

Comparative Study of Serum Potassium Level in Diabetic and Non-Diabetic Pre-Dialytic Chronic Kidney Disease Patients on Angiotensin Receptor Blockers Treatment

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ABSTRACT

Background: Angiotensin Receptor Blocker (ARB) drugs are widely used to reduce blood pressure among the predialytic diabetic and nondiabetic CKD (Chronic Kidney Diseases) patients. ARB usually increases serum K⁺ level. The aim of the present study is to compare the changes of serum potassium level in diabetic CKD patients to that of non-diabetic CKD patients who are on ARB treatment.

Materials and methods: This cross sectional comparative study was done on 100 patients of diabetic and non diabetic CKD (50 in each group) admitted in the Nephrology and Medicine wards of Chittagong Medical College Hospital, over a period of 6 months from 1st January 2012 to 30th June 2012. Inclusion criteria was all the CKD patients admitted in ward who gave consent for study. Exclusion criteria was patients who were on renal replacement therapy (Dialysis or Renal transplantation) Pattern of serum potassium level were analyzed in relation to different doses and formulation of ARB in both diabetic and non diabetic CKD patients. Data was analyzed by SPSS-15.

Results: Among the 100 patients, three types of ARB were used by both groups Losartan (70%), Olmesartan (22%) and Valsartan (8%). Maximum patients were found in stage 5 (77%) of CKD, 11% were in each stage 4 and 3 and 1 patient in stage 2. Losartan users had low serum potassium (4.79 mg/dl) than Valsartan users (5.56 mg/dl). Higher serum potassium was found in higher different stages of CKD patients. In both diabetic and non diabetic groups Valsartan users had more serum potassium than Losartan or Olmesartan users. Non diabetic (Stage 5) CKD patients had higher serum potassium than diabetic (Stage 5) patients. In all three ARB groups, serum potassium is higher in Losartan and Valsartan group but lower in Olmesartan in diabetic subject. Progressive increase of CKD stages shows progressive increase of serum potassium level. Higher serum potassium level was found among the higher dose of ARB users in both groups. Increase of dose grading was associated with increase level of serum potassium in Losartan and Valsartan users and it was not true for Olmesartan.

Conclusion: ARB is related to changes in serum potassium level with diabetic patients than the non-diabetic patients with CKD. Moreover, different types of ARB have influence on serum potassium in different way.

Key word: ARB (Angiotensin Receptor Blocker); CKD (Chronic Kidney Diseases); DM (Diabetes Mellitus).

Introduction

Hyperkalemia is an established complication of reduced renal function in patients suffering from either CKD or acute renal failure and it is long considered a potentially life-threatening condition because of the risk of ventricular arrhythmias and cardiac arrest when serum K⁺ is severely elevated^{1,2}. Although decreasing renal function and the associated interference with potassium excretion is a major cause for potassium elevation, in clinical practice, the development of hyperkalaemia is usually the result of a combination

of factors superimposed on renal dysfunction, such as diabetes mellitus with high glucose levels or hyporeninemic hypoaldosteronism, advanced stages of heart failure with accompanying reductions in renal perfusion, concurrent high-potassium diet, use of potassium-based salt substitutes, and use of medications interfering with potassium homeostasis like Angiotensin-Converting Enzyme Inhibitors (ACEIs) Angiotensin Receptor Blockers (ARBs). Aldosterone receptor antagonists, β -blockers and others^{3,4}.

For several years, one of the main concerns of physicians treating patients with CKD was to balance between the undisputed benefits of ACEIs and ARBs toward renal function preservation in proteinuric nephropathies and the associated risk of hyperkalaemia with these agents^{4,5}. This issue became even more important because of the accumulating evidence suggesting the potential benefits of the ACEI/ARB combination or adjunct Aldosterone blockade toward renoprotection as well as the data suggesting beneficial effects of medications that interfere with potassium homeostasis on other conditions commonly present in patients with CKD, such as the effect of Aldosterone blockers on chronic heart failure or resistant hypertension or the use of β -blockers for cardio-protection and effective hypertension control⁶⁻⁸.

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ARB or ACEIs are commonly used in hypertension with diabetes to reduce the blood pressure, also to reduce the renal protein loss. ARB/ACEIs have established influence on potassium homeostasis. So the present study will estimate either the potassium levels and prevalence of hyperkalaemia (among other CKD complications) with decreasing levels of renal function or the incidence of hyperkalaemia associated with CKD stage, medication use, and other hyperkalaemia factors⁹⁻¹⁰.

