Urinary tract infection is associated with hypokalemia: a case control study

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Abstract

Background

Hypokalemia is a common clinical problem. The association between urinary tract infection (UTI) and hypokalemia is not clear. Hypokalemia is common in patients with UTI in clinical observation. The aim of the study is to determine if UTI is associated with hypokalemia.

Methods

Patients hospitalized with UTI and the control group were retrieved from the Longitudinal Health Insurance Database 2005. The control group was patients hospitalized with other reasons and were matched for the confoundings of UTI and hypokalemia. We analyze the risk of hypokalemia using logistic regression and calculate the odds ratio (OR) and 95% confidence interval (CI) of OR.

Results

We analyzed 44952 UTI patients and 44952 matched control patients. The percentage (10.3%, n=4625) of hypokalemia was higher in UTI patients than that (5.2%, n=2342) in control patients (chi-square, $p < 0.001$). UTI was associated with hypokalemia ($p < 0.001$) and the OR was 2.04 (95% CI 1.94 - 2.16). Cerebrovascular accident, chronic obstructive pulmonary disease, diabetes, hypertension, congestive heart failure, and medications including diuretics, beta-blockers, insulin, and laxatives were also associated with hypokalemia. Recurrent UTI was associated with hypokalemia in patients with UTI.

Conclusions

Hypokalemia is linked to urinary tract infection and potassium should be tested in UTI patients. The association of hypokalemia and UTI is independent of patients' comorbidities and medications.

Background

Hypokalemia is a common electrolyte abnormality in hospitalized patients. Unrecognized hypokalemia may trigger arrhythmias [1] and is associated with increased mortality in patients with chronic diseases such as heart failure, diabetes, or chronic kidney disease [2, 3]. Urinary tract infection (UTI) is a common bacterial infection in women and the elderly [4–6]. Clinical manifestations of UTI include dysuria, frequency, urgency, fever, nausea, vomit, and gross hematuria. It may not be surprised that hypokalemia may be occurred because of increased potassium loss after vomit and fever. However, the association between UTI and hypokalemia is not clear [7–11]. We observed that hypokalemia is common among UTI patients in clinical settings. This study was conducted to determine the association between UTI and hypokalemia. Inpatients were selected because serum potassium is rarely measured in outpatient settings as UTI has not been considered as a risk factor for hypokalemia.

Methods

We extracted data from the longitudinal health insurance database 2005 (LHID2005) as prescribed in the previous study [12]. The dataset is a de-identified secondary data and is released to the public for research purposes. A review of the institutional review board is not required in conducting this study.

All inpatients between 1 January 2000 and 31 December 2008 were included. Patients hospitalized with UTI were identified with ICD-9-CM code 599 on admission. Hypokalemia was identified using ICD-9-CM code (276.8) in the same hospitalization.

The first hospitalization for UTI was selected in patients with more than one episode of UTI. The control patients are the patients who hospitalized for other reasons except for UTI. The control patients were patients who are hospitalized for other reasons with matching for confoundings including cerebrovascular accident (CVA), chronic obstructive pulmonary disease (COPD), diabetes mellitus (DM), hypertension (HTN), chronic kidney disease (CKD), congestive heart failure (CHF), Cushing syndrome, hyperthyroidism, vaginal infection, medications, and urethral catheterization with a ratio of 1:1. These confoundings were used because they are associated with UTI or hypokalemia in the literature.

The comorbidities diagnosed before the episode of UTI in at least 3 visits were used. The ICD-9-CM codes of comorbidities include CVA (ICD-9-CM code 430–436 and 438), COPD (490–496), vaginal infection (616), DM (250), HTN (401–405), CKD (585), CHF (428), Cushing's syndrome (255.0), hyperthyroidism (242), and hypothyroidism (244). Urethral catheterization (47013–47014) in one week before hospitalization was also extracted. Recurrent UTI was defined as individuals who had more than two episodes of UTI in 6 months or three episodes in one year [13]. Medications including diuretics (ATC code C03), Beta-blockers (C07), antibiotics (J01CA, J01CR, J01GB, A01AB04), insulin (A10), steroid (H02AB), potassium binders (V03AE01), laxatives (A06AG07), and theophylline (C03) were also extracted.

Statistical Analysis

Data are expressed as number (percentage) for categorical variables, mean (standard deviation), or median (interquartile range) for continuous variables. The differences of variables between two groups were tested using Chi-square tests for categorical variables and t-test or Mann–Whitney U test for continuous variables. The risk of hypokalemia was analyzed with univariable logistic regression followed by multivariable logistic regression. The odds ratios (ORs) and 95% confidence interval (CIs) of ORs were calculated. All statistical analyses were carried out using SAS statistical package, version 9.3 (SAS Inc., NC, USA). All comparison tests were two-sided. A P-value of less than 0.05 was considered as statistically significant.

