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A STUDY OF SERUM POTASSIUM LEVELS IN NEWLY DETECTED HYPERTENSIVE PATIENTS PUT ON ANGIOTENSIN CONVERTING ENZYME INHIBITORS: A ONE YEAR HOSPITAL BASED CROSS SECTION STUDY

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ABSTRACT **BACKGROUND AND OBJECTIVES:** Although deterioration of renal parameters in patients of renal insufficiency has been known and assessed, clinical significant cases of life threatening hyperkalemia in patients of normal renal function on ace-inhibitors needs to be assessed. Thus the objective of this study was to ascertain the level of rise of serum potassium levels from baseline in patients of hypertension with normal renal function put on ace-inhibitors over a duration of time (4 wks) and compare the dose of ace-inhibitor being used, the diabetic status of the patient and effect of baseline levels of serum potassium levels on such a rise in patients subjected to such a therapy.

METHOD: The present study was conducted on 50 newly detected patients of primary hypertension, either diabetic or non-diabetic visiting outpatient department as well as getting admitted in our hospital, detailed history, clinical examination and laboratory tests were done to each patient. The patient was put on Ace inhibitor of adequate dosage and asked to come for follow up after four weeks with Sr. K+ levels and ECG. The degree of rise of Sr. K+ levels from baseline was thus calculated.

RESULTS: 54% (27 patients) of the total patients were non diabetic and 46% (23 patients) were diabetic. 40 patients (80%) were in the age group of 51 – 65 yrs. In this study 77.77% of non- diabetics and 82.60 % of diabetics were in the age group of 51 – 65 yrs. Thus, a baseline of 3.5 – 4 mmol/L was present in 38% of patients, 4.1- 4.5 mmol/L in 46 % and 4.6-5 mmol/L in 16 % of total pts. In this study, hyperkalemia defined by S.K+ >5.5 mmol/L has been seen in none (0%) of the patients. Only Three patients in the study had 0.5 mmol/L rise of Sr. K+ levels from baseline. Conclusions: Our study concluded that in a patient with normal renal parameters defined by S. creatinine levels < 1.5 mg/dl, baseline Sr. K+ <5.4 mmol/L put on ACE-inhibitors the level of rise of potassium values is insignificant. However since this study had small sample size further studies are mandated.

KEYWORDS : hypertension, hyperkalemia, ace inhibitors, diabetes mellitus

INTRODUCTION:

Systemic hypertension is the most important modifiable risk factor for all-cause morbidity and mortality worldwide and is associated with increased probability of cardiovascular disease (CVD). Less than half of those with hypertension are aware of their condition, and many others are aware but not treated or unsatisfactorily treated, although successful management of hypertension reduces the global burden of disease and overall mortality. The aetiology of hypertension involves the complex interplay of environmental, pathophysiological factors as well as genetic predisposition **Oparil S, et al(2018).**[1] Detailed evaluation of hypertensive patients includes accurate standardized blood pressure (BP) measurement, assessing patients predicted risk of atherosclerotic CVD, evidence of target organ damage (TOD), detection of secondary causes of hypertension and presence of comorbidities, including CVD and kidney disease. Lifestyle changes, including dietary modifications and increased physical activity, are effective in lowering BP and preventing hypertension and its CVD sequelae. Pharmacological therapy is very effective in lowering BP and preventing CVD outcomes in most patients; first line antihypertensive medications include angiotensin-converting enzyme (ACE) inhibitors, angiotensin II receptor blockers, dihydropyridine calcium channel blockers and thiazide diuretics **James PA, et al (2014).** [2]Angiotensin-Converting Enzyme (ACE) inhibitors are the drug of choice in diabetes and have a huge role in the improvement of left ventricular hypertrophy (LVH), retinopathy and nephropathy due to uncontrolled hypertension. Although deterioration of kidney function tests in patients of renal insufficiency has been known, the cases of life threatening hyperkalemia in patients of normal renal function on ace- inhibitors has not been predicted extensively **Cordonnier DJ, et al (2001)[3].**

