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Original Paper

Serum Potassium Profile and Associated Factors in Incident Peritoneal Dialysis Patients

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Key Words
Serum potassium • Continuous ambulatory peritoneal dialysis • Incident peritoneal dialysis

Abstract
Background/Aims: Abnormal potassium profiles are common in peritoneal dialysis (PD) patients. We studied the factors associated with serum potassium profiles in incident PD patients. ***Methods:*** Patients were enrolled from two hospital-facilitated PD centers from May 2013 to May 2016 and January 2009 to December 2015. A total of 319 incident PD patients were examined for factors associated with serum potassium profile. Average serum potassium levels were obtained for analysis during the first 3 months after PD initiation. Clinically factors and parameters associated with PD were assessed by logistic regression. ***Results:*** There were 168 men and 151 women (mean age, 50.8 years). Blood urea nitrogen (BUN), creatinine (Cr), and intact parathyroid hormone levels were significantly increased in patients in the higher serum potassium group. There were no significant risk factors for hypokalemia, including sex, age, diabetes, blood examination parameters, medication use, or PD-related parameters by multivariate logistic regression analysis. BUN (adjusted odds ratio [OR] 1.02, 95% CI 1.01–1.03, p = 0.001) and Cr (adjusted OR 1.08, 95% CI 1.01–1.16, p = 0.029) levels were significant risk factors for hyperkalemia by multivariate logistic regression analysis. ***Conclusion:*** Hyperkalemia and blood BUN and Cr levels were significantly associated in incident PD patients.

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Introduction

Potassium clearance in peritoneal dialysis (PD) is mainly dependent upon potassium diffusion from the extracellular fluid to the hypertonic peritoneal dialysis solution. Bulk flow of extracellular water during hypertonic PD does not correlate with a proportionately

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increased rate of potassium removal in the absence of a concentration gradient for net diffusion [1]. However, potassium clearances and maximal potassium removal rates are relatively low with PD compared to hemodialysis and kayexalate enema techniques [1]. The maximum potassium clearance with hypertonic peritoneal dialysis in PD studies was 26 mL/min during the dwell time [1].

It is well known that hemodialysis results in more potassium clearance than PD. However, hypokalemia in PD is more prevalent than in hemodialysis. One possible explanation is the greater movement of potassium into the cells mediated by insulin, secondary to glucose absorption from the PD solution. The reported prevalence of hypokalemia in PD patients ranges from 10% to 36% [2-8], and nearly 10–30% of patients need potassium supplementation [8, 9]. Risk factors for hypokalemia in PD patients are race, cultural diet preferences, poor nutritional intake, coexisting comorbid conditions, and different dialysis schedules [5, 9-10]. In contrast, the prevalence of hyperkalemia is relatively low in PD patients at 0.8%–13% [3, 11]. Risk factors for hyperkalemia in PD are the use of angiotensin-converting enzyme inhibitors (ACEi), angiotensin II receptor blockers (ARB), and potassium-containing salt substitutes [11-13]. Szeto et al. reported no association of residual renal function with hypokalemia in incident PD patients [5]. Moreover, Xu et al. reported no association of baseline serum potassium levels with hypokalemia in incident PD patients [7].

Potassium dysregulation in PD patients has been reported to be an independent predictor of shorter survival time [5-7]. In one study from the DaVita facilities, the adjusted hazard ratio for all-cause mortality was 1.51 for potassium < 3.5 mEq/L and 1.52 for potassium ≥ 5.5 mEq/L [6]. In another study from a Chinese incident PD population, the adjusted hazard ratio for all-cause mortality was 1.79 for potassium < 3.0 mEq/L and 1.28 for potassium ≥ 5.0 mEq/L [7]. The exact mechanisms remain to be elusive. A study in hemodialysis patients revealed higher potassium removal, indicating by higher potassium gap between pre and post-hemodialysis, leading to a better myocardial performance at the end of hemodialysis session [14]. However, blood potassium concentrations in PD patients are relative constant than hemodialysis patients. Therefore, investigating factors associated with serum potassium profiles in PD patients is important for applying appropriate therapeutic strategies.