Thus, the aim of this study was to examine the prevalence and potential determinants of different levels of potassium in a population of predialytic CKD patients who are grouped into diabetic and non diabetic groups on ARB treatment.

Materials and methods

Present study was conducted in the Department of Nephrology and Medicine, Chittagong Medical College Hospital (CMCH) and the duration of the study was 6 (six) months. Sample size of the study was 100 (Diabetic 50, Non-diabetic 50) and patients were selected purposively. Inclusion criteria were all chronic kidney disease patient admitted during the period of study and patients or attendants giving written consent to take part under study. Exclusion criteria were patients on renal replacement therapy (Transplantation or Dialysis). Diagnosed patients of diabetic and non diabetic predialytic CKD patients were thoroughly informed about the aims, objectives and detail procedure of the study before examination. He/She were encouraged for voluntary participation and allowed freedom to withdraw from the study whenever he/she liked even after participation. Patients were screened for whether they were taking ARB or not. Those who are on ARB treatment consent were taken from them. Clinical history were taken and clinical examination were done to elicit findings related to chronic renal diseases, DM and their complication. Related investigations like urine and blood examination were also be done. Blood sample were collected with proper aseptic technique as per direction of the laboratory and were sent for analysis before starting of hemolysis which might have some impact on the serum potassium results. All relevant data were noted in the pre tested data sheet. All data were checked and rechecked to avoid error. The urine and blood were collected by researcher himself. All relevant investigations were done in the Clinical Pathology Departments of CMCH or if needed in modern laboratory of Chattogram. Cost were beard by the researcher himself. Data were processed and analyzed by using computer bases software SPSS-15 (Statistical Package for Social Science). Different statistical method were applied for data analysis. Qualitative variable will be analyzed by frequency, percentage and chi squared test and quantitative variables were analyzed by mean, standard deviation, t test and ANOVA etc. p value were considered as statistically significant when it was less than 0.05. Before commence the study ethical clearance was obtained from the proper authority.

Results

Table I : Serum potassium level and ARB type

ARB type	Mean (Serum potassium in mg/dl)	No. of patients	Std. Deviation
Losartan	4.79	70	.79271
Olmesartan	4.58	22	1.03877
Valsartan	5.57	8	.41582
Total	4.81	100	.85879

Table I showing patients who were using Losartan had low serum potassium level (4.79 mg/dl) than patients who were using Valsartan (5.57 mg/dl).

Table II: Mean serum potassium in both groups with different ARB

	Losartan Mean (mg/dl)	Olmesartan Mean (mg/dl)	Valsartan Mean (mg/dl)
Mean (mg/dl) Serum potassium in Diabetic group (n=50)	4.81	4.43	5.64
Mean Serum potassium in Non Diabetic group (n=50)	4.79	4.69	5.10

Table II showing in both diabetic and non diabetic groups of patients who were using Valsartan had more serum potassium level (5.64 vs 5.10) than others who were using Losartan (4.81 vs 4.79) or Olmesartan (4.43 vs 4.69).

Table III : Comparison of serum potassium in both groups with ARB

	Serum Potassium		p value
	Diabetic group Mean (mg/dl)	Non diabetic group Mean (mg/dl)	
Losartan	4.81	4.79	>0.05
Olmesartan	4.43	4.69	>0.050
Valsartan	5.64	5.10	<0.05

Table III showing in all three ARB drugs serum potassium is higher in Losartan and Valsartan group but lower in Olmesartan group in diabetic subject.

Table IV : ARBs and stages of CKD

	Losartan		Olmesartan		Valsartan	
	Type of subject		Type of subject		Type of subject	
	Diabetic group	Non Diabetic group	Diabetic group	Non Diabetic group	Diabetic group	Non Diabetic group
	Mean (mg/dl)	Mean (mg/dl)	Mean (mg/dl)	Mean (mg/dl)	Mean (mg/dl)	Mean (mg/dl)
Stage 2			4.20			
Stage 3	3.80	4.33		4.22		
Stage 4	4.92	4.13				
Stage 5	4.83	5.07	4.46	4.90	5.64	5.10
p value	>0.05	<0.05		>0.05		

Table IV showing increasing stages was related with increasing of serum potassium in non diabetic CKD patients.

