Analysis of Influencing Factors and a Prediction Model of Abnormal Serum Potassium in Patients with Chronic Kidney Disease

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Abstract

Objective

The high incidence of abnormal serum potassium in patients with chronic kidney disease have resulted in frequent cardiovascular adverse events and even death. Through a retrospective analysis of the clinical data of 273 patients with CKD, we analyzed the correlation between the general data of patients and serum potassium levels, and the risk factors for abnormal serum potassium, and constructed risk prediction models for abnormal serum potassium.

Methods

In this paper, 273 patients with CKD who were admitted to the Second Affiliated Hospital of Xuzhou Medical University were selected for this retrospective analysis. The subjects were divided into two groups based on the presence of abnormal serum potassium. Preliminary literature retrieval was conducted to extract the risk factors that might affect serum potassium. Independent sample *t* test was used to analyze the differences between two groups, Pearson or Spearman test was used to analyze the linear correlation of data, and Logistic regression equation was used to construct the multiple regression analysis.

Results

The use of diuretics ($P=0.046$), the use of renin-angiotensin and aldosterone (RAAS) inhibitors ($P=0.040$) and low score of Renal Adherence Questionnaire (RAAQ) ($P<0.001$) were independent risk factors for abnormal serum potassium. There was a positive linear correlation between serum potassium and age, serum creatinine, blood urea nitrogen, anion gap and RAAQ score in patients with CKD; each influencing factor was independent. Subgroup analysis showed that the use of diuretics, low RAAQ score and peritoneal dialysis were more likely to lead to hypokalemia, while hypertension, diabetes, use of RAAS inhibitors, low RAAQ score and hemodialysis were more likely to result in hyperkalemia.

Conclusion

Poor compliance is a risk factor for abnormal serum potassium. On this basis, the use of diuretics and peritoneal dialysis may increase the risk of hypokalemia, and the use of RAAS, hypertension, diabetes, and peritoneal dialysis may increase the risk of hyperkalemia.

Introduction

Chronic Kidney Disease (CKD) refers to the chronic progressive damage of renal parenchyma caused by various reasons, which could result in obvious atrophy of the kidney and renal dysfunction. The main clinical manifestations of CKD include the retention of metabolites, water-electrolyte imbalance, acid-base imbalance and systemic symptoms. In the past 30 years, the incidence of CKD has doubled and been increasing^[1], with a variety of causes for resulting deaths^[2], including abnormal serum potassium. Abnormal serum potassium is classified into hyperkalemia and hypokalemia. Hyperkalemia not only increases the risks of arrhythmia and sudden death^[4], but also helps predict poor prognosis in patients with CKD^[3]. Hypokalemia is more commonly seen in CKD patients than hyperkalemia^[5]. Evidence suggested that hypokalemia is associated with the progression of CKD^[6]. A U-shaped association between serum potassium and CKD mortality was found, with both high and low serum potassium associated with an increased risk of all-cause mortality^[7]. Based on the above findings, early intervention is vital for patients with CKD who are at the risk of hyperkalemia or hypokalemia^[8] to reduce the incidence of all-cause mortality and cardiovascular adverse events.

Risk prediction refers to the inference and analysis of the potential risk status, influencing factors and changing trend, which is the basis of decision-making. In recent years, disease risk prediction has also become a research hotspot; it is no longer limited to the assessment of the risk of death, and more attention has been given to the risk prediction of the risk of infection, malnutrition, and so forth. At present, many studies have been conducted on the disease progression and cardiovascular and cerebrovascular complications in CKD patients so as to build a risk prediction model, which can be used to guide clinical practice through external verification^[9, 10]. To date, most domestic and overseas studies focused on hyperkalemia^[11], and there has been no risk prediction model established for abnormal serum potassium in patients with CKD.

In this study, we retrospectively analyzed the general clinical data of 273 patients with CKD. We examined the correlation between the patients' general data and serum potassium values, identified the risk factors for abnormal serum potassium, and built a risk prediction model for abnormal serum potassium.

Patients And Methods

Patients

A total of 273 patients with CKD admitted to the Department of Nephrology, The Second Affiliated Hospital of Xuzhou Medical University from January to December 2021 were selected as study subjects of this retrospective analysis.

Inclusion criteria

Conform to the diagnostic criteria of the 2015 Guidelines for the Diagnosis and Treatment of Chronic renal failure by Integrated Chinese and Western Medicine;

Age $\geq$ 18 years;

The patient (family member) consented to participate voluntarily.

