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MANAGEMENT OF HYPERTENSION: COMPARISON OF TELMISARTAN WITH OTHER ANTIHYPERTENSIVE DRUGS

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ABSTRACT

Angiotensin II type 1 receptor antagonists (ARBs) are highly effective antihypertensive drugs used clinically for the management of hypertension, prevention of heart failure, and protecting diabetic nephropathy. Hypertension is the most prevalent lifestyle disease affecting the cardiovascular system and a major risk factor for stroke. The ARBs are very effective in decreasing elevated blood pressure (BP) to a normal level. Additionally, they do not have side effects like cough and angioedema, as shown by other classes of antihypertensive drugs like angiotensin-converting enzyme inhibitors. This feature makes ARBs the most preferred therapeutic strategy for hypertension. Telmisartan is an ARB, approved by the Food and Drug Administration for the treatment of hypertension in 1998, and is proven to provide efficient and lasting BP control when compared to other agents. This review highlights several clinical trials carried out to compare the efficacy, safety, and tolerability of telmisartan with other antihypertensive agents.

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1. INTRODUCTION

Angiotensin II receptor blockers (ARBs) are highly prescribed antihypertensive medications. These drugs selectively and specifically prevent the action of angiotensin II. Angiotensin II is a potent vasoconstrictor peptide. This peptide has a plethora of physiological effects on blood pressure (BP) and its regulation. ARBs are becoming more popular for the treatment of hypertension because they are effective and very well tolerated. [1] Antihypertensive agents differ in

their ability to control 24 h BP. Ideally, antihypertensive therapy should maintain control of BP throughout the 24 h dosing cycle and especially in the last 6 hours of the cycle. [2]

Telmisartan is a nonpeptide type of drug. It is a very potent blocker of the angiotensin II type-1 (AT1) receptor. Being a long-lasting antagonist of the AT1 receptor, telmisartan is clinically used for the treatment of essential hypertension. It is a selective blocker of the AT1 receptor and prevents activation of the receptors by angiotensin II. Telmisartan does not interact with other receptors involved in cardiovascular regulation, thus offering a selective action without significant adverse effects that generally arise due to the non-specific interaction of drugs with non-target receptors. Telmisartan is a poorly watered drug. It has a high volume of distribution. These two properties indicate that telmisartan will have good permeability characteristics and will have clinical benefits due to its lipophilicity. [3]

Telmisartan was found to be effective in controlling BP throughout the 24 hand during the early morning, probably due to the longer duration of action resulting from a high volume of distribution, which is sustained throughout the 24 h dosing period. [2,4] Several clinical studies that compared the safety, efficacy, and tolerability of telmisartan are discussed below.

2. Comparison of pharmacokinetic parameters of ARBs

Most clinically used ARBs have common molecular structures resembling the first marketed ARB losartan. However, small structural changes have resulted in a significant change in their lipophilicity, protein-interaction, and pharmacokinetics. [5] Various pharmacokinetic parameters for telmisartan and other ARBs are tabulated in table 1.

Table 1. Angiotensin II receptor blockers (ARBs) and their pharmacokinetic prpoerties.[5,6]

Pharmacokinetic parameters for various Angiotensin II Receptor Antagonists							
Pharmacokinetic parameter	Losartan	Valsartan	Irbesartan	Candesartan	Eprosartan	**Telmisartan**	Olmesartan
T_{max} (h)	3-4	2-4	1.5 -2	3-4	1-2	**0.5-1**	1-2
$T_{1/2}$ (h)	6-9	6	11-15	9	5-9	**24**	13
V_d (L)	12	17	53-93	5-15	308	**500**	17
Prodrug	Yes	No	No	Yes	No	**No**	Yes
Bioavailability (%)	33	25	60-80	15	13	**42-58**	26
CYP-450 interaction	Yes	No	Yes	No	No	**No**	No
Effect of food on absorption	Decrease by 10 %	Decrease by 40 -50 %	None	None	Decrease by 25 %	**Decrease by 10-20%**	None
Renal clearance (% Oral dose)	10	13	20	33	7	**<1%**	35-50%

It can be concluded that among all the ARBs, telmisartan has a rapid onset of action and longer half-life due to the high volume of distribution. Therefore, telmisartan is suitable for once-a-day oral administration. [6] It also offers additional benefits like no interaction cytochrome P-450 pathway and minimal renal clearance. Since its introduction into clinical practice, telmisartan has been compared with other ARBs as well as other antihypertensive drugs for safety, efficacy, and tolerability.

