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RESEARCH ARTICLE

Hyperkalemia in Chronic Kidney Disease Patients under Conservative Treatment

Salama E Farag[1], Sameh A Soliman[1],Tarek A Ghonemy[1,3], Ahmed A Hamdy[2,3]

1 Internal medicine Department, Zagazig University Hospital, Egypt .
2 Mansoura urology and nephrology center, Egypt.
3 Hamad Medical Corporation, Qatar.

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Corresponding Author

Salama E Farag

Abstract

Background: Hyperkalemia is one of such disturbances that have a great concern in CKD patients for its possible potential for associated adverse cardiac outcomes. The principal causes of hyperkalemia in CKD patient include an impaired glomerular filtration rate (GFR) combined with a frequently high dietary potassium intake relative to residual renal function, a commonly observed extracellular shift of potassium caused by the metabolic acidosis of renal failure and, most importantly, recommended treatment with renin angiotensin aldosterone system (RAAS) blockers that inhibit renal potassium excretion. The aim of this study is to examine the prevalence and potential determinants of hyperkalemia in a population of predialysis CKD patients under conservative therapy. **Patients and Methods:** This is a 4 month cross-sectional study in predialysis CKD patients under regular follow-up in the LCC. 78 patients are recruited for the study. Information of serum potassium and different other laboratory variables, Co-morbidities, and the using medications are recorded for each participant. In univariate analysis, clinical and laboratory parameters were compared for patients to identify factors associated with hyperkalemia (potassium >5.5 meq/L).**Results:** From total 74 patients recruited for the study, 14 (17.9%) of them had serum potassium level > 5.5 meq/l. They are older than patients without hyperkalemia but with no statistical difference. Also, they are more obese, more hypertensive but with no statistical differences. There was no statistical significant difference between male and female patients and no statistically significant effect of causes of CKD and comorbitidies on hyperkaemia. Use of angiotensin-converting enzyme inhibitors or angiotensin receptor blockers was not associated with hyperkalemia. The GFR was lower in hyperkalemic patients, but with no statistically significant difference, however, the bicarbonate level was lower in hyperkalemic patients with highly statistical difference to patients without hyperkalemia p 0.015.**Conclusion:**Hyperkalemia is common in stable predialysis CKD patients. The most important risk factors are low GFR, low serum bicarbonate level. Using of ACEi or ARBs is not associated with high risk hyperkalemia

Introduction

Chronic kidney disease (CKD) is a common disease of healthcare problems, affecting a growing number of the population, and it may be associated with a variety of electrolyte disturbances[1].Hyperkalemia is one of such disturbances that has a great concern in CKD patients for its possible potential for associated adverse cardiac outcomes.[2,3]

Patients with CKD may be predisposed to hyperkalemia for a variety of reasons. Principal causes include an impaired glomerular filtration rate (GFR) combined with a frequently high dietary potassium intake relative to residual renal function, a commonly observed extracellular shift of potassium caused by the metabolic acidosis of renal failure,[1,2] and, most importantly, recommended treatment with renin angiotensin- aldosterone system (RAAS) blockers that inhibit renal potassium excretion.[4,5]

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 [6] and the associated risk of hyperkalemia with these agents [4,7]

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 [8,9] 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 [10,11] or the use of b-blockers for cardioprotection and effective hypertension control [12].

Because of the increasing complexity of the above field, recent studies have attempted to delineate the relationship between CKD and hyperkalemia. These studies estimated either the potassium levels and prevalence of hyperkalemia (among other CKD complications) with decreasing levels of renal function [13,14] or the incidence of hyperkalemia associated with CKD stage, medication use, and other hyperkalemic factors [15,16]however, there is a paucity in current literature on hyperkalemia and associated factors in predialysis patients not in the general population, but followed in a structured nephrology environment, an issue that is perhaps more relevant to everyday clinical practice.

Thus, the aim of this study is to examine the prevalence and potential determinants of hyperkalemia in a population of predialysis CKD patients on conservative therapy.

Patients and Methods

This is a cross-sectional study in patients with predialysis CKD under regular follow-up in the low clearance clinic (LCC) of nephrology department, Hamad Medical Corporation , Qatar. The LCC generally accepts referrals from other nephrology clinics of patients with estimated GFR (eGFR) below 20 ml/min per 1.73 m2 or anticipated start of dialysis within 1 year. The aim of the clinic is to optimize the care of the patients in the predialysis period preparing them for renal replacement therapy including methods of dialysis or preemptive renal transplantation or offer them conservative treatments accordingly. Patients are seen in the clinic by a nephrology physician at intervals ranging from 2 weeks to 3 months. In routine practice, all laboratory tests obtained in the clinic are checked by the LCC staff on the same or next day.