Exclusion criteria

Complicated with trauma and shock of other organs;

The patient has mental illness and communication disorder.

Methods

After enrolment in strict accordance to the inclusion criteria, the patients were divided into the normal potassium group and the abnormal potassium group based on their blood biochemistry results for serum potassium, with potassium values of 3.5–5.5 mmol/L considered normal while the values lower than 3.5 mmol/L or higher than 5.5 mmol/L considered abnormal. The patients with abnormal serum potassium were treated according to the relevant measures in Management of Chronic Kidney Disease 2019^[12].

Influencing factors

In this retrospective study, we included 12 potential influencing factors, i.e., age, gender, hypertension, diabetes, use of diuretics, use of renin-angiotensin and aldosterone (RAAS) inhibitors, renal function, serum creatinine (Scr), urea nitrogen (BUN), anion gap (AG), dietary adherence, and the type of dialysis.

Assessment tools

The Renal Adherence Questionnaire (RAAQ)^[13] was used to evaluate the dietary adherence of patients with CKD, with higher scores indicating better dietary compliance. The Cronbach's α coefficient of each dimension of the scale ranged from 0.68 to 0.88^[14].

Statistical analysis

The collected data were confirmed and recorded by two researchers. SPSS 24.0 and GraphPad prism 8 were used for statistical analysis and plotting, with mean, standard deviation, standard error of mean, median, range, and 95% confidence interval as descriptive statistics. Inter-group comparison was performed using *t* test, the linear correlation of data was analyzed using Pearson or Spearman correlation coefficient, and the correlation between serum potassium and related variables was analyzed using multiple linear regression analysis. For all the above analyses, two-tailed $P < 0.05$ was considered statistically significant.

Results

General data analysis

The 273 patients with CKD were aged from 24 to 89 years, with a mean age of 62.90 ± 13.33 years. Among them, 117 were female, accounting for 42.86%, and 156 were male, accounting for 57.14%. There were 90 cases (32.96%) with abnormal serum potassium, 72 cases (80.0%) with hypokalemia, and 18 cases (20.0%) with hyperkalemia. The patients' CKD stage ranged 1–5, Scr ranged 49–1652 $\mu\text{mol/L}$, BUN ranged 2.9–46 mmol/L, and AG ranged 3.3–27.1 mmol/L (Fig. 1, Table 1).

Table 1
General data of 273 patients with CKD

Item	Normal potassium group	Abnormal potassium group	χ^2 or t	P
Age	62.04 ± 11.95	64.66 ± 12.96	1.654※	0.099
Gender			0.796	0.372
Male	108	48		
Female	75	42		
CKD stage			1.056	0.788
1–2	41	16		
3a	11	5		
3b	14	6		
4–5	117	63		
Hypertension			2.106▲	0.349
Yes	140	69		
No	40	17		
Unknown	3	4		
Diabetes			3.146▲	0.207
Yes	71	44		
No	108	43		
Unknown	4	3		
Scr (umol/L)			3.741	0.316
60–120	43	13		
121–177	8	11		
178–442	49	14		
443–707	31	16		
707	43	28		
Unknown*	9	8		
BUN (mmol/L)			3.670▲	0.299
3.6	3	0		
3.6–9.5	42	24		
9.5	129	58		
Unknown*	9	8		
AG (mmol/L)			1.954▲	0.376
8	11	2		
8 ~ 16	119	62		
16	53	26		
Use of diuretics			6.168	0.046
Yes	61	44		
No	93	35		
Unknown	29	11		
Use of RAAS inhibitors			6.436	0.040
Yes	70	49		
No	85	31		
Unknown	28	10		

Item	Normal potassium group	Abnormal potassium group	χ^2 or t	P
RAAQ score			45.210▲	0.001
110–130	57	7		
90–109	71	20		
70–89	51	51		
50–69	4	12		
26–49	0	0		
Type of dialysis			5.300	0.071
NA	112	42		
Hemodialysis (HD)	26	19		
Peritoneal dialysis (PD)	45	29		

Note: ※ = t value and ▲ = χ^2 value with correction, with $P < 0.05$ indicating statistical significance; unknown * = emergency electrolytes did not include this item

Analysis of influencing factors

After normality test of measurement data, Pearson or Spearman analysis was used to find a linear correlation between serum potassium value and age, Scr, BUN, AG and RAAQ score (Figure 2).

