine levels in plasma.

A.12 d) SMOKING CESSATION

Cigarette smoking is one of the strongest contributors to the risks of cardiovascular diseases, including coronary heart disease, stroke, sudden death, peripheral artery disease, and aortic aneurysm[27]. Considerable reductions in the risk of cardiovascular diseases occur immediately after the discontinuation of cigarette smoking[28].Alterations in blood pressure (BP), heart rate (HR), and autonomic nervous function are thought to be at least in part responsible for the rapid reduction in the risk of cardiovascular diseases after quitting.

A.12 e) MODERATE CONSUMPTION OF ALCOHOL

Consumption of alcohol is restricted in hypertensive population as it can leads to elevation in blood pressure. High alcohol consumption leads to increased risk for cerebrovascular accidents. Not more than 30 ml of alcohol per day is advised to hypertensive subjects.

A.12 f) DIET

Diet with increased usage of fruits, vegetables and low-fat dairy products and includes whole grains, nuts, poultry and fish[29]. It has low quantities of fats, red meat, sweets and sugar-containing beverages. It is thus rich in potassium, magnesium, calcium

and fiber and has low amounts of total fat, saturated fat and cholesterol is advised in hypertension[30]. Some example for the above includes vegan's diet, dash diet, Mediterranean diet[31]. Animal products meat and it's product have been shown to rise in BP, were fish has shown to reduce BP because of omega -3 fatty acid.

A.13 ORAL ANTIHYPERTENSIVE DRUGS

Drugs that are used to treat hypertension are called as antihypertensive drugs. Antihypertensive therapy is meant to prevent the complications of high blood pressure, such as stroke, myocardial Infarction. Reduction of the blood pressure by 5 mmHg can decrease the risk of stroke by 34%, of ischemic heart disease by 21%, and reduce the likelihood of dementia, heart failure, and mortality from cardiovascular disease

A.13a) DIURETICS

These classes of drug are very important in hypertensive treatment. The diuretics are also known as water pills – as they help body get rid of water and salt through urine. Diuretics bring out an alteration in Na^+ balance and decrease in extra cellular volume. They are used either alone or in combination with other antihypertensive drugs. Diuretics are used in treatment of several pathological conditions like high blood pressure, heart failure, kidney and liver problems and glaucoma etc.

The exact mechanism for arterial blood pressure reduction by diuretics is not certain .Initially the interaction with thiazide –sensitive Na-cl co transporter in kidney decreases the extra cellular volume which can produce fall in cardiac output. Reduction in blood pressure is produced and maintained in long term therapy because of reduced vascular resistance.

Diuretics are wildly used to treat hypertension. Thiazide diuretics having additive effect with other antihypertensive drugs, this reason sounds for its combination regimen with other antihypertensive drugs. Diuretics show an advantage of minimizing the salt

and water retention that is commonly produced by vasodilators and some sympatholytic drugs.

The most commonly used diuretics are hydrochlorothiazide, furosemide, and torsemide. The combination of triamterene and hydrochlorothiazide and metolazone are also used in antihypertensive therapy. Thiazide diuretics are used in indication like hypertension and to treat edema in heart failure. Loop diuretics are used in subjects with congestive heart failure symptoms and in emergency symptoms. Potassium sparing diuretics are mainly suggested in CHF.

Omitting or underutilization of diuretics leads to "resistant hypertension"

A.13 b) SYMPATHOLYTIC AGENTS

Both α and β adrenergic receptor antagonist drug shows antihypertensive action. Early invented sympathetic drugs were poorly tolerated and adverse side effects. Many of new sympathetic drugs are currently used in antihypertensive therapy. They primarily used in treatment of angina pectoris and their arterial blood pressure lowering activity is latterly investigated.

Reduction of blood pressure by β adrenergic agents are achieved through different mechanisms including, reduction in myocardial contractility, heart rate, and cardiac output. On general consideration blood pressure reduction is produced by blocking action of adrenaline receptor. Beta blockers are prescribed in population with heart disease, angina, or history a heart attack.

Examples: propranolol, metoprolol,atenolol.

Alpha$_1$ adrenergic antagonist drugs are used in therapy of hypertension. They reduce arteriolar resistance and increase venous capacitance; hence the reduction in blood pressure is obtained. The α_1 adrenergic receptor blockers are not recommended as monotherapy for hypertensive patients but suggested to use in combination with diuretics and β blockers. Enhanced effect of α_1 adrenergic receptor blocker is observed on

combining with β receptor antagonist. Since α_1 adrenergic receptor blocker improves urinary symptoms they are attractive drugs for hypertensive patient with benign prostatic hyperplasia.

Examples: prazosin, terazosin, doxazosin.

A.13 c) COMBINED α_1AND β ADRENERGIC RECEPTOR ANTAGONISTS

The drugs with combined α_1 and β adrenergic receptor antagonist action are also there in anti hypertensive category; they include labetelol, carvedilol etc. In that labetelol is given intravenously to reduce the blood pressure rapidly so used in treatment of hypertensive emergencies. Another drug carvedilol reduces the mortality in patients with systolic dysfunction and heart failure when used with diuretics and ace inhibitors.

Centrally acting antihypertensive agents like methyldopa, clonidine, guanfacine and adrenergic neuron blockers are also comes under the sympatholytic agents.

A.13 d) CALCIUM CHANNEL BLOCKERS

Calcium Channel Blockers(CCBs) are a group of drugs used in treatment of hypertension. The antihypertensive action is quick and long acting preparations are available for once a day administration. The CCBs monotherapy is effective in -50%hypertensive subjects. CCBs voltage sensitive calcium channel blocking action reduces the entry of extracellular calcium into cells cause cardiac and smooth muscle relaxation. These above change leads to vasodilation and a corresponding reduction in BP. CCBs blood pressure regulation is independent of patient rennin status. CCBs are effective in lowering of blood pressure and decreasing cardiovascular events in the elderly with isolated systolic hypertension.

Examples: nifedipine, diltiazem, verapamil, nicardipine, amlodipine, foelodipine.

A.13 e) ANGIOTENSIN CONVERTING ENZYME (ACE) INHIBITORS

The ACE inhibitors are one of the first choice drugs in all grades of essential as well as renovascular hypertension. Most patients require relatively lower doses. Used alone they control hypertension in patients, and addition o f a diuretic / β blocker extends efficacy to 90%. The ACE facilitates production of angiotensin II, which has a major role in regulating arterial BP. ACE is distributed in many several different cell types including endothelial cells. The major site for angiotensin II production is the blood vessels. ACE inhibitors block the conversion of angiotensin I to angiotensin II, a potent vasoconstrictor and stimulator of aldosterone secretion. ACE inhibitors also block the degradation of bradykinin and stimulate the synthesis of other vasodilating substances including prostaglandinE2 and prostacyclin. The fact that ACE inhibitors lower BP in patients with normal plasma renin activity suggests that bradykinin and perhaps tissue production of ACE are important in hypertension.

ACE inhibitors widen or dilate blood vessels to improve the amount of blood heart pumps and lower blood pressure.ACE inhibitors also increase blood flow, which helps to decrease the amount of work heart has to do and can help protect the kidneys from the effects of hypertension and diabetes. ACE inhibitors are used in many indications including high blood pressure, heart failure, heart attack, and preventing kidney damage associated with high blood pressure and diabetes.

Examples: captoril, enalapril, lisinopril, quinapril, ramipril, fosinopril.

A.13 f) ANGIOTENSIN II RECEPTOR ANTAGONISTS (ARBs)

ARBs produce blood pressure reduction by antagonizing the effects of angiotensin II, thus relaxation of smooth muscle is produced which leads to vasodilation, increase renal salt and water excretion, reduce plasma volume and decrease cellular hypertrophy. The ARBs have the same effects as ACE inhibitors but work by different mechanism. ARBs also overcomes some disadvantages of ACE inhibitors, which not only prevents the conversion of angiotensin I to angiotensin II but also prevent the ACE – mediated degradation of bradykinin.

Clinical trials comparing ARBs with active controls have reported significant reductions in stroke in ARB treated patients. Data on ARBs and other drugs that activate the RAS support a potential role for RAS in protecting against stroke[32].

Clinical trials havealso demonstrated that ARBs effecting against in reducing the risk of CV mortality, stroke, HF, and a new onset atrial fibrillation[33]. Ongoing trials are expected to confirm and may be extend the place of such agents for improving CV outcomes[34].

The addition of thiazide diuretic can increase the efficacy significantly.ARB therapy offers a significant reduction in progression of nephropathy in hypertensive patients with diabetes and a reduction in risk of CV events in patients with LV dysfunction. ARBtherapy is an alternative to ACE inhibitor therapy in intolerant patients. ARB_s show the lowest incidence of side effects compared with other antihypertensive drugs. The ARB_S have advantage over ACE inhibitors since they didn't produce dry cough.

. Examples: losartan, candesartan, lrbesartan, valsartan, telmisartan

A.13 g) VASODILATORS:

The vasodilators directly act on arteries and with little action on veins. Vasodilators produce better reduction in diastolic blood pressure than systolic blood pressure. Vasodilators are combined with diuretics and sympatholytic agents for achieving better therapeutic response. Vasodilators are used in hypertensive crisis and are administered intravenously to rapid lowering of blood pressure.

Examples:

Arterial: hydralyzine, minoxidil, diazoxide, fenoldopam.

Arterial and venous: nitroprusside.

2. DIABETESMELLITUS

The diabetes mellitus is a commonest endocrine disorder. This is a chronic condition and is characterized by hyperglycemia due to impaired insulin secretion with or without insulin resistance. Diabetes is developed in people when the pancreas does not produce enough insulin or when the cells in the muscles, liver and fat do not use insulin properly or due to combination of both of the above reasons. Due to this the amount of glucose in the blood increases while the cells are starved of energy. High blood glucose, also called hyperglycaemia. The most common forms of diabetes are type 1 (10%), which is an autoimmune disorder and type 2 (90%), which is associated with obesity. Gestational diabetes is the form of diabetes occurring during pregnancy. Other forms of diabetes are rare and are caused by a single gene mutation.

It is a metabolic disorder which is characterized by chronic hyperglycemia with disturbances in carbohydrate, fat and protein metabolism resulting due to defects in insulin secretion, insulin action or both.

2.1 DEFINITION

Diabetes mellitus (DM) is a group of metabolic disorders characterized by hyperglycemia and abnormalities in carbohydrate, fat, and protein metabolism.It results from defects in insulin secretion, insulin sensitivity, orboth. Chronic microvascular, macrovascular, and neuropathic complicationsmay ensue.

2.2 CLASSIFICATION OF DIABETES MELLITUS:

Out of many types, the most common ones are[35]

1. Type 1 Diabetes Mellitus

- Immune Mediated
- Idiopathic

2. Type 2 Diabetes Mellitus

3. Other specific types of diabetes

- Genetic defects of islet β-cell function
- Genetic defects of insulin action
- Diseases of the exocrine pancreas
- Endocrinopathies.
- Drug-or chemical-induced diabetes
- Other genetic syndromes

2.3 EPIDEMIOLOGY

In 2000, according to the WHO, at least 171 million people worldwide suffer from diabetes which is about 2.8% of the population. The incidence of diabetes is increasing rapidly. By 2030 it is estimated that this number will almost double. Diabetes mellitus occurs throughout the world, but it is more common (especially type 2) in the developed countries. The greatest increase in incidence is, expected to occur in Asia and in Africa, where most patients will probably be found by 2030. The increase in incidence of diabetes in developing countries is due to the trend of urbanization and lifestyle changes, perhaps most importantly due to their 'Western-style' diet.

Diabetes mellitus prevalence is expected to increase with age and the number of older persons with diabetes is expected to increase as the number of elderly population increases. Type 1 diabetes accounts for 5-10% of cases that affects 1 of 400 children and adolescents. Type 2 diabetes accounts for about 90-95% of all cases of diabetes and is relatively common. It can go undiagnosed for many years. But the number of cases that are being diagnosed is also rising rapidly and that leads to reports of a diabetes epidemic.

2.4 DIAGNOSIS OF DIABETES MELLITUS

Diagnosis of diabetes is done by measuring blood/plasma glucose level[36].

- Fasting plasma glucose (FPG).
- Oral Glucose Tolerance Test (OGTT).
- 2 Hour Post Prandial Plasma Glucose Level (2HPG).
- Glycosylated Haemoglobin (HbA_1C):

2.4 PATHOPHYSIOLOGY

2.4 a) PATHOPHYSIOLOGY OF TYPE 1 DIABETES/IDDM:

It is characterized by absolute insulin deficiency either through autoimmune attack on pancreas, a viral infection or is idiopathic. As a result cells in the islets of Langerhans in the pancreas are destroyed resulting in hypoinsulinaemia. The cause of type 1 diabetes is still not fully understood but it is believed to be of immunological origin.

2.4 b) PATHOPHYSIOLOGY OF TYPE 2 DIABETES

The two metabolic defects that characterize type 2 diabetes are

1. The derangement in β-cell secretion of insulin
2. The inability of the peripheral tissues to respond to insulin.

2.5 TREATMENT:

The two main goals of treatment are[37]:

1. Reduction of mortality and concomitant morbidity due to assorted diabetic complications.
2. Preservation of quality of life.

2.5 a) NON PHARMACOLOGICAL TREATMENT OR DIABETES

Life style modifications are the cornerstone of management of diabetes of diabetes mellitus and include the prescription of a healthy diet, regular exercise, the management of stress, and avoidance of tobacco.

2.5 b) PHARMACOLOGICAL TREATMENT

1. **BIGUANIDES:** Metformin.
2. **THIAZOLIDINEDIONES:**Pioglitazone ,Rosiglitazone.
3. **SULFONYLUREAS:**First-generation:-Tolbutamide,Chlolrpropamide.
   Second-generation:-Glipizide,Glibenclamide,Glimepiride,
   Glicazide
4. **MEGLITINIDES:**Repaglinide and Nateglinide[38].
5. **ALPHA GLUCOSIDASE INHIBITORS:**Acarbose, Miglitol and Voglibose.

2. REVIEW OF LITERATURE

P.R. Anandvijayakumar et al.,[39]**(2013)** conducted a study on the pleiotropic effects of Telmisartan and Olmesartan in hypertensive patients with metabolic syndrome.Telmisartan20mg/day and Olmesartan 10mg/day were administered to group A & B respectively for two months. The blood pressure, lipid profile (TC, TGL, LDL and HDL&VLDL)& FBS were measured on baseline and at the end of study. Both of the study drugs demonstrate the significant reduction in blood pressure, FBS, LDL and VLDL. And telmisartan is considered as an ideal agent in patients with elevated lipid profile because of its significant increase ($p<0.05$) in the levels of HDL after two months of treatment. The pleiotropic effects of Telmisartan showed within two months of study recommend the use of the drug in metabolic syndrome patients**.**

Yuji Shimizu et al.,[40]**(2012)**has studied the metabolic effect of combined Telmisartan and Nifedipine therapy in patients with essential hypertension. The Patients were initiated on Telmisartan (40 mg/day). If their office BP was not reduced to 140/90 mmHg after 6 weeks, Nifedipine(20–40 mg per day) was added for 18 weeks. In the study Telmisartan showed a reduction in blood pressure and (HOMA-IR), but didn't reduced the adiponectin or leptin levels. Telmisartan sounds for favorable metabolic effect in hypertensive patients without preexisting metabolic disorders.

Naziayasmeen et al.,[41]**(2011)** has conducted a study on efficacy and tolerability of different antihypertensive drugs in patients withessential hypertension. Drugs used were Atenolol (A) 50mg, Enalapril(E)5mg, Nifedipine (N)10mg and Furosemide (F) 40mg in monotherapy (n=86) and in 2 and 3 drugs combination (n=166). After 8 weeks oftherapy patients were assessed for efficacy and tolerability. In the study highest decrease in SBP was seen with A+E+N combination (29.2%) and in DBP with N+F combination (17.7%). All the drug groups from monotherapy and combination therapy reduced BP effectively. Mosteffective groups were A+E+N and N+F combination. Enalapril was effective and mostfrequently used drug.

SE Kjeldsen et al;[42]**(2010)** has studied the Effects of Losartan vs Candesartan inreducing cardiovascular events in theprimary treatment of hypertension. There was no difference in blood pressurereduction when comparing the Losartan and Candesartangroups during

follow-up. Compared with the Losartangroup, the Candesartan group had a lower adjusted hazardratio for total CVD, Heart failure, Cardiac arrhythmias, and Peripheral artery disease. The observations of study suggesting that, since there is no difference in blood pressure reduction then thedivergent clinical outcomes are due to difference in the pharmacological properties of thedrugs.

R.M Nixon et al.,[43] **(2009)**Conducted a study on Valsartan VS other angiotensin II receptor blockers in the treatment of hypertension .Six studies include trial arms with Candesartan, Six Irbesartan,13 Losartan, two Olmesartan, five Telmisartan and 12 Valsartan. The study reported change in systolic and diastolic blood pressure from base line to follow upping 12 weeks The weighted average reduction in mean SBP and DBP for Valsartan 160 mg 15.32/11.3 mmHg and for Valsartan 320 mg was 15.85/11.97mm Hg; these are statistically significantly greater reduction compared with Losartan 100 mg, which was 12.01mm Hg and 9.37mm Hg for SBP and DBP respectively. This paper shows that Valsartan at doses of 160 mg or 320 mg is more effective at lowering blood pressure than Losartan 100 mg. For other ARBs at comparable doses, valsartan achieves comparable antihypertensive efficacy.

Paolo verdecchia et al.,[44]**(2009)**conducted a study named - "Comparative assessment of angiotensin receptor blockers in different clinical settings". The primary outcome was the time to onset of diabetic nephropathy, defined by persistent albuminuria. The primary endpoint was achieved by 14.9% of patients with placebo, 9.7% of patients with Irbesartan 150 mg ($P = 0.08$) and 5.2% of patients with Irbesartan 300 mg ($P = 0.001$). These effects were independent of BP changes. The overall message of the trials examined in this review is that intervention with ARBs at different steps of the cardiovascular disease continuum is effective to slow down or block the disease progression, with consequent measurable benefits. The study results show that, Telmisartan reduced cardiovascular events in a broad population of patients with high cardiovascular risk, with a protective effect similar to the ACE-inhibitor comparator Ramipril. Losartan was superior to the beta-blocker atenolol in reducing the risk of stroke in patients with hypertension and LV hypertrophy. In patients with type 2 diabetes and nephropathy, Losartan in addition to conventional therapy reduced protenuria and the

progression to end stage renal disease. In patients with chronic heart failure, Losartan proved to be an alternative therapeutic option in patients intolerant to ACE-inhibitors.

