Original Research Paper

Medicine

A STUDY OF SERUM POTASSIUM LEVEL IN HYPERTENSIVE PATIENTS TREATED WITH RAMIPRIL VS TELMISARTAN

Gian Chand	Associate professor, Department of Medicine, Govt. Medical College, Amritsar.
Rabinder Kumar	Junior Resident, Department of Medicine, Govt. Medical College, Amritsar
Pritam Singh Sandhu	Professor, Department of Medicine, Govt. Medical College, Amritsar

ABSTRACT Hypertension is a major independent risk factor for coronary artery disease, stroke, heart failure, renal failure and peripheral arterial disease.[1] The two major classes of drugs that target the RAAS are the angiotensin converting enzyme inhibitors (ACEIs) and the selective angiotensin receptor blockers (ARBs).[2] Hyperkalemia is one of the important side effects of ACEIs/ARBs. Our study mainly aims to study serum potassium level and compare efficacy of BP lowering with ramipril and telmisartan in hypertensive patients at baseline, 1 week and 1 month. There was significant rise in serum potassium levels from baseline with both drugs but on comparison, no significant rise in serum potassium level was seen. There was significant fall in blood pressure with both drugs but telmisartan was more effective in lowering blood pressure as compared to ramipril.

KEYWORDS : ACEI angiotensin converting enzyme inhibitor, ARB- angiotensin receptor blocker, Hypertension

INTRODUCTION:
Globally, cardiovascular disease accounts for approximately 17 million deaths a year, nearly one third of the total.[3] Of these, complications of hypertension account for 9.4 million deaths worldwide every year.[4] Hypertension is responsible for at least 45% of deaths due to heart disease (total ischemic heart disease mortality) and 51% of deaths due to stroke.[3] RAAS inhibitors, such as ACEIs, ARBs, aldosterone receptor antagonists (ARAs), and, direct renin inhibitors (DRIs) are associated with an increased risk of hyperkalemia.[5] The incidence appears to be relatively common in those with renal insufficiency but there are few reports that have correlated ACEIs/ARBs with hyperkalemia in patients with normal renal functions. Serum potassium monitoring shortly after initiation of therapy can assist in preventing hyperkalemia.[6]

MATERIALS AND METHODS:
Ethics: Approval of institutional thesis and ethical committee was granted before initiating the present prospective comparative study.

Study Design: This was a prospective comparative study done on 100 patients of primary hypertension aged 30-65 years attending Guru Nanak Dev Hospital, Amritsar.

Inclusion criteria: Diagnosed cases of primary hypertension aged between 30 to 65 years.

Exclusion criteria: Secondary hypertension, diabetic nephropathy, drug allergy to ACEIs/ARBs, renal insufficiency (serum creatinine >1.5), Age > 65 years and <30 years, congestive cardiac failure, patients on diuretics, heparin, cyclosporine, ketoconazole, tacrolimus, trimethoprim, pentamidine, beta-blockers

All the study subjects were then subjected to ECG, FBS, RBS, blood urea, Serum creatinine, S. Na[+], S. K[+], lipid profile.

STATISTICS:
For the purpose of making comparisons, the study population was divided into two groups. Group 1 was started on tablet telmisartan 40 mg once daily and Group 2 was started on ramipril 5 tablet mg once daily. Patients were followed after 1 week and 1 month of

therapy and blood pressure, ECG, serum potassium level and serum creatinine level were measured on every follow up. One way x^2-test (Chi-square test) and paired t test was applied to calculate p values. Statistical significance was defined as $p<0.05$.

