Medical Manual of Telblok /Telblok-H

Introduction:

Cardiovascular disease caused 2.3 million deaths in India in the year 1990, and this is projected to double by the year 2020.(1)

Hypertension is the most common cardiovascular disease.It is responsible for 57% of all stroke deaths and 24% of all coronary heart disease deaths in India.The prevalence of hypertension in Indian population is about 30-40%.(1)

Hypertension causes pathological changes in the vasculature and hypertrophy of the left ventricle.As a consequence it is the principle cause of stroke. It is a major risk factor for coronary artery disease and is a major contributor to the cardiac failure and renal insufficiency.

Hypertension is commonly associated with diabetes,affecting 20-60% of individuals with diabetes.The prevalence of hypertension in diabetic population is 1.5 to3 times higher than that of non diabetic age matched group.(2)

In addition to hyperglycemia and dyslipidemia, hypertension is a major risk factor to the development and progression of macro and microvascular complications in patients with diabetes. Therefore, diagnosis and effective treatment of hypertension is important in preventing cardiovascular disease in people with diabetes.

Hypertension is commonly defined as systolic blood pressure more than 140mmHg and diastolic blood pressure more than 90 mmHg.However,because of the high cardiovascular risk associated with a blood pressure reading >130/80 mmHg in patients with diabetes, 130/80 mmHg is considered as the treatment goal of hypertension in diabetics.(2)

The Third National Health and Evaluation Survey (1988-1994) demonstrates that 55% of diabetic individual on treatment had a blood pressure >140/90.This shows how far we have to go to effectively address hypertension in people with diabetes.(2)

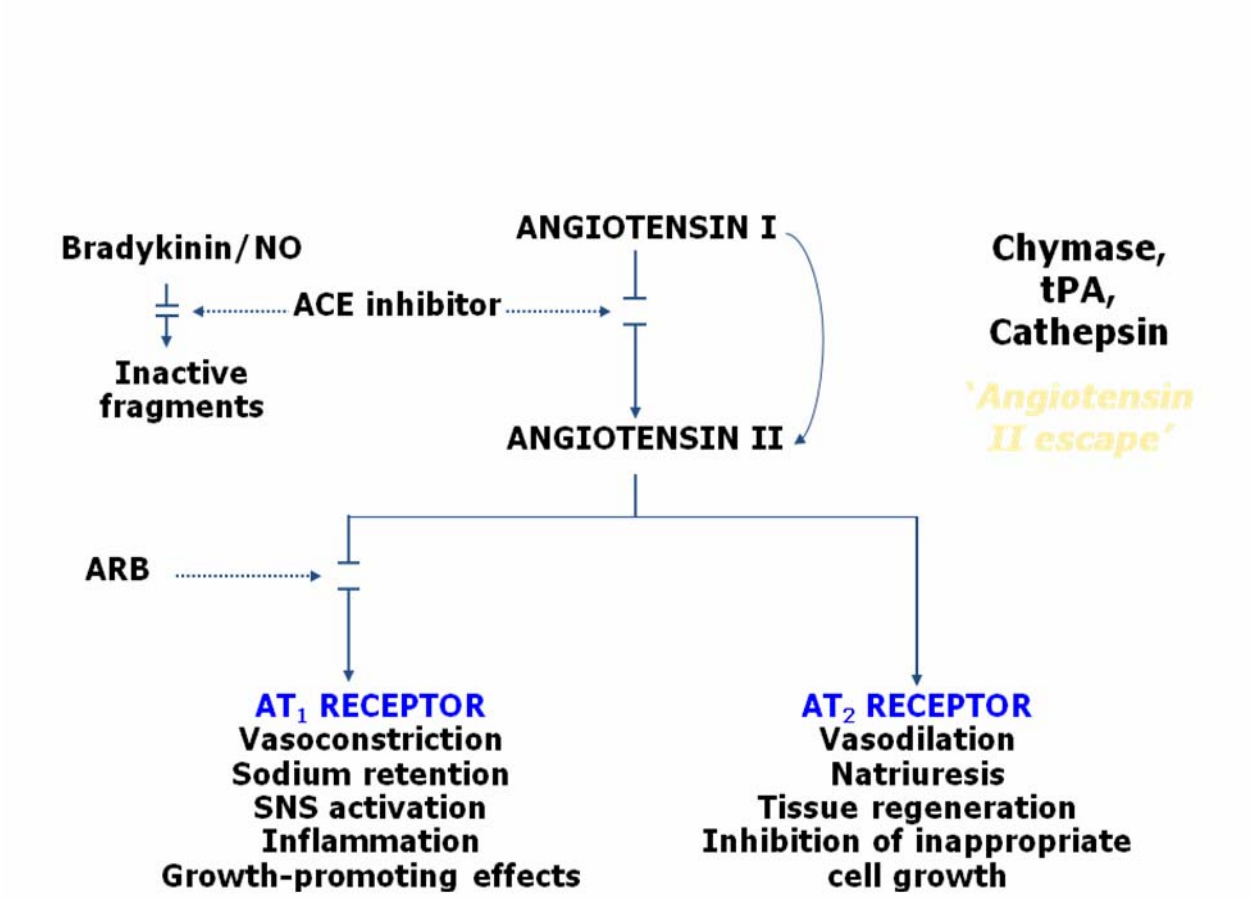
Suboptimal control of hypertension is a major attributable risk for death all over the world. The sixth annual report of the Joint National Committee stated that optimal drug formulations should provide 24 hrs efficacy with a once daily dose. Thus, an effective antihypertensive should provide sustained and smooth reductions in blood pressure over 24hrs, reducing the risk of blood pressure variability.(2,3)