Shiho nakayama et al.,[45]**(2008)**studied the effects of Olmesartan and Telmisartan on Blood Pressure and metabolic Parameters in Early-Stage Type-2 Diabetics with Hypertension, in this open-label prospective crossover study, theycompared the effects of Olmesartan (20 mg/day) and Telmisartan (40 mg/day). They analyzed the blood pressure lowering effects of each drug by 24-h ambulatory blood pressure monitoring at 0, 8, and 16 weeks, and metabolic parameters and inflammation markers. Olmesartan lowered mean systolic and diastolic blood pressure more significantly than Telmisartan. While there were no differences between the groups in metabolic parameters.

Derosa et al.,[46]**(2007)**studied the metabolic effects of Telmisartan and Irbesartan in type 2 diabetic patients with metabolic syndrome treated with Rosiglitazone. Evaluation were done on mass index, glycosylated haemoglobin, fasting plasma glucose, fasting plasma insulin, homeostasis model assessment-index, total cholesterol , low density lipoprotein , high density lipoprotein-cholesterol, triglycerides, systolic blood pressure, diastolic blood pressure, adiponectin and resistin during 12 months of this treatment.In addition to a comparable antihypertensive effect for Telmisartan and Irbesartan after 6 and 12 months, both treatments were associated with a significant reduction in TC and LDL plasma levels compared with baseline. After 6 months of treatment, only the telmisartan group experienced a significant improvement in (HbA(1c)), FPG, Homa-IR, adiponectin and resistin compared with the baseline values, whereas both drug regimens were associated with a significant improvement in these parameters after 12 months. However, the improvements observed in the Telmisartan group were significantly larger than that noted in the Irbesartan group. FPI significantly decreased only after 12 months of treatment in both groups, but again, the reduction was significantly larger in the Telmisartan-treated subjects. Telmisartan seemed to improve glycaemic and lipid control and metabolic parameters of the metabolic syndrome better than irbesartan.

Nagel et al.,[47] **(2006)** compared Telmisartan 40 mg versus placebo in 20 individuals with insulin resistance (homeostatic model assessment [HOMA] index >2.3) and abdominal obesity (body mass index [BMI] >25 kg/m^2 and waist circumference >95 cm in males or

80 cm in females) in a randomized, crossover trial lasting 12 weeks. Compared to placebo, Telmisartan promoted a significant reduction in the glucose area under the curve (AUC) during an oral glucose tolerance test (11%;p = .04). Non significant changes in the HOMA index (11% reduction;p = .06) and adiponectin (6%;p = increas.09) were also present during telmisartan treatment.

R Asmar et al.,[48] **(2005) -**conducted a study on effectiveness of angiotensin receptor blockers in blood pressure control. Variation in blood pressure with individual ARBs are taken into comparison in the study. The study drugs included were Losartan, Irbesartan, Candesartan, Telmisartan, and Olmesartan. Several newer ARBshave been reported to provide equivalent antihypertensive efficacy to Amlodipine and greater efficacy than Losartan, Valsartan or both. Secondly, increases in dose may improve the antihypertensive efficacy of agents such as Valsartan, although clinical studies are necessary to provide characterization of new, higher-dose monotherapy. Thirdly, fixed dose combinations with hydrochlorothiazide (HCTZ) increase the antihypertensive effect of all ARBs.

Vitale et al., [49]**(2005)**conducted a study on metabolic effect of Telmisartan and Losartan in hypertensive patients with metabolic syndrome. At baseline and end of treatment fasting and post pradinal plasma glucose, lipid profile, insulin sensitivity, and systolic and diastolic pressures were determined.After 3 months' treatment, Telmisartan reduced 24-hour mean SBP and DBP significantly more than Losartan. There was no significant correlation between the decrease in blood pressure and the change in FPG ($p = 0.020$) or FPI ($p = 0.012$).Both Telmisartan and Losartan were well tolerated.On comparison it is founded that the Telmisartan but not Losartan, significantly ($p<0.05$) reduce free plasma glucose. The results of this study explains as well as providing superior blood pressure control, Telmisartan unlike, Losartan, displayed insulin sensitizing activity.

DerosaG et al.,[50]**(2004)** has studied the effects of Telmisartan compared with Eprosartan on blood pressure control, glucose metabolism and lipid profile in hypertensive, type 2 diabetic patients. Evaluated the antihypertensive activity, glucose homeostasis and plasma lipid profile. Compared with baseline, a significant reduction ($p<0.01$) in seated trough systolic blood pressure (SBP) was detected after 12-month treatment with either

Telmisartan or Eprosartan. The antihypertensive effect of Telmisartan was significantly superior ($p<0.05$). No change in body mass index or glucose metabolism was observed with either active treatment, or with placebo. Telmisartan, but not Eprosartan, significantly improved plasma total cholesterol ($p<0.01$), low-density lipoprotein cholesterol ($p<0.01$) and triglycerides ($p<0.05$) compared with Eprosartan. The 12-month Telmisartan treatment produced a significantly greater reduction in DBP than Eprosartan and significantly improved plasma lipids.

Michael schupp et al.,[51]**(2004) -** has studied,angiotensin Type 1 Receptor Blockers Induce Peroxisome Proliferator–Activated Receptor-γ Activity.The findings of the study sounds that, ARB Losartan enhanced aP2 expression only at high concentrations, whereas Eprosartan had no significant effects, Irbesartan and Telmisartan (10 μmol/L) markedly induced transcriptional activity of PPARγ. Irbesartan and Telmisartan also induced PPARγ activity in an AT_1R-deficient cell model, demonstrating that these ARBs stimulate PPARγ activity independent of their AT_1R blocking actions. The study demonstrates that a specific subset of ARBs induces PPARγ activity, thereby promoting PPARγ-dependent differentiation in adipocytes. The activation of PPARγ demonstrates new pleiotropic actions of certain ARBs, providing a potential mechanism for their antidiabetic effects.

UjalaVerma et al.,[52] **(2004)**did a study on Antihypertensive Efficacy of Carvedilol and Amlodipine in patients of mild to moderate hypertension . Blood pressure was recorded in the sitting and standing position during followup visits at 2,4,8 and 12 weeks. Dosage adjustments if neededwere made at 4 and 8 weeks of study. Both Carvedilol and Amlodipine produced a statisticallysignificant ($P<0.001$) and dose related fall in SBP and DBP. On comparative analysis of the effect of Carvedilol andAmlodipine on BP, Amlodipine produced a greater fall in sitting and standing SBP at all study intervals ascompared to carvedilol, with statistically significant fall at 8 and 12 weeks ($P<0.01$). The findings of the study indicate that Carvedilol has become an alternative treatment for mild to moderate hypertension.

Daholf B et al.,[53]**(2002)** conducted a study on cardiovascular morbidity and mortality in the Losartan.LVH ascertained by electrocardiography (ECG).They observed out that blood pressure fell by 30.2/16.6 (SD 18.5/10.1) and 29.1/16.8 mm Hg (19.2/10.1) in the

Losartan and Atenolol groups, respectively. New-onset diabetes was less frequent with Losartan. Interpretation Losartan prevents more cardiovascular morbidity and death than atenolol for a similar reduction in blood pressure and is better tolerated. Losartan seems to confer benefits beyond reduction in blood pressure.

Lerch M et al.,[54]**(1998)** studied the effects of angiotensin II-receptor blockade with losartan on insulin sensitivity, lipid profile, and endothelin in normotensive offspring of hypertensive parents. Insulin sensitivity index (SI), determined by the Minimal Model Method of Bergman, fasting plasma insulin and glucose concentrations, serum total and HDL cholesterol, serum triglycerides, and plasma ET-1 levels were assessed. Compared with placebo, Losartan administration did not significantly modify SI, fasting plasma insulin and glucose. Plasma ET-1 levels also did not differ significantly between the placebo and Losartan serum total cholesterol and triglycerides decreased significantly with losartan treatment. Body weight, BMI, heart rate (HR), blood pressure (BP), and 24-h urinary sodium, potassium, and creatinine values were stable throughout the study. These findings demonstrate that Losartan 50 mg daily, does not alter insulin sensitivity and ET-1 in normotensive offspring of essential hypertensive parents.the study shows that the Losartan significantly reduced serum total cholesterol and total triglyceride levels.

Pedro Luis de Pablosvelasco et al., [55]**(1998)** has studied the effects of Losartan and Diltiazem on Blood Pressure, Insulin Sensitivity, Lipid Profile and Microalbuminuria in Hypertensive Type 2 Diabetic Patients. At baseline and after 3 months, plasma glucose, glycated haemoglobin, uric acid, lipid profile, albumin excretion rate and creatinine clearance, Insulin sensitivity was estimated by an insulin suppression test, and ambulatory blood pressure was monitored for 24 hours. Differences between the two treatments were not significant. Insulin sensitivity and lipid profile were not modified by any of the treatments and no adverse effects were reported. Both drugs were well tolerated and effectively reduced blood pressure and albuminuria, but did not modify insulin sensitivity or lipid profile.

3. DRUG PROFILE

3.1 LOSARTAN POTASSIUM

NAME: Losartan potassium

BRAND NAMES: cozaar

DESCRIPTION[56]:

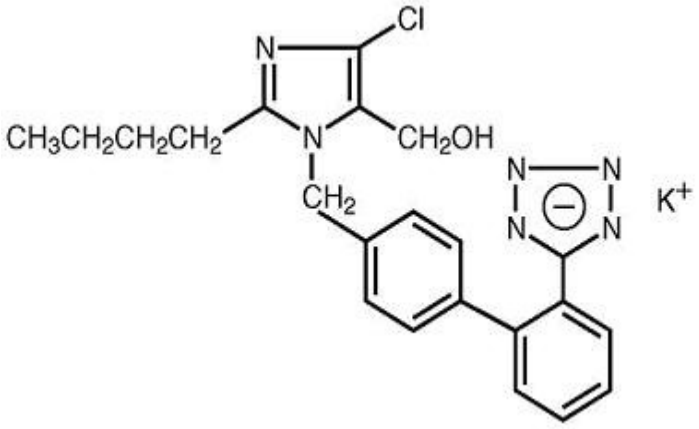
Losartan potassium is an Antihypertensive drug belongs to the class ARB (Angiotensin receptor II antagonist). Losartan potassium is a non peptide molecule shows high affinity to the Angiotensin receptor II, and the drug inhibits the action of the angiotensin receptor II on vascular smooth muscles. As the result of inhibitory action a reduction in blood pressure is obtained.

CHEMICAL IUPAC NAME:

Mono potassium salt of 4-butyl-4chloro-1-[[2'-(1*H*-tetrazol-5-yl)[1,1'-biphenyl]-4-yl]methyl]-1*H*-imidazole -5-methanol.

CHEMICAL FORMULA: $C_{22}H_{22}ClKN_6O$

CHEMICAL STRUCTURE:



MOLECULAR WEIGHT: 461.0 Daltons

STATE: White to off-white crystalline powder

MELTING POINT: 461.01^{0} **C**

THERAPEUTIC CATEGORY:

Antihypertensive (Angiotensin receptor II antagonist)

PHARMACOLOGY:

Angiotensin II [formed from angiotensin I in a reaction catalyzed by angiotensin converting enzyme (ACE, kininase II)], is a potent vasoconstrictor, the primary vasoactive hormone of the renin-angiotensin system and an important component in the pathophysiology of hypertension. It also stimulates aldosterone secretion by the adrenal cortex. Losartan and its principal active metabolite block the vasoconstrictor and aldosterone-secreting effects of angiotensin II by selectively blocking the binding of angiotensin II to the AT1 receptor.

MECHANISM OF ACTION:

Angiotensin II [formed from angiotensin I in a reaction catalyzed by angiotensin converting enzyme (ACE, kininase II)], is a potent vasoconstrictor, the primary vasoactive hormone of the renin-angiotensin system and an important component in the pathophysiology of hypertension. It also stimulates aldosterone secretion by the adrenal cortex. Losartan and its principal active metabolite block the vasoconstrictor and aldosterone-secreting effects of angiotensin II by selectively blocking the binding of angiotensin II to the AT1 receptor found in many tissues, (e.g., vascular smooth muscle, adrenal gland). There is also an AT2 receptor found in many tissues but it is not known to be associated with cardiovascular homeostasis. Both Losartan and its principal active metabolite do not exhibit any partial agonist activity at the AT1 receptor and have much greater affinity (about 1000-fold) for the AT1 receptor than for the AT2 receptor. Neither Losartan nor its active metabolite inhibits ACE (kininase II, the enzyme that converts angiotensin I to angiotensin II and degrades bradykinin); nor do they bind to or block

other hormone receptors or ion channels known to be important in cardiovascular regulation.

DOSAGE FORM:

Form: Tablet

Route: Oral

PHARMACOKINETICS:

ABSORPTION:

The drug is well absorbed. Administration along with food shows a slight decrease in absorption and it has only minor effect on losartan or active metabolite AUC. Systemic bioavailability of losartan is about 33%**.**

DISTRIBUTION:

Volume of distribution is 34 L(losartan) and 12 L (metabolite)

PROTEIN BINDING:

Losartan and active metabolite are highly binds to plasma protein, primarily albumin. Neither Losartan nor metabolite accumulates in plasma upon repeated daily dosing.

METABOLISM:

Losartan undergoes substantial first – pass metabolism by CYP-450 2CP and 3A4 enzymes. Fourteen percent of an oral dose is converted to an active carboxylic acid metabolite that is responsible for most of the angiotensin II receptor antagonist activity.

ELIMINATION:

The $t_{1/2}$ of Losartan 2 hr and that of metabolite is 6 to 9 hr. Renal clearance of Losartan is 75 ml/min and that of metabolite is 25 ml/ min. Biliary excretion contributes to the elimination of Losartan and metabolite. About 4% is excreted unchanged in the urine and 6% excreted as active metabolite in metabolite in urine.

INDICATION:

The drug is used alone or in combination with other classes of antihypertensive drugs. It is used in treatment of hypertension, diabetic nephropathy in hypertensive patients with type 2 diabetes mellitus; reduce risk of stroke in patients with hypertension and left ventricular hypertrophy.

CONTRAINDICATION: Losartan potassium tablets are contraindicated in patients who are hypersensitive to any components of this product.

INTRACTION:

Drug – Drug:

Fluconazole: Fluconazole elevates plasma level of Losartan, which will leads to increase the antihypertensive and adverse effects.

Indomethacin: The antihypertensive effect of Losartan may be blunted.

Rifamycins: Rifamycins like Rifampin reduces plasma levels of Losartan thus antihypertensive effects of Losartan got reduced.

Drug and lifestyle:

Alcohol use: It enhances the hypotensive effects of the drug. Avoid use of alcohol and drug together.

ADVERSE REACTION:

The adverse drug reactions Losartan potassium includes, hypotension, orthostatic hypotension, CNS side effects, GI side effects, UTI Infection, hypersensitivity reaction.

SPECIAL POPULATION:

Close monitoring must be practiced in patients with hepatic impairment, renal impairment .During the pregnancy Losartan is suggested to be stopped.

Pregnancy:

When used in pregnancy during the second and third trimester, drugs that act directly on renin angiotensin system can cause injury and even death to the developing fetus. When pregnancy is detected, discontinue therapy as soon as possible.

Children:

Safety and efficacy not established in hypertensive patients younger than 6 yr of age or in children's.

Renal function:

Use caution in treating patients whose renal function may depend on the rennin-angiotensin – aldosterone system.

Hepatic function:

A lower starting dose is recommended for patients with hepatic impairment.

3.2Telmisartan

NAME: Telmisartan

BRAND NAMES: Micardis, Tazloc, Telday

DESCRIPTION[57]:

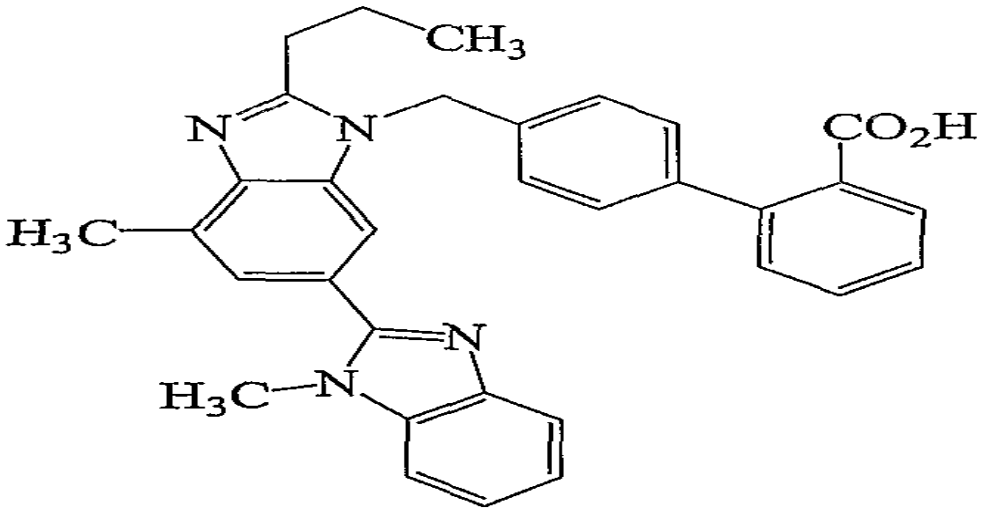
Telmisartan is an antihypertensive drug belongs to the class ARB (angiotensin receptor II antagonist). Telmisartan shows high affinity to the angiotensin receptor II, and the drug inhibit the action of the angiotensin II on vascular smooth muscles. As the result of inhibitory action a reduction in blood pressure is obtained .As per the suggestions of recent studies, Telmisartan also having beneficial metabolic effects because of PPAR-gamma agonistic action.

CHEMICAL IUPAC NAME:

4′ - [1(1, 4′ - Dimethyl - 2′ - propyl [2, 6′ - bi - 1*H* - benzimidazol] - 1′ - yl) methyl] - [1,1′ - biphenyl] - 2 - carboxylic acid

CHEMICAL FORMULA: $C_{33}H_{30}N_4O_2$

CHEMICAL STRUCTURE:



MOLECULAR WEIGHT: 514.6169 Daltons

STATE: White solid

MELTING POINT: 261-263^{0}C

THERAPEUTIC CATEGORY:

Antihypertensive (Angiotensin receptor II antagonist)

PHARMACOLOGY:

Telmisartan is a non peptide molecule, which orally active. It selectively binds and inhibits the angiotensin II AT1receptor subtype. Telmisartan shows much greater affinity (> 3,000 fold) for the AT_1 receptor than for the AT_2 receptor. Angiotensin II is the principle factor of rennin angiotensin system. Telmisartan inhibitory action brings out the desirable effects like relaxation of smooth muscle thereby vasodilation,increased renal excretion of salt and water and reduced plasma volume. Telmisartan also have beneficial metabolic effects because of PPAR-gamma agonistic action. PPAR-gamma is a nuclear

receptor related to the insulin sensitizing effect, PPAR-gamma agonistic action improve insulin sensitivity and lipid profile in patients with metabolic syndrome.