Because of the importance of potassium management in PD patients, we hypothesized serum potassium levels could be influenced by clinical factors in incident PD patients. Therefore, we examined the association between relevant clinical factors and serum potassium levels in these patients in the present study. Factors such as social characteristics, comorbid diseases, laboratory examination findings, and PD-related parameters were analyzed.

Materials and Methods

Patient selection

Subjects who initiated regular PD for at least 3 months in two hospital-facilitated PD centers were selected for analysis. Patients were enrolled from May 2013 to May 2016 in the Tianjin First Center Hospital, China, and from January 2009 to December 2015 in the Kaohsiung Chang Gung Memorial Hospital, Taiwan. Utilizing demographic and laboratory data, PD-related parameters were recorded. Comorbid illnesses including hypertension and diabetes were also recorded.

Data collection

Data were collected from the PD home record including body weight index (BMI), ultrafiltration amount, and concentration of the PD solution used. Laboratory data, including hemograms and biochemical results, were generally examined at monthly intervals. All blood samples were measured with commercial kits and an autoanalyzer. The albumin level was measured by using the bromocresol green method.

A standard peritoneal equilibration test (PET) was performed 1 to 3 months after PD commencement. The procedure used a 4-hour dwell for a 2.27% glucose-containing PD solution. Twenty-four-hour urine and dialysate samples were collected for measurement of residual glomerular filtration rate, total weekly urea, and creatinine clearance.

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Table 1. Baseline clinical and social characteristics among three stratified potassium groups

Characteristics	Total	Group 1	Group 2	Group 3	*p*
		< 3.5 mEg/L	3.5-5.0 mEg/L	≥ 5.0 mEg/L	
Numbers	319	13	251	55	
K (mEq/L)*	4.4±0.6	3.3±0.1	4.3±04	5.4±0.6	< 0.001
Gender					0.825
Male (%)	168(52.7)	7(53.8)	130(51.8)	31(56.4)	
Female (%)	151(47.3)	6(46.2)	121(48.2)	24(43.6)	
Age (y)	50.8±14.7	49.8±17.6	51.6±13.8	47.6±17.5	0.177
BMI (kg/m^2)	23.3±4.1	21.1±3.2	23.5±4.1	23.1±4.1	0.109
Comorbid disease					
Hypertension (%)	238(74.6)	10(76.9)	188(74.9)	40(72.7)	0.927
Diabetes (%)	55(17.2)	3(23.1)	46(18.3)	6(10.9)	0.356
Blood Parameters					
Hb (g/dL)	10.5±1.8	10.1±1.7	10.6±1.8	10.3±1.8	0.370
BUN (mg/dL)	72.1±33.0	59.7±26.1	69.9±32.6	84.8±33.7	0.004
Cr (mg/dL)	10.9±4.7	9.9±4.3	10.7±4.9	12.3±3.6	0.009
Alb (g/dL)	3.6±0.5	3.5±0.5	3.6±0.5	3.6±0.4	0.457
Ca (mg/dL)	8.7±0.9	8.5±0.6	8.7±0.9	8.8±1.0	0.565
P (mg/dL)	5.2±1.4	4.7±0.9	5.1±1.4	5.4±1.5	0.198
iPTH (pg/mL)#	204(99.9-378)	170.2(63.1-365.2)	199.1(91.2-354)	259.4(138.7-459)	0.021
Medication use					
ACEi (%)	119(37.3)	4(30.8)	91(36.3)	24(43.6)	0.524
ARB (%)	89(27.9)	2(15.4)	73(29.1)	14(25.5)	0.556
Diuretic (%)	27(8.5)	1(7.7)	19(7.6)	7(12.7)	0.377
β-blocker (%)	126(39.5)	3(23.1)	98(39.4)	25(45.5)	0.338
K supplement (%)	9(2.8)	1(7.7)	8(3.2)	0(0.0)	0.183
Laxative (%)	138(43.3)	4(30.8)	110(43.8)	24(43.6)	0.707