Correlation analysis of influencing factors

The correlation matrix was used to analyze the correlation between various influencing factors (Table 2).

Table 2 Correlation matrix of influencing factors in 273 patients with CKD

RAAQ score			Gender	Diabetes	BUN	Age	RAAS inhibitors	Type of dialysis	Hypertension	AG	Diuretics	CKD stage	Scr
Correlation	RAAQ score	1.000											
	Gender	-0.080	1.000										
	Diabetes	-0.049	0.018	1.000									
	BUN	0.038	-0.029	-0.013	1.000								
	Age	0.136	0.064	-0.065	-0.001	1.000							
	RAAS inhibitors	-0.204	0.214	-0.025	-0.121	-0.027	1.000						
	Type of dialysis	0.063	0.145	0.040	0.284	0.099	-0.119	1.000					
	Hypertension	0.067	-0.030	-0.222	0.035	-0.080	-0.381	0.135	1.000				
	AG	0.027	0.124	0.026	-0.191	0.024	0.026	-0.043	-0.055	1.000			
	Diuretics	0.166	-0.348	0.051	0.147	0.022	-0.490	-0.029	-0.058	-0.048	1.000		
	CKD stage	0.081	-0.065	-0.137	0.210	-0.295	0.044	-0.273	-0.104	-0.003	-0.225	1.000	
	Scr	-0.067	-0.066	0.109	0.431	0.166	0.041	-0.450	-0.084	-0.273	-0.002	0.330	1.000

Multiple regression analysis

The clinical data of 273 patients with CKD were analyzed using subgroup analysis and logistic regression analysis to avoid the mutual cancellation effect of the influencing factors for hyperkalemia and hypokalemia, as shown in Table 3 and 4.

Table 3 Multivariate regression analysis for hypokalemia						
Item	β value	Standard error	<i>t</i>	<i>P</i>	Tolerance	VIF
Constant	2.047	0.344	5.948	0.000		
Age	0.003	0.003	1.029	0.305	0.819	1.221
Gender	-0.013	0.083	-1.159	0.874	0.813	1.230
Hypertension	0.155	0.113	1.377	0.017	0.584	1.713
Diabetes	-0.005	0.080	-0.069	0.945	0.884	1.131
CKD stage	0.021	0.043	0.485	0.628	0.316	3.161
RAAQ score	0.016	0.002	6.864	0.000	0.877	1.140
Diuretics	-0.263	0.133	-1.446	0.014	0.587	1.798
RAAS inhibitors	0.325	0.112	2.906	0.004	0.442	2.263
Type of dialysis	-0.076	0.067	-1.357	0.169	0.427	2.340
Scr	0.000	0.000	-1.203	0.234	0.239	4.185
BUN	0.031	0.006	5.515	0.000	0.461	2.170
AG	-0.014	0.012	-1.114	0.266	0.576	1.763
Table 4 Multivariate regression analysis for hyperkalemia						
Item	β value	Standard error	<i>t</i>	<i>P</i>	Tolerance	VIF
Constant	3.645	0.377	9.496	0.000		
Age	0.002	0.004	0.503	0.616	0.776	1.289
Gender	0.032	0.089	0.357	0.721	0.757	1.321
Hypertension	0.196	0.116	2.681	0.045	0.576	1.736
Diabetes	0.132	0.086	1.534	0.127	0.809	1.236
CKD stage	0.004	0.045	0.085	0.932	0.300	3.329
RAAQ score	-0.003	0.003	-1.553	0.112	0.809	1.237
Diuretics	-0.026	0.113	-0.232	0.817	0.478	2.092
RAAS inhibitors	0.545	0.112	4.402	0.000	0.471	2.124
Type of dialysis	-0.128	0.082	-1.184	0.137	0.420	2.380
Scr	0.000	0.000	-1.022	0.247	0.242	4.138
BUN	0.038	0.006	6.516	0.000	0.407	2.456
AG	-0.013	0.014	-0.940	0.349	0.521	1.919

The prediction model for serum potassium

Through subgroup analysis and regression analysis, the prediction model for serum potassium in CKD patients was preliminarily established:

(1) Prediction model for hypokalemia: potassium value $Y = 2.047 + 0.15 \times \text{hypertension (yes=1, no=0)} + 0.016 \times \text{RAAQ score} + 0.325 \times \text{use of RAAS inhibitors (yes=1, no=0)} - 0.263 \times \text{use of diuretics (yes=1, no=0)} - 0.076 \times \text{type of dialysis (NA=0, HD=-1, PD=1)} + 0.031 \times \text{BUN}$.