Pathophysiology of Essential hypertension:

There is still much uncertainty about the pathophysiology of essential hypertension.A number of physiological factors are involved in the maintenance of normal blood pressure and their derangement may play a part in the development of hypertension. These include salt intake , obesity , sympathetic nervous system and renin angiotensin system.

The **renin angiotensin aldosterone system (RAAS)** is the most important of the endocrine system that affect the control of blood pressure. Renin is an enzyme secreted from juxtaglomerular apparatus of the kidney in response to glomerular hypoperfusion or a reduced salt intake or sympathetic stimulation.Renin is responsible for converting renin substrate, angiotensinogen to angiotensin I.Angiotensin I is physiologically inactive and is rapidly converted to angiotensin II by angiotensin converting enzyme (ACE). Most of the biological effects of angiotensinII are mediated by the AT_1 receptor. The AT_1 receptor exists in the blood vessels, liver kidney adrenal cortex and heart and the cardiovascular effects of AT II are mediated by this receptor. The functional role for AT_2 receptor are poorly defined however, evidence suggests that AT_2 receptors may exert antiproliferative, proapoptotic and vasodilatory effects.

Angiotensin II binds to angiotensin I receptor and act as a potent vasoconstrictor and therefore is implicated in hypertension.In addition to its vasoconstrictor effect, angiotensin II also mediates vascular hypertrophy, atherosclerosis.Angiotensin II is also involved in the development of left ventricular hypertrophy, a major risk factor for cardiovascular morbidity and mortality, and in the progression of renal disease.



Angiotensin II also facilitates peripheral noradrenergic neurotransmission by increasing norepinephrine release from sympathetic nerve

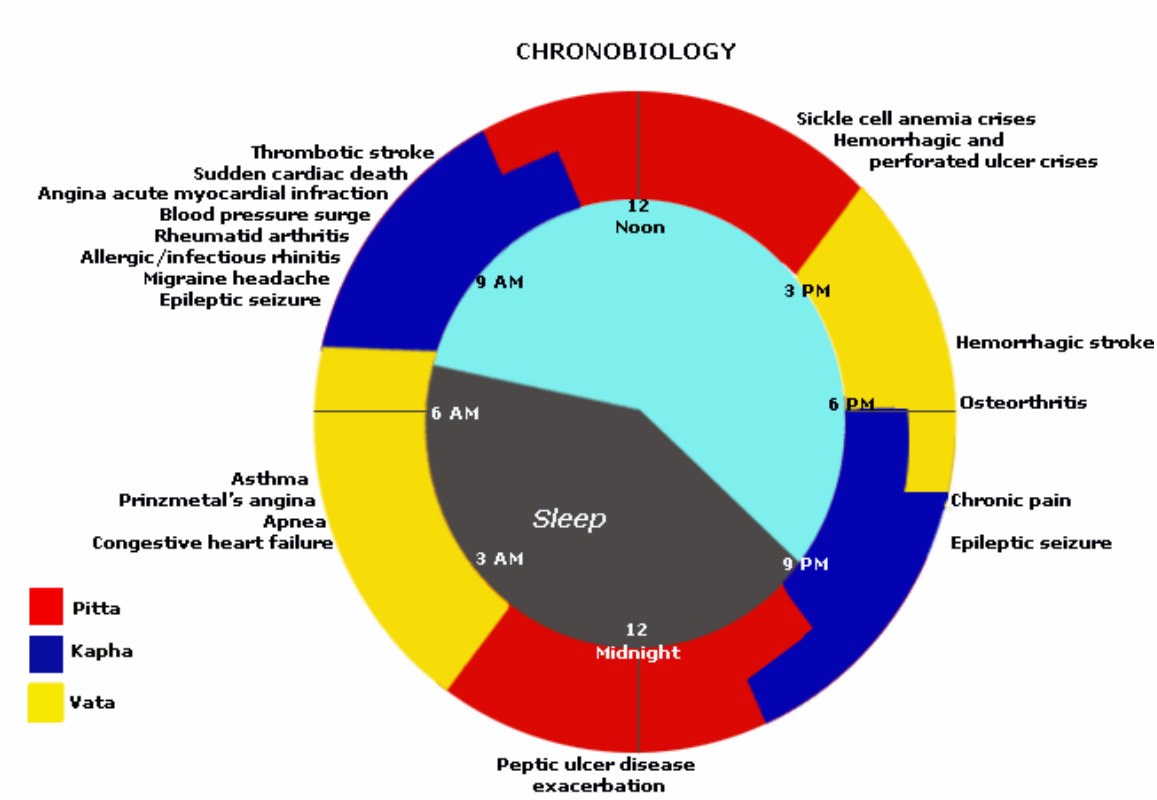
terminals. Angiotensin II enhances the vascular response to norepinephrine and potentiates sympathetic nervous system induced coronary vasoconstriction.Blocking the RAAS with angiotensin receptor antagonists like telmisartan will also protect against the deleterious effects of sympathetic nervous system activation.