For the purpose of this study, we collected data at a single time point (i.e., at the first scheduled visit during a prespecified period of 4 months from 1stof May 2012 to 1st of September 2012) for all patients regularly attending the clinic. Before each regular LCC visit, blood samples were drawn by the central laboratory qualified persons. 130 patients are followed in low clearance clinic, 78 of them are recruited and 54 patients are excluded because of many reasons; 23 patients went to hemodialysis, 15 patients went for peritoneal dialysis, 3 patients had Renal transplantation , 9 patients were hospitalized and 4 patients missed their regular appointment in the clinic.

Data Collection

We collected routine data on demographics, cause of CKD, comorbidities (hypertension, diabetes, coronary heart disease, stroke, heart failure, liver disease, and history of malignancy), and blood biochemical parameters (potassium, sodium, bicarbonate, urea, creatinine, and others) for each participant.in addition, we recorded the using of different medications that can affect K regulation including ACEIs, ARBs, renin inhibitors, aldosterone blockers, b-blockers, thiazides, loop diuretics, insulin and oral hypoglycemic agents, heparin, trimethoprim, pentamidine, cyclosporine, tacrolimus, digoxin, resin K+ exchangers, sodium docusate, lactulose, senna, and sodium bicarbonate.

Definitions:

Hyperkalemia was defined as serum potassium.5.5 meq/L or more . Hypokalemia was defined as serum potassium, 3.5 meq/L or less.

GFR was estimated from serum creatinine levels with the use of the Modification of Diet in Renal Disease equation [17]

Statistical Analyses

Statistical analyses were performed with Statistical Package for Social Sciences version 17.0 for Windows (SPSS Inc., Chicago, IL). Continuous variables are presented as mean ± SD or median and range, and categorical variables are presented as absolute and relevant frequencies. In univariate analyses, clinical and laboratory parameters were compared for patients stratified by potassium levels using chi-square test. Probability values of P 0.05 (two-tailed) were considered statistically significant.

Results:

In univariate analysis, the total numbers of patients were 78, 14 (17.9%) of them have hyperkalemia with no statistical significant difference between male and female patients P 0.59. Also, no statistically significant effect of causes of CKD and comorbitidies on hyperkaemia P 0.39 (Table 1)

Patients with hyperkalemia are older than patients without hyperkalemia but with no statistical difference. Also, they are more obese, more hypertensive but with no statically differences.

The GFR is lower in hyperkalemic patients, but with no statistically significant difference

The bicarbonate level is lower in hyperkalemic patients with highly statistical difference to patients without hyperkalemia p 0.015 (Table 2)

Table 3 shows information about using medications that can affect the serum K level. There is no significant affection on serum K by using ACEi, ARBs, B blockers, oral hypoglycemic, digoxin,senna and lactulose. There is significant lower level of serum k in patients using loop diuretics and insulin p 0.05

Table 1: Demographic and clinical characteristics of total patients and those with high potassium levels

	Total patients	**K < 5.5 meq/l**	**K ≥ 5.5 meq/l**
No of patients	78	64 (81.1%)	14 (17.9%)
Male/Female	44/34	41/23	8/6
Causes of CKD:			
• **Unknown**	4	3	1
• **Interstitial nephritis**	2	1	1
• **DM**	34	28	6
• **FSGS**	2	1	1
• **Pyelonephrtis**	1	1	0
• **HTN**	31	27	4
• **APKD**	3	2	1
• **Neurogenic bladder**	1	1	0
Co morbidities:			
• **CAD**	4	4	0
• **PVD**	2	2	0
• **Hypothyroidism**	6	5	1
• **Hep C**	1	0	1
• **Gout**	2	2	0
• **CHF**	1	1	0
• **CLD**	1	1	0
• **COPD**	2	2	0
• **Synthetase syndrome**	1	1	0

DM(Diabetes Mellitus), HTN (hypertension), PVD (peripheral vascular disease), Hep C (Hepatitis C), CHF (Congestive Heart Failure), CLD (Chronic Liver Disease), COPD (Chronic Obstructive Pulmonary Disease), FSGS (Focal Segmental Glomerulosclerosis), APKD (Adult Polycystic Kidney Disease)

Table 2: clinical and laboratory characteristics of the patients with and without elevated potassium levels