Abbreviations: K, potassium; BMI, body mass index; Hb, hemoglobin; BUN, blood urea nitrogen; Cr, creatinine; Alb, albumin; Ca, calcium; P, phosphate; iPTH, intact parathyroid hormone; ACEi, angiotensin converting enzyme inhibitor; ARB, angiotensin receptor blocker

*: averaged serum potassium levels in the first three months after peritoneal dialysis initiation

#: median (interquartile range)

Timing of serum potassium measurement and management

Averaged serum potassium levels in the first 3 months after PD initiation were calculated for analysis. We defined hypokalemia as a serum potassium level < 3.5 mEg/L and hyperkalemia as a serum potassium level ≥ 5.0 mEg/L. Patients with hypokalemia were generally managed with potassium-containing pills and were instructed to increase vegetable and fruit intake. Hyperkalemia was treated with potassium chelating agents and patients were advised to reduce fruit and vegetable intake. Medication use that might affect potassium levels such as ACEis, ARBs, diuretics, β-blockers, potassium supplements, and laxatives was also recorded.

The data review protocol for this study was approved by the Committee on Human Research at the Kaohsiung Chang Gung Memorial Hospital in Taiwan (100-2661B) and Tianjin First Center Hospital in China (2015009s), and the study was conducted in accordance with the principles of the Declaration of Helsinki. Written informed consent was not required according to retrospective data review regulations by the Committee on Human Research at Kaohsiung Chang Gung Memorial Hospital in Taiwan and Tianjin First Center Hospital in China.

Statistical analysis

The baseline characteristics of the participants are summarized and presented as mean ± standard deviation (SD), median (interquartile range), and frequency (percentage). Differences in baseline characteristics between the groups were estimated by using the χ^2 test, Fisher's exact test, and analysis of variance (ANOVA) tests (Tables 1 and 2). The association between the baseline variables and serum potassium categories (Group 1: serum K < 3.5 mEq/L, Group 2: serum K 3.5–5.0 mEq/L, Group 3: serum K ≥ 5.0 mEq/L) in the study period were analyzed by using univariate and multivariate logistic regression (Tables 3 and 4). Multivariate logistic regression analyses were used to derive adjusted odds ratios (ORs) for serum potassium profile changes. The 95% confidence interval (95% CI) and p-value were used to determine statistical significance. A p value less than 0.05 was considered statistically significant. All statistical analyses were conducted using STA-

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Table 2. Baseline peritoneal dialysis-related parameters among three stratified potassium groups

Characteristics	Total	Group 1	Group 2	Group 3	*p*
		< 3.5 mEg/L	3.5-5.0 mEg/L	≥ 5.0 mEg/L	
Numbers	319	13	251	55	
PD mode					0.073
CAPD (%)	150(47.0)	4(30.8)	122(48.6)	24(43.6)	
APD (%)	29(9.1)	2(15.4)	26(10.4)	1(1.8)	
DAPD (%)	140(43.9)	7(53.8)	103(41.0)	30(54.6)	
PD exchange volume (mL)#	6000(6000-8000)	7800(6000-8000)	6000(6000-8000)	6000(6000-8000)	0.332
Ultrafiltration volume (mL)#	300(100-480)	260(42-455)	300(100-490)	250(100-400)	0.294
Urine volume (mL/day)#	850(500-1300)	800(400-1050)	800(450-1300)	1000(650-1500)	0.148
Total Kt/V urea	2.1±0.7	2.2±0.5	2.1±0.7	1.9±0.4	0.209
Renal Kt/V urea	0.9±0.7	0.7±0.6	0.9±0.7	0.9±0.5	0.501
Dialysate Kt/V urea	1.4±0.5	1.6±0.5	1.4±0.5	1.2±0.4	0.024
WCCr total (L/w/1.73m^2)	70.8±30.1	70.9±21.8	70.7±32.3	71.2±20.3	0.994
WCCr renal (L/w/1.73m^2)	36.8±26.5	33.8±23.7	36.5±27.5	38.9±22.4	0.762
WCCr dialysate (L/w)	34.2±18.7	37.1±12.0	34.2±20.2	33.2±12.2	0.793