Circadian rhythm:

Chronobiology of cardiovascular system demonstrates that blood pressure, heart rate and peripheral resistance display circadian variations.

Circadian variation in blood pressure occur such that blood pressure is at its lowest at 3a.m.,and starts to rise in early morning hours with the sharpest increase between 6 a.m. and 9 a.m.Similarly various pathophysiological events within the cardiovascular system such as stroke, myocardial infarction, angina and sudden cardiac death etc. also display circadian pattern.(4)

The onset of various acute cardiovascular events shows highest incidence of morbidity and mortality in the morning hours.Therefore,the role of hypertension is suggested in the onset of acute cardiovascular events.(5,6)



Various antihypertensives which are used in the management of hypertension include beta blockers, ACE inhibitors, Calcium channel blockers and angiotensin receptor blockers.

Angiotensin receptor blockers(ARBs) have emerged as a first line of therapy in patients of hypertension with diabetes.ARBs are more specific in their action than ACE inhibitors.ARBs block the effects of angiotensin II generated by pathways other than RAAS system (e.g. by the enzyme chymase) by binding to the AT_1 receptor.This specificity for the AT_1 receptor translates into a more favourable side effect profile, like ACE inhibitors are commonly associated with cough,which is not seen with ARBs.Various ARBs have been developed like losartan, valsartan, candesartan, olmesartan and **Telmisartan.**(7)

Telmisartan (Telblok) is a angiotensin II receptor blocker with high affinity for AT_1 receptor.It selectively and insurmountably inhibits AT_1 receptor without affecting other systems involved in cardiovascular regulation.

Among various ARBs, telmisartan has the strongest binding affinity to AT_1 receptor. The rank order of affinity is telmisartan > olmesartan > candesartan > valsartan > losartan.**This high affinity of telmisartan for AT_1 receptor may be responsible for long lasting blood pressure lowering effects and superior cardioprotective properties in patients with hypertension.**(8)

The oral bioavailabilty of telmisartan is 40-60%.Following oral administration peak concentration is achieved in 0.5-1 hour(Tmax).It has a half life of 24 hours.

Telmisartan is extensively distributed in body tissues (mean apparent volume of distribution is 460-510 L).Telmisartan is metabolized to form inactive acylglucuronide.The cytochrome P450 isoenzymes are not involved in its metabolism.The primary rout of elimination of telmisartan and its metabolite is biliary- fecal excretion.(4)Telmisartan can work as a partial agonist of PPAR-γ receptor and reverse insulin resistence.(9) Various studies have shown that side effect profile of telmisartan resembles to that of a placebo and may cause headache,dizziness, bodyache,flulike symptom etc.(10) Very few drug interactions have been reported with telmisartan.Plasma concentration of digoxin and lithium may increase in presence of telmisartan.Potassium supplements may increase the risk of hyperkalemia.

Telmisartan is the only sartan with

- **Longest half life of 24 hours**
- **Highest lipophilicity and tissue penetration**
- **PPAR-γ modulating activity**
- **Minimal urinary excretion**
- **Placebo like side effects**

Table 1 : Pharmacokinetic parameters of angiotensin II receptor blockers(7,8)

Parameters	Telmisartan	Losartan	Olmesartan	Valsartan	Irbesartan
Half Life (hrs.)	24	6 to 9	13	6	11 to 15
T max	0.5 - 1 hr.	3-4 hrs.	1-2 hrs.	2-4 hrs.	1.5-2 hrs.
Bioavailability (%)	43	33	26	25	
Route of elimination	Renal 0.49 % Hepatic > 97 %	Renal 35 % Hepatic 60 %	Renal 35 -50 % Hepatic 50-65 %	Renal 13 % Hepatic 83.7 %	Renal 20 % Hepatic 80 %
PPAR gamma activity	Yes	No	No	No	No
Last 6 hrs. BP control	Yes	No	No	No	No
Dissociation rate constant	0.003248	0.008561	0.004171	0.01027	NA

Role of Telmisartan in controlling early morning blood pressure surge(EMBPS)

As mentioned earlier most of the cardiovascular events like stroke, angina and myocardial infarction occur in the morning hours, which may be precipitated by early morning surge in blood pressure. Morning BP surge is also significantly associated with hypertensive target organ damage.(6)

Various mechanisms may be involved in the association between BP variability and cardiovascular disease. The impact of this association may be augmented in the morning.Increased sympathetic activity , particularly the α-adrenergic component may contribute to the morning BP surge.An increase in plasma cortisol levels could enhance coronary artery sensitivity to the vasoconstrictor effects of catecholamines. The renin angiotensin aldosterone system (RAAS) is also activated in the morning and could contribute to morning BP surge and morning increase in cardiovascular risk.(6)

Various studies have demonstrated that telmisartan provide sustained and effective control of blood pressure over 24 h.Telmisartan also effectively controlled early morning surge in blood pressure when compared with other antihypertensives including losartan. Telmisartan has also been shown to produce greater reductions in diastolic and systolic blood pressure than losartan during the last 6 hours of the 24 hour dosing interval.

