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Original Research Article

Comparative Study of Efficacy and Safety of Ramipril and Telmisartan on Serum Electrolytes in Newly Diagnosed Hypertensive Patients

Krishna Singh[1], Rahul Vaish[2], Ashwani Kumar Gupta[3]

[1]Assistant Professor, Department of Pharmacology, Hind Institute of Medical Sciences, Barabanki, Uttar Pradesh

[2]Senior Resident, Department of Pharmacology, Hind Institute of Medical Sciences, Barabanki, Uttar Pradesh

[3]Professor and Head, Department of Pharmacology, DR BR Ambedkar State Institute of Medical Sciences, Mohali, Punjab

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Corresponding Author: Dr. Krishna Singh

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Abstract:

Introduction: ACEIs (angiotensin converting enzyme inhibitor) and ARBs (angiotensin II receptor blockers) are two medications that are frequently recommended to treat heart conditions and hypertension. It is now crucial to assess and investigate into how these medications affect the variations in serum electrolytes.

Objective: To compare the effects of Ramipril and Telmisartan on blood pressure, serum potassium and serum sodium.

Materials and Methods: The prospective study, which lasted 24 weeks and involved patients in the age range of 30 to 60 who had recently been diagnosed with grade 1 hypertension, was carried out at the Department of Pharmacology in collaboration with the Department of Cardiology at a tertiary care teaching hospital. A total of 120 patients completed the research. According to randomization, patients were instructed to take either Ramipril 2.5 mg (Group 1, n = 58) or Telmisartan 40 mg (Group 2, n = 62). The student's t-test is used for statistical analysis, and all data are expressed as mean ±SD.

Results: At the fourth follow-up visit, or 24 weeks, there is a significant ($p<0.001$) decrease in mean SBP and mean DBP compared to the baseline visit for both groups 1 (Ramipril) and 2 (Telmisartan). However, when group 1 and group 2 are compared at the fourth visit, there is no statistically significant difference in mean SBP and mean DBP ($p>0.05$). In relation to serum electrolytes, there was no significant difference between baseline and fourth visit in group 1 in serum potassium (4.00 ± 0.54 to 4.07 ± 0.53) and serum sodium (139.00 ± 5.67 to 138.3 ± 5.17). Similarly, between the baseline visit and the fourth visit in group 2, there was also not a significant difference in the serum potassium (4.15 ± 0.55 to 4.17 ± 0.52) or sodium (137.74 ± 5.41 to 137.45 ± 7.74) ($p>0.05$). Additionally, it was found that there was no statistically significant difference between the two groups' mean serum potassium and mean serum sodium at the fourth visit ($p>0.05$).

Conclusion: Our study's conclusion is that the antihypertensive efficaciousness of Telmisartan and Ramipril as monotherapy is nearly equal and regarding safety the both medications have minimal effects on serum potassium and sodium levels. For a period of six months, it indicates a lower risk of cardiac and other issues associated to hyperkalemia and hyponatremia. But before prescribing the medication, especially to an elderly patient, one must carefully assess their comorbid illnesses, and should be closely monitored for potassium and sodium levels.

Keywords: Hypertension, Ramipril, Telmisartan, Serum Electrolyte, Serum Potassium And Serum Sodium.

Introduction

One of the main concerns is the rising incidence of hypertension in developing nations. Two thirds of hypertensive individuals reside in developing nations, according to latest estimates from the World Health Organization [1]. Angiotensin II receptor antagonists (ARBs) and angiotensin-converting enzyme inhibitors (ACEIs) are drugs that are mostly used to treat hypertension, congestive heart failure and diabetic nephropathy. In a variety of patients and situations, treatment with angiotensin-converting enzyme inhibitors (ACEIs) or angiotensin receptor blockers (ARBs) has been repeatedly demonstrated to lower the risk of renal and cardiovascular morbidity and mortality. [2,3] These advantageous effects are, at

least partially, mediated by how they affect albuminuria and blood pressure.