	GROUP 1	GROUP 2	P value
Number of patients (M/F)	50 (31/19)	50 (30/20)	-
Age (in years)	51.94	52.16	0.8318
FBS (mg/dL)	90.2	90.3	0.6939
Serum creatinine (mg/dL)	1.09	1.03	0.0573
Serum Na^{+} (mEq/L)	139.58	139.28	0.5341
Serum K^{+} (mEq/L)	4.22	4.18	0.5609
Serum cholesterol (mg/dL)	178.94	177.44	0.8177
Serum triglyceride (mg/dL)	185.08	186.18	0.8491
Serum HDL (mg/dL)	43.04	41.43	0.2087
Serum LDL (mg/dL)	98.88	98.56	0.9857

TABLE 1 BASELINE CHARACTERISTICS BETWEEN TWO GROUPS

RESULTS :
In group 1, there were 31 males and 19 females while in group 2, there were 30 males and 20 females. The mean age in group 1 was 51.94 years and in group 2 was 52.16 years. On follow up at 1 week, the mean fall in SBP/DBP in group 1 was 7.04/5.04 mmHg (p value= 0.0001/0.0001) and in group 2 was 6.00/4.08 mmHg (p value= 0.0001/0.0001) and at 1 month the mean fall in SBP/DBP in group 1 was 9.52/7.16 mmHg (p value = 0.0001/0.0001) and in group 2 was 7.68/5.28 mmHg (p value =0.0001/0.0001). There was significant fall in SBP/ DBP from baseline in both groups at 1 week and at 1 month but on comparison, telmisartan was more effective than ramipril in lowering blood pressure at 1 week (p value= 0.0016/0.0141) and at 1 month (p value= 0.0001/0.0001). The mean rise in serum potassium level from baseline at 1 week was 0.226 mEq/L in group 1 (p value= 0.0011) and 0.248 mEq/L in group 2 (p value= 0.0008) and at 1 month was 0.354 mEq/L in group 1 (p value= 0.0001) and 0.356 mEq/L in group 2 (p value= 0.0001) which was statistically significant but on comparison, there was no statistically significant difference between two groups at 1 week (p value= 0.3268) and at 1 month (p value= 0.9008). The mean rise in serum creatinine from baseline at 1 week in group 1 was 0.024 mg/dl and in group 2 was 0.122 mg/dl and at 1 month in group 1 was 0.008 mg/dl and in group

2 was 0.03 mg/dl. On comparison, there was no statistically significant difference between two groups (p value= 0.2282).
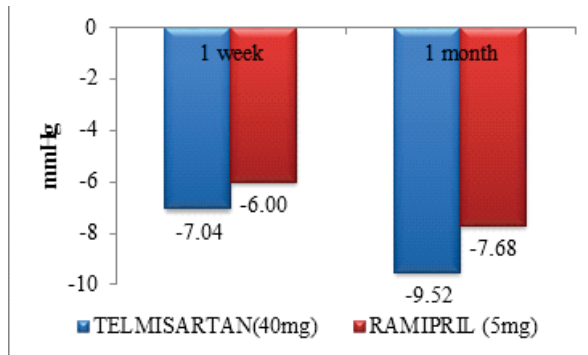

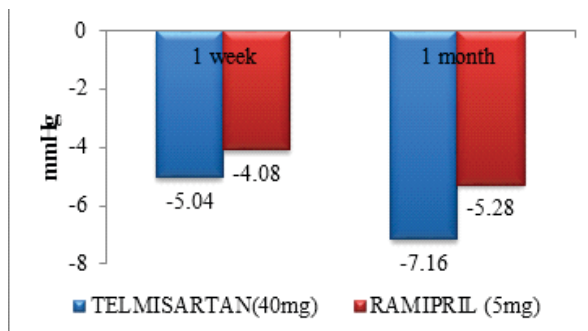**FIG1. COMPARISON OF MEAN FALL IN SBP**

FIG. 2 COMPARISON OF MEAN FALL IN DIASTOLIC BLOOD PRESSURE
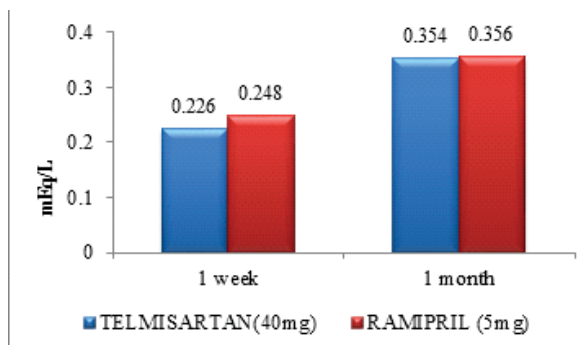