MECHANISM OF ACTION:

Telmisartan binds with the angiotensin II ATI receptor in adrenal gland and vascular smooth muscle, mode of binding is selective and reversible. The systemic vascular resistance is produced by the blockade of the angiotensin II. The angiotensin II is a vasoconstrictor which produces elevation in blood pressure. Telmisartan is a selective antagonist of angiotensin II receptor because it doesn't inhibit the angiotensin converting enzyme, other hormone receptors, or ion channels. Studies also suggest that telmisartan having partial agonist activity towards PPAR gamma. PPAR gamma is an established target for antidiabetic drugs. This sounds that telmisartan can improves carbohydrate, lipid metabolism and controls insulin resistance.

DOSAGE FORM:

FORM: Tablet

ROUTE: Oral

PHARMACOKINETICS:

ABSORPTION:

The bioavailability of drug depends on dosage. Administration of telmisartan with food shows a 6% decrease in bioavailability. Peak plasma concentration generally reached at 0.5 – 1 hour following oral administration.

DISTRIBUTION:

Volume of distribution is 500 L

PROTEIN BINDING:

Protein binding is > 99.5%, principally albumin and α_1- acid glycoprotein.

METABOLISM:

Metabolized in liver, conjugated into inactive acylglucuronide it has been identified in human plasma and urine.

ELIMINATION:

When administered orally duration of action is 24 hours. The drug is excreted unchanged in the feces via biliary excretion mainly; small amount of drug is eliminated through urine.

INDICATION:

The drug is used alone or in combination with other classes of antihypertensive drugs. It is used in treatment of hypertension, diabetic nephropathy in hypertensive patients with type 2 diabetes mellitus, and in congestive heart failure population who can't tolerate ACE inhibitors.

CONTRAINDICATION:

Drug is contraindicated in pregnancy and in patients who hypersensitive to drugs and its components. Cautious usage is suggested in patients with biliary obstruction disorders, renal or hepatic insufficiency and in those with an activated rennin – angiotensin system.

INTRACTION:

Drug – Drug:

Digoxin:

Telmisartan increases digoxin plasma levels. Digoxin levels must be monitored closely.

Warfarin:

Telmisartan decreases the plasma warfarin level, patient must be monitored closely.

Drug and lifestyle:

Alcohol use: It enhances the hypotensive effects of the drug. Avoid use of alcohol and drug together.

ADVERSE REACTION:

Upper respiratory tract infection, sinusitis, pharyngitis, back pain, diarrhoea.

SPECIAL POPULATION:

Close monitoring must be practiced in patients with hepatic impairment, renal impairment. Drug must not be used in pregnancy and lactation.

Pregnant patients:

Use of drug is contraindicated during pregnancy because of potential risk of fetal and neonatal morbidity and death.

Breast feeding patients:

Assess risks and benefits before continuing drug in breast feeding women.Because it is not known telmisartan is secreted in human milk.

Pediatric patients:

Safety and efficacy in children have not been established.

Geriatric patients:

No significant difference has been reported compared to younger patients.

4. AIM AND OBJECTIVES

SCOPE OF THE STUDY

Hypertension is currently affects, approximately one billion adults globally. It is a major risk factor for cardiovascular diseases (CV) and stroke. The high prevalence of hypertension has contributed to the present pandemic of CV disease, which now accounts for 30% of all deaths worldwide.

As the population ages and the prevalence of contributing factors such as obesity, sedentary lifestyle and smoking rise, this figure is projected to increase by 60% to 1.56 billion by the year 2025.

The risk of hypertension increases with age and is associated with gender and ethnicity. The morbidity and mortality associated with uncontrolled hypertension result in a substantial economic burden as a result of drug costs, hospitalizations, surgery and other healthcare resources. This cost is compounded by the humanistic burden and effect on quality of life associated with lifestyle modifying adverse events.

Angiotensin receptor blockers (ARBs) have become established as a major class of antihypertensive on the basis of their powerful effects on blood pressure (BP), excellent tolerability and pleiotropic end-organ-protective effects. However, individual ARBs vary in antihypertensive efficacy, which may be important to clinical outcome. It is well established that achieving ambitious BP targets improves long-term clinical outcomes in the management of hypertension

The present study was to compare the efficacy of Losartan potassium and Telmisartan, both are belongs to the above mentioned class of angiotensin receptor blockers (ARBs). Of the above Losartan potassium is the prototype and Telmisartan is a newly introduced ARB.

AIM:

- The aim of the present study was to compare the efficacy of Losartan potassium 50 mg Vs Telmisartan 40 mg in patients with hypertension.

OBJECTIVE:

PRIMARY

- To compare the efficacy of Losartan potassium 50 mg Vs Telmisartan 40 mg

- To assess the mean change in Systolic Blood Pressure (SBP) and Diastolic Blood Pressure (DBP) with Losartan potassium and Telmisartan in a treatment period of three months.

SECONDARY

- To assess the mean change in Fasting Blood Sugar (FBS) and Post Pradinal Blood Sugar (PPBS).

5. PLAN OF WORK

The present dissertation work was planned to conduct a comparative study on efficacy of losartan versus telmisartan in hypertensive patients. The study conducted at Manohar Hospital, Calicut, Kerala.

The Plan of Work Includes:

i. Submission of the protocol for getting the approval from ethical committee.
ii. To get the consent letter from patient.
iii. Select hypertensive patients for the study.
iv. To design a data collection form.
v. Select monitoring parameters.
vi. Patients divided into two groups A & B.
vii. Each group containing 30 patients.
viii. Prescribing drug for group A: Losartan potassium 50 mg.
ix. Prescribing drug for group B: Telmisartan 40 mg.
x. Checking of SBP&DBP, FBS&PPBS on specified visit.
xi. Carrying out statistical analysis and recorded.

6. METHODOLOGY

STUDY SITE : Manohar hospital, (170 bedded), Calicut- Kerala.

STUDY DESIGN : Prospective observational study.

DURATION OF STUDY : 3 months.

DOSAGE : Losartan potassium 50 mg.

: Telmisartan 40 mg.

- A total of 60 patients were enrolled in the treatment program.
- A prospective and observational study was carried out to compare efficacy of losartan potassium versus telmisartan 40 mg in patients with hypertension.
- The selected patients were divided into two groups. Group A, group B.
- Group A (30 patients) were to be treated with Losartan potassium 50 mg.
- Group B (30 patients) were to be treated with Telmisartan 40 mg.

STUDY CRITERIA

Inclusion criteria

- Patients aged between 30 -59 years.
- Patient's who having sustained diastolic blood pressure >90 mm Hg accompanied by elevated systolic blood pressure > 140 mm Hg.
- Patient's who agreed with prescribed consent form.

Exclusion criteria

- Patient with secondary hyper tension.
- Patient who having other medication with known effects on blood pressure.
- Patient who refuse to participate in study or withdrawing prescribed consent.
- Pregnant and lactating women.

PARAMETERS

Primary parameters

- Systolic blood pressure.
- Diastolic blood pressure.
- FBS.
- PPBS.

Secondary parameters

- Height.
- Weight.
- BMI.

STASTSTICAL ANALYSIS:

The information collected regarding all the selected cases were recorded in a Master Chart. Data analysis was done with the help of computer (Microsoft exel 2007)

Using this software range, frequencies, percentages, means, standard deviations, and 'p' values were calculated. The Students T test was used to test the significant difference of quantitative variables, chi squre test was used to test the significant difference of qualitative variables. A 'p' value less than 0.05 is taken to denote significant relationship.

7. Observations and results

The work entitled comparative study of efficacy of Losartan potassium 50 mg versus Telmisartan 40 mg in patients with hypertension was carried out in Department of General Medicine at Manohar hospital, Calicut, kerala. A total number of 60 patients were enrolled in this study. These patients were divided into two groups (A&B). Group A (30 patients) were treated with Losartan potassium 50 mg and Group B(30 patients)Telmisartan 40 mg.

All primary and secondary parameters were recorded in the initial visit, systolic and diastolic blood pressure recorded at each follow up of 15 days interval and the FBS and PPBS and weight were recorded at the end of the study. All the recorded parameters were compared to assess the efficacy.

Group A: Losartan potassium 50 mg

Group B: Telmisartan 40 mg

A. CHARECTERISTICS OF CASES STUDIED

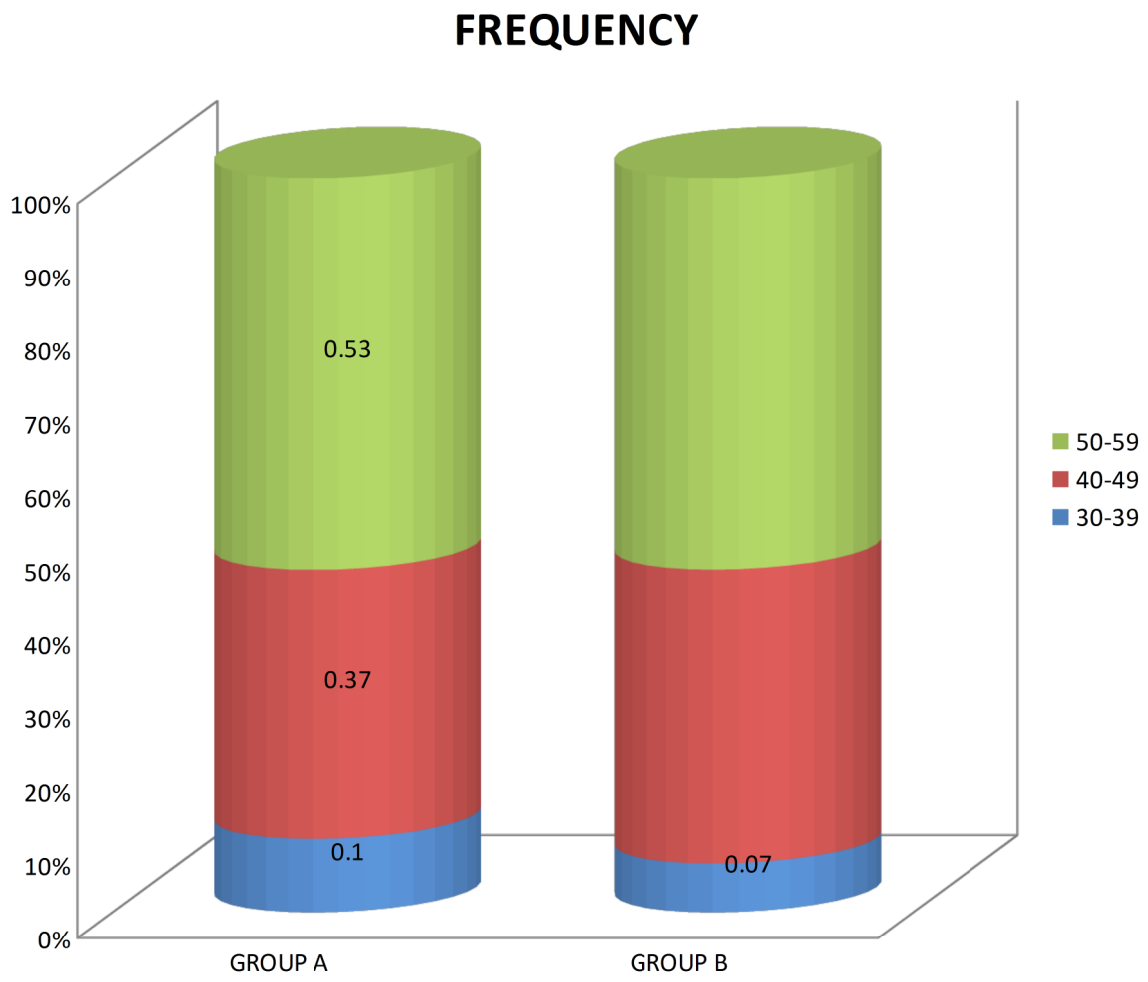
Table 3: Age distribution

Age group (in years)	Group A		Group B	
	No	%	No	%
30 – 39 years	3	10	2	6.67
40 – 49 years	11	36.66	12	40
50 – 60 years	16	53.34	16	53.33
Total	30	100	30	100
Range	38 - 59		30 – 60	
Mean	50.17		50.47	
SD	6.62		6.25	

Out of 60 patients, 30 patients were of group A, out of these 3 patients (10%) between the age group of 30-39 years,11 patients (36.66%) between the age group of 40-49 years, 16 patients (53.34%) between the age group of 50-60 years.

Out of 60 patients, 30 patients were of group B, out of these 2 patients (6.67%) between the age group of 30-39 years, 12 patients (40%) between the age group of 40-49 years, 16 patients (53.33%) between the age group of 50-60 years.

Age distribution



Fig,no 1

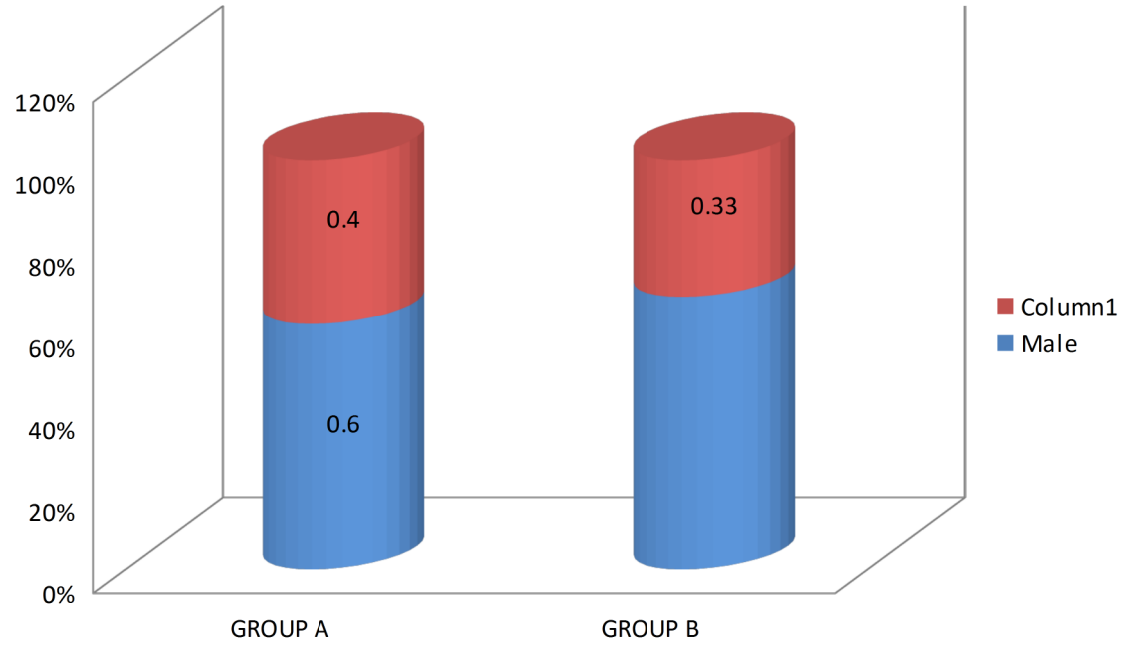
The mean age of group A was 50.17± 6.62 years and group B was 50.47 ± 6.25 years.

Table 4: Sex distribution

Sex	Group A		Group B	
	No	**%**	**No**	**%**
Male	18	60	20	66.67
Female	12	40	10	33.34
Total	30	100	30	100

A total of 60 patients were screened and randomized into two treatment group. Out of which 30 patients were of GROUP A, 18 patients (60%) were males, 12 patients (40%) were females. In case of GROUP B, 20, patients (66.67%) were males, 10 patients (33.34%) were females.

Sex distribution



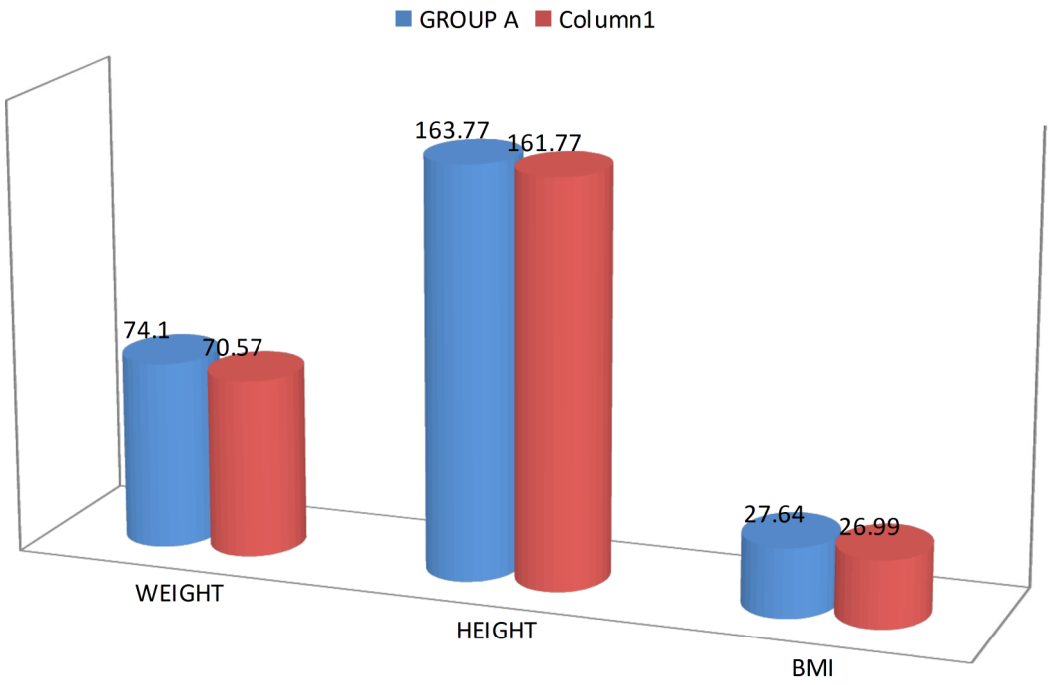
Fig,no 2

Table 5: Physiological parameters

Variable	Group A		Group B		'p' value
	Mean	**SD**	**Mean**	**SD**	
Weight (in kg)	74.1	5.97	70.57	5.84	
Height (in cm)	163.77	6.32	161.77	6.95	
BMI	27.64	1.73	26.99	1.92	0.1767

The average weights of patients were 74.1±5.97 in GROUP A and 70.57±5.84 in GROUP B. The average height of patients was 163.77 ±6.32 in GROUP A and 161.77±6.95 in GROUP B. The average BMI of patients were 27.64±1.73 in GROUP A and 26.99±1.92 in GROUP B.