Prior studies have previously explored the correlation between increases in serum potassium and sodium caused by ACEIs or ARBs with cardiovascular morbidity or death. It has been reported that ACEI and ARB inhibit the expression of renin and the sodium channel in renal tubules. By inhibiting the sodium channel, these characteristics would reduce the absorption of sodium. [4] Reduced renal tubular potassium secretion and sodium reabsorption are the results of angiotensin II mediated aldosterone-releasing and vasoconstricting mechanisms, which are inhibited by ACEI and ARB [5].

Serum sodium concentrations below 135 mmol/L, or hyponatremia, are a highly frequent electrolyte problem that are linked to significant mortality and disability as well as increased morbidity, duration of hospital stay, and use of hospital resources [6]. The use of ARB and ACEI medications raises serum potassium levels, raising the possibility of hyperkalemia. Hyperkalemia can be fatal and can affect heart function. [7] According to a study by Lambers Heerspink HJ et al. [8] subjects with serum potassium levels between 4.0 and 4.5 mmol/l had the lowest risk of cardiovascular and renal events. This means that even slight variations in serum potassium levels above 5.0 mmol/l (4.5 mmol/l for renal outcomes) or below 4.0 mmol/l were linked to higher risks of cardiovascular or renal events. Nonetheless, because they don't often cause the same side effects as other antihypertensive medications, angiotensin-converting enzyme (ACE) inhibitors and angiotensin type 1 receptor blockers (ARBs) are well-liked among antihypertensive medications.

However, there is a dearth of information regarding the relative effects of monotherapy (Ramipril versus Telmisartan) on serum potassium and serum sodium, particularly in the Indian population. Thus, the study's objectives were to assess how Telmisartan and Ramipril affected newly diagnosed grade 1 hypertension patients' systolic and diastolic blood pressure as well as their serum potassium and sodium levels.

Materials and Methods

Study Design and Settings: This study was prospective in nature and was carried out at the Shri Ram Murti Smarak Institute of Medical Sciences, a tertiary care teaching hospital in Bareilly, Uttar Pradesh, in coordination with the Department of Cardiology.

Selection of Cases: Patients who met the inclusion criteria were enrolled in the study after receiving permission from the Institutional Ethical Committee and Scientific Review Committee (Ref. No. SRMSIMS 2016-17/67-E) and getting informed consent from the patients in a vernacular language.

Inclusion Criteria: Patients of any gender who met the following criteria were included in the study:

a) Aged between 30 and 60 years; b) Patients with Grade-1 hypertension, defined as systolic 140-159 mm Hg and/or diastolic 90-99 mm Hg.

Exclusion Criteria: Patients excluded who were a) under 30 years old or older, b) uncontrolled hypertension (systolic pressure >160 mm Hg and/or diastolic pressure >100 mm Hg), c) pregnant or nursing women, and d) patients with congestive heart failure, post myocardial infarction, unstable angina, malignant hypertension, hepatic and renal dysfunction and secondary hypertension e) Individuals consuming two or more antihypertensive medications.

Study population and Sample size: Following a total of 154 screenings, 133 individuals were randomly assigned to receive either ramipril 2.5 mg (Group 1, n = 65) or telmisartan 40 mg (Group 2, n = 68). Seven from the Ramipril group and six patients from the Telmisartan group were lost to follow-up. In the end, total of 120 patients, 58 in the Ramipril group and 62 in the Telmisartan group completed the research.

Study groups and treatment protocol:

Group – 1 (n=58): Prescribed tablet ramipril 2.5 mg, taken once daily in the morning.

Group – 2 (n=62): Prescribed tablet telmisartan 40 mg, taken once daily in the morning.

Study duration: This study duration was 14 months; every participant in the study had a 24-week participation period.