(2) Prediction model of hyperkalemia: potassium value $Y = 3.645 + 0.196 \times \text{hypertension (yes =1, no =0)} + 0.132 \times \text{diabetes (yes =1, no =0)} - 0.003 \times \text{RAAQ score} + 0.545 \times \text{use of RAAS inhibitors (yes=1, no=0)} - 0.128 \times \text{type of dialysis (NA=0, HD=-1, PD=1)} + 0.038 \times \text{BUN}$.

Discussion

CKD is associated with higher rate of abnormal serum potassium

A survey in 2018 in the United States showed that the incidence of hyperkalemia in CKD patients was 6.35%, which was slightly better than 6.86% in Australia^[16]; while the incidence of hypokalemia was as high as 21%^[15]. The incidence of hyperkalemia in patients with CKD in Asian countries is 6.79%,

slightly higher than that in many countries such as United States^[17]. Of the 273 patients included in this study, 90 (32.97%) had abnormal serum potassium, 72 (26.37%) had hypokalemia, and 18 (6.59%) had hyperkalemia. Our findings showed that the incidence of hyperkalemia in China was similar to that in other countries, but the incidence of hypokalemia was higher than that in other countries. Despite the importance of hyperkalemia, hypokalemia should not be neglected due to its harm and incidence. Patients with hypokalemia are at a higher risk of death than those with mild-to-moderate hyperkalemia^[18]. Therefore, the attention of clinical nursing needs to be slightly reallocated. In addition to paying attention to hyperkalemia, the harm of hypokalemia should not be underestimated.

The impacts of diuretics, RAAS indicators, and low RAAQ score

Our findings suggested that the use of diuretics and RAAS inhibitors, and low RAAQ score had varying degrees of impacts on the serum potassium status in patients with CKD. In clinical nursing works, we need to pay attention to the serum potassium status in patients with high BUN, use of diuretics or RAAS inhibitors, and low RAAQ score, so as to reduce the incidence of adverse events caused by abnormal serum potassium. The most common side effects of diuretics are dose-related and involve electrolyte and metabolic abnormalities. Studies have shown that the risk ratio for the progression of CKD was 1.59 in patients with a high-potassium diet compared to those with a low-potassium diet^[19]. Excessive limitation of potassium intake may lead to hypokalemia^[20], malnutrition^[21], and increased risk of poor prognosis^[22]. However, a study showed a controversial finding that dietary potassium was not associated with serum potassium levels^[23]. Nonetheless, it has been demonstrated that patients with higher RAAQ scores are at a lower risk of all-cause mortality from CKD^[24]. Some types of diuretics may increase the excretion of potassium, and thus potassium supplementation is needed as appropriate for patients using these diuretics. Clinical nurses also need to promote diet and health education, so as to improve patients' RAAQ score, as higher scores indicate better prognosis.

Subgroup Analysis

Low RAAQ scores, use of diuretic, and peritoneal dialysis were associated with hypokalemia

Thiazides are the most commonly used diuretics in clinical practice. Some types of diuretics have an effect of potassium, sodium and chlorine excretion; thus, the long-term use of these diuretics is likely to cause hypokalemia. Collins et al. suggested that the use of diuretics was strongly associated with hypokalemia^[25]. Therefore, thiazide diuretics should be used together with potassium-sparing diuretics or potassium supplementation as needed. In the present study, thiazide diuretics are associated with increased risk of hypokalemia, even with potassium-sparing diuretics or potassium supplementation in time. In addition, CKD patients with a higher RAAQ score had a lower risk of abnormal serum potassium. Peritoneal dialysis can lead to greater loss of potassium, as compared to hemodialysis^[26]. In CKD patients with low RAAQ scores, the compliance of oral potassium supplementation could not be ensured, and diuretics and peritoneal dialysis could lead to more potassium loss than intake, which might increase the risk of hypokalemia. Therefore, as clinical nurses, we need to implement targeted education and management to improve patients' RAAQ score, which reflects patient compliance. Patients at high risk of hypokalemia should be timely supplemented with potassium if symptoms such as fatigue, poor appetite, palpitation and abdominal distension occur, so as to reduce the duration of serum potassium and improve patients' quality of life.