Physiological parameters



±

Fig,no 3

Table 6: Change in BMI

BMI	GROUP A			GROUP B		
	First visit	Final value	Difference	First visit	Final value	Difference
MEAN	27.64	26.58	1.05	26.99	25.91	1.08
SD	± 1.73	± 1.75	± 0.39	± 1.92	± 1.71	± 0.71

The average BMI of patients after 3 month were 26.58±1.75 in GROUP A with difference of 1.05±0.39 from initial value 27.64 and 25.91±1.71 in GROUP B with difference of 1.08±0.71 from initial value 26.99.

Change in BMI

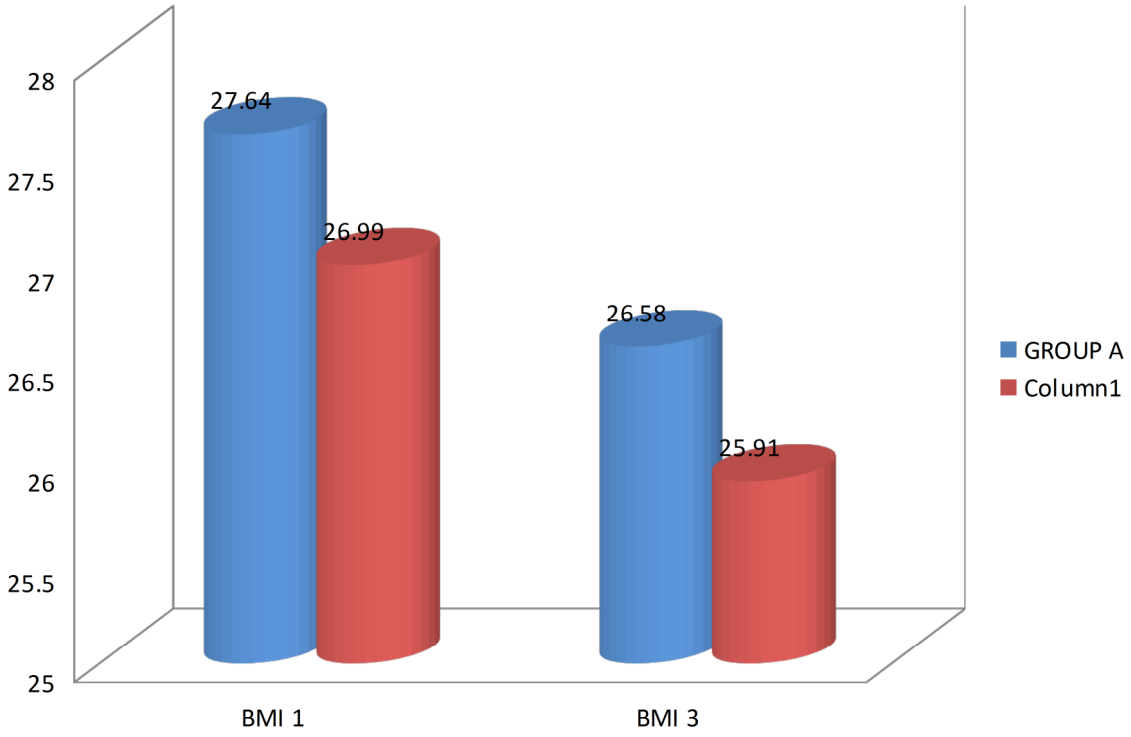


Fig.no 4

B. EFFICACY OF THE TWO REGIMENS

Table 7: Change in systolic blood pressure (SBP) – in mm Hg

SBP Values at	SBP Values				'p' Values
	Group A		Group B		
	Mean	SD	Mean	SD	
First visit	152.93	6.53	148.80	7.28	0.02
Second visit	147.06	6.30	140.94	7.12	P<0.001
Third visit	142.87	6.50	134.06	7.11	P<0.001
Fourth visit	137.48	6.77	127.80	6.99	P<0.001
Fifth visit	131.14	6.6	122.00	6.90	P<0.001
Sixth visit	125.00	6.96	115.53	6.40	P<0.001
Decrease (First visit – sixth visit)	27.94	3.09	33.27	3.42	P<0.001

The systolic blood pressure showed significant reduction in the both group. The reduction was greater in GROUP B who was treated with Telmisartan 40 mg, than in GROUP A who were treated with Losartan potassium 50 mg.

The mean systolic blood pressure reduction in GROUP B was (33.27±3.42) & GROUP A was (27.94± 3.09) at the end of 3 months, which shows that the regimen B have better impact on systolic blood pressure than GROUP A with statistically significant 'p' value less than 0.001

Change in systolic blood pressure (SBP)

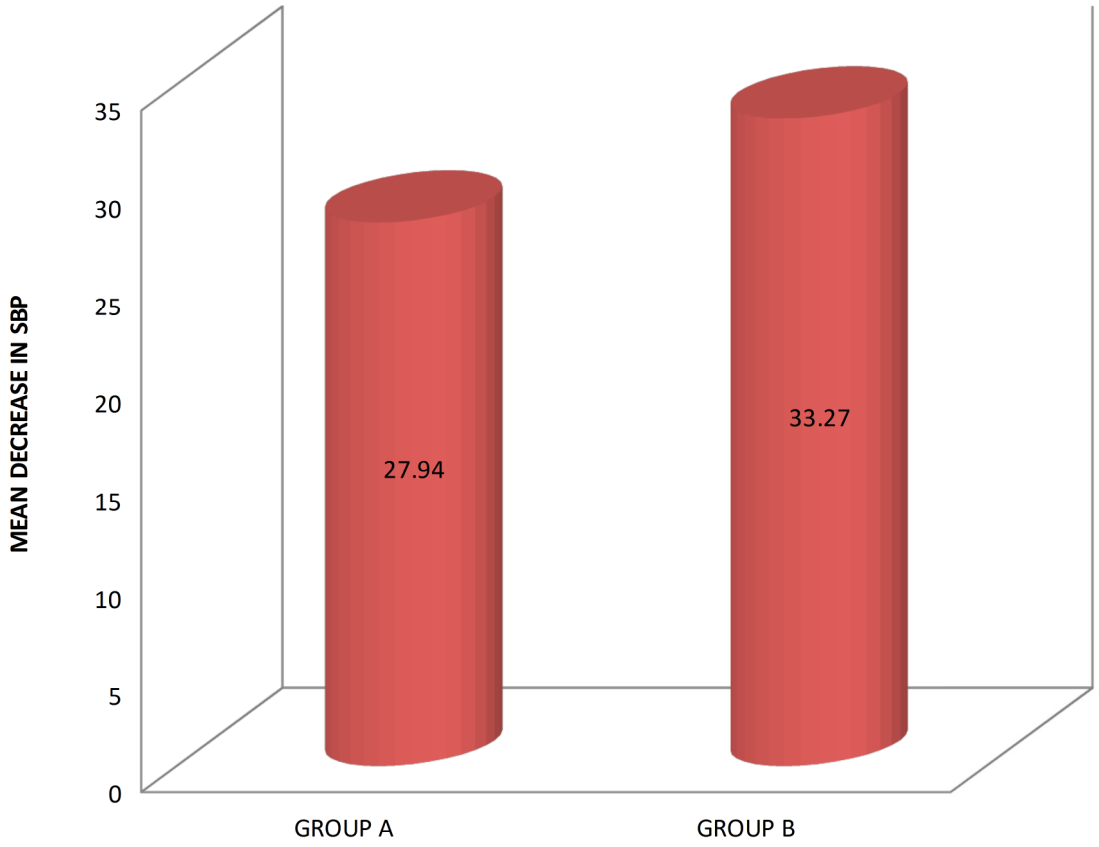


Fig.no 5

Change in systolic blood pressure in 2 week intervals.

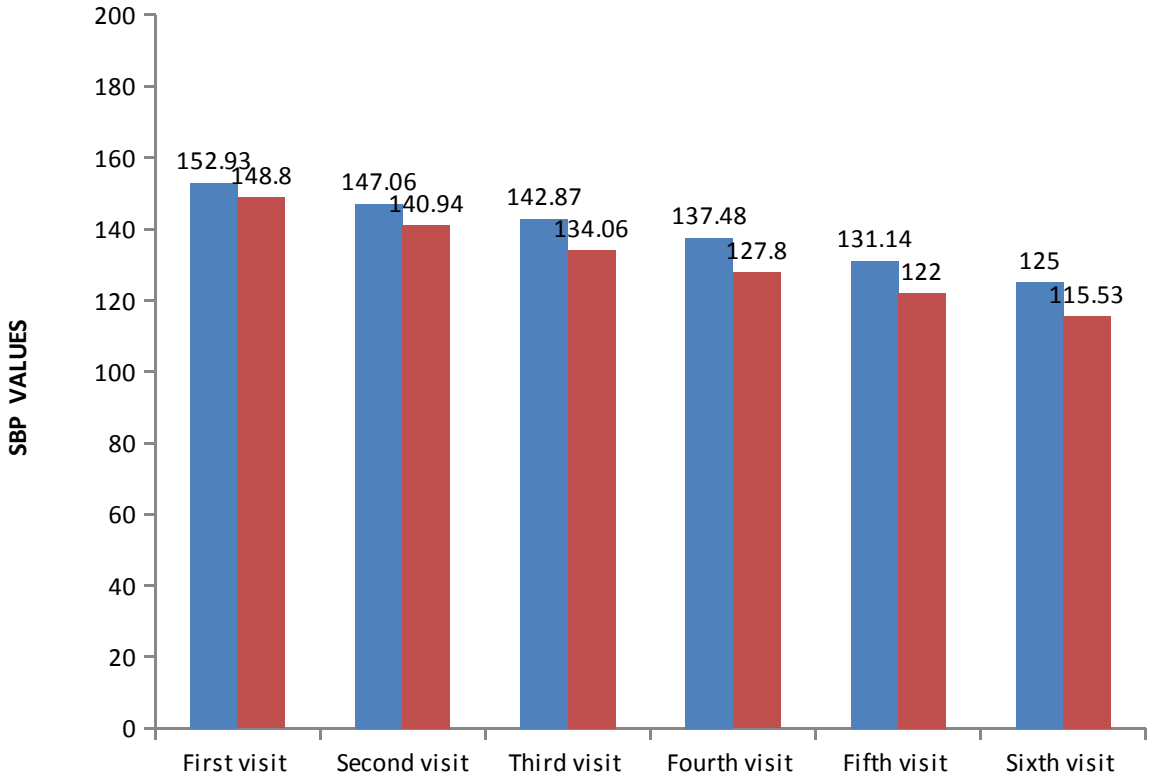


Fig.no.6

\The SBP values of GROUP A and GROUP B were initially 152.93±6.53 & 148.8±7.28 respectively and that was changed to 147.06±6.30& 140.94±7.12 on Second visit , then it changed to the levels of 142.87±6.50 &134.06±7.11, 137.48 ±6.77 & 127.8±6.99, 131.14±6.60 & 122±6.90, 125±6.96 & 115.53±6.40 in further third, fourth ,fifth ,sixth visits.

Table 8:

DBP Values at	DBP Values				'p' Values
	Group A		Group B		
	Mean	SD	Mean	SD	
First visit	93.73	3.39	93.27	2.75	0.561
Second visit	90.74	2.94	88.80	2.99	0.01
Third visit	87.33	2.53	85.14	3.18	0.004
Fourth visit	85.60	2.75	82.54	3.32	P<0.001
Fifth visit	84.20	2.59	81.20	3.22	P<0.001
Sixth visit	82.20	2.53	78.80	3.13	P<0.001
Decrease (First visit – sixth visit)	11.54	2.27	14.47	2.33	P<0.001

The diastolic blood pressure showed significant reduction in the both group. The reduction was greater in GROUP B who was treated with telmisartan 40 mg, than in GROUP A who are treated with losartan potassium 50 mg.

Diastolic blood pressure decreased significantly in GROUP B (14.47± 2.33) than in GROUP A (11.54 ± 2.27) at the end of 3 months, which showed that the regimen B had a significantly better impact on systolic blood pressure ($p < 0.05$) than GROUP A.

Change in diastolic blood pressure (DBP)

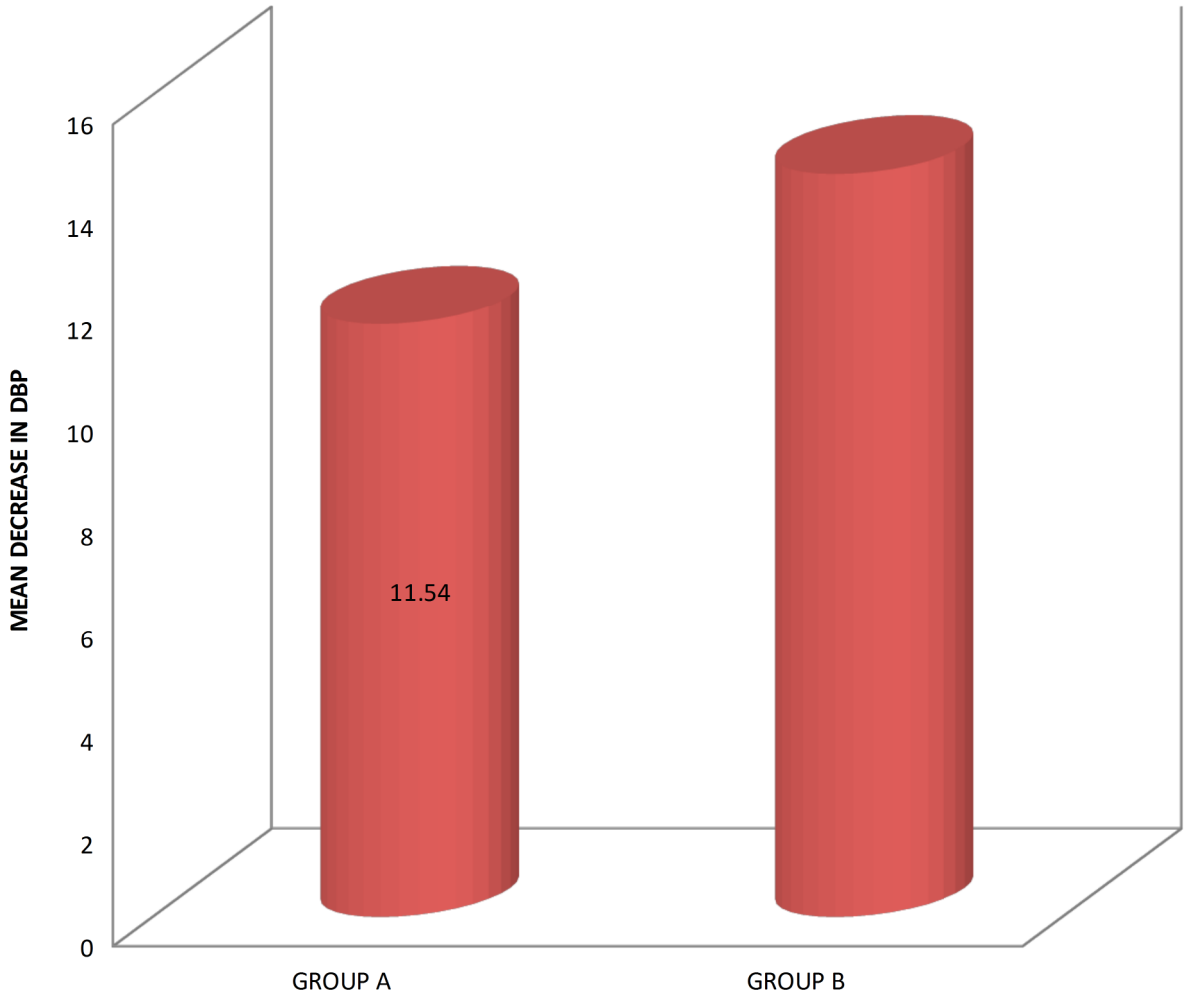


Fig.no. 7

Change in diastolic blood pressure in 2 week interval.

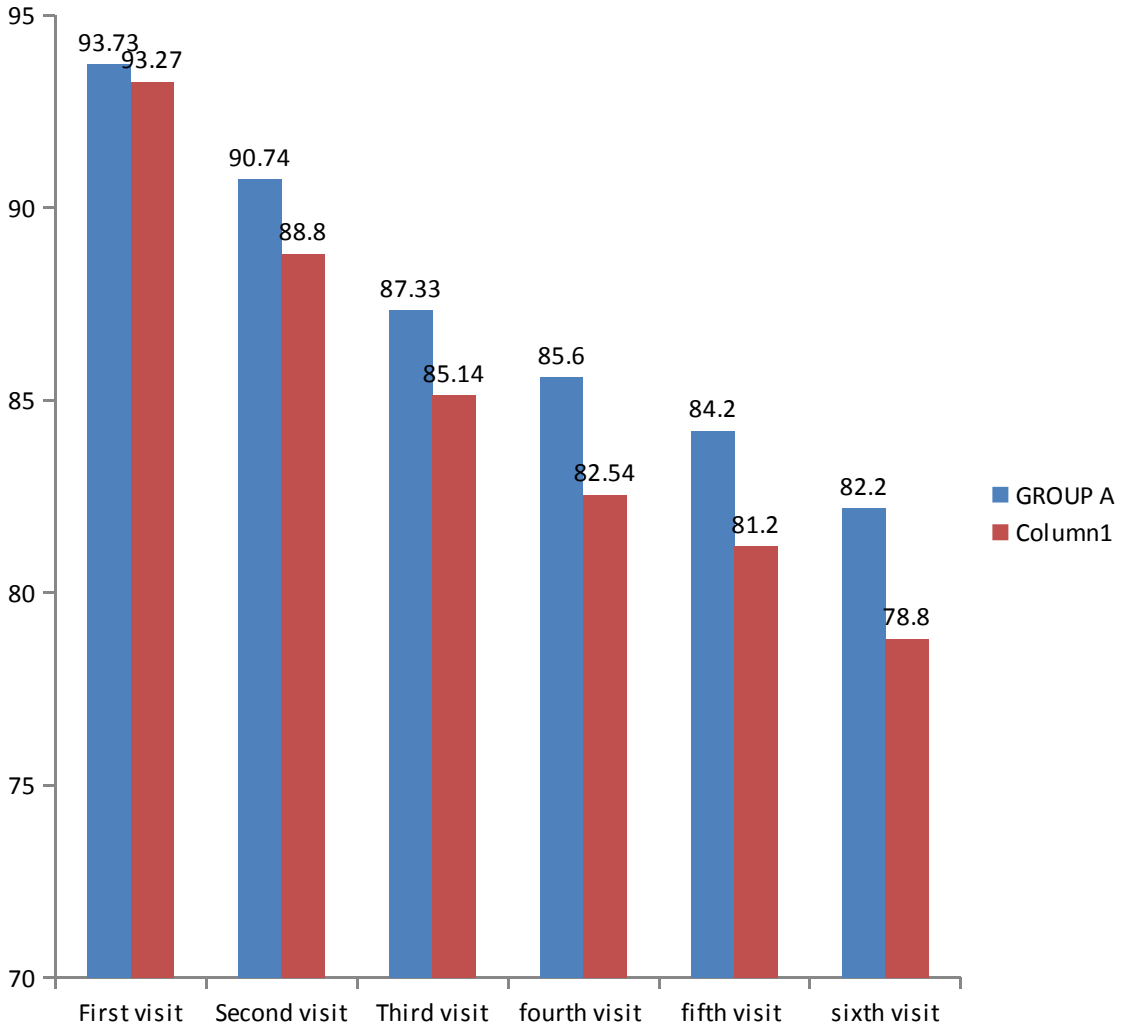


Fig.no. 8

Initial DBP values of GROUP A and GROUP B were 93.73±3.39&93.27±2.75respectively and that was changed to 90.74±2.94 & 88.80±2.99 on second visit , then it changed to the levels of 87.33±2.53 & 85.14±3.18, 85.60 ±2.75 & 82.54±3.32,84.20±2.59 & 81.27±3.32, 82.20±2.53 & 78.80±3.13 in further third, fourth, fifth and sixth visits.