Study conduct: Each case had a comprehensive clinical examination, a detailed history, and laboratory investigations performed at the baseline visit, after the informed consent, measurements of blood pressure, serum electrolytes, lipid profiles, renal and liver function tests, and other parameters were taken in both groups before treatment in the Department of Cardiology.

Follow up period: For duration of 24 weeks, the patients were scheduled for follow-up visits every 6 weeks to have their systolic and diastolic blood pressure measured. The JNC 8 guidelines were followed to determine whether telmisartan and ramipril were effective. The reduction of SBP and DBP to the target level (SBP/DBP =<140/90 mm Hg) was used to measure the efficacy of both medications. If, at any follow-up visit, the patient's SBP was greater than 160 mm Hg or DBP was greater than 100 mm Hg, telmisartan was titrated to 80 mg and ramipril to 5 mg, respectively. At the

second visit, or 12 weeks, and the fourth visit, or 24 weeks, serum potassium and serum sodium were examined.

Statistical analysis: Data was statistically analyzed using Microsoft Excel (Windows 2010). Values obtained before and after treatment within the group were compared using a Paired Student's t-test; between-group comparisons were made using unpaired t-tests. The mean ±SD is used to express all data. Less than 0.05 two-tailed p values were regarded as statistically significant.

Results

Table 1: Patient demographics, baseline blood pressure, serum potassium, and serum sodium for Groups 1 and 2

Characteristics		Ramipril (n = 58) Group- 1	Telmisartan(n = 62) Group- 2	P – value
Age(in yrs)		53.67 ± 5.35	53.95 ± 4.67	0.50
Gender	Male	38	37	
	Female	20	25	0.637
BMI		23.69 ± 3.86	23.72 ± 3.18	0.96
Smoking Habit	Smoker	10	12	
	Non- Smoker	48	50	0.948
SBP (mmHg)		154.18 ± 4.58	153.32 ± 4.55	0.30
DBP (mmHg)		93.18 ± 3.12	93.56 ± 3.78	0.32
Serum Potassium(mg/dl)		4.00 ± 0.54	4.15 ± 0.55	0.13
Serum Sodium(mg/dl)		139.00 ± 5.67	137.74 ± 5.41	0.23

The values are given as mean ± SD.

Demographic data of patients: In both groups, every patient was less than 60 years of age. In group 1, the mean age of the patients was 53.67 ± 5.35 years, while in group 2, it was 53.95 ± 4.67 years. The two study groups in the current study were homogeneous at baseline in terms of the patients' age, gender, weight, height, BMI, smoking habit, BMI, SBP, DBP, and serum K+ and Na+ levels.

There was also no significant difference between the two groups (p>0.05) (Table 1).

Table 2: Mean systolic blood pressure (SBP) and mean diastolic blood pressure (DBP) of patients in groups 1 and 2 at baseline, first, second, third, and fourth follow-up visits.

No of Visits		Ramipril (n = 58) Group- 1	Telmisartan(n = 62) Group- 2	P – value
Base line visit	**SBP**	154.18 ± 4.58	153.32 ± 4.55	0.30
	DBP	93.18 ± 3.12	93.56 ± 3.78	0.32
First visit	**SBP**	153.01 ± 8.05	149.91 ± 7.32	0.02
	DBP	92.15 ± 7.01	88.06 ± 7.26	0.002
Second visit	**SBP**	147.71 ± 7.50	145.56 ± 7.36	0.17
	DBP	87.15 ± 7.61	85.64 ± 6.92	0.25
Third visit	**SBP**	142.06 ± 7.01	140.72 ± 6.26	0.27
	DBP	84.82 ± 7.00	83.95 ± 6.41	0.47
Fourth visit	**SBP**	138.87 ± 6.00	136.93 ± 7.85	0.12
	DBP	82.41 ± 7.26	81.75 ± 6.70	0.60

At the baseline visit, first visit, second visit, third visit, and fourth visit follow-up, there was no discernible difference in either SBP or DBP between the two groups (p>0.05).