Shilpa Vijayakumar, et al (2019)[4] studied the major risk factors for development of hyperkalaemia are an estimated glomerular filtrationrate (eGFR) <45 mL/min/1.73m^2 and/or a serum potassium level on appropriate diuretics for kidney function of >4.5 mmol/L. Thus, in these settings, hyperkalaemia is a common complication of RAASi (renin-angiotensin aldosterone system inhibitor (includes ace inhibitors) therapy and is often a reason for their discontinuation or suboptimal dosing. However, these agents offer a proven mortality benefit, slow progression of kidney disease, and decrease risk of hospitalization in people with HF. With the current limitations for management of hyperkalaemia, there is a substantial gap between recommendations in treatment guidelines and everyday prescribing patterns for RAASi, given that the patients who would gain the greatest cardiovascular and renal benefit from these therapies are at the highest risk of developing hyperkalaemia. The fact that many clinical trials have specifically excluded high-risk patients (such as those with Stage 3b or higher CKD) furthers this therapeutic dilemma. Although deterioration of renal parameters in patients of renal insufficiency has been known and predicted, the sporadic cases of life threatening hyperkalemia in patients of normal renal function on ace- inhibitors has never been predicted and whether to stop or continue with ace inhibitors under different clinical scenarios.Thus the need of this study is to ascertain the level of rise of serum potassium levels from baseline in patients of hypertension with normal renal function put on ace-inhibitors over a duration of time and compare the effect of dose of ace-inhibitor being used, the diabetic status of the patient and effect of baseline levels of serum potassium levels on such a rise in patients subjected to such a therapy.**The objectives of the present study are: 1.**To study the outcome of Angiotensin converting enzyme (ACE) inhibitor administration on serum potassium levels. 2. To compare the level of rise of serum potassium of hypertensive diabetic patients with that of non-diabetic population who did not have nephropathy. 3. Effect of dose of ACE inhibitor used on rise of serum potassium levels. 4. Effect of baseline levels of serum potassium on degree of rise.

METHODS:

The present study was conducted on 50 NEWLY detected patients of primary hypertension, either diabetic or non-diabetic visiting outpatient department as well as getting admitted in Medicine Department of ASCOMS and Hospital, JAMMU during 1st November 2019 to 31st October 2020. It is a Cross-sectional study,50 NEWLY detected patients of primary hypertension visiting outpatient department as well as getting admitted in Medicine Department of ASCOMS and Hospital, Jammu who fulfilled the inclusion criteria and

were willing for follow up.The sample was calculated considering 80% of the average number of admissions as well as outpatient department patients over last three years taking into consideration the willingness of the patient for follow up.

Selection Criteria:

Inclusion Criteria - NEWLY diagnosed primary hypertensives.

Exclusion Criteria

1. Secondary hypertension
2. Diabetic nephropathy
3. Drug Allergy to ace inhibitors.
4. Renal insufficiency (creatinine >1.5) and Congestive cardiac failure. 5 Patients on diuretics (High ceiling and potassium sparing), NSAIDS.

Diagnostic Criteria: Patients with systolic blood pressure > 130 mm Hg and diastolic blood pressure > 80 mm Hg. Whelton PK, *et al.* (2017 ACC/AHA Guidelines).

Method Of Collection Of Data:

50 NEWLY detected Primary hypertensive patients irrespective of their diabetic status visiting outpatient department as well as those getting admitted in Medicine Department of ASCOMS and Hospital, Jammu were randomly screened. After applying the selection criteria patients were included. These study participants were informed in detail about the study, the need for follow up and a written informed consent was obtained from them. The study participants eligible for enrollment and who provided consent (Annexure II) for participation in the study were subjected to an interview for history, clinical examination and investigations which included baseline renal parameters. The patient was put on T. Ramipril of adequate dosage and asked to come for follow up after four weeks. The study of renal parameters, more importantly S. potassium levels were done at baseline and follow up. ECG readings at baseline and follow up at four weeks were also done. Meticulous care was done to measure the degree of rise of serum potassium levels from baseline. The rise of serum potassium levels thus measured was compared with the dose of ace-inhibitor being used, the diabetic status of the patient andbaseline levels of serum potassium levels. The patients were categorized into diabetic hypertensives and non-diabetic hypertensives. Thus an objective assessment was done to determine whether the rise of serum potassium levels on follow up was dependent on the patient being diabetic, whether the baseline levels of S. potassium made any difference to subsequent rise at follow up and whether the dose of ace-inhibitor determined the level of rise of S. potassium levels. The ACE-inhibitor being used was indicated for the patient's hypertensive status and no modification was done with regard to therapy to suit the study. The results were then analyzed.