Clinical studies

Study1.
The effect of telmisartan and ramipril on early morning blood pressure surge : a pooled analysis of two randomized clinical trials.(11)

Objective: To investigate the effect of telmisartan and ramipril on early morning blood pressure surge.

Method: Data from two prospective randomized, open-label, blinded end point studies involving 1279 patients compared telmisartan and ramipril.Patients with mild to moderate hypertension were included and were assessed using 24-h ambulatory blood pressure monitoring.

Results: Telmisartan changed the overall mean (SE) systolic surge by -1.5(0.47) mmHg ,and ramipril by +0.3 (0.47) mmHg (p=0.0049).The magnitude of surge reduction was greatest in the quartile with the highest baseline systolic surge : telmisartan -12.7 (0.91), ramipril -7.8 (1.02) mmHg (p= 0.0004).Telmisartan also reduced the surge compared with ramipril in dippers. But there were no differences between the two groups in non dippers.

Conclusion : Telmisartan significantly reduced the early morning systolic blood pressure surge compared with ramipril.

Study 2
Efficacy and safety of telmisartan vs. losartan in control of mild to moderate hypertension : a multi centre, randomized, double blind study.(12)

Objective : To compare the safety and efficacy of telmisartan and losartan in mild to moderate hypertension

Method: In this double blind , double dummy, parallel group study, 330 patients with mild to moderate hypertension were randomly assigned to receive once daily treatment with telmisartan 40 mg (n=164) or losartan 50 mg (n=166)

Results: After 4 weeks treatment , mean trough seated blood pressure was reduced significantly more in the telmisartan group than in the losartan group (SBP 12.5 mmHg vs 9.4 mmHg,p=0.037;DBP 10.9 mmHg vs 9.3 mmHg, p=0.030).The over all DBP response rate (reduction from baseline in mean seated DBP> or =10 mmHg and or a mean seated DBP <90 mmHg) at the end of study in the telmisartan

group was higher than in the losartan group (70.1% vs. 58.7%, p= 0.020).Adverse events with the two treatments were comparable (telmisartan vs. losartan 23.2% vs.22.9%, p=0.952).

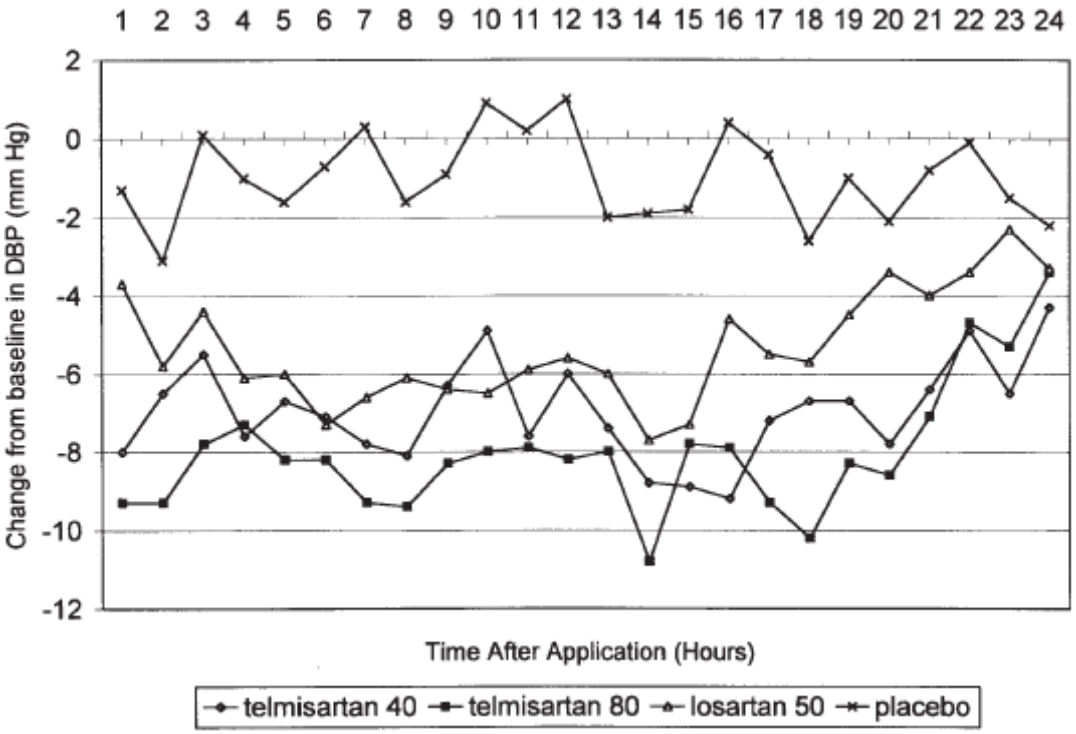
Conclusion: Telmisartan administered once daily can reduce SBP and DBP effectively than losartan.