Here are a few comparative clinical studies involving telmisartan.

3. COMPARATIVE CLINICAL STUDIES

3.1. Morning *versus* evening dosing of telmisartan

Several studies have demonstrated the difference between morning dosing and evening dosing for several ARBs. Due to diurnal variations in the hormonal levels, the difference in the pharmacokinetics and pharmacodynamics is observed depending on the dosing time of an antihypertensive drug. To determine the antihypertensive efficacy of the telmisartan, a prospective trial was carried out in Spain. Clinicians compared the BP data of 48 h ambulatory BP in patients with essential hypertension. Telmisartan was administered as a single drug either in the morning after awakening from night-time sleep or at bedtime. The treatment was continued for three months, and thereafter the data of BP was analyzed. The dose of telmisartan was 80 mg/d. Once-a-day monotherapy of telmisartan efficiently and similarly reduced BP for the entire 24 h in both the patterns of dosing. However, bedtime administration of telmisartan was more efficient in reducing nocturnal BP and, thus, significantly increased the sleep time–the relative decline of BP. [1] Moreover, the number of patients with a non-dipper BP pattern at baseline was unaltered after ingestion of telmisartan on awakening but significantly reduced when the medication was ingested at bedtime. This may be clinically relevant because, although the mechanism underlying the lack of nocturnal decline in BP is unclear, no dipping has been related to an increase in end-organ injury and cardiovascular events. Moreover, night-time BP seems to be a better predictor of cardiovascular mortality than the diurnal or 24 h BP means. [7]

3.2. Telmisartan *versus* other ARBs

3.2.1. Telmisartan *versus* Olmesartan

An open-label prospective crossover study was carried out in Japanese hypertensive patients having type-2 diabetes mellitus. Effects of telmisartan were compared with that of olmesartan. [7] Dose of telmisartan and olmesartan was 40 and 20 mg/day, respectively. Olmesartan lowered mean systolic and diastolic BP more significantly than telmisartan in 8 weeks of treatment. Both the groups showed similar results for metabolic parameters, including HbA1c and adiponectin. The decreases in serum interleukin-6 and highly sensitive C-reactive protein were more significant in olmesartan treatment. This indicates that olmesartan has more potent anti-inflammatory effects. Olmesartan also had a more significant effect on lowering arterial BP in type-2 diabetes mellitus patients having hypertension.[7] Later on, in another study, the effects of telmisartan and olmesartan were compared in 20 hypertensive Japanese patients with chronic heart failure and metabolic syndrome. In contrast to the previous study, this study showed that telmisartan had more beneficial effects on glucose and lipid profiles in patients with relatively high HbA1c, serum total and low-density lipoprotein cholesterol, and triglyceride levels. It was concluded that telmisartan was more beneficial than olmesartan for controlling BP in the early morning, as well as for improving glucose and lipid profiles in patients with hypertension, chronic heart failure, and metabolic syndrome. [8]

3.2.2. Telmisartan *versus* Losartan

In a prospective meta-analysis of data from two randomized, double-blind, double-dummy, titration-to-response studies, the ability of telmisartan and losartan to reduce mean diastolic BP over the last six h of the 24 h dosing interval, measured using ambulatory BP monitoring, was compared. [9] The study was conducted in USA and Europe in patients with mild-to-moderate hypertension. After a 4-week placebo run-in period, patients received

once-daily telmisartan 40 mg or losartan 50 mg. Uptitration after four weeks of treatment to telmisartan 80 mg or losartan 100 mg once daily, respectively, was performed if seated diastolic BP was 90 mm of Hg or higher. The 24 h profiles of ambulatory systolic BP hourly mean reductions were similar to those for diastolic BP. Both telmisartan and losartan showed good safety and tolerability profile. It was concluded that telmisartan 40 or 80 mg is superior to losartan 50 or 100 mg. Because telmisartan controlled diastolic BP at the end of the 24 h dosing interval and also controlled systolic BP at the end of the dosing interval. [9]