	K <5.5 meq/l (no. 64)	K≥5.5 meq/l (no. 14)	P value
Age (years)	56.5±12.5	58±13.6	0.709
BMI (kg/m^2)	28.3±4.3	29.0±4.6	0.608
Systolic BP (mmHg)	146.4±15.8	149.4±15.7	0.588
Diastolic BP(mmHg)	74.1±7.1	74.7±8.9	0.786
Urea (mmol/l)	21.4±8.2	19.6±4.3	0.422
Creatinine(mmol/l)	394.9±142.6	403.03±99.6	0.820
eGFR(ml/min per 1.73 m^2)	14.3±5.9	12.3±3.6	0.211
Sodium (meq/l)	142.9±3.5	142.3±2.9	0.578
Potassium(meq/l)	4.6±0.44	5.8±0.2	0.000
Serum Bicarbonate (meq/l)	21.9±3.6	19.3±2.8	0.015

Table 3: Use of medications that could interfere with potassium regulation in patients with and without elevated potassium levels

	K <5.5 meq/l (no. 64)	K ≥5.5 meq/l (no. 14)	P value
ACEi	7	1	0.560
ARBs	14	1	0.190
B blockers	32	8	0.426
Thiazide	6	1	0.632
Loop diuretics	43	6	0.05
Senna	3	3	0.06
Insulin	43	6	0.05
Oral hypoglycemic	10	3	0.425
Digoxin	1	0	0.821
Lactulose	3	1	0.555

ACEi :Angiotensin convertor enzyme blockers, ARBs: Angiotensin Receptor Blockers, B blockers: Beta Blockers

Discussion:

The prevalence of hyperkalemia in our patients was high with around 17.9 % of all patients have hyperkalemia with serum K level is > 5.5 meq /l and the incidents of hyperkalemia was more in patients with lower GFR but without statistically significant difference. This result is in consisting with many studied which were done before on hyperkalemia in CKD patients. One of them is a French cohort of 1038 outpatients with stages 2–5 CKD not on dialysis, the prevalence of hyperkalemia defined as serum potassium.5 mmol/L or treatment with ion exchange resin was 17% of the total population and around 42% in the subset of 184 individuals with eGFR,20 ml/min per 1.73 m$^{2(14)}$.

Two other recent studies have examined the incidence of hyperkalemia in individuals with CKD. The first study was a posthoc analysis of the African-American Study on Kidney Disease (AASK), which included 1094 African-American nondiabetic adults with hypertensive CKD and eGFR=20–65 ml/min per 1.73 m2 that were followed for 3.0–6.4 years.With hyperkalemia defined as serum potassium.5.5 meq/L during follow-up visits, a total of 80 events (1.2% of laboratory records) in 51 patients was identified[15]. Finally, the largest study of the field included a retrospective analysis of records of 245,808 individuals (including 70,873 individuals with CKD stages 3–5) hospitalized over 1 year in the Veterans Health Administration Hospitals in the United States; a total of 66,259 hyperkalemic events was captured (3.2% of total laboratory values) [16].

Among a wide range of study parameters, we found that the incident of hyperkalemia was higher in male patients (10.2%) than female patients (7.6%) but with no statisticaldifference. Also hyperkalemia was more in older patients and in patients with more weight and in patients with higher blood pressure but without statistically significant differences.

Also, we found that hyperkalemia was statistically significant higher in Patients with low sodium bicarbonate. Also, no statistically significant hyperkalemia in patients who were on RAAS inhibitors and beta blockers and no significant effect of the causes of CKD and the associated comorbiditeis on the incident of hyperkalemia. These results are in consisting with the result done by Pantelis et al[18] who studied 238 patients on low clearance clinic and found in univariate analysis that patients with k > 5.5 had significantly higher urea and lower eGFR and serum bicarbonate level. Also, they found that using of RAAS inhibitors was not associated with hyperkalemia. In another study done by Takaichi et al[13], they found that serum potassium level was higher in diabetic patients and in patients using RAAS inhibitors, but this study, however, was limited by the use of only creatinine values for measurements of kidney function and absence of multivariate analysis.

In french study[16], they found that hyperkalemia was significantly higher in male patients with no independent associations with age, causes of CKD, diabetes, BMI and BP control.Also, they noticed lower odds of hyperkalemia with increased age.Most other studies have shown older age to slightly increase hyperkalemia risk [15-16]

Finally, limited sample size enrolled in our study, so the prevalence of hyperkalemia among CKD patient under conservative therapy should be further examined in a prospective design with a larger number of subjects.

Conclusion

This study shows that hyperkalemia is common in stable predialysis patients. Among different risk factors of hyperkalemia, the most important are low GFR, low serum bicarbonate level. Additional studied are needed to evaluate the clinical significance of hyperkalemia for morbidity and mortality in this type of population.

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