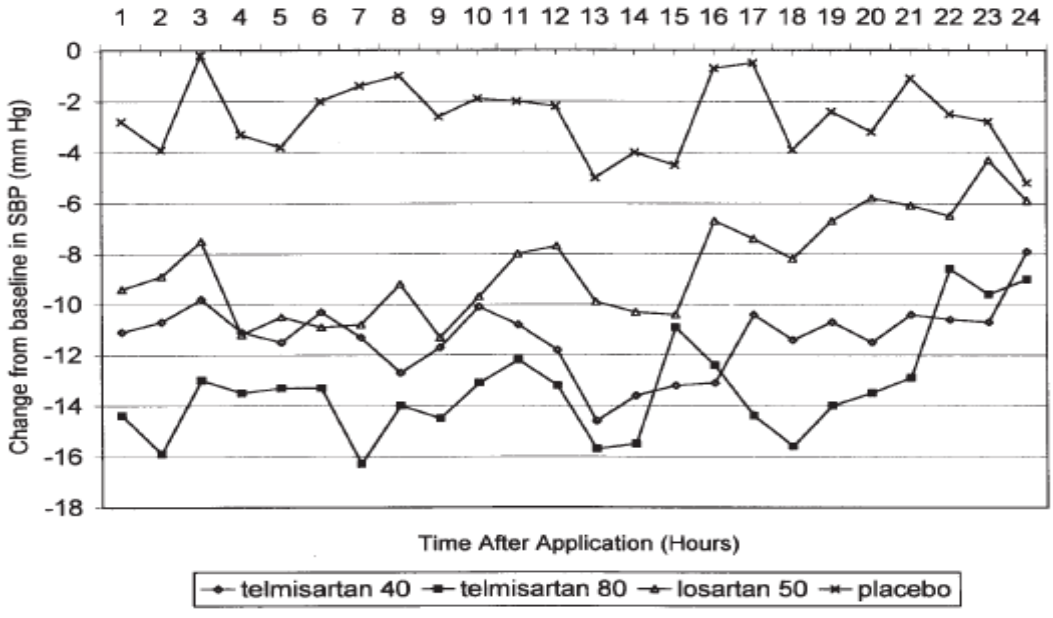
Study 3
ABPM comparison of the antihypertensive profiles of the selective angiotensin II receptor antagonists telmisartan and losartan in patients with mild to moderate hypertension(13)

Objective: To compare the efficacy and tolerability of telmisartan and losartan in mild to moderate hypertension

Method: Telmisartan and losartan were compared with placebo in a six week multinational,multicentre, randomized, double blind, parallel group study of 223 patients with mild to moderate hypertension. After a 4 week single blind placebo run in, eligible patients were randomized to receive telmisartan 40mg, telmisartan 80 mg, losartan 50 mg, or placebo.

Result: Ambulatory blood pressure monitoring (ABPM) after 6 weeks of therapy showed that all active treatment produced significant ($p< 0.01$) reduction from baseline in 24 hr mean SBP and DBP compared with placebo.During the 18 to 24 hrs period after dosing, the reductions in SBP/DBP with telmisartan 40 mg (10.7/6.8 mmHg) and 80 mg (12.2/7.1 mmHg) were each significantly ($p < 0.05$) greater than those observed for losartan 50 mg (6.0/3.7 mmHg), and losartan was no better than placebo.Also for the 24 h mean blood pressure , telmisartan40 mg and 80 mg were significantly ($p<0.05$) better than losartan 50mg.Compared with losartan , telmisartan 80 mg produced significantly ($p < 0.05$) greater reduction in SBP and DBP during all monitored period of the 24 hrs period, while telmisartan 40 mg produced significantly greater reductions in SBP andDBP in the night time period (10.01 pm to 5.59 am) ($p< 0.05$) and in DBP in the morning period (6.00 am to 11.59 am) ($p < 0.05$).All treatments were comparably well tolerated.
Conclusion: Telmisartan 40 mg and 80mg once daily were effective and well tolerated in the treatment of mild to moderate hypertension, producing sustained 24 – h blood pressure control which compared favourably with losartan.





Study 4: Comparison of telmisartan versus losartan : meta-analysis of titration to response studies(14)

Objective: To compare the ability of telmisartan and losartan to reduce mean diastolic blood pressure (DBP) during the last 6 h of the 24-h dosing interval in a prospectively planned meta-analysis of ambulatory blood pressure monitoring (ABPM) data from 2 independent studies.