Abbreviation: CAPD, continuous ambulatory peritoneal dialysis; APD, automated peritoneal dialysis; DAPD, automated peritoneal dialysis at daytime; WCCr, weekly creatinine clearance
: median (interquartile range)

TA version 11.1 (Stata Corp.2009. Stata Statistical software: Release 11. College Station, Texas, Stata Corp LP., USA)

Results

A total of 319 patients were identified for analysis. The mean age was 50.8±14.7 year-old. Male was predominant. In the analysis of social characteristics among potassium-stratified patients, there were no significant differences in sex, BMI, age, or comorbid diseases. Blood urea nitrogen (BUN), creatinine (Cr), and intact parathyroid hormone (iPTH) levels were significantly increased in the patients in the higher serum potassium strata (Table 1).

Table 3. Associations between clinical characteristics and low potassium levels (serum K < 3.5 mEq/L) by logistic regression. (n=264)

Characteristics	COR	95% CI	*p*	AOR	95% CI	*p*
Gender, Female	0.92	0.30 - 2.82	0.885	0.72	0.17 - 3.05	0.656
Age (y)	0.99	0.95 - 1.03	0.644	0.99	0.95 - 1.04	0.663
Diabetes (%)	1.34	0.35 - 5.05	0.669	1.17	0.25 - 5.39	0.839
Blood Parameters						
BUN (mg/dL)	0.99	0.97 - 1.01	0.264	1.00	0.97 - 1.03	0.834
Cr (mg/dL)	0.85	0.71 - 1.02	0.081	0.82	0.67 - 1.01	0.057
Alb (g/dL)	0.56	0.21 - 1.45	0.231	0.63	0.18 - 2.22	0.473
Ca (mg/dL)	0.71	0.38 - 1.36	0.305	0.97	0.44 - 2.14	0.941
P (mg/dL)	0.78	0.50 - 1.22	0.280	0.78	0.48 - 1.27	0.319
iPTH (pg/mL)	1.00	1.00 - 1.00	0.862	1.00	1.00 - 1.00	0.572
Medication use						
ACEi (%)	0.78	0.23 - 2.61	0.688	0.76	0.19 - 3.10	0.701
ARB (%)	0.44	0.10 - 2.05	0.298	0.65	0.11 - 3.86	0.640
Diuretic (%)	1.02	0.13 - 8.25	0.987	0.74	0.07 - 7.70	0.801
β-blocker (%)	0.47	0.13 - 1.74	0.258	0.48	0.10 - 2.19	0.340
K supplement (%)	2.53	0.29 - 21.91	0.399	3.75	0.28 - 49.71	0.316
Laxative (%)	0.57	0.17 - 1.90	0.360	0.78	0.17 - 3.55	0.746
PD mode						
CAPD (%)	1.00			1.00		
APD (%)	2.35	0.41 - 13.49	0.339	1.70	0.16 - 18.59	0.664
DAPD (%)	2.07	0.59 - 7.28	0.255	2.46	0.42 - 14.55	0.321
PD exchange volume (mL)	1.00	1.00 - 1.00	0.487	1.00	1.00 - 1.00	0.551
Ultrafiltration volume (mL)	1.00	1.00 - 1.00	0.517	1.00	1.00 - 1.00	0.651
Urine volume (mL/day)	1.00	1.00 - 1.00	0.395	1.00	1.00 - 1.00	0.369
Total Kt/V urea	1.15	0.63 - 2.08	0.648	1.35	0.66 - 2.76	0.415
WCCr total (L/w/1.73m^2)	1.00	0.98 - 1.02	0.984	1.00	0.98 - 1.02	0.854

COR: Crude odds ratio estimated by univariate logistic regression.
AOR: Adjusted odds ratio estimated by multivariate logistic regression.