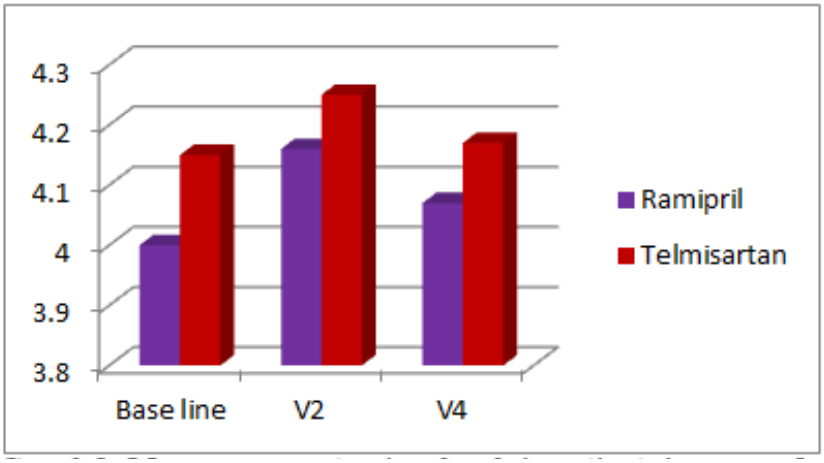
Blood pressure-Systolic BP (SBP) and Diastolic BP (DBP): When comparing the mean SBP at the fourth follow-up visit to the baseline visit, there was a significant (p<0.001) decrease in both group 1 (154.18 ± 4.58 to 138.87 ± 6.00) and group 2 (153.32 ± 4.55 to 136.93 ± 7.85). Similar to the baseline visit, there was a significant (p<0.001) decrease in mean DBP at the fourth visit for both groups 1 (93.18 ± 3.12 to 82.41 ± 7.26) and group 2 (93.56 ± 3.78 to 81.75 ± 6.70).

However, when group 1 and group 2 were compared at the fourth visit, there was no statistically significant difference in mean SBP and mean DBP (p>0.05) (Table 2).

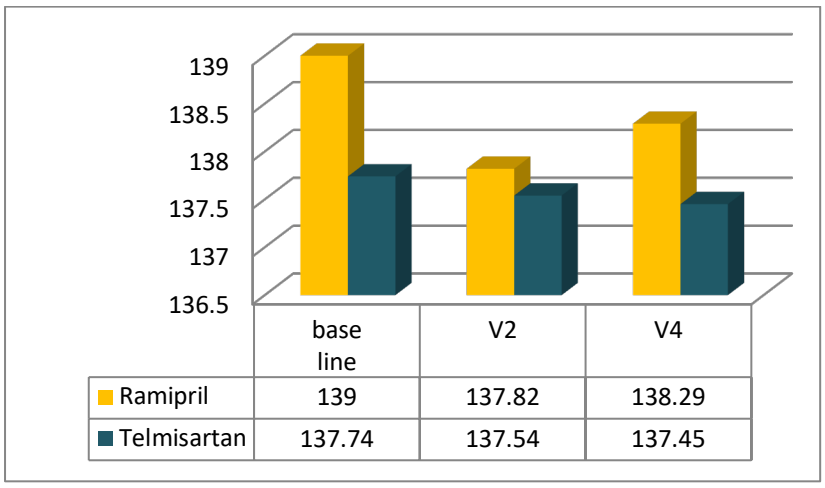
Table 3: Mean serum potassium and mean serum sodium of patients in groups 1 and 2 at baseline, second and fourth follow-up visits.