RESULTS

Table No. 1:

DISTRIBUTION OF STUDY GROUP: A total of 50 sample cases were taken in the study. 29 patients (58%) were males and 21 patients (42%) were females. Out of the total of 50 patients. 40 patients (80%) were in the age group of 51 – 65 yrs similar to that in the general population of incidence of primary hypertension.

Age in years	No. of males (n=29)	No. of females (n=21)	Total
40-45	1	1	2
46-50	3	1	4
51-55	7	4	11
56-60	8	8	16
61-65	7	6	13
66-70	3	1	4

Table No. 2:

Distribution Of Total Patients According To Their Diabetic Status. Out of total cases, 27 pts (54%) were non diabetics and 23 pts (46%) were diabetics. So 21 of the 27 pts or 77.77 % of non-diabetics were in the age group of 51 – 65 yrs. Similarly 82.60 % of diabetics were in the age group of 51 – 65 yrs.

Age in years	Non- Diabetic (n=27)	Diabetic (n=23)	Total
40-45	1	1	2
46-50	3	1	4
51-55	6	5	11
56-60	8	8	16
61-65	7	6	13
66-70	2	2	4

Table No. 3: Distribution Of Hypertensive Males With Respect To Their Diabetic Status: Total Male patients – 29 (58 %), Diabetics – 12 (24%) of total, Non diabetics – 17 (34%) of total.

Age in years	Non- Diabetic	Diabetic	Total
40-45	1	0	1
46-50	2	1	3
51-55	4	3	7
56-60	4	4	8
61-65	4	3	7
66-70	2	1	3

Table No.4:

Distribution Of Hypertensive Females With Respect To Their Diabetes Status: . Total females – 21 (42%) of total. Non diabetic females – 10 (20 % of total) Diabetic females – 11 (22 % of total).

Age in years	Non- Diabetic	Diabetic	Total
40-45	0	1	1
46-50	1	0	1
51-55	2	2	4
56-60	4	4	8
61-65	3	3	6
66-70	0	1	1

Table No.5:

Distribution Of Patients With Respect To Serum Potassium Levels At Baseline: Baseline of 3.5 – 4 mmol/L was present in 38% of patients, 4.1- 4.5 mmol/L in 46 % and 4.6-5 mmol/L in 16 % of total pts.

Baseline Sr. K+ Level (mmol/L)	Males (n=29)	Females (n=21)	Total (n=50)
3.5-4.0	10	9	19
4.1-4.5	14	9	23
4.6-5.0	5	3	8

Table No.6:

Fragmentation Of Baseline S. Potassium Levels With Respect To Their Diabetic Status: Statistical analysis of distribution of patients with respect to their baseline levels gives a chi- square – 0.45 and P = 0.67. Thus the diabetic status of the patient and the baseline S. K^+ levels are independent of each other

Baseline Sr. K+	Non- Diabetic		Diabetic	
Level (mmol/L)	Males	Females	Males	Females
3.5-4.0	6	4	4	5
4.1-4.5	8	4	6	5
4.6-5.0	3	2	2	1

Table No.7:

Distribution Of Total Patients According To Rise Of S. K^+ Levels From Baseline At Follow Up Of 4 Weeks: In this table 18 % of total patients had a rise of Sr. K^+ of 0.1 mmol/L while 38% had a 0.2 mmol/L rise and 28% and 10 % had a rise of 0.3 mmol/L and 0.4 mmol/L respectively. Thus 76 % of total patients had a rise of 0.2 – 0.4 mmol/L of Sr. K^+ levels. The chi-square is 0.33 and P = 0.81 is not significant. Hence the diabetic status of patient is independent of the rise of Sr. K^+ at follow up.