Table 2 showed the results of the association analysis between clinical characteristics and low serum potassium levels by the logistic regression method. There were no significant risk factors for hypokalemia including sex, age, diabetes, blood examination parameters, me-

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Table 4. Associations between clinical characteristics and high potassium levels (serum K ≥ 5.0 mEq/L) by logistic regression. (n=306)

Characteristics	COR	95% CI	*p*	AOR	95% CI	*p*
Gender, Female	0.83	0.46 - 1.50	0.539	1.21	0.57 - 2.57	0.629
Age (y)	0.98	0.96 - 1.00	0.065	0.97	0.95 - 1.00	0.036
Diabetes (%)	0.55	0.22 - 1.35	0.190	0.98	0.34 - 2.80	0.966
Blood Parameters						
BUN (mg/dL)	1.01	1.00 - 1.02	0.004	1.02	1.01 - 1.03	0.001
Cr (mg/dL)	1.07	1.01 - 1.13	0.025	1.08	1.01 - 1.16	0.029
Alb (g/dL)	1.04	0.57 - 1.89	0.895	0.71	0.33 - 1.54	0.390
Ca (mg/dL)	1.05	0.76 - 1.45	0.764	1.24	0.85 - 1.83	0.267
P (mg/dL)	1.14	0.94 - 1.39	0.182	1.01	0.79 - 1.29	0.965
iPTH (pg/mL)	1.00	1.00 - 1.00	0.019	1.00	1.00 - 1.00	0.304
Medication use						
ACEi (%)	1.36	0.75 - 2.46	0.307	1.01	0.49 - 2.08	0.974
ARB (%)	0.83	0.43 - 1.62	0.589	0.72	0.30 - 1.73	0.466
Diuretic (%)	1.78	0.71 - 4.47	0.219	2.41	0.79 - 7.41	0.124
β-blocker (%)	1.30	0.72 - 2.34	0.381	1.40	0.67 - 2.92	0.374
Laxative (%)	0.99	0.55 - 1.79	0.980	0.65	0.28 - 1.51	0.315
PD mode						
CAPD (%)						
APD (%)	0.20	0.03 - 1.51	0.118	0.20	0.02 - 2.02	0.174
DAPD (%)	1.48	0.81 - 2.69	0.198	2.56	0.93 - 7.03	0.069
PD exchange volume (mL)	1.00	1.00 - 1.00	0.216	1.00	1.00 - 1.00	0.310
Ultrafiltration volume (mL)	1.00	1.00 - 1.00	0.137	1.00	1.00 - 1.00	0.599
Urine volume (mL/day)	1.00	1.00 - 1.00	0.099	1.00	1.00 - 1.00	0.045
Total Kt/V urea	0.56	0.29 - 1.06	0.075	0.55	0.24 - 1.22	0.138
WCCr total (L/w/1.73m^2)	1.00	0.99 - 1.01	0.916	1.00	0.99 - 1.02	0.523

COR: Crude odds ratio estimated by univariate logistic regression.
AOR: Adjusted odds ratio estimated by multivariate logistic regression.

dication use, and PD-related parameters by multivariate logistic regression analysis. Table 4 showed the similar analysis for hyperkalemia. BUN (adjusted odds ratio [OR] 1.02, 95% CI 1.01–1.03, p = 0.001) and Cr (adjusted OR 1.08, 95% CI 1.01–1.16, p = 0.029) levels were correlated with a significantly higher risk for hyperkalemia by multivariate logistic regression analysis. Urine volume was correlated with a significantly neutral effect for hyperkalemic risk (adjusted OR 1.00, 95% CI 1.00–1.00, p = 0.045).