FIG. 3 COMPARISON OF MEAN RISE IN SERUM POTASSIUM LEVEL

DISCUSSION

Renin angiotensin aldosterone system (RAAS) is an important contributor to the maintenance of blood pressure. Two major classess of drugs that act on RAAS are angiotensin converting enzyme inhibitors (ACEIs) / angiotensin receptor blockers (ARBs) that are among the first line drugs in the treatment of hypertension. [7] Hyperkalemia is one of the important side effects of ACEIs/ARBs. The present study was a prospective comparative study done on 100 newly diagnosed hypertensive patients, it mainly aims to study serum potassium level and compare efficacy of BP lowering with ramipril and telmisartan. The study population was divided into two groups, group 1 was started on telmisartan 40 mg once daily and group 2 was started on ramipril 5 mg once daily, patients were followed after 1 week and 1 month The mean rise in serum potassium level from baseline at 1 week was 0.226 mEq/L in group 1 (p value= 0.0011) and 0.248 mEq/L in group 2 (p value= 0.0008) and at 1 month was 0.354 mEq/L in group 1 (p value= 0.0001) and 0.356 mEq/L in group 2 (p value= 0.0001), there was significant rise in serum potassium levels from baseline at 1 week and at 1 month. But on comparison between two drugs, the rise in serum potassium

level was not significant at 1 week (p value= 0.3268) and at 1 month (p value= 0.9008). In the study done by Park I et al, serum potassium levels were measured after initiating ARBs, 5.3 % of patients developed hyperkalemia, which were frequently seen among patients with reduced GFR, congestive heart failure (CHF) or taking other interacting medication. 52.4% of all hyperkalaemic events occurred during the first week and around 80% of hyperkalemia occurred within 2 weeks.[8] In a study by Mcgill et al, the mean rise in serum potassium levels from baseline after 2 weeks of initiation of telmisartan 40 mg was 0.123 mEq/L, which was comparable to our study.[9] In a study by Bakris et al, the mean rise in serum potassium level after 1 month in ARB group was 0.1 mEq/L and in ACEI group, it was 0.3 mEq/L.[9] In the study done by Kumar P et al, the mean increase in serum potassium level at 9 months with telmisartan group was 0.140 mEq/L and with ramipril group was 0.142 mEq/L, there was no significant difference on comparison.[11]

On follow up at 1 week, the mean fall in SBP/DBP in group 1 was 7.04/5.04 mmHg (p value= 0.0001/0.0001). and in group 2 was 6.00/4.08 mmHg (p value= 0.0001/0.0001) ,there was significant fall in SBP/ DBP from baseline in both groups at 1 week but on comparison, telmisartan was more effective than ramipril in lowering blood pressure at 1 week (p value= 0.0016/0.0141). In study done by Raja M et al the mean fall in SBP/DBP at 1 week was 5.76/4.56 mmHg with telmisartan group and 6.6/4.44 mmHg with ramipril.[12]

At 1 month the mean fall in SBP/DBP in group 1 was 9.52/7.16 mmHg (p value= 0.0001/0.0001) and in group 2 was 7.68/5.28 mmHg (p value =0.0001/0.0001), there was significant fall in SBP/ DBP from baseline in both groups at 1 month but on comparison, telmisartan was more effective than ramipril in lowering blood pressure at 1 month (p value= 0.0001/0.0001). In another study by Heerspink HJ et al, the mean fall in SBP/DBP after 6 weeks in telmisartan group was 7.4/5.0 mmHg and in ramipril group was 6.4/4.3 mmHg, these results were comparable to our study results.[13]