3.2.3. Telmisartan *versus* Olmesartan *versus* Losartan

Hypertension in India is rising. There is about a 25% increase in the population with hypertension in urban areas, whereas rural areas have 10% of the population being affected. Therefore, a study was carried out on Indian stage I hypertensive patients. The efficacy and tolerability of losartan, telmisartan, and olmesartan were analyzed in an open-label, parallel study. [10] All the three study drugs were well tolerated, and no treatment-related serious adverse events were reported. The patients experiencing treatment-related adverse events were 5% in the olmesartan (headache), 5.2% in the telmisartan (dizziness) group, and none in the losartan group. It was concluded that olmesartan was more effective in reducing BP in stage I hypertensive patients; however, telmisartan had more favorable effects on lipid profile. Serum triglycerides, total cholesterol, and low-density lipoprotein cholesterol were significantly decreased in telmisartan treated patients. [10]

3.3. Telmisartan *versus* other antihypertensive drugs

3.3.1. Telmisartan *versus* Enalapril

In a randomized, double-blind, parallel-group study in Taiwanese patients (n=147) with mild-to-moderate essential hypertension, the efficacy, and tolerability of once-daily telmisartan 40 mg were compared with that of enalapril 10 mg. [11] Six weeks of therapy was well tolerated in both the groups, however, telmisartan was more effective than the ACE inhibitor enalapril in reducing trough seated diastolic BP. The incidence of increased cough was markedly lower with telmisartan than with enalapril, indicating the superior therapy with telmisartan. [11] Earlier, an eight weeks clinical trials in patients with severe hypertension has proved that supine diastolic BP control was achieved in 55% and 35% of the patients on the telmisartan and enalapril regimens, respectively.[12]

3.3.2. Telmisartan *versus* Lisinopril

Telmisartan was compared with lisinopril in a year-long randomized, multicenter, double-blind, dose-titration study in patients with mild-to-moderate essential hypertension (n=578). [13] The monotherapy and also the combination therapy with hydrochlorothiazide were compared for both the drugs. Treatment-related side effects occurred in fewer telmisartan-treated patients (28%) than in lisinopril-treated patients (40%). At the end of the titration period, diastolic BP control was achieved on monotherapy by 67% and 63% of the telmisartan and lisinopril patients, respectively. At the end of the maintenance period, supine diastolic BP was controlled in 83% and 87% of the telmisartan and lisinopril patients, respectively. This study concluded that telmisartan is extremely effective in the treatment of mild-to-moderate hypertension both as monotherapy and combination with hydrochlorothiazide and is at least comparable in efficacy to lisinopril with a better tolerability profile as observed from reduced incidence of adverse events.[13]

3.3.3. Telmisartan *versus* Amlodipine *versus* Ramipril

A clinical study compared to therapy of telmisartan, amlodipine, and ramipril in patients (n= 18, 22, and 17 respectively) with mild-to-moderate hypertension therapy. The analytical parameters were antihypertensive

effects and the duration of action. For the same ambulatory, BP monitoring was carried out. [14] Telmisartan and amlodipine showed a similar clinical response in reducing blood pressure. The results were not statistically different for ambulatory BP during daytime and night-time when the treatment was given for two months. Ramipril provided significant reductions in ambulatory systolic and diastolic BP from 2-6 h post-dose (peak effect), but it failed to induce significant reductions in mean daytime and night-time ambulatory BP. The response was more effective for ambulatory BP when the treatment was given with telmisartan and amlodipine. This effect was attributed to the significantly elevated activity of plasma renin. Ramipril could show an increase in renin activity during the first four h of the administration interval. [14]