Rise Sr. K+ from baseline (mmol/L)	Non- Diabetic	Diabetic	Total
0.1	6	3	9
0.2	10	9	19
0.3	6	8	14
0.4	4	1	5
0.5	1	2	3

Table No.8 Distribution of cases according to rise in S. Potassium on follow up among non diabetics: Out of the Total 27 pts (54 %) were non diabetics. Thus 74.07 % of non-diabetics have a rise of S. Potassium levels between 0.2 – 0.4 mmol / L from baseline at 4 weeks of follow up

Rise Sr. K+ from baseline (mmol/L)	Non- Diabetic (%)
0.1	22.22
0.2	37.04
0.3	22.22
0.4	14.81
0.5	3.7

Table No. 9:

Distribution Of Patients According To Rise Of S. Potassium Levels At Follow Up Of 4 Weeks Among Diabetics: Among a total of 23 diabetics (46% of total), 78.26 % have a rise of 0.2 – 0.4 mmol/L of S. Potassium at 4 weeks of follow up.

Rise Sr. K+ from baseline (mmol/L)	Diabetic (%)
0.1	13.04
0.2	39.13
0.3	34.78
0.4	4.35
0.5	8.7

Table No.10:

Distribution according to dosage of ace inhibitor (Tab. Ramipril) and the rise of S. K+ levels at follow up. Out of the total of 50 cases, 16 pts or 32 % were on 2.5mg/day of T. Ramipril 19 pts or 38 % were on 5 mg/day of T. Ramipril 15 pts or 30% were on 7.5mg/day of T. Ramipril. The above table has a chi-square of 0.53 and P = 0.76. Thus the rise of Sr. K+ from baseline is independent of dosage of T. Ramipril.

Sr. K+ rise from baseline in (mmol/L)	Pts on 2.5mg (in % of total patients)	Pts on 5 mg (in % of total patients)	Pts on 7.5mg (in % of total patients)	Total (n=50) (in % of total patients)
0.1	3	6	0	9
0.2	9	2	8	19
0.3	1	8	5	14
0.4	3	2	0	5
0.5	0	1	2	3

Table No.11:

Distribution of patients on Tab. Ramipril with respect to their diabetic status: Out of total of 27 non diabetics, 33.33% were on 2.5 mg, 29.62 % on 5 mg and 37.03 % on 7.5 mg. Out of 23 diabetics 30.43 % were on 2.5 mg, 47.82 % on 5mg and 21.73 % on 7.5 mg.

Dosage of Ramipril	Non diabetic (n=27) (in % of total non diabetics)	Diabetic (n=23) (in % of total diabetics)
2.5 mg	9	7
5 mg	8	11
7.5 mg	10	5

Table No.12:

Distribution of patients on T. Ramipril of various dosages at 4 weeks of follow up with respect to their rise from baseline and diabetic status: In the non-diabetic population 25.92 % of patients have 0.2 – 0.4 mmol / L rise of Sr. K+ levels on 2.5mg and 29.62 % of patients were on 5 mg, while the 7.5mg group has a 0.2 – 0.4 mmol/L rise in 37.03 % of patients. There is a rise of 0.2 – 0.4 mmol/L of Sr. K+ in 2.5mg, 5mg and 7.5mg in diabetic groups showing incidence of 30.43 %, 47.82 % and 21.73 % respectively.

Sr. K+ rise from baseline in (mmol/L)	Non diabetic (n=27) (in % of total non diabetics)			Diabetic (n=23) (in % of total diabetics)		
	2.5mg (in % of non diabetics)	5 mg (in % of non diabetics)	7.5mg (in % of non diabetics)	2.5mg (in % of Diabetic)	5 mg (in % of Diabetic)	7.5mg (in % of Diabetic)
0.1	2	4	0	1	2	0
0.2	4	1	5	5	1	3
0.3	0	2	4	1	6	1
0.4	3	1	0	0	1	0
0.5	0	0	1	0	1	1

Table No. 13:

Distribution of baseline sr. k+ levels and subsequent rise of S. K+ at follow up: Among patients with baseline of 3.5 – 4 mmol/L (89.47 %) have rise of Sr. K^+ between 0.2 – 0.4 mmol/L. Among baseline of 4.1 – 4.5 mmol/L and 4.6 – 5 mmol/L ranges there is a 0.2 – 0.4 mmol/L in 82.60 % and 62.50 % of patients respectively