Methods: Data from two independent randomized, double blind, double dummy,titration to response studies conducted in patients with mild to moderate hypertension (seated cuff DBP 95-105 mmHg, 24 h mean ambulatory DBP > =85 mmHg).After a 4 week placebo run in period, patients received once daily telmisartan 40mg or losartan 50 mg, with uptitration after 4 weeks to telmisartan 80 mg or losartan 100 mg respectively.Blood pressure were recorded using ABPM.

Results: Titration to higher dose was required in 60.1% of telmisartan patients and 69.5% of losartan patients (p=0.01).Reduction from baseline in the last 6 h mean ambulatory DBP with telmisartan and losartan were 6.6+/-0.4 mmHg, respectively (p<0.01,adjusted for baseline and study).During last 6 h of the 24 h dosing interval, telmisartan produced greater reductions in 3 each of the observed hourly mean ambulatory DBP values over the entire 24 h dosing interval.Reductions from baseline in the last 6 hr adjusted mean ambulatory systolic blood pressure (SBP) for telmisartan and losartan were 9.9 +/-0.6 and 7.8+/- 0.6 mmHg,respectively (p=0.01).The 24 h profiles of ambulatory SBP hourly mean reductions were similar to those for DBP.Both telmisartan and losartan were found to be safe and well tolerated.
Conclusion: Telmisartan 40mg/80mg is superior to losartan 50/100 in controlling DBP and SBP during the last 6 h of the 24 h dosing interval.

Role of telmisartan in renal protection

There is a close link between cardiovascular and renal changes due to cardiovascular risk factors such as hypertension and diabetes.Albuminuria and decreased renal function, which are both primarily known to predict renal outcome, have now been identified as excellent predictors of cardiovascular morbidity and mortality.Albuminuria is related to intrarenal pressure, podocyte function and increased permeability provoked by endothelial dysfunction.(15)

The endothelium is a major regulator of vascular homeostasis, with functional integrity being essential for the maintenance of blood flow and antithrombotic activity.Nitric oxide(NO), formed from L-arginine in presence of NO synthase, is released by vascular endothelial cells and brings about relaxation of vascular tissue and inhibition of platelet aggregation and adhesion.(15)

Angiotensin II, which is widely implicated in endothelial dysfunction, increases oxidative stress, which causes stimulation of NO breakdown. In the long term, endothelial dysfunction results in atherosclerosis and subsequent target organ damage leading to overt cardiovascular disease and chronic kidney disease.(15)

Telmisartan has been shown to improve endothelial function and reduce albuminuria in hypertensive patients with diabetes.

Study1

Impact of telmisartan versus ramipril on renal endothelial function in patients with hypertension and type 2 diabetes (15)

Objective: To analyze effect of RAAS blockade on renal endothelial function.

Method: In a multicentre, prospective double blind , forced titration, randomized study,96 patients with type 2 diabetes,hypertension,glomerular filtration >80ml/min, and normo or microalbuminuria were treated once daily with 40/80 mg or 5/10 mg ramipril for 9 weeks.

Results: The mean ± SE fall in renal plasma flow (RPF) in response to intravenous N^G-monomethyl-L-arginine (L-NMMA), reflecting the magnitude of nitric oxide (NO) activity, increased with telmisartan from 71.9 ± 9.0 ml/min before therapy to 105.2 ± 9.7 ml/min at the end of treatment ($P < 0.001$). With ramipril, RPF response to L-NMMA increased from 60.1 ± 12.2 to 87.8 ± 9.2 ml/min ($P = 0.018$). The adjusted difference between treatments was –17.1 ± 13.7 ml/min ($P = 0.214$). In accordance, telmisartan increased RPF at rest (i.e., without L-NMMA) from 652.0 ± 27.0 to 696.1 ± 31.0 ml/min ($P = 0.047$), whereas ramipril produced no significant changes in RPF. The more the basal NO activity improved, the greater was the vasodilatory effect on renal vasculature ($r = 0.47$, $P < 0.001$).

Conclusion: In patients with type 2 diabetes, telmisartan and ramipril both increased NO activity of the renal endothelium significantly, which in turn may support the preservation of cardiovascular and renal function.

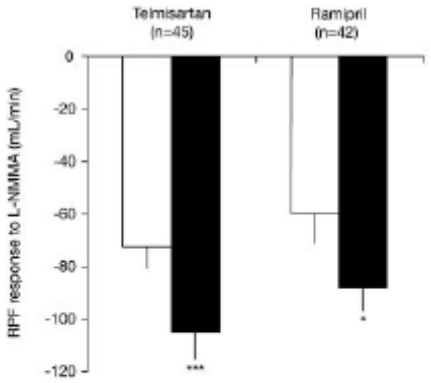


Figure 1—*Effects of 40/80 mg telmisartan and 5/10 mg ramipril for 9 weeks on the mean ± SE RPF in response to 5 mg/kg L-NMMA infusion compared with pre–L-NMMA infusion values. □, baseline; ■, end of treatment. *P = 0.018 vs. baseline; ***P < 0.001 vs. baseline.*

Study 2

The differential effects of angiotensinII type 1 receptor blockers on microalbuminuria in relation to low grade inflammation in metabolic hypertensive patients.(16)

Objective: To investigate difference between the effects of telmisartan and valsartan with respect to microalbuminuria reduction, and the association with improvement of metabolic features or suppression of the inflammatory state.