Discussion

Xu et al. reported that serum potassium levels had variability in the follow-up period in incident PD patients [7]. In the present study, we used averaged serum potassium levels in the first 3 months after PD initiation for statistical analysis. We found that patients with hyperkalemia had higher blood BUN, Cr, and iPTH levels than hypokalemic and normokalemic patients.

We found no significant differences for medication use and PD-related parameters. A reasonable explanation for this result is greater freedom in dietary choices in the PD patients with hyperkalemia. This result implies there is an important role for dietary education of new PD patients. In our prior study, failure to comply with medication use was the only significant factor contributing to hyperphosphatemia in new PD patients [15]. Therefore, educational instruction about adherence to medication in new PD patients is still a challenge in the care of PD patients.

In PD patients, potassium balance is mainly achieved through potassium redistribution between the extracellular and intracellular compartments [16]. These patients frequently have hypokalemia caused by potassium redistribution into the intracellular compartment that is stimulated by insulin release secondary to continuous peritoneal glucose infusion

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[16]. In the present study, we did not observe any relationship between diabetes and the serum potassium profile of new PD patients. The short-term observation period may have contributed to this result.

We did not find any significant association between serum potassium levels and drugs such as diuretics, ACEis, ARBs, laxatives, or potassium-containing pills. Prior studies demonstrated influences of the aforementioned drugs on serum potassium levels in PD patients [2, 4, 8, 9, 11, 17]. However, some studies also reported that ACEis did not affect serum potassium levels in PD patients [5, 18, 19]. The present study did not measure serial potassium levels and only used a short-term observation period. It seems likely that individual dietary potassium intake, bowel habit changes, PD exchange volume, and progressively declining residual urine volume may result in long-term serum potassium variability.

We found blood BUN, Cr, and iPTH levels were proportionately increased in association with increased serum potassium. However, the only significant risk factors for hyperkalemia after fully adjusted multivariate logistic regression analysis were blood BUN and Cr levels. Previous studies demonstrated a significant correlation between serum potassium levels and albumin levels [7]. In the present study, we did not find any significant difference in nutritional indices including BMI, serum albumin levels, or hemoglobin levels among the three groups. Moreover, PD-related parameters and urine volume also did not correlate with a significantly increased risk for hyperkalemia by multivariate logistic analysis. Therefore, a possible reason for our observations is the free dietary intake in these patients was contributing to hyperkalemia. The relationship between nutritional indices and serum potassium levels in PD patients needs further research with longer observation periods and a larger patient group.

In the present study, we did not find an association of PD-related parameters with serum potassium profile in new PD patients. Prior studies revealed that an increased dialysate volume was independently related to decreased serum potassium levels [7, 20, 21]. In adjusted multivariate logistic regression analysis, urine volume demonstrated a neutral effect for hyperkalemic risk with marginal statistical significance. We did not measure PD exchange volume or daily urine volume in the PD patients with different PD modes. Based on the above limitations, however, we cannot construct an exact model of the relationship between PD modes and residual urine volume with serum potassium profiles in new PD patients.

Although the present study provides promising evidence of clinical factors associated with serum potassium profiles in incident PD patients, there are limitations to the methods used. First, we only recorded a short-time averaged serum potassium level in incident PD patients. The direct causality cannot be drawn without selection bias. Second, we did not measure daily potassium intake or the amount of urine and dialysate potassium removal. As a result, an assessment of potassium balance in the patients is not available. It is not clear how strongly this data contributes to serum potassium profiles in PD patients. Third, there are relatively few patients presenting with abnormal serum potassium levels in the present study. Hence, the weight of the statistical significance of the analysis may be reduced.

Conclusion

Our study demonstrated a stronger association between incident PD patients with hyperkalemia and higher blood BUN and Cr levels than those with hypokalemia or normokalemia. The result implies a freely dietary intake may contribute to the higher serum potassium levels in new PD patients.

Disclosure Statement

The authors of this manuscript state that they do not have any conflict of interests and nothing to disclose.

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