	Rise of Sr. K+ from baseline in % of baseline ranges					Total
Baseline Sr. K+ ranges mmol/L	0.1	0.2	0.3	0.4	0.5	numbers
3.5-4.0	2	6	9	2	0	19
4.1-4.5	4	10	4	3	2	23
4.6-5.0	3	3	1	0	1	8

DISCUSSION:

ACE inhibitors have a wide range of use in clinical medicine. It has been estimated that ACE inhibitors accounted for 24% of the antihypertensive agents prescribed. In other conditions, such as congestive heart failure and diabetic nephropathy, they have been shown to improve important clinical outcomes **Pugh D(2020)**[5]. Hyperkalemia is a known complication of ACE inhibitors use. Hyperkalemia with such a use appears to be relatively low in patients with normal renal function but becomes increasingly common in those with renal insufficiency **Raebel, MA. (2012)**[6]. A total of 50 sample cases were taken in the study of which 29 patients (58 %) were males and 21 patients (32%) were females. Out of the total of 50 patients, 40 patients (80%) were in the age group of 51 – 65 yrs. similar to that in the general population of incidence of primary hypertension. Out of total cases, 27 patients (54%) were non-diabetics and 23 patients (46%) were diabetics. So 21 of the 27 non diabetics (77.77 %) were in the age group of 51 – 65 yrs. Similarly 82.60 % of diabetics were in the age group of 51 – 65 yrs. Total male patients were 29 (58% of total) out of which 12 patients (24% of total) were diabetics and 17 patients (34 % of total) were non-diabetics. Among total of 21 females, 20 % (10 patients) of entire study population were non diabetic and 22 % (11 patients) were diabetic. A baseline serum potassium of 3.5 – 4 mmol/L was present in 38% (19 patients), 4.1-4.5 mmol/L in 46% (23 patients) and 4.6-5 mmol/L in 16 % (8 patients) of total. Statistical analysis of distribution of patients with respect to their baseline levels gives a chi-square – 0.45 and P = 0.67. Thus the diabetic status of the patient and the baseline S. K^+ levels are independent of each other. In the present study conducted in 50 newly detected hypertensives, significant hyperkalemia defined by serum potassium levels >6.0 mmol/L has been seen in none (0%) of the patients. Only Three patients in the study had 0.5 mmol/L rise of Sr. K+ levels from baseline. This study also inferred that 18 % of total patients had a rise of Sr. K^+ of 0.1 mmol/L while 38% had a 0.2 mmol/L rise and 28% and 10 % had a rise of 0.3 mmol/L and 0.4 mmol/L respectively. Thus 76 % of total patients had a rise of 0.2 – 0.4 mmol/L of Sr. K^+ levels. The chi-square is 0.33 and P = 0.81 is not significant. Hence the diabetic status of patient is independent of the rise of Sr. K^+ at follow up. Also 82.73 % of non-diabetics and 78.25 % of diabetics had a rise of Sr. K+ levels between 0.2 – 0.4 mmol/L from baseline at 4 weeks of follow up. Out of the total of 50 cases, 16 patients (32%) were on 2.5mg/day, 19 patients (38%) were on 5 mg/day and 15 patients (30%) were on 7.5mg/day of T. Ramipril. This tabulation has a chi-square of 0.59 and P = 0.82 which is not significant indicating that the rise of Sr. K+ from baseline is independent of dosage of Ramipril. In the non-diabetic population 25.92 % of patients have 0.2 – 0.4 mmol / L rise of Sr. K+ levels on 2.5mg and 14.81 % of patients were on 5 mg, while the 7.5mg group has a 0.2 – 0.4 mmol/Lrise in 42 % of patients. There is a rise of 0.2 – 0.4 mmol/L of Sr. K+ in 2.5mg, 5mg and 7.5mg in diabetic groups showing incidence of 26.08 %, 34.78 % and 17.39 % respectively. From these data, the following is suggested. Serum potassium levels should be measured in all patients after beginning therapy with ACE inhibitors. Should mild hyperkalemia develop while receiving ACE inhibitors, patients younger than 70 years with normal renal function can safely continue to use the drug since the frequency of severe hyperkalemia is low and frequent monitoring is not required. Those patients with either of the factors predicting severe hyperkalemia warrant either judicious surveillance of potassium levels or reconsideration of the use of ACE inhibitor **Espinel E (2013)**[7]**.**