Methods: Fifty three patients with metabolic syndrome who had been taking valsartan were recruited. All patients were randomly assigned to replace valsartan by telmisartan (telmisartan group; n=30) or to keep taking valsartan (control group; n=21).Various parameters were measured at baseline and 12 weeks after randomization.

Results: There was a significant increase in high molecular weight adiponectin in the telmisartan group(4.6 v 5 mcg/ml,p=0.024).The reductions of microalbuminuria and high sensitivity C reactive proteins were significant in telmisartan group(28.1 v 18.9mg/g.Cr and 0.77 v 0.60 mg/L, respectively, p=0.001 and 0.022).Whereas there was no significant change in the control group.

Conclusion: The dual ARB/PPAR- γ agonist telmisartan achieved more microalbuminuria reduction than an ARB with no PPAR- γ agonistic action.

Role of Telmisartan in Left ventricular hypertrophy (LVH)

Pathological alterations in cardiovascular structures may involve hypertrophy(an increase in tissue mass) and/ or remodeling (redistribution of mass within a structure) such as increased wall to lumen ratio in blood vessels associated with hypertension, hypertrophy associated with hypertension, heart failure and myocardial infarction.These morbid changes in cardiovascular structure are due to increased migration, proliferation and hypertrophy of cells as well as to increased extracellular matrix.

Angiotensin II has been shown to stimulate migration, proliferation and hypertrophy of vascular smooth muscle cells.Angiotensin II also causes hypertrophy of cardiac myocytes and increases extracellular matrix production by cardiac fibroblast.

Left ventricular hypertrophy is a cardinal manifestation of preclinical cardiovascular disease that strongly predicts myocardial infarction, stroke and cardiovascular death in hypertensive patients and patients with coronary artery disease. Cardiovascular events are 2-4 fold higher in the presence of LVH.Several studies suggest that regression of hypertensive LVH is associated with improved prognosis.**Telmisartan has been shown to reduce left ventricular mass in patients with hypertension**.

Clinical Study

Three-dimensional echocardiographic and magnetic resonance assessment of the effect of telmisartan compared with carvedilol on left ventricular mass a multicenter, randomized, longitudinal study.(17)

Objective: To compare the effects of telmisartan and carvedilol on 24-h mean ambulatory BP and left ventricular mass (LVM) regression, measured using three-dimensional echocardiography (3-DECHO) and magnetic resonance imaging (MRI).

Methods: A total of 82 patients with mild-to-moderate hypertension and an optimal echocardiographic acoustic window were randomized to receive once-daily telmisartan 80 mg or carvedilol 25 mg for 44 weeks.

Results: The 24-h mean ambulatory systolic/diastolic BP reductions were similar in both treatment groups (telmisartan, from 159.6 +/- 10.2/97.8 +/- 5.4 to 128.6 +/- 6.5/78.2 +/- 5.8 mm Hg; carvedilol, from 157.8 +/- 11.1/95.7 +/- 11.9 to 128.2 +/- 5.6/78.7 +/- 5.2 mm Hg). However, night-time and last 6-h mean BP reductions were nonsignificantly greater with telmisartan. Using 3-DE, telmisartan (P< .001) and carvedilol (P< .001) progressively reduced LVM index by 21.97 +/- 5.84 (15.7%) and 12.31 +/- 3.14 (9.1%) g/m2, respectively, at week 44. Similar magnitudes of reductions were observed using MRI (15.5% and 9.6%, respectively). Reductions in LVM index achieved with telmisartan were statistically superior to carvedilol (P< or = .001).

Conclusion: The superior LVM regression with telmisartan versus carvedilol suggests telmisartan has a mechanism that may be beyond that of lowering BP in hypertensive patients.

Role of telmisartan in metabolic syndrome:

The metabolic syndrome is a common precursor of cardiovascular disease type 2 diabetes that is characterized by the clustering of insulin resistance, dyslipidemia and increased blood pressure.Recently, telmisartan (the only ARB) was found to act as a partial agonist of peroxisome proliferators activated receptor-γ (PPAR- γ)

PPAR- γ activity influences the gene expression involved in carbohydrate and lipid metabolism and improve insulin resistance.Moreover there is growing body of evidence that activators of PPAR- γ exert anti inflammatory, antioxidative and anti-proliferative effects on vascular wall cells, thus decreasing the risks for atherosclerosis.These observations suggest that due to its unique PPAR- γ modulating activity, **telmisartan** may become a promising cardiometabolic sartan that targets both diabetes and cardiovascular disease in hypertensive patients.

Clinical study
Metabolic effect of telmisartan and losartan in hypertensive patients with metabolic syndrome (18)

Objective: To compare the glucometabolic effect of telmisartan and losartan in patients with metabolic syndrome.