CONCLUSION

Our chief observation in the present study was that in hypertensive patients with normal renal function treated with telmisartan (40 mg) or ramipril (5 mg), there was mild but significant rise in serum potassium levels from baseline. But on comparison between two drugs, the rise in serum potassium level was not significant, none of the patients developed hyperkalemia during the study period. There was significant fall in systolic blood pressure and diastolic blood pressure with both drugs but telmisartan was more effective in lowering systolic blood pressure and diastolic blood pressure as compared to ramipril.

REFERENCES:

1. Mackay J, Mensah GA, Mendis S, Greenlund K. The atlas of heart disease and stroke. Geneva: World Health Organization; 2004.
2. Unger T, Jakobsen A, Heroys J, Ralph A, Rees T, Shaw M. Targeting cardiovascular protection: the concept of dual renin–angiotensin system control. Medscape J Med. 2008;10:S4.
3. Causes of Death 2008: Data Sources and Methods. WHO; Geneva, Switzerland: 2011. Availableonline: http://www.who.int/healthinfo/global_burden_disease/cod_2008_sources_methods.pdf.
4. Lim SS, Vos T, Flaxman AD, Danaei G, Shibuya K, Adair-Rohani H et al. A comparative risk assessment of burden of disease and injury attributable to 67 risk factors and risk factor clusters in 21 regions, 1990-2010: a systematic analysis for the Global Burden of Disease Study 2010. Lancet. 2012;380(9859):2224-60
5. Rimmer JM, Horn JF, Gennari FJ. Hyperkalemia as a complication of drug therapy. Arch Intern Med. 1987;147(5):867-9.
6. Raebel MA. Hyperkalemia Associated with Use of Angiotensin-Converting Enzyme Inhibitors and Angiotensin Receptor Blockers. Cardiovascular Therapeutics. 2012;30:156–66.
7. James PA, Oparil S, Carter BL, Cushman WC, Dennison HC, Handler J, et al. Evidence-based guideline for the management of high blood pressure in adults: report from the panel members appointed to the Eighth Joint National Committee (JNC 8). J Amer Med Asso. 2014;311(5):507-20.
8. Park I, Sheen S, Yoon D, Lee S, Shin G, Kim H et al. Onset time of hyperkalaemia after angiotensin receptor blocker initiation: when should we start serum potassium monitoring? J Clin Pharm Ther. 2013;39(1):61-8.
9. McGill J, Reilly P. Telmisartan plus hydrochlorothiazide versus telmisartan or hydrochlorothiazide monotherapy in patients with mild to moderate hypertension: a multicenter, randomized, double-blind, placebo-controlled, parallel-group trial. Clin Ther. 2001;23(6):833-50.
10. Bakris GL, Weir MR. Angiotensin-converting enzyme inhibitor–associated elevations

in serum creatinine: is this a cause for concern? Arch Intern Med. 2000;160(5):685-93.

11. Kumar P, Kapoor AK, Singh HK, Kulshrestha M. Randomized, interventional, prospective, comparative study to evaluate the antihypertensive efficacy and tolerability of ramipril versus telmisartan in stage 1 hypertensive patients with diabetes mellitus. Internet Journal of Medical Update. 2015;10(1):15-25.

12. Raja M, Shukla AK, Mehani R, Agnihotri A. Comparative study of telmisartan and ramipril as an antihypertensive in mild to moderate hypertension. National Journal of Physiology, Pharmacy and Pharmacology. 2016;6(5):388-93

13. Heerspink HJ, Gao P, de Zeeuw D, Clase C, Dagenais GR, Sleight P, et al. The effect of ramipril and telmisartan on serum potassium and its association with cardiovascular and renal events: results from the ONTARGET trial. Eur J Prev Cardiol. 2014;21(3):299-309.