FBS Values at	**FBS Values**		**'p'**
	Group A	**Group B**	

					Values
	Mean	**SD**	**Mean**	**SD**	
First visit	145.47	16.40	136	13.06	0.0163
Sixth visit	138.06	15.83	123.16	13.32	0.0002
Decrease (First visit – sixth visit)	7.40	1.35	12.83	4.86	0.0001

Table 9: Fasting blood sugar (FBS) Values

The fasting blood sugar values reduced significantly in both groups, the reduction of fasting blood sugar was greater in Group B 12.83±4.86 than in Group A 7.40±1.35.

The Group B shows better significant reduction in fasting blood sugar than Group A at the end of 3 month study with a p value of <0.05.

Change in Fasting blood sugar (FBS)

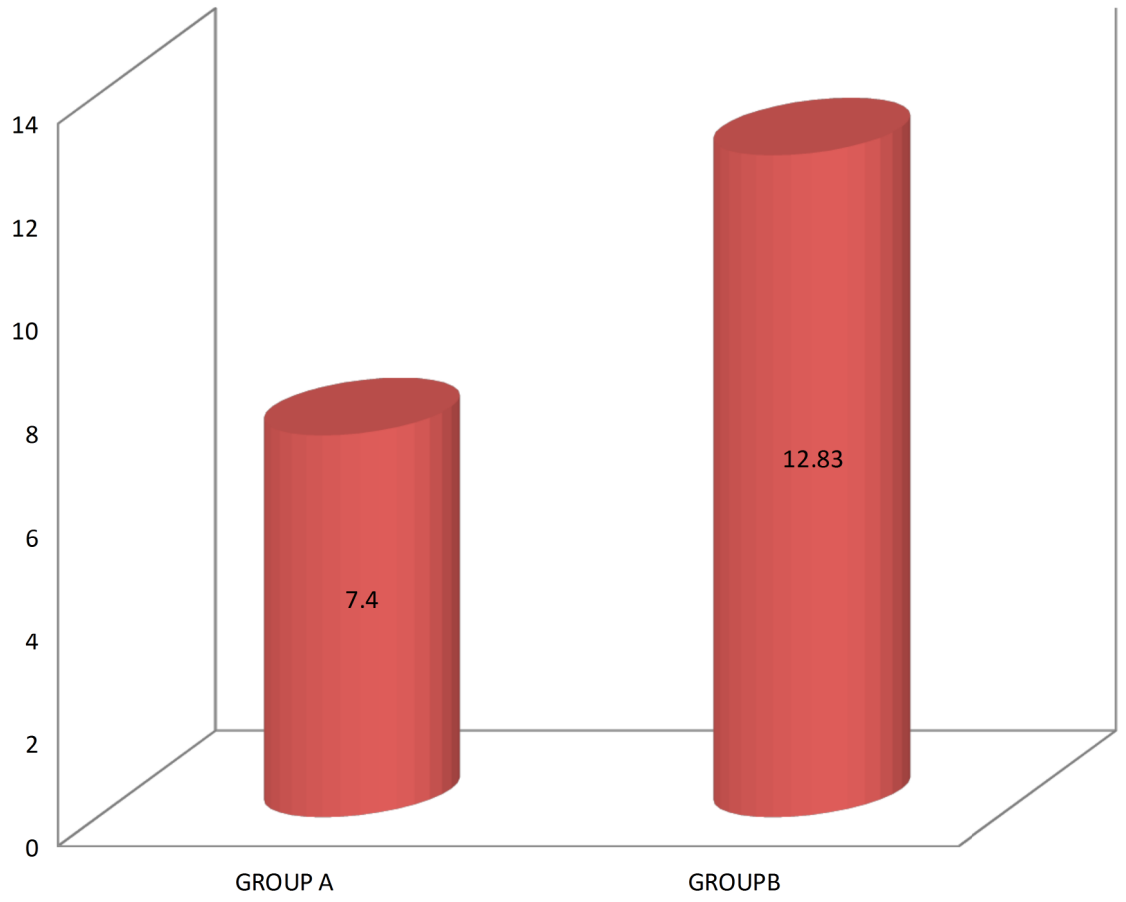


Fig.no 9

Table 10: Change in Post prandial blood sugar (PPBS)

PPBS Values at	PPBS Values				'p' Values
	Group A		Group B		
	Mean	SD	Mean	SD	

First visit	247	21.81	247.87	17.02	0.8643
Sixth visit	229.81	19.92	217.47	15.81	0.0098
Decrease (First visit – sixth visit)	17.14	3.69	30.40	8.92	0.0001

The PPBS values reduced significantly in both groups, the reduction of fasting blood sugar was greater in Group B 30.40±8.92 than in Group A 17.14±3.69.

The Group B shows better significant reduction in PPBS than Group A at the end of 3 month study with a p values<0.05.

Change in Post pradinal blood sugar (PPBS)

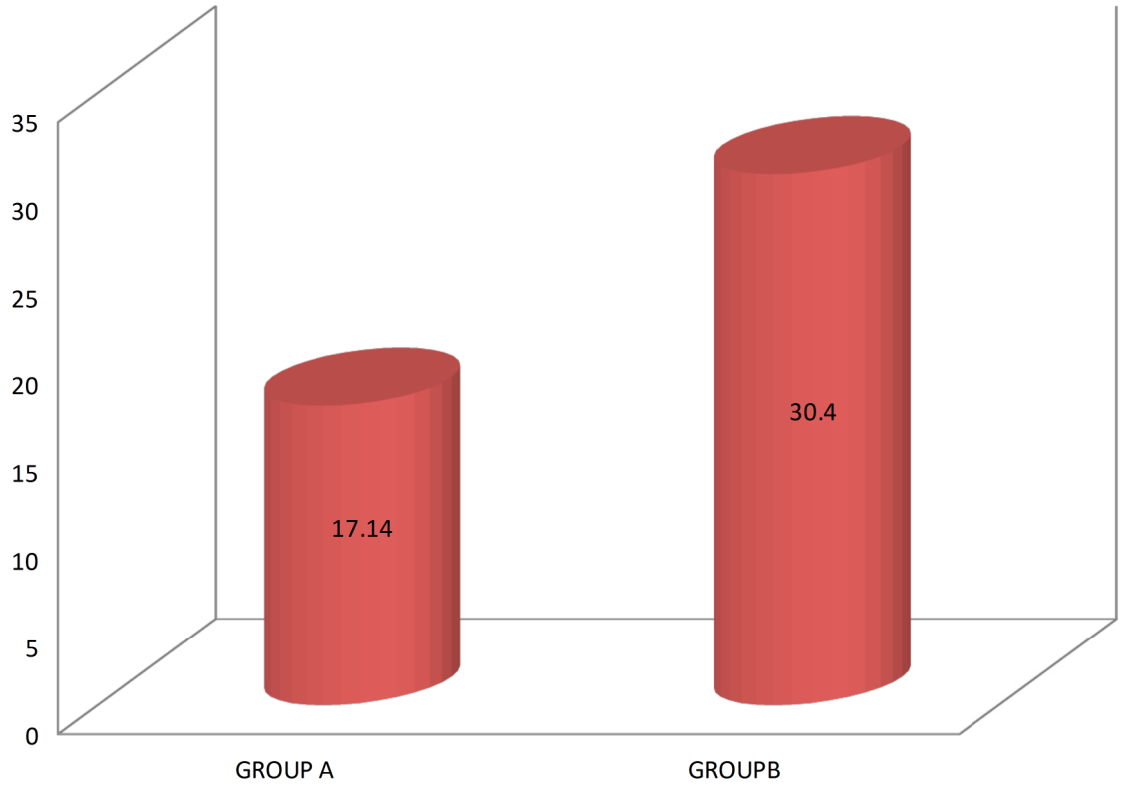


Fig.no 10

Table 11: Change in Fasting Blood Sugar- FBS (Patients Treated with Metformin HCL 500 mg)

FBS Values at	Group A			Group B			P- Value
	Mean	SD	Range	Mean	SD	Range	

First visit	137.3	19.79	119-166	130.9	9.33	114-145	0.315
Sixth visit	130.9	19.77	113-160	120	10.78	102-137	0.105
Decrease(First visit – sixth visit)	6.4	0.97	5-8	10.92	1.89	8-14	P<0.001

A total number of 11&13 patients who were under antidiabetic treatment with Metformin HCl 500 mg belong to hypertensive patient category Group A (Losartan Potassium 50 mg) and were in hypertensive category Group B respectively.

The observed change in Fasting Blood Sugar value was from 137.3 ± 19.79 to 130.9 ±19.77 with a mean decrease of 6.4 ± 0.97 in Group A, and that was from 130.9 ± 9.33 to 120 ± 10.78 in Group B with a mean decrease of 10.92 ± 1.89 Group B have better reduction in FBS than Group A.

Change in Fasting Blood Sugar- FBS (Metformin HCL 500 mg)

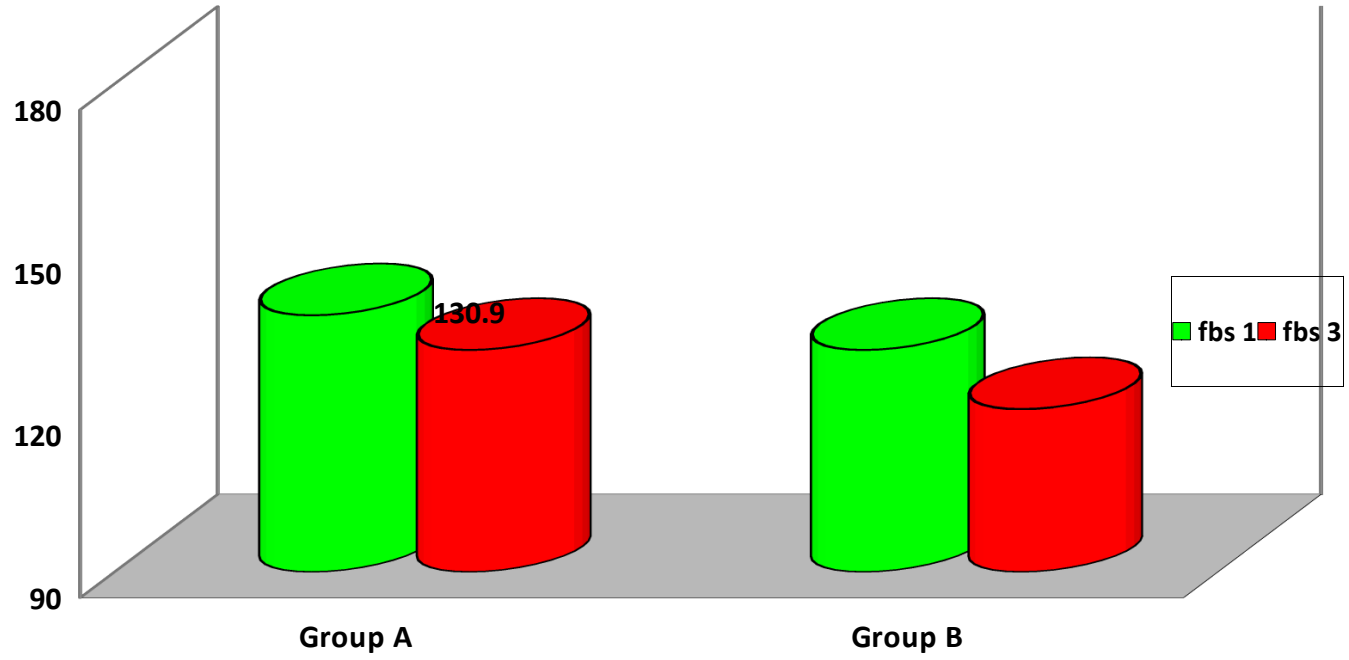


Fig.no 11

Table 12: Change in Post prandial Blood Sugar-PPBS (Patients Treated with Metformin HCL 500 mg)

PPBS Values at	Group A			Group B			P- Value
	Mean	SD	Range	Mean	SD	Range	

First visit	229.8	19.86	200-256	245.77	16.74	215-274	0.048
Sixth visit	214.3	17.26	190-240	217.6	15.01	198-236	0.628
Decrease(First visit – sixth visit)	15.5	4.03	10-21	28.15	6.58	17-38	P<0.001

A total number of 11&13 patients who were under antidiabetic treatment with Metformin HCl 500 mg belong to hypertensive patient category Group A (Losartan Potassium 50 mg) and Group B (Telmisartan 40 mg) respectively .

The observed change in Post Prandial Blood Sugar value was from 229.8 ± 19.86 to 214.3 ± 17.26 with a mean decrease of 15.5 ± 4.03 in Group A, and that was from 245.77 ± 16.74 to 217.6 ± 15.01 in Group B with a mean decrease of 28.15 ± 6.58 Group B have better reduction in PPBS than Group A.

Change in Post Prandial Blood Sugar-PPBS (Metformin HCL 500 mg)

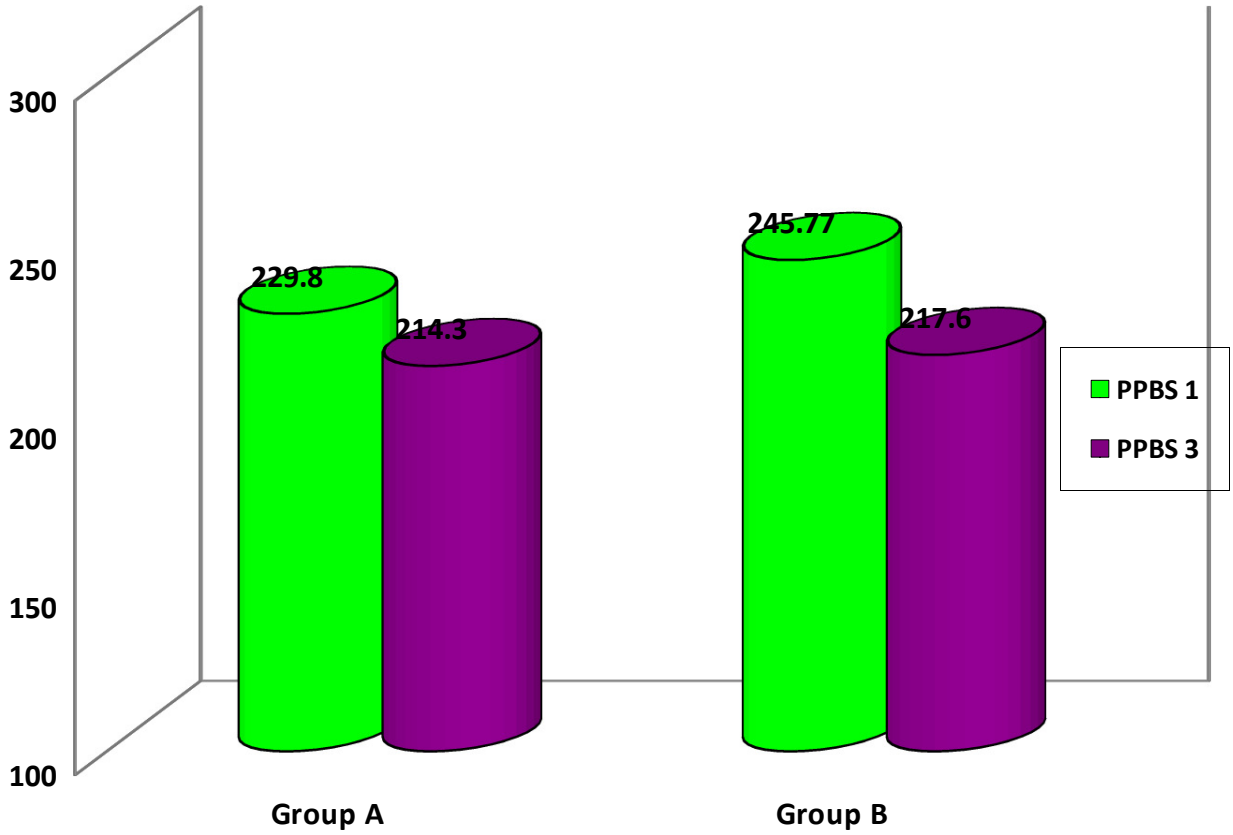

300
250
200
150
100
229.8
214.3
245.77
217.6
PPBS 1
PPBS 3
Group A
Group B

Fig.no 12

Table 13: Change in Fasting Blood Sugar-FBS (Patients Treated with Glimepiride 1 mg+ Metformin HCL 500 mg)

FBS Values at	Group A			Group B			P- Value
	Mean	SD	Range	Mean	SD	Range	
First visit	150.28	12.84	130-167	143	16.85	120-180	0.3597
Sixth visit	142	12.61	122-158	127.11	18.65	107-165	0.0921
Decrease(First visit – sixth visit)	8.28	1.11	7-10	15.88	7.47	11-32	0.02

A total number of 7&9 patients who were under antidiabetic treatment with Metformin HCl 500 mg + Glimepiride 1 mg, belong to hypertensive patient category Group A (Losartan Potassium 50 mg) and Group B(telmisartan 40 mg) respectively.