4. CONCLUSION

In conclusion, treatment with telmisartan for mild to moderate hypertension showed similar efficacy when compared to that of enalapril, lisinopril, ramipril, and amlodipine. Treatment with telmisartan showed better tolerability as there were fewer incidences of adverse events compared to other antihypertensive medications. When compared with the other ARBs, it was superior to losartan and equally effective to olmesartan. Efficacy data are conflicting when telmisartan and olmesartan therapy has been compared in patients with comorbidity.

References

1. Hermida RC, Ayala DE, Fernandez JR, Calvo C. Comparison of the efficacy of morning versus evening administration of telmisartan in essential hypertension. *Hypertension.* 2007;50(4):715-722.
2. Akhrass PR, McFarlane SI. Telmisartan and cardioprotection. *Vasc Health Risk Manag*. 2011;7:677-683.
3. Wienen W, Entzeroth M, van Meel JC, et al. A review on telmisartan: a novel, long-acting angiotensin II-receptor antagonist. *Cardiovascular drug reviews*. 2000;18(2):127-154.
4. Williams B, Lacourcière Y, Schumacher H, Gosse P, Neutel JM. Antihypertensive efficacy of telmisartan vs ramipril over the 24-h dosing period, including the critical early morning hours: a pooled analysis of the PRISMA I and II randomized trials. *Journal of Human Hypertension.* 2009;23(9):610-619.
5. Michel MC, Foster C, Brunner HR, Liu L. A systematic comparison of the properties of clinically used angiotensin II type 1 receptor antagonists. *Pharmacological reviews*. 2013;65(2):809-848.
6. White WB. Comparative effects of telmisartan in the treatment of hypertension. *J Clin Hypertens (Greenwich).* 2002;4(4 Suppl 1):20-25.
7. Nakayama S, Watada H, Mita T, 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: official journal of the Japanese Society of Hypertension.* 2008;31(1):7-13.
8. Sasaki T, Noda Y, Yasuoka Y, et al. Comparison of the effects of telmisartan and olmesartan on home blood pressure, glucose, and lipid profiles in patients with hypertension, chronic heart failure, and metabolic syndrome. *Hypertension research: official journal of the Japanese Society of Hypertension.* 2008;31(5):921-929.
9. Smith DH, Cramer MJ, Neutel JM, Hettiarachchi R, Koval S. Comparison of telmisartan versus losartan: a meta-analysis of titration-to-response studies. *Blood pressure monitoring*. 2003;8(3):111-117.
10. Kalikar M, Nivangune KS, Dakhale GN, et al. Efficacy and Tolerability of

Olmesartan, Telmisartan, and Losartan in Patients of Stage I Hypertension: A Randomized, Open-label Study. *Journal of pharmacology & pharmacotherapeutics*. 2017;8(3):106-111.

11. Chen JH, Cheng JJ, Chen CY, et al. Comparison of the efficacy and tolerability of telmisartan 40 mg vs. enalapril 10 mg in the treatment of mild-to-moderate hypertension: a multicentre, double-blind study in Taiwanese patients. *International journal of clinical practice Supplement*. 2004(145):29-34.
12. Neutel JM, Smith DH, Reilly PA. The efficacy and safety of telmisartan compared to enalapril in patients with severe hypertension. *International journal of clinical practice*. 1999;53(3):175-178.
13. Neutel JM, Frishman WH, Oparil S, Papadimitriou V, Guthrie G. Comparison of telmisartan with lisinopril in patients with mild-to-moderate hypertension. *American journal of therapeutics*. 1999;6(3):161-166.
14. Poirier L, de Champlain J, Larochelle P, Lamarre-Cliche M, Lacourcière Y. A comparison of the efficacy and duration of action of telmisartan, amlodipine and ramipril in patients with confirmed ambulatory hypertension. *Blood pressure monitoring*. 2004;9(5):231-236.