Hypertension, diabetes, use of RAAS inhibitors, low RAAQ score, and hemodialysis were associated with hyperkalemia

Kidney is an important organ that regulates plasma potassium concentration. With the decline of renal function, kidney excretion of potassium decreases, leading to increased incidence of hyperkalemia^[27]. RAAS inhibitors can decrease urinary potassium excretion and increase serum potassium by inhibiting the secretion of adrenal aldosterone. In the present study, our findings were basically consistent with previous results. According to the prediction model of hyperkalemia constructed in this study, the use of RAAS inhibitors was associated with an increase of serum potassium by 0.545 mmol/L, which greatly increased the risk of hyperkalemia; furthermore, it was also an independent risk factor for hyperkalemia. Despite the risk induced by RAAS inhibitors, this type of drugs is still widely used in clinical practice. Over a decade ago, it was demonstrated that RAAS inhibitors could slow down the progression of kidney diseases^[28], showing combined effects of anti-hypertension, hemodynamics, anti-proteinuria, etc. The combination of diuretics and RAAS inhibitors might be beneficial to cardiovascular events and the resulting mortality, but also might increase the risk of hyperkalemia in patients with CKD who were on dialysis^[29]. We should timely inform high-risk patients with hyperkalemia to come to the hospital for treatment in case of muscle weakness, unresponsiveness, palpitations and other symptoms, so as to reduce the occurrence of cardiovascular events caused by hyperkalemia. Recently, the use of novel potassium binding agents has been demonstrated to have a positive effect on relieving hyperkalemia induced by RAAS inhibitors^[30].

In summary, poor compliance (reflected by low RAAQ scores) is a risk factors for abnormal potassium status. On this basis, the use of diuretics and peritoneal dialysis might cause excessive potassium loss, resulting in hypokalemia. Patients with hypertension, diabetes and hemodialysis who used RAAS inhibitors were more likely to develop hyperkalemia. Clinical nurses should provide timely diet-related guidance according to the general data of patients, as well as promote patient education about their own serum potassium status. On the basis of active prevention, we should also inform the doctor of patients' abnormal potassium status and take corresponding measures in time.

Limitations and Prospects

In this study, data from only 273 subjects were collected from the department of nephrology of a single hospital, which might introduce biases that affected statistical significance. In view of this limitation, prospective design can be used to optimize the model and increase the sample size future studies. In this way, it can not only avoid the bias caused by retrospective data and small sample size mentioned above, but also avoid the methodological defects in model establishment that need to adjust the assignment score.

The prediction models for hypokalemia and hyperkalemia have been preliminarily established in this study, but it needs to be verified and generalized with the involvement of more patients with CKD. Hopefully, the prediction models could help guide timely intervention for patients with CKD to reduce the rate of emergency admission and incidence of adverse events due to abnormal serum potassium.

Declarations

Ethics approval and consent to participate

All methods were carried out in accordance with relevant guidelines and regulations. Informed consent was obtained from all subjects and from legal guardian of dead patients. The experimental protocol was approved by the Ethics Committee of the Second Affiliated Hospital of Xuzhou Medical University (2021 011001).

Consent for publication

Not applicable.

Availability of data and materials

The data used and/or analyzed during the current study are available from the corresponding author on reasonable request.

Competing interests

The authors declare that they have no conflicts of interest.

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Authors' contributions

Hong Song, Rui Li and Yue Wu conceived the study, participated in its design and drafted the manuscript. Xiaofeng Zheng and Lu Ma participated in data analysis. All of the authors read and approved the final manuscript.

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Figures

Figure 1 General data distribution of 273 patients with CKD

Figure 1

General data distribution of 273 patients with CKD.

Note: A, B: ratio of serum potassium status in the 127 patients with CKD; C: gender distribution; D: distribution of dialysis methods; E: distribution of CKD stage and Scr; F: distribution of BUN and AG levels; G: distribution of potassium status and RAAQ score.

Figure 2 Correlation analysis of potassium in 273 patients with CKD

Figure 2

Correlation analysis of potassium in 273 patients with CKD

Note: The slope r ranges from -1 to 1, with a positive r indicating positive correlation and a negative r indicating negative correlation. $P < 0.05$ indicates that the difference is statistically significant.