The observed change in Fasting Blood Sugar value was from 150.28 ± 12.84 to142 ± 12.61 with a mean decrease of 8.28 ± 1.11in Group A, and that was from 143 ± 16.85 to 127.11±18.65 in Group B with a mean decrease of 15.88 ± Group B have better reduction in FBS than Group A.

Change in Fasting Blood Sugar-FBS (Glimepiride 1 mg+ Metformin HCL 500 mg)

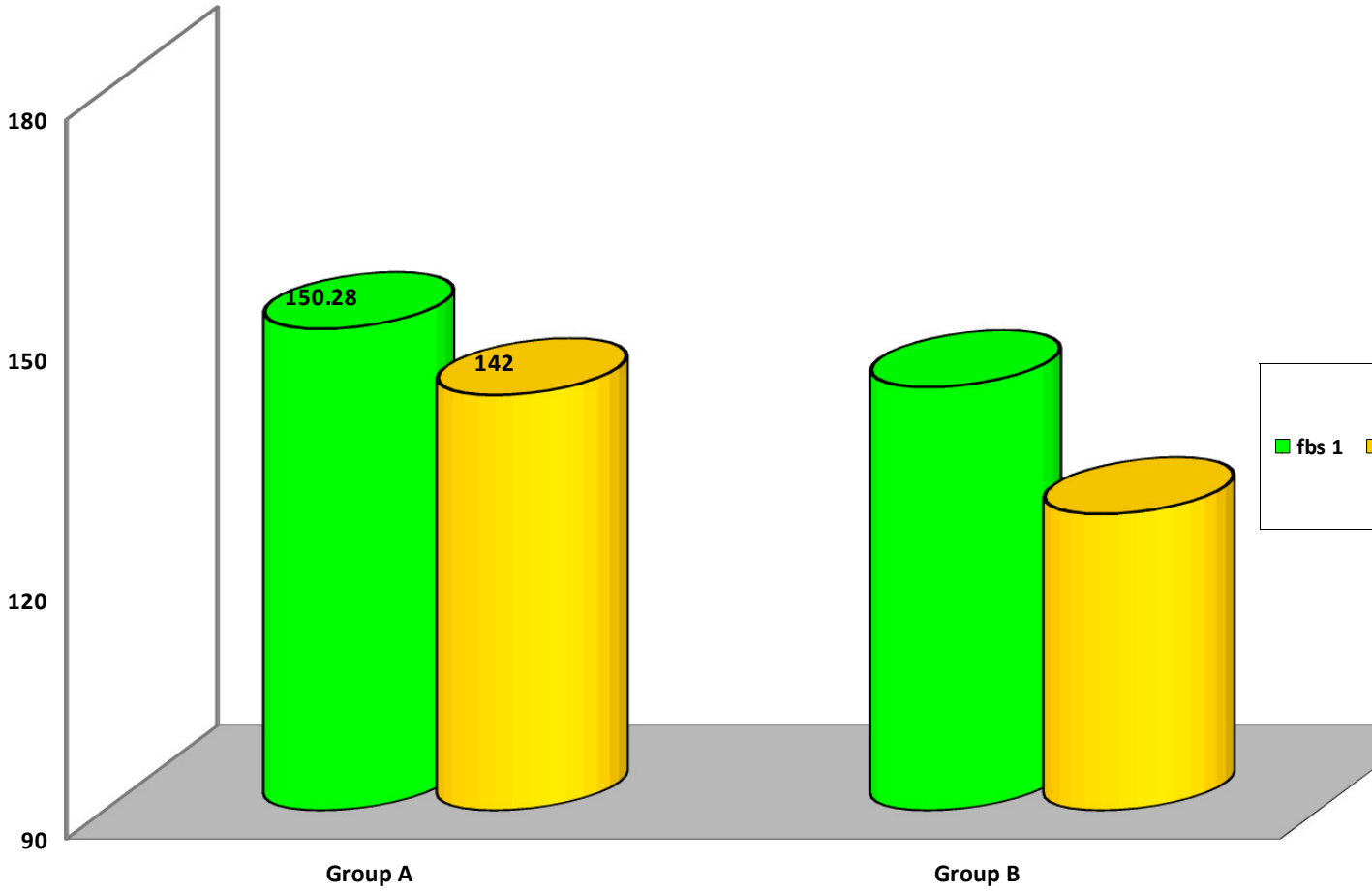


Fig.no 13

Table 14: Change in Post prandial Blood Sugar-PPBS (Patients Treated with Glimepiride 1 mg+ Metformin HCL 500 mg)

FBS Values at	Group A			Group B			P- Value
	Mean	SD	Range	Mean	SD	Range	

First visit	262	13.35	130-167	253.56	15.63	220-270	0.2581
Sixth visit	245	11.46	122-158	216.4	13.65	200-246	P<0.001
Decrease(First visit – sixth visit)	17.28	3.59	7-10	37.11	9.94	20-49	P<0.001

A total number of 7&11 patients who were under antidiabetic treatment with Glimepride 1 mg + Metformin HCl 500 belong to hypertensive patient category Group A (Losartan Potassium 50 mg) and Group B (telmisartan 40 mg) respectively.

The observed change in Post Prandial Blood Sugar value was from 262 ± 13.35 to 245 ± 11.46 with a mean decrease of17.28 ± 3.59 in Group A, and that was from 253.56 ± 15.63 to 216.4 ± 13.65 in Group B with a mean decrease of 37.11 ± 9.94.Group B have better reduction in PPBS than Group A.

Change in Post Prandial Blood Sugar-PPBS (Glimepiride 1 mg+ Metformin HCL 500 mg)

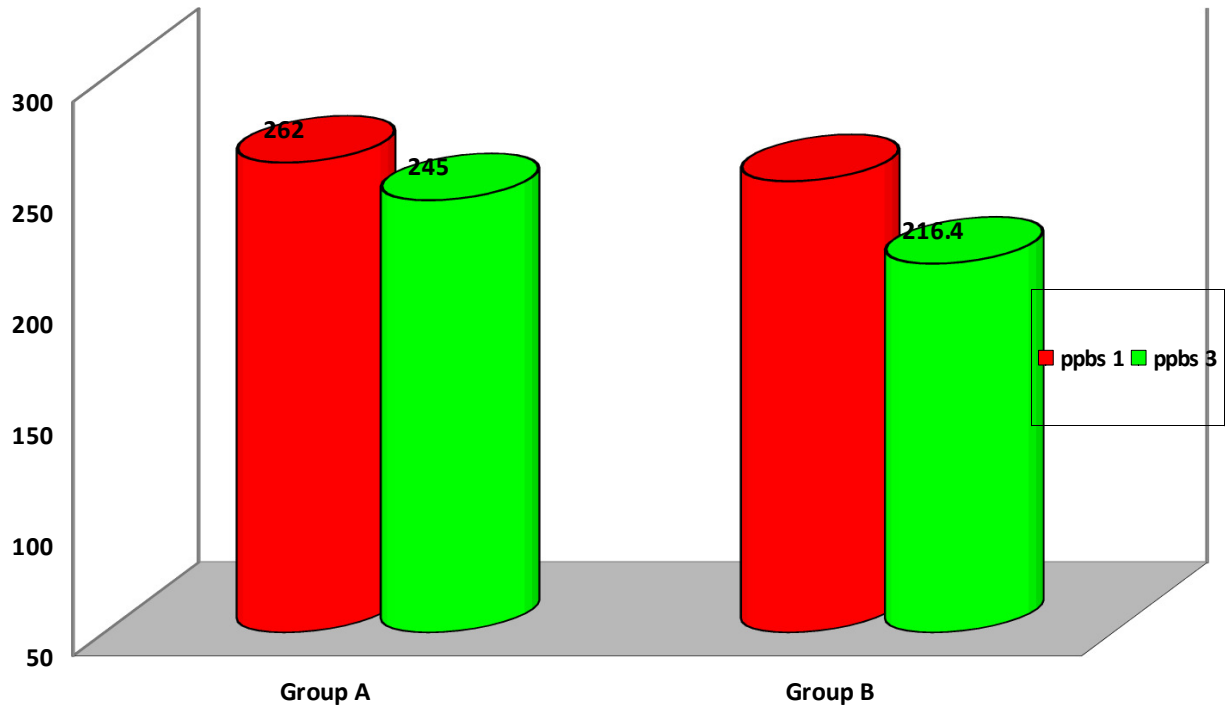


Fig.no 14

Table 15: Change in Fasting Blood Sugar-FBS (Patients Treated with Glimepiride 1 mg)

FBS Values at	Group A	Group B	P- Value

	Mean	SD	Range	Mean	SD	Range	
First visit	155.43	16.19	129-180	132.4	6.06	124-140	0.013
Sixth visit	147.57	15.05	124-170	119.8	6.02	114-128	0.003*
Decrease(First visit – sixth visit)	7.85	1.77	5-10	12.6	2.61	9-16	0.0036*

A total number of 7&5 patients who were under antidiabetic treatment with Glimepiride 1 mg were belong to hypertensive patient category Group A (Losartan Potassium 50 mg) and Group B (telmisartan 40 mg) respectively.

The observed change in Fasting Blood Sugar value was from 155.43 ± 16.19 to 147.57 ± 15.05 with a mean decrease of 7.85 ± 1.77 in Group A, and that was from 132.4 ± 6.06 to 119.8 ±6.02 in Group B with a mean decrease of 12.6 ± 2.61 Group B have better reduction in FBS than Group A.

Change in Fasting Blood Sugar-FBS (Glimepiride 1 mg)

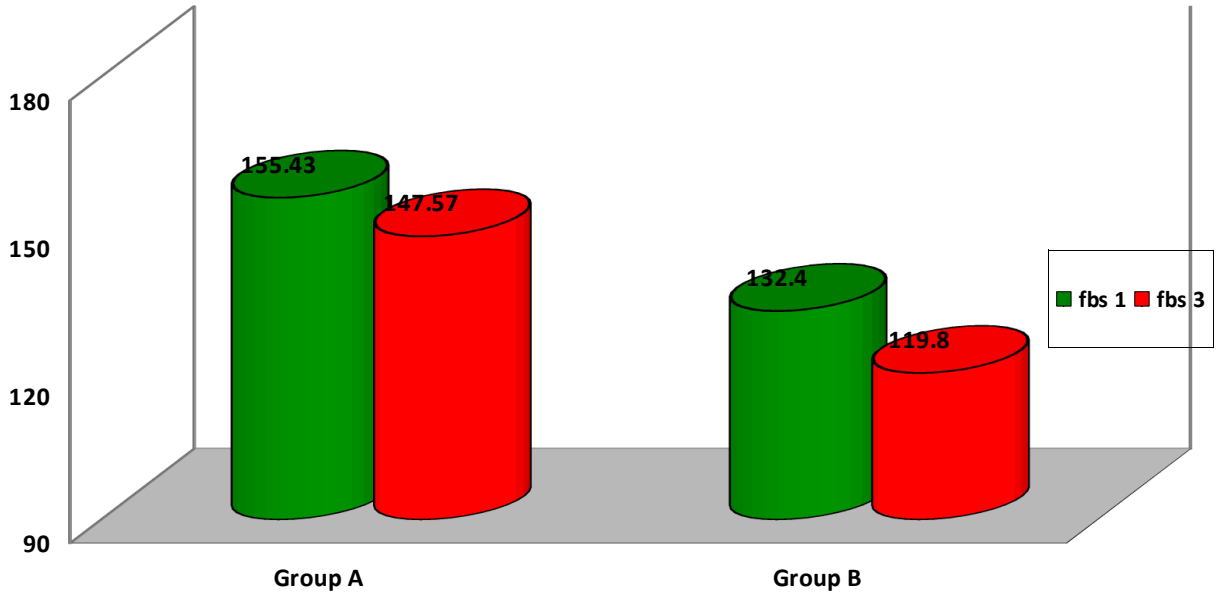


Fig.nlo 15

Table 16: Change in Post prandial Blood Sugar (Patients Treated with Glimepiride 1 mg))

PPBS Values	Group A			Group B			P- Value
	Mean	SD	Range	Mean	SD	Range	

at							
First visit	256.14	23.31	219-279	236.8	15.62	210-250	0.139
Sixth visit	237	22.42	202-264	209.8	17.21	190-236	0.046
Decrease(First visit – sixth visit)	19.14	3.71	15-24	27	9.94	14-39	0.081

A total number of 7&5 patients who were under antidiabetic treatment with Glimepiride 1 mg belong to hypertensive patient category Group A (Losartan Potassium 50 mg) and were Group B (telmisartan 40 mg) respectively.

The observed change in Post Prandial Blood Sugar value was from 256.14 ± 23.31 to 237 ± 22.42 with a mean decrease of 19.14 ± 3.71 in Group A, and that was from 236.8 ± 15.62 to 209.8 ± 17.21 in Group B with a mean decrease of 27 ± 9.94. Group B have better reduction in PPBS than Group A.

Change in Post Prandial Blood Sugar-PPBS (Glimepiride 1 mg)

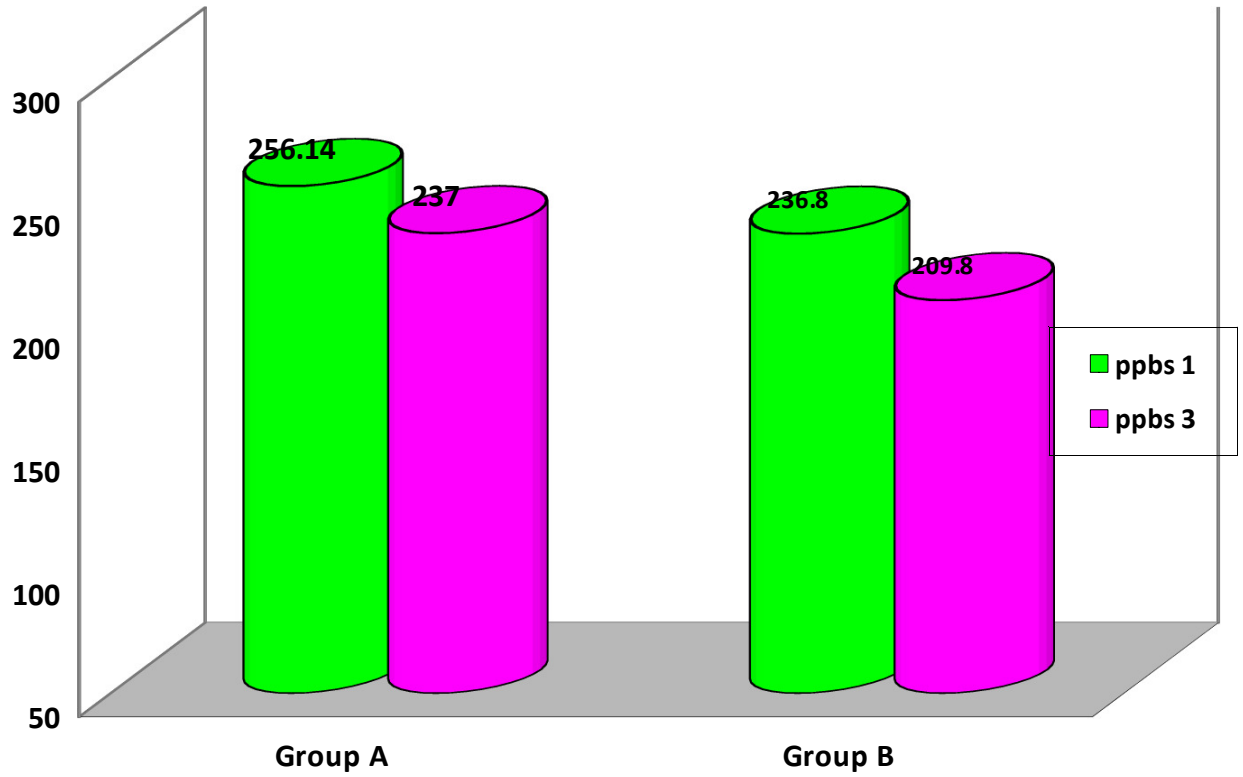


Fig.no 16

Table 17: Change in Fasting Blood Sugar (Patients Treated with Voglibose 0.2 mg)

FBS Values	Group A	Group B	P- Value

at	Mean	SD	Range	Mean	SD	Range	
First visit	142.5	2.12	141-144	154	-	154	-
Sixth visit	135	2.82	133-137	137	-	137	-
Decrease(First visit – sixth visit)	7.5	0.71	7-8	17	-	17	-

A total number of 2&1 patients who were under antidiabetic treatment with Voglibose 0.2 mg belong to hypertensive patient category Group A (Losartan Potassium 50 mg) and Group B (telmisartan 40 mg) respectively.

The observed change in Fasting Blood Sugar value was from 142.5 ± 2.12 to 135 ± 2.82 with a mean decrease of 7.5 ± 0.71 in Group A, and that was from 154 to 137 in Group B with a mean decrease of 17. Group B have better reduction in FBS than Group A.