CONCLUSION:

The present study was conducted on 50 newly detected patients of primary hypertension, either diabetic or non-diabetic visiting outpatient department as well as getting admitted in Medicine Department of ASCOMS and Hospital during 1st November 2019 to 31st October 2020. The following were the observations of this study. Of the 50 sample cases males outnumbered females in this study where 29 patients (58%) were males and 21 patients (42%) were females. 54% (27 patients) of the total patients were non diabetic and 46% (23 patients) were diabetic. 40 patients (80%) were in the age group of 51 – 65 yrs. In this study 77.77% of non-diabetics and 82.60 % of diabetics were in the age group of 51 – 65 yrs. Thus, a baseline of 3.5 – 4 mmol/L was present in 38% of patients, 4.1- 4.5 mmol/L in 46 % and 4.6-5 mmol/L in 16 % of total pts. In this study, hyperkalemia defined by S.K+ >5.5 mmol/L has been seen in none (0%) of the patients. Only Three patients in the study had 0.5 mmol/L rise of Sr. K+ levels from baseline. Thus in a patient of normal renal function put on ACE-inhibitor the level of rise of potassium at follow up is insignificant. The level of rise of S.K+ at follow up was found to be independent of their baseline levels in patients on ACE-inhibitors. In other words patients

with higher baseline levels of Sr. K+ need not produce larger levels of rise of serum potassium. This study also concurred that 76% of total patient's had a rise of 0.2 –0.4 mmol/L of Sr. K+ levels at follow up of 4 wks which is insignificant. 74.07% were non diabetics and 78.26 % were diabetics. In this study 16 patients (32%) were on 2.5mg/day, 19 patients (38%) were on 5 mg/day and 15 patients (30%) were on 7.5mg/day of T. Ramipril. The level of rise of Sr. K+ levels was found to be independent of the dosage of ACE-inhibitor in use.

REFERENCES

1. Oparil S, Acelajado MC, Bakris GL, et al. Hypertension. Nat Rev Dis Primers. 2018;4:18014. Published 2018 Mar 22. doi:10.1038/nrdp.2018.14
2. James PA, Oparil S, Carter BL, et al. 2014 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). JAMA. 2014;311(5):507–520. doi:10.1001/jama.2013.284427.
3. Cordonnier DJ, Zaoui P, Halimi S. Role of ACE inhibitors in patients with diabetes mellitus. Drugs. 2001;61(13):1883-92. doi: 10.2165/00003495-200161130-00001. PMID: 11708761.
4. Vijayakumar S, Butler J, Anker SD. New treatments for hyperkalaemia: clinical use in cardiology. Eur Heart J Suppl. 2019 Feb;21(Suppl A):A41-A47. doi: 10.1093/eurheartj/suy031. Epub 2019 Feb 26. PMID: 30837804; PMCID: PMC6392415.
5. Pugh D, Gallacher PJ, Dhaun N. Management of Hypertension in Chronic Kidney Disease [published correction appears in Drugs. 2020 Sep;80(13):1381]. *Drugs*. 2019;79(4):365-379. doi:10.1007/s40265-019-1064-1
6. Raebel M.A., (2012), Hyperkalemia Associated with Use of Angiotensin-Converting Enzyme Inhibitors and Angiotensin Receptor Blockers. Cardiovascular Therapeutics, 30: e156-e166. doi:10.1111/j.1755-5922.2010.00258
7. Espinel E, Joven J, Gil I, et al. Risk of hyperkalemia in patients with moderate chronic kidney disease initiating angiotensin converting enzyme inhibitors or angiotensin receptor blockers: a randomized study. BMC Res Notes. 2013;6:306. Published 2013 Aug 1. doi:10.1186/1756-0500-6-306