Table V : Relation of serum potassium and dose of ARB

Grading of dose					
Low dose		Medium dose		High dose	
Type of subject		Type of subject		Type of subject	
Diabetic group	Non diabetic group	Diabetic group	Non diabetic group	Diabetic group	Non diabetic group
Serum potassium	Serum potassium	Serum potassium	Serum potassium	Serum potassium	Serum potassium
Mean (mg/dl)	Mean (mg/dl)	Mean (mg/dl)	Mean (mg/dl)	Mean (mg/dl)	Mean (mg/dl)
4.56	4.56	4.79	4.81	5.06	5.17

Table V showing higher serum potassium level was found among the patients who were on higher dose of ARB in both diabetic and non diabetic groups.

Table VI : Serum potassium in low dose of ARB

	Grading of dose			
	Low dose			
	ARB type			
	Losartan	Olmesartan	Valsartan	p value
	Mean (mg/dl)	Mean (mg/dl)	Mean (mg/dl)	
Low dose	4.30	4.57	.	>0.05.
Medium dose	4.82	4.63	.	>0.05
High dose	4.75	.	5.57	<0.05

Table VI showing increase of dose grading was associated with increase level of serum potassium in Losartan and Valsartan where it was not true for Olmesartan.

Discussion

There are different traditional and non-traditional risk factors for chronic kidney disease. Different traditional cardiovascular risk factors like physical inactivity, diabetes mellitus, hypertension, dyslipidemia, smoking and left ventricular hypertrophy are more predominant in the stage 5 CKD patients¹¹. For hypertensive patient with CKD, with or without diabetes different types of anti-hypertensive drugs are used among which Angiotensin Receptor Blocker (ARB) are common.

Staging of the chronic kidney disease was done by estimating eGFR with CKD-EPI equation where most of the patients were found in stage 5(77%) of CKD, but for stage 4 and stage 3 percentage were 11% for each stage and 1 patient were found in stage 2. As Chittagong Medical College Hospital is a tertiary care hospital and patients admitted here at terminal stages, for that reason most of the patients were found at stage 5 of CKD. This finding is consistent with the previous study¹¹.

Three types of ARB were used by both groups Losartan (70%) Olmesartan (22%) and Valsartan (8%). These three are most commonly prescribed ARB antihypertensive in Bangladesh.

Patients who were using Losartan had low serum potassium level (4.79 mg/dl) than patients who were using Valsartan (5.56 mg/dl). Progressive increase of serum potassium

was observed as CKD progresses to end stage. A few studies that examined the prevalence of various CKD complications with decreasing renal function also provided some data on hyperkalemia. In a cross-sectional analysis of retrospectively collected electronic medical records of 1216 individuals with various levels of renal function, the prevalence of potassium > 5 meq/L rose from about 10% to 18% and 22%, and the actual levels of potassium rose from 5.2 to 5.3 and 5.5 meq/L for subjects with eGFR=30–60, 15–30, and <15 ml/min per 1.73 m², respectively¹². In this study, however, patients with renal function<15 ml/min per 1.73 m² were a very small percentage of the study population (5.7%).

In both diabetic and non diabetic groups patient who were using Valsartan had more serum potassium level than others though there was limitation due to small size patient. Non diabetic stage 5 CKD patients had more serum potassium level than diabetic stage 5 patients. Higher serum potassium level was found among the patients who were on higher dose of ARB in both diabetic and non diabetic groups. Increase of dose grading was associated with increase level of serum potassium in Losartan and Valsartan where it was not seen for Olmesartan.

Taka chi et al observed serum potassium levels to be higher in patients with diabetes and patients using an ACEI/ARB up to serum creatinine of 2 mg/dl and not for groups with lower renal function. This study, however, is limited by the use of only creatinine values¹³. In the aforementioned French study, the odds ratio of hyperkalaemia in multivariate analysis was significantly higher for males and subjects using an ACEI/ARB, it was lower with increasing eGFR, and it was marginally lower for black individuals. Age, cause of CKD, diabetes, body mass index and BP control did not show independent associations. Despite the lack of clear evidence some authors have stated that the increase in serum potassium is less pronounced during therapy with ARBs and that the risk of hyperkalemia is higher in patients treated with ACEIs¹⁴. Hypertension is a well known risk factor for coronary heart disease, stroke, transient ischaemic attack, and diabetes-induced chronic kidney disease¹⁵. Few guidelines for hypertension recommend Angiotensin II Receptor Blockers (ARBs) as the first drug of choice for treating hypertension¹⁶.

Conclusion

This study shows that serum potassium level gradually increases as CKD also progress to end stages. Antihypertensive like ARB types and their dose influence the level of serum potassium among both diabetic and non-diabetic CKD patients. Fluctuation of serum potassium is more among the patients with CKD with DM then CKD without DM.

Disclosure

All the authors declared no competing interests.

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