No of visits		Ramipril (n = 58) Group- 1	Telmisartan(n = 62) Group- 2	P –Value
Base line visit	Serum K^+	4.00 ± 0.54	4.15 ± 0.55	0.13
	Serum Na^+	139.00 ± 5.67	137.74 ± 5.41	0.23
Second visit	Serum K^+	4.16 ± 0.54	4.25 ± 0.47	0.29
	Serum Na^+	137.82 ± 5.16	137.54 ± 5.23	0.76
Fourth visit	Serum K^+	4.07 ± 0.53	4.17 ± 0.52	0.31
	Serum Na^+	138.3 ± 5.17	137.45 ± 7.74	0.35

Values given in milligrams/dl. Between the two groups, there was no significant change in serum potassium or sodium levels at the baseline, second, or fourth visit follow-up ($p>0.05$).



Graph 1: Mean serum potassium levels in patients in groups 1 and 2 at baseline, second and fourth follow-up visits



Graph-2: Mean serum sodium levels in patients in groups 1 and 2 at baseline, second and fourth follow-up visits

Table 4: Serum potassium and sodium levels in patients were compared between group 1 and group 2 between the baseline and fourth visits.

No of visits		Base line visit	Fourth visit	P –Value
Ramipril (n = 58) Group- 1	Serum K^+	4.00 ± 0.54	4.07 ± 0.53	0.12
	Serum Na^+	139.00 ± 5.67	138.3 ± 5.17	0.28
Telmisartan(n =62) Group-2	Serum K^+	4.15 ± 0.55	4.17 ± 0.52	0.73
	Serum Na^+	137.74 ± 5.41	137.45 ± 7.74	0.50

Serum electrolytes (serum potassium and serum sodium): At the fourth visit, the mean serum potassium and mean serum sodium for groups 1 and 2 were 4.07 ± 0.53, 4.17 ± 0.52, and 138.3 ±

5.17, 137.45 ± 7.74, respectively, shows that there was no statistically significant difference between the two groups' mean serum potassium and mean serum sodium Table 3 (Graph1,2). Additionally, between the baseline visit and the fourth visit in group 1, there was also no significant difference in serum potassium (4.00 ± 0.54 to 4.07 ± 0.53, p= 0.12) or sodium (139.00 ± 5.67 to 138.3 ± 5.17, p= 0.28). Likewise, there was no significant change in group 2's serum potassium (4.15 ± 0.55 to 4.17 ± 0.52, p=0.73) or sodium (137.74 ± 5.41 to 137.45 ± 7.74, p=0.50) between the baseline and fourth visits (Table 4) (Graph 1, 2).

Table 5: Percentage changes in serum potassium and sodium between baseline and subsequent visits for each group

% changes in K^+ and Na^+ from baseline visit to different visits		Ramipril (n = 58) Group- 1	Telmisartan (n =62) Group-2
Second visit	**% changes in K^+**	4.23 ± 8.72	3.16 ± 10.13
	% changes in Na^+	0.77 ± 2.54	0.11 ± 2.09
Fourth visit	**% changes in K^+**	2.14 ± 8.44	0.97 ± 9.41
	% changes in Na^+	0.41 ± 3.29	0.15 ± 2.45

The values are given as mean (%) ± S.D.(%).

Percentage changes in serum potassium and serum sodium: The mean serum potassium percentage increased in group 1 from the baseline visit to the fourth visit by 2.14 ± 8.44% and in group 2 by 0.97 ± 9.41%, respectively, but the results did not differ statistically. Between the first and second groups, the percentage decrease in mean serum sodium was 0.41 ± 3.29% and 0.15 ± 2.45%, respectively, from the baseline visit to the fourth visit; however, there were no significant differences observed (Table 5).

Discussion

The present study aimed to investigate the blood pressure-lowering effects of ramipril and telmisartan as monotherapy, as well as any changes in serum potassium and sodium levels during the course of the six-month treatment.

Effect on Blood Pressure (SBP and DBP): The primary finding of the current study was that, for patients with grade-1 hypertension, once-daily telmisartan and ramipril significantly reduced both SBP and DBP at the fourth visit when compared to the baseline visit in both groups. The telmisartan group experienced a greater reduction in blood pressure than the ramipril group, but there was no statistically significant difference in blood pressure reduction between the two groups, indicating that both medications are equally effective and safer in terms of their antihypertensive effects. It should be mentioned that the standard initial dosage for the treatment of hypertension is 40 mg of telmisartan.