Methods: In a double blind, parallel group, randomized study, patients with WHO criteria for metabolic syndrome received once-daily doses of telmisartan (80mg,n=20) or losartan (50 mg, n=20) for 3 months.At baseline and end of treatment, fasting and post prandial plasma glucose, insulin sensitivity, glycosylated hemoglobin (HBA1c) and 24 hour mean systolic and diastolic blood pressures were determined.
Results: Telmisartan, but not losartan, significantly ($p<0.05$) reduced free plasma glucose,free plasma insulin, homeostasis model assessment of insulin resistence and HbA1c.Following treatment, plasma glucose and insulin were reduced during the oral glucose tolerance test by telmisartan, but not by losartan.Telmisartan also

significantly reduced 24 hour mean systolic blood pressure ($p<0.05$) and diastolic blood pressure ($p<0.05$) compared with losartan.

Conclusion: Apart from providing superior 24- hour blood pressure control, telmisartan, unlike losartan, displayed insulin-sensitizing activity, which may be explained by its partial PPAR- γ activity.

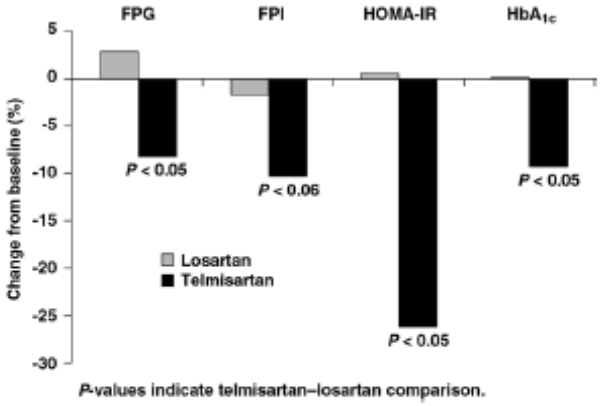


Figure 1
Effect of telmisartan and losartan on measures of glycaemia and insulin resistance in 40 patients with metabolic syndrome. FPG = fasting plasma glucose, FPI = fasting plasma insulin, HOMA-IR = homeostatic model assessment – insulin resistance, HbA_{1c} = glycosylated haemoglobin.

Smoothness Index

The smoothness index has been introduced as a more precise, reproducible,and clinically relevant alternative to the trough/peak ratio for evaluating the homogeneity of 24 hour blood pressure reduction by an antihypertensive agent.The index is calculated from the mean of 24 individual hourly blood pressure changes induced by treatment, divided by the standard deviation.**Telmisartan has a significantly superior smoothness index compared with losartan (18)**

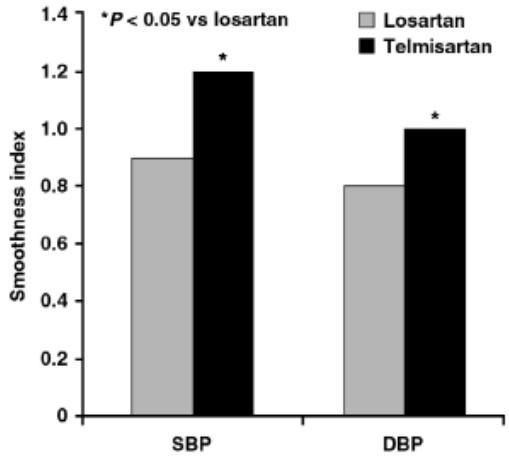


Figure 3
Effect of telmisartan and losartan on the smoothness index at endpoint.

Salient features of telmisartan (Telblok)

- **Telmisartan(Telblok) is a ARB with potent , selective and insurmountable antagonism of AT1 receptor, thereby contributing to its long duration of action.**

- **Telmisartan (Telblok) is indicated for the treatment of hypertension.**

- **Telmisartan (Telblok) has a very high lipophilicity and high volume of distribution which indicate its high tissue penetration.**

- **Telmisartan (Telblok) has a longer half life (24hrs) than other sartans, which make it suitable for once a day dosing.**

- **Telmisartan (Telblok) effectively control early morning surge in blood pressure than other sartans including losartan.**

- **Telmisartan (Telblok) is the only sartan with PPAR-γ modulating activity, therefore has favorable effect on glycemic control and metabolic syndrome.**

- **Telmisartan (Telblok) is not metabolized by cytochrome P450, therefore has a lower risk for cyt.P450 based drug interactions.**

- **Telmisartan (Telblok) is mainly eliminated through hepatic rout, hence can be safely used in patients with mild to moderate renal failure**.

Telmisartan (Telblok) is indicated in

- *All age group hypertensives including diabetic hypertensives*
- *ACE Inhibitors intolerant patients (dry cough, angioedema)*
- *Diabetic microalbuminuria and type 2 diabetic nephropathy*
- *LVH and heart failure*

Dosage : Dosage must be individualized.The usual starting dose of telmisartan is 20 mg once a day orally. Blood pressure response is dose related over the range of 20-80 mg.