Change in Fasting Blood Sugar-FBS (Voglibose 0.2 mg)

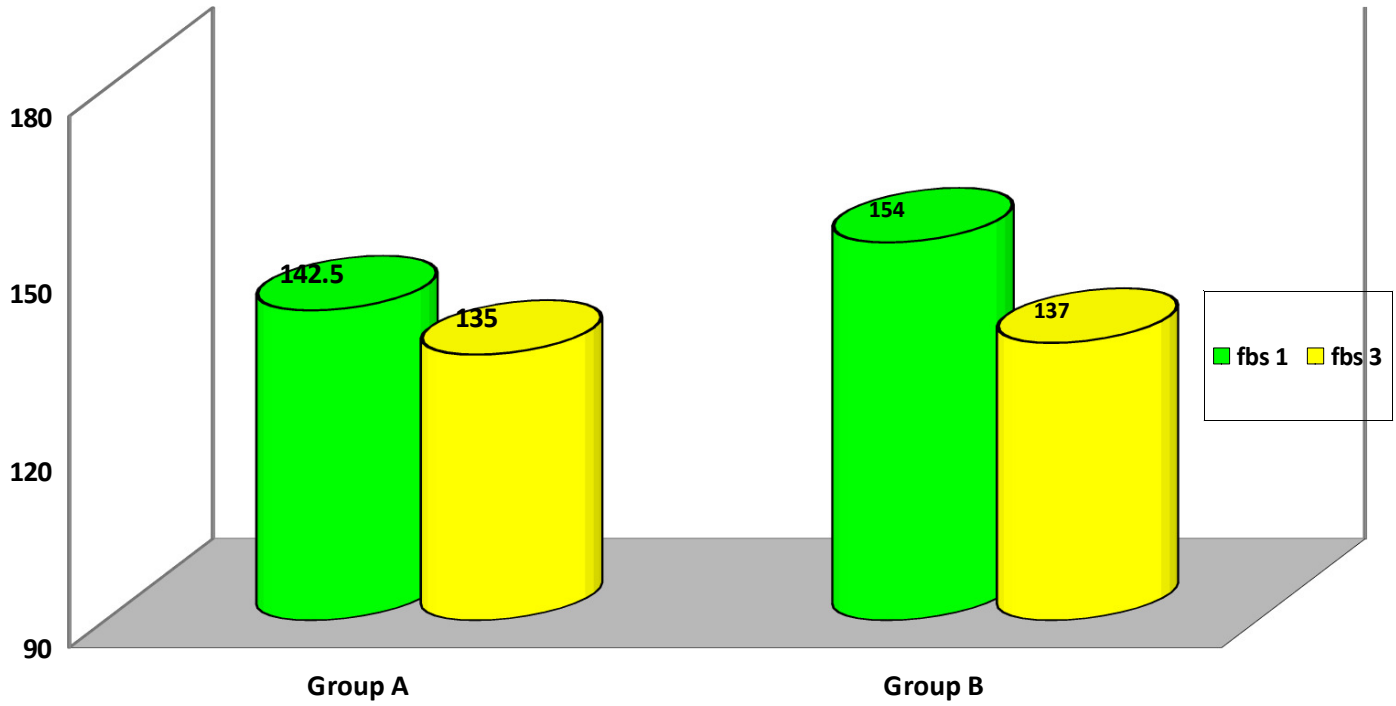


Fig.no 17

Table 18: Change in Post prandial Blood Sugar (Patients Treated with Voglibose 0.2 mg))

PPBS Values at	Group A			Group B			P- Value
	Mean	SD	Range	Mean	SD	Range	
First visit	259	1.41	258-260	270	-	270	-
Sixth visit	241.5	2.12	240-243	246	-	246	-
Decrease(First visit – sixth visit)	17.5	3.53	15-20	24	-	24	-

A total number of 2&1 patients who were under antidiabetic treatment with Voglibose 0.2 mg belong to hypertensive patient category Group A (Losartan Potassium 50 mg) and Group B (telmisartan 40 mg) respectively.

The observed change in Post Prandial Blood Sugar value was from 259 ± 1.41 to 241.5 ± 2.12 with a mean decrease of 17.5 ± 3.53 in Group A, and that was from 270 to 246 in Group B with a mean decrease of 24. Group B have better reduction in PPBS than Group A.

Change in Post Prandial Blood Sugar-PPBS (Voglibose 0.2 mg)

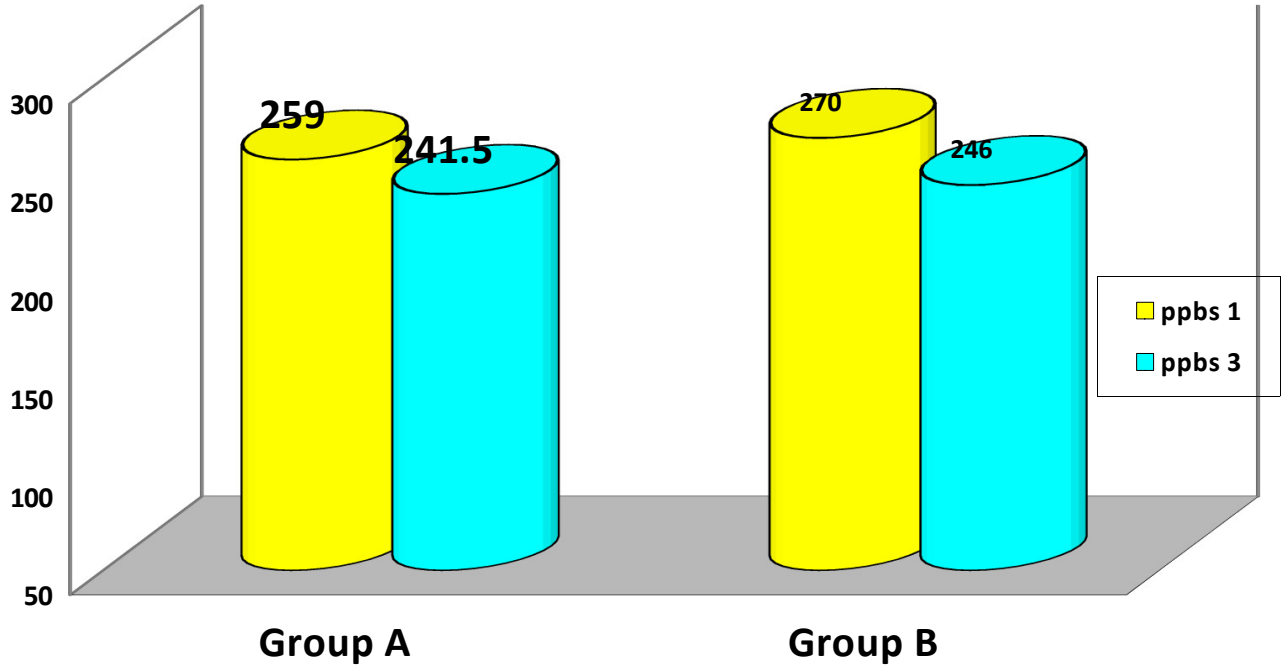


Fig.no 18

Table 19:Change in Fasting Blood Sugar (Patients Treated with Metformin HCL 500+ Voglibose 0.2 mg))

FBS Values at	Group A			Group B			P- Value
	Mean	SD	Range	Mean	SD	Range	
First visit	139	3.46	137-143	137.5	17.68	125-150	0.886
Sixth visit	131.7	3.79	129-136	127.5	16.26	116-139	0.675
Decrease(First visit – sixth visit)	7.33	0.58	7-8	10	1.41	9-11	0.053

A total number of 3&2 patients who were under antidiabetic treatment with Metformin HCl 500 mg + Voglibose 0.2 mg belong to hypertensive patient category Group A (Losartan Potassium 50 mg) and Group B (telmisartan 40 mg) respectively.

The observed change in Fasting Blood Sugar value was from 139 ± 3.46 to 131.7 ± 3.79 with a mean decrease of 7.33 ± 0.58 in Group A, and that was from 137.5 ± 17.68 to 127.5 ± 16.26in Group B with a mean decrease of 10 ± 1.41. Group B have better reduction in FBS than Group A.

Change in Fasting Blood Sugar-FBS (Metformin HCL 500 mg + Voglibose 0.2 mg))

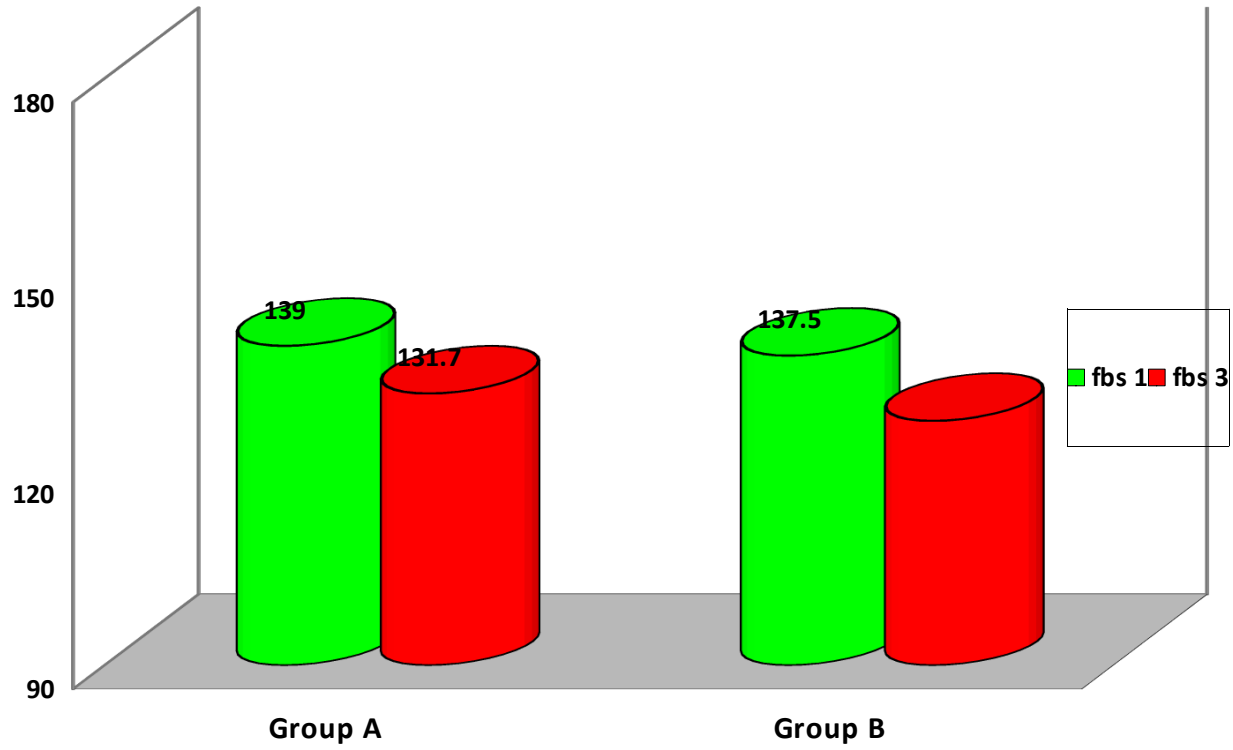


Fig.no19

Table 20: Change in Post prandial Blood Sugar (Patients Treated with Metformin HCL 500 mg + Voglibose 0.2 mg))

	Group A			Group B			P- Value
	Mean	SD	Range	Mean	SD	Range	
First visit	238.3	10.41	230-250	252.5	24.75	235-270	0.419
Sixth visit	221	7.54	214-229	226	24.04	209-243	0.742
Decrease(First visit – sixth visit)	17.33	3.21	15-21	26.5	0.71	26-27	0.032*

A total number of 3&2 patients who were under antidiabetic treatment with Metformin HCl 500 mg + Voglibose 0.2 mg belong to hypertensive patient category Group A (Losartan Potassium 50 mg) and Group B (telmisartan 40 mg) respectively.

The observed change in Post Prandial Blood Sugar value was from 238.3 ± 10.41 to 221 ± 7.54 with a mean decrease of 17.33 ± 3.21 in Group A, and that was from 252.5 ± 24.75 to 226 ± 24.04 in Group B with a mean decrease of 26.5 ± 0.71 Group B have better reduction in PPBS than Group A.

Change in Post Prandial Blood Sugar-PPBS (Metformin HCL 500 mg + Voglibose 0.2 mg))

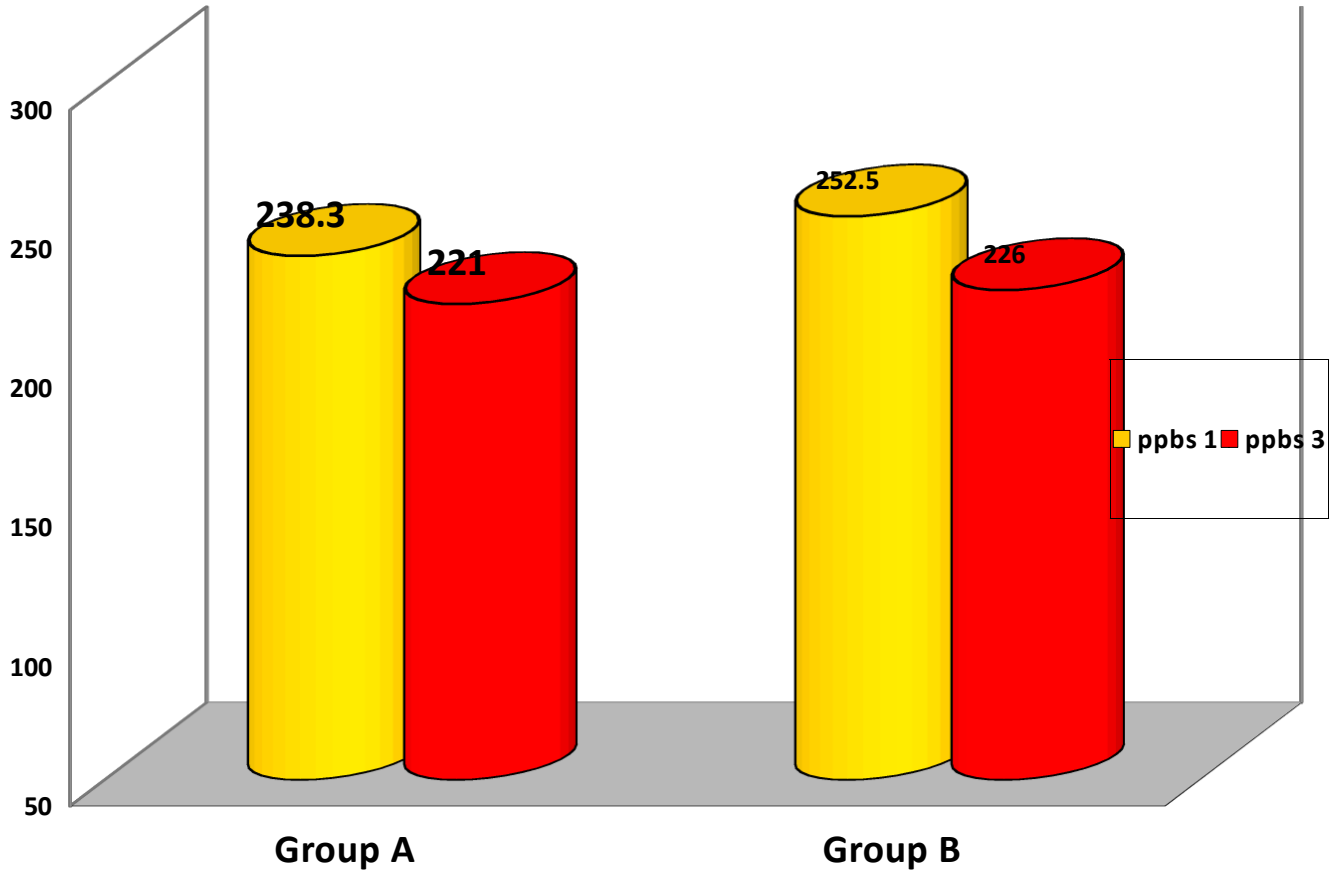


Fig.no20

8. DISCUSSION

Angiotensin II receptor antagonists provide a more specific blockade to the renin-angiotensin system and have better tolerability when compared with ACE inhibitors. In addition, the evidence available thus far for this new class of antagonists has established that their efficacy is equal to that of ACE inhibitors in hypertension. Therefore, it is conceivable that angiotensin II receptor blockers will take a growing place in the management of hypertensive patients. However, the place of angiotensin II receptor antagonists in the management of hypertension will of course, depend on the results of morbidity and mortality trials.

In this study comparison of efficacy of Losartan and Telmisartan in hypertensive patients was carried out. Patients with hypertension were enrolled for the study as per inclusion and exclusion criteria. They are divided into Group A (30 patients who were treated with Losartan potassium 50 mg) &Group B (30 patients who were treated with Telmisartan 40 mg). The parameters that used tothe efficacy comparison were - SBP, DBP, and FBS& PPBS. SBP & DBP were recorded from baseline to three months in an interval of 15 days. And the FBS & PPBS were recorded in the base line and at the end of the study. Then the comparison was done with the help of computational statistical method.

In this prospective study we observed that both Losartan potassium and Telmisartan reduces the blood pressure. Telmisartan was significantly superior to losartan in reduction of the Systolic blood pressure& Diastolic blood pressure with a p value(< 0.05) and Telmisartan the same shows superior reduction blood sugar levels than Losartan potassium with significant p value <0.05.

AGE:

A number of 60 patients were enrolled for the study and their age distribution was as below -

30 patients were of group A, out of these 3 patients (10%) between the age group of 30-39 years, 11 patients (36.66%) between the age group of 40-49 years, 16 patients (53.34%) between the age group of 50-60 years,

Out of 60 patients, 30 patients were of group A, out of these 2 patients (6.67%) between the age group of 30-39 years, 12 patients (40%) between the age group of 40-49 years, 16 patients (53.33%) between the age group of 50-60 years,

The age group A was 50.17± 6.62 years and group B was 50.34 ± 6.25 years. A total number of 32 patients comes under the age category 50-60 years ie, 53.33% of total study population this will cement the age correlation of hypertension " As the age increases the risk for hypertension also increases"

SEX:

A total of 60 patients were screened and randomized into two treatment group. Out of which 30 patients were of GROUP A, 18 patients (60%) were male, 12 patients (40%) were female. In case of GROUP B, 20, patients (66.67%) were male, 10 patients (33.34%) were female.

In our study population, numbers of males with hypertension were higher than the females, this may be due to the life style difference between the males and females, especially using of tobacco and alcohol.

PHYSIOLOGICAL PARAMETERS:

The average weights of patients were 74.1±5.97 in GROUP A and 70.57±5.84 in GROUP B. The average BMI of patients were 27.64±1.73 in GROUP A and 26.99±1.92 in GROUP B. The was no statistically significant difference in the mean weight and BMI of two groups (P>0.05)

SYSTOLIC BLOOD PRESSURE:

The mean systolic blood pressure of Group A and Group B were (152.93±6.53mm Hg& 148.8±7.28 mm Hg) respectively, at the base line (First visit). The group A who were treated with Losartan potassium 50 mg showed a mean reduction of (27.94± 3.09mm Hg) but that was lower than that produced by the Telmisartan in Group B (33.27± 3.42 mm Hg).

Both of the study drug produced reduction in the systolic blood pressure during the study time and of that, the Telmisartan 40 mg is found to be superior in SBP reduction which is statistically significant when compare to Losartan potassium 50 mg with a p value <0.05.