The recommended starting dose of ramipril is 2.5 mg; however, many patients did not achieve adequate control of their blood pressure during the follow-up period, which is defined as a blood pressure of ≥ 160/90 mmHg. Of these patients, 44 out of 58 received 5 mg of ramipril during follow-up visits, and 14 patients in group 1 continued to take 2.5 mg of ramipril for six months. Similarly, in group 2, 45 patients remained to receive 40 mg of telmisartan for six months, whereas 17 (27.41%) of the 62 patients received 80 mg during follow-up visits. The present study's findings coincide with earlier research by J Petrovic et al [9] and Christian Delles et al [10], which also shown no discernible variation in blood pressure values between the telmisartan and ramipril groups. With cardiovascular events following a similar circadian rhythm and an increase in incidence linked to the early morning blood pressure surge, the extended action of telmisartan may theoretically offer advantages in preventing these events. [11,12].

Effect on serum electrolytes: Our investigation revealed that when comparing the mean serum potassium and mean serum sodium of the two groups to their respective baseline visits on the second and fourth visits (p>0.05), there was no significant difference observed in either group during monotherapy with ramipril and telmisartan. Little variations in serum potassium and serum sodium levels were observed, which may have been related to the effects of ramipril [13]. However, as has been observed in other similar studies, there was no significant difference in mean serum potassium and serum sodium after six months between the ramipril and telmisartan groups. [14]

The results of this study showed that among patients using ramipril and telmisartan for six months, neither hyperkalemia nor hyponatremia occurred. But this differs from previous studies13. A study on patients receiving losartan had also reported the occurrence of hyponatremia at a mean age of 76.4 years indicated that substantial fall in the serum sodium level. [15] This finding may be explained by variations in the kinetics and dynamics of medications in older people.

According to a study by Aranda P et al. [16], there was not a significant change in the S. potassium level. But unlike this retrospective observational cohort analysis by Sadjadi SA et al. [17] the prevalence of hyperkalemia was compared in participants on ARBs and ACEIs. 20.4% of

patients taking ACEIs and 31.0% of patients taking ARBs had hyperkalemia (>5 mEq/l). Among ACEI users, 0.8% had severe hyperkalemia (6 mEq/l or greater), while 2.8% used ARBs. Hyperkalemia was substantially correlated with diabetes mellitus, blood glucose, creatinine, and estimated GFR in univariate logistic regression studies. In the ONTARGET trial, this specifically compared ramipril and telmisartan in terms of reducing cardiovascular-related death and morbidity in patients with vascular disease or high-risk diabetes. The proportion of patients in the ramipril and telmisartan groups who experienced a rise in potassium levels of more than 5.5 mmol/l was 3.3% and 3.4%, respectively [18,19].

According to these earlier studies, conditions such as established atherosclerotic vascular disease, diabetes mellitus with end-organ damage, higher doses of ramipril and telmisartan for moderate to severe hypertension with longer duration or as an adverse effect of other certain medications can cause serum sodium levels to fall or potassium levels to rise. This could possibly be because, in comparison to other age groups, cardiovascular disorders and incidence of hyponatremia or hyperkalemia are more common in the elderly specially those over 60 years and as a result, a higher number of the older population is using medication.

Conclusion

Our study's conclusion is that the antihypertensive efficaciousness of telmisartan and ramipril as monotherapy is nearly equal and regarding safety the both medications have minimal effects on serum potassium and sodium levels. For a period of six months, it indicates a lower risk of cardiac and other issues associated to hyperkalemia and hyponatremia. But before prescribing the medication, especially to an elderly patient, one must carefully assess their comorbid illnesses, and should be closely monitored for potassium and sodium levels.

Limitations: We can better generalize the study's findings and improve its power by extending the study's duration and sample size.

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