DIASTOLIC BLOOD PRESSURE:

The mean Diastolic blood pressure of Group A and Group B were (93.73±3.39mm Hg & 93.27± 2.75 mm Hg) respectively, at the base line (First visit). The group A who were treated with Losartan potassium 50 mg showed a mean reduction of (11.54± 2.27 mm Hg) but that was lower than that produced by the Telmisartan 40 mg in Group B (14.47± 2.33 mm Hg).

Both of the study drug produced reduction in the systolic blood pressure during the study time and of that the Telmisartan 40 mg is found to be superior in SBP reduction which is statistically significant when compare to Losartan potassium 50 mg with a p value <0.05.

EFFECT OF STUDY DRUGS IN BLOOD SUGAR LEVELS OF STUDY POPULATION

FASTING BLOOD SUGAR(FBS)

The fasting blood sugar values reduced in both groups, the reduction of fasting blood sugar was greater in Group B(Telmisartan 40 mg)12.83±4.86 than in Group A (Losartan potassium 50 mg) 7.40±1.35.

The Group B shows better reduction in fasting blood sugar than Group A at the end of 3 month study with a statistically significant p value of <0.05.

The fasting blood sugar changes among the study population who were under different anti diabetic therapy was observed as follows;

Metformin HCL 500 mg:

Values were decreased from base line value 137.3 ± 19.79 to 130.9 ± 19.77 with a decrease of 6.4 ± 0.97 in Group A and in Group B it was from base line value 130.9 ± 9.33 to 120 ± 10.78 with a decrease of 10.92 ± 1.89. It was found to be higher reduction in Group B than in Group A.

Metformin HCL 500 mg + Glimepiride 1 mg:

Values were decreased from base line value 150.28 ± 12.84 to 142 ± 12.61 with a decrease of 8.28 ± 1.11 in Group A and in Group B it was from base line value 143 ± 16.85 to 127.11 ± 18.65 with a decrease of 15.88 ± 7.47. It was found to be higher reduction in Group B than in Group A.

Glimepiride 1 mg:

Values were decreased from base line value 155.43 ± 16.19 to 147.57 ± 15.05 with a decrease of 7.85 ± 1.77 in Group A and in Group B it was from base line value 132.4 ± 6.06 to 119.8 ± 6.02 with a decrease of 12.6 ± 2.61. It was found to be higher reduction in Group B than in Group A .

Voglibose 0.2 mg:

Values were decreased from base line value 142.5 ± 2.12 to 135 ± 2.82 with a decrease of 7.5 ± 0.71 in Group A and in Group B it was from base line value 154 to 137 with a decrease of 17. It was found to be higher reduction in Group B than in Group A.

Metformin HCL 500 mg + Voglibose 0.2 mg:

Values were decreased from base line value 139 ± 3.46 to 131.7 ± 3.79 with a decrease of 7.33 ± 0.58 in Group A and in Group B it was from base line value 137.5 ± 17.68 to 127.5 ± 16.26 with a decrease of 10 ± 1.41. It was found to be higher reduction in Group B than in Group A.

POST PRANDIAL BLOOD SUGAR (PPBS)

The PPBS values reduced in both groups, the reduction of post prandial blood sugar was greater in Group B(Telmisartan 40 mg) 30.40±8.92 than in Group A (Losartan potassium 50 mg)17.14±3.69.

The Group B shows better significant reduction in PPBS than Group A at the end of 3 month study with a p values<0.05.

From the above findings it can assess that the partial PPAR-gamma activity of telmisartan sounds for the superior reduction in blood sugar values.

The post prandial blood sugar changes among the study population who were under different anti diabetic therapy were observed as follows;

Metformin HCL 500 mg:

Values were decreased from base line value 229.8 ± 19.86 to 214.3 ± 17.26 with a decrease of 15.5 ± 4.03 in Group A and in Group B it was from base line value 245.77 ± 16.74 to 217.6 ±15.01 with a decrease of 28.15 ± 6.58. It was found to be higher reduction in Group B than in Group A.

Metformin HCL 500 mg + Glimepiride 1 mg:

Values were decreased from base line value 150.29 ± 12.84 to 142 ± 12.61with a decrease of 8.28 ± 1.11 in Group A and in Group B it was from base line value 253.56 ± 15.63 to 216.4 ± 13.65 with a decrease of 37.11 ± 9.94. It was found to be higher reduction in Group B than in Group A.

Glimepiride 1 mg:

Values were decreased from base line value 256.14 ± 23.31 to 237 ± 22.42 with a decrease of 19.14 ± 3.71 in Group A and in Group B it was from base line value 236.8 ± 15.62

to 209.8 ± 17.21 with a decrease of 27 ± 9.94. It was found to be higher reduction in Group B than in Group A.

Voglibose 0.2 mg:

Values were decreased from base line value 259 ±1.41 to 241.5 ± 2.12 with a decrease of 17.5 ± 3.53 in Group A and in Group B it was from base line value 270 to 246 with a decrease of 24. It was found to be higher reduction in Group B than in Group A.

Metformin HCL 500 mg + Voglibose 0.2 mg:

Values were decreased from base line value 238.3 ± 10.41to 221 ± 7.54 with a decrease of 17.33 ± 3.21 in Group A and in Group B it was from base line value 252.5 ± 24.75 to 226 ± 24.O4 with a decrease of 26.5 ± 0.71. It was found to be higher reduction in Group B than in Group A.

9.CONCLUSION

In this present prospective observational study, treatment of hypertension with two study drugs losartan potassium 50 mg and telmisartan 40 mg were carried out in a population of 60 patients. They were instructed to follow a healthy diet with proper exercise.

After 3 months study it is observed that, both of the study drugs have good impact on blood pressure lowering. But the Telmisartan 40 mg showed superior reduction in blood pressure when compare to Losartan potassium 50 mg.

The second objective of the study ie; effect of study drugs Losartan potassium 50 mg and telmisartan 40 mg in blood sugar levels of population on diabetic therapy. The FBS and PPBS were the parameters observed for the study, there was reduction in FBS and PPBS values in both Group A Group B. And it is observed that the reduction is higher in Group B when compare with Group A. It can be suggested that the partial PPAR gamma agonist activity of Telmisartan accounts for the higher reduction in blood sugar levels.

PROFORMA

COMPARATIVE STUDY ON EFFICACY OF LOSARTAN VERSUS TELMISARTAN IN HYPERTENSIVE PATIENTS

DEMOGRAPHICDATA:

1. NAME: 2. AGE: 3. SEX: M/F 4: OPNO:

5. WEIGHT: 6. HEIGHT: 7. BMI:

7. ADDRESS:

8. PATIENT HISTORY:

9. DIAGNOSIS:

10. DRUG USED: LOSARTAN POTASSIUM 50 MG ☐

TELMISARTAN 40 MG ☐

11. OTHER CO-MORBIDITIES:

12. OTHER DRUGS USED:

BASE LINE(First visit)

DATE:

PARAMETERS

PRIMARY

SYSTOLIC BLOOD PRESSURE: mm Hg

DIASTOLIC BLOOD PRESSURE:mm Hg

SECONDARY

FBS:

PPBS:

SECOND VISIT DATE:

PARAMETERS

SYSTOLIC BLOOD PRESSURE: mm Hg

DIASTOLIC BLOOD PRESSURE:mm Hg

THIRD VISIT DATE:

PARAMETERS

SYSTOLIC BLOOD PRESSURE: mm Hg

DIASTOLIC BLOOD PRESSURE:mm Hg

FOURTH VISIT DATE:

PARAMETERS

SYSTOLIC BLOOD PRESSURE: mm Hg

DIASTOLIC BLOOD PRESSURE:mm Hg

FIFTH VISIT DATE:

PARAMETERS

SYSTOLIC BLOOD PRESSURE: mm Hg

DIASTOLIC BLOOD PRESSURE:mm Hg

SIXTH VISIT DATE:

PARAMETERS

PRIMARY **SECONDARY**

SYSTOLIC BLOOD PRESSURE: mm Hg FBS:

DIASTOLIC BLOOD PRESSURE:mm Hg PPBS:

Body weight: Kg

Pharmacist signature Physician signature

BIBLIOGRAPHY

1. Wolf –Mair k et al., hypertension prevalence and blood pressure levels in 6 Europian countries, Canada and the United states. JAMA 2003;289(18):pgno:2363-2369
2. Gupta R, Trends in hypertension epidemiology in India. J HUM hypertens , 2004;18:pg no:73-8.
3. Madhuri Devabhaktuni, Fixed combination of amlodipine and atorvastatin in cardiovascular risk management: patient perspectives.vascular health and risk management, 2009;5: pg no:377-387.
4. Stella – Maria G et al., Effects of Antihypertensive Treatment With Angiotensin II Receptor Blockers on Lipid Profile: An Open Multi Drug Comparison Trial. Hellenic J Cardiol,2006;47:pg no: 21 -28.
5. Franz H. messerli et al; Efficacy and Safety of Coadministered Amlodipine and Atorvastatin in Patient With Hypertension and Dyslipidemia: Results of the Avolon Trial.THE JOURNAL OF CLINICAL HYPERTENSION,2006;vol(8);pg no: 8.
6. George Nickening, Should angiotensin II receptor blockers and statins be combined. Circulation, JOURNAL OF THE AMERICAN HEART ASSOCIATION, 2004;110: pg no:1013-1020.
7. Marry J Mycok,Lippincott's Illustrated reviews. pharmacology 2nd edition, Judith E Thomson; 1998;pg no: 179-191.
8. RS Sathoker, PHARMACOLOGY AND PHARMACOTHERAPUETICS.19th edition, Popular prakashan; 2005; pg no: 404 -407.
9. Padmaja Udayakumar, Medicinal pharmacology,3rd edition; CBS publishers; 2011;pgno:169-177.
10. Roger Walker, clinical pharmacy and therapeutics,3rd edition; Churchill living stone; 1994; pgno:265 - 275.
11. Anderson JL, ST segment elevation acute myocardial infarction and complications of myocardial infarction. Saunders Elsevier, 2011;chap 73.
12. Badr KF., Vascular injury to the kidney. In. eds. Harrison's Principals of Internal Medicine,17th ed. New York, NY: McGraw Hill; 2008:chap 280.
13. Goodmaan&Gliman's, The pharmacological Basis of therapeutics,10th edition; The MC Graw Hill; 2001;pg no:845-866.

14. KD Tripathi, Essentials of medical pharmacology, 4th edition, Jay Pee brothers;1999;pg no:539-550.
15. National High Blood Pressure Education Program Working Group Report on Primary Prevention of Hypertension. Arch Inter Med,1993;153: pg no:186-208.
16. N Murugesh, A Concise Text Book of PHARMACOLOGY,6th edition, SATHYA PUBLISHERS; pg no: 133-139.
17. Joseph dippiro, Pharmacotherapy Handbook,7th edition,McGraw Hill; 2009; pg no:111-114.
18. Arm V Chobanian et al., The Seventh Report of Joint National committeeon Prevention , Detection , Evaluation ,and treatment of High Blood Pressure. The JNC 7 Report, 2003;vol(289):pg no:2560-2572.
19. Trials of Hypertension Prevention Collaborative Research Group, Effects of Weight loss and sodium reduction interventionon blood pressure and hypertension incidence in overweight people with high - normal blood pressure.The Trials of Hypertension Prevention,Phase II.Arch Intern Med,1997;157(6): pg no:657-667.
20. Blair SN et al., Cardiorespiratory Fitness and Risk of Nonfatel Cardiovascular Disease in Men and Women. AM J Hypertens, 2007;20(6):pg no: 608-615.
21. Maxwell et al., BP changes in obese hypertensive subjects during rapid weight loss. Comparison of restricted v unchanged salt intake. Arch Intern Med, 1984; 144(8): pg no: 1581 -1584.
22. Kagan A et al., Dietary and other risk factors for stroke in Hawaiian Japanese men. Stroke JOURNAL OF THE AMERICAN HEART ASSOCIATION, 1985; 16:pg no: 390-396.
23. Niels AG et al; Effects of Sodium Restriction on Blood Pressure, Renin, Aldosterone, Catecholamines, Cholesterols, and TriglycerideA Meta-analysis. JAMA,1998;279(17):pg no:1383-1391.
24. Sacks FM et al., Effect on blood pressure of reduced dietary sodium and the Dietary Approaches to Stop Hypertension (DASH) diet. N Engl J Med 2001; 344 (1): pg no: 3-10.
25. Nelson L et al., Effect of changing levels of physical activity on blood pressure and haemodynamics in essentional hypertension. lancet,1986; 2(8505):pg no: 473-476.

26. Kohno et al., Renal depressor mechanisms of physical training in patients with essential hypertension.Am J Hypertens,1997;10(8): pg no: 859-868.
27. Jonas MA et al, Statement on smoking and cardiovascular disease for health care professionals. Circulation Stroke, JOURNAL OF THE AMERICAN HEART ASSOCIATION, 1992;86:pg no1664–1669.
28. LaCroix AZ., Smoking and mortality among older men and women in three communities. N Engl J Med,1991;324(23):pg no:1619–1625.
29. Davey GK et al., Hypertension and blood pressure among meat eaters, fish eaters, vegetarians and vagans in EPIC – Oxford. Public Health Nutr, 2002; 5(5): pg no: 645-654.
30. Lawrence J et al., Dietary Approaches to prevent and Treat Hypertension: A Scientific Statement From the American Heart Association. Hypertension JOURNAL OF THE AMERICAN HEART ASSOCIATION, 2006;47:pg no:296-308.
31. Psaltopoulou T et al., Olive oil, the Mediterranean diet and arterial blood pressure: the Greek European Prospective Investigation into Cancer and Nutrition (EPIC) study[1-3].Am J ClinNutr,2004;80:pg no:1012-1018.
32. Epstien BJ et al., Can the renin – angiotensin system protect against stroke ? A focus on angiotensin II receptor blockers. Pharmacotherapy,2005;25(4):pg no: 531 -539.
33. Weber M et al; Achieving blood pressure goals: should angiotensin II receptor blockers become first-line treatment in hypertension?.J Hypertens Suppl, 2009;27(5):pg no: 9 -14.
34. George nickening et al., Clinical Evidence for the Cardiovascular Benefits of Angiotensin Receptor Blockers. JRAAS, 2006;7: Pg no:1- 6.
35. National clinical guideline for the management in primary and secondary care. Pg no:06-17
36. National diabetic information clearinghouse.US Department of Health and Human Services, 2005; pgno:1-11.
37. National diabetes fact sheet.Department of Health and Human Service Centers for Disease control and prevention 2007; pg no:1-14.
38. L H Bosenberg et al, The mechanism of action of oral antidiabetic drugs. JEMDSA,2008;13(3): pg no: 80-88.
39. Dr. P. R. AnandVijayakumar et al., To Compare the Pleiotropic Effects of Telmisartan and Olmesartan in Hypertensive Patients with Metabolic

Syndrome Based On ATP III Criteria. Iosr Journal Of Pharmacy,2013;3(1): Pg no: 59-67.

40. Yuji Shimizu et al., Metabolic effect of combined telmisartan and nifedipine CR therapy in patients with essential hypertension. Int J Gen Medcine, 2012; 5:pg no:753-758.
41. Nazia yasmeen et al., Efficacy and Tolerability of Different Antihypertensive Drugs in Patients with Mild to Moderate Hypertension in a Teritiary Care Hospital. Sholars Resech library ,Archives of Applied Science Reserch, 2011; 3(1):pg no: 436-443.
42. SE Kjeldsen et al; The Effects of losartan vs candesartan in reducing cardiovascular events in theprimary treatment of hypertension. J Hum Hypertens,2010;24(4):pg no:263-273.
43. RM Nixon et al; Valsartan vs. other angiotensin II receptor blockers in the treatment of hypertension. Int J ClinPract, 2009;63(5):pg no: 766–775.
44. Paolo Verdecchia et al., Comparative assessment of angiotensin receptor blockers in different clinical settings.Vasc Health Risk Manag, 2009; 5:pg no: 939–948.
45. Shiho Nakayama et al., Comparison of Effects of Olmesartan and Telmisartan on Blood Pressure and Metabolic Parameters in Japanese Early-Stage Type-2 Diabetics with Hypertension.Hypertension Research, (2008); 31:pg no: 7–13.
46. Derosa G et al. Metabolic effects of telmisartan and irbesartan in type 2 diabetic patients with metabolic syndrome treated with rosiglitazone. J Clin Pharm Ther, 2007;32:pg no:261-268.
47. Nagel et al., The effect of telmisartan on glucose and lipid metabolism in nondiabetic, insulin-resistant subjects Metabolism. Clinical and Experimental, 2006;pg no: 1149 - 1154
48. Asmar R et al., Targeting effective blood pressure control with angiotensin receptor blocker. Int J Clin Pract,2006;60(3):pg no: 315 – 320.
49. Cristiana Vitale et al., Metabolic effect of telmisartan and losartan in hypertensive patients with metabolic syndrome. Cardiovascular Diabetology, 2005;4(6) pg no:1-8.
50. Derosa G et al., Effects of telmisartan compared with eprosartan on blood pressure control, glucose metabolism and lipid profile in hypertensive, type 2

diabetic patients: a randomized, double-blind, placebo-controlled 12-month study Hypertens, 2004; 27:pg no:457-464.

51. Schupp M et al., Angiotensin type 1 receptor blockers induce peroxisome proliferator-activated receptor-g activity. Circulation 2004; 109: pg no:2054-2057.
52. UjalaVerma et al., Antihypertensive Efficacy of carvedilol and Amlodipine in patients of mild to moderate hypertension-A Comparative Study.j k science,2004;6(4); pg no:193-196.
53. Dahlof B et al., Cardiovascular morbidity and mortality in the Losartan Intervention For Endpoint reduction in hypertension study (LIFE): a randomised trial against atenolol.Lancet,2002; 359:pg no: 995-1003.
54. Lerch M et al., Effects of angiotensin II-receptor blockade with losartan on insulin sensitivity, lipid profile, and endothelin in normotensive offspring of hypertensive parents. J Cardiovasc Pharmacol,1998; 31(4) :pg no: 576-580.
55. Pedro Luis de Pablos Velasco et al., Effects of Losartan and Diltiazem on Blood Pressure, Insulin Sensitivity, Lipid Profile and Microalbuminuria in Hypertensive Type 2 Diabetic Patients.1998; 16(5):pg no: 361-370
56. Indian Pharmacopoeia. 2007;vol(1):pg no:1319-1321.
57. The Merck Index, An Encyclopedia of CHEMICALS, DRUGS AND BIOLOGICALS,13th edition: merck research laboratories, 2001;pg no:1628-1629.