Results

We analyzed 44952 inpatients with UTI and 44952 matched control patients. The UTI patients were 70 years old (interquartile range 54 to 79) and 60% of them were female. Fifty-eight percent of them had HTN, 33.8% had DM, 30.2% had COPD, 28% had CVA, and 13.7% had CHF. There was no difference in the patients' age, the percentage of gender, comorbidities, medications, urethral catheterization between the

UTI and the control patients (Table 1). There was no difference in the proportions of medications used between the two groups. The percentages of patients with urethral catheterization were both 6.7%.

Table 1
Clinical characteristics of patients with and without urinary tract infection (UTI)

Factor	UTI(-) N = 44952	UTI(+) N = 44952	P
Hypokalemia n(%)	2342 (5.2)	4625 (10.3)	< 0.001
Age year(IRQ)	70 (54–79)	69 (53–79)	0.90
Male n(%)	17924 (39.9)	17924 (39.9)	-
Comorbidity n(%)			
CVA	12635 (28.1)	12581 (28.0)	0.69
COPD	13689 (30.5)	13577 (30.2)	0.421
DM	15179 (33.8)	15179 (33.8)	-
HTN	26331 (58.6)	26103 (58.1)	0.13
CKD	3386 (7.5)	3386 (7.5)	-
CHF	6213 (13.8)	6156 (13.7)	0.59
Cushing syndrome	297 (0.7)	283 (0.6)	0.59
Hyperthyroidism	714 (1.6)	700 (1.6)	0.73
Vaginal infection	318 (0.7)	354 (0.8)	0.18
Medications n(%)			
Diuretics	2178 (4.8)	2178 (4.8)	-
Beta-blockers	1334 (3.0)	1334 (3.0)	-
Antibiotics	296 (0.7)	298 (0.7)	0.97
Insulin	732 (1.6)	747 (1.7)	0.71
Steroid	968 (2.2)	968 (2.2)	-
Potassium binders	105 (0.2)	105 (0.2)	-
Laxatives	4458 (9.9)	4458 (9.9)	-
Xanthium	1777 (4.0)	1777 (4.0)	-
Urethral catheterization	3034 (6.7)	3034 (6.7)	-

CVA: cerebrovascular accident, COPD: chronic obstructive pulmonary disease, DM: diabetes mellitus, HTN: hypertension, CKD: chronic kidney disease, CHF: congestive heart failure

As shown in Table 2, UTI was associated with hypokalemia in univariable and multivariable logistic regression ($p < 0.001$ and < 0.001). The ORs were 2.16 (95% CI: 2.05–2.28) in univariable logistic regression and 2.04 (95% CI: 1.94–2.16). Other factors associated with hypokalemia were patients' age, CVA, COPD, DM, HTN, and CHF. The ORs was 1.02 (95% CI: 1.02–1.02) for every one additional year, 1.28 (95% CI: 1.21–1.36) for CVA, 1.27 (95% CI: 1.20–1.34) for COPD, 1.21 (95% CI: 1.14–1.28) for DM, 1.12 for HTN (95% CI: 1.05–1.19), and 1.85 (95% CI: 1.74–1.97) for CHF in multivariable logistic regression. Diuretics (OR: 1.80, 95% CI: 1.65–1.96), beta-blockers (OR: 1.55, 95% CI: 1.35–1.79), insulin (OR: 1.32, 95% CI: 1.14–1.52), laxatives (OR: 1.28, 95% CI: 1.18–1.39) were positively associated with hypokalemia. Antibiotics were negatively associated with hypokalemia (OR: 0.43, 95% CI: 0.30–0.61, $p < 0.001$)

Table 2
Factors associated with hypokalemia in univariable and multivariable logistic regression

Factors	**Univariable**			**Multivariable**		
	ORs	**95%**	**CIs**	**ORs**	**95%**	**CIs**
UTI	2.16	2.05	2.28	2.04	1.94	2.16
Age	1.03	1.03	1.03	1.02	1.02	1.02
Comorbidity						
CVA	2.20	2.09	2.32	1.28	1.21	1.36
COPD	1.91	1.82	2.01	1.27	1.20	1.34
DM	1.65	1.57	1.74	1.21	1.14	1.28
HTN	2.27	2.15	2.40	1.12	1.05	1.19
CHF	2.76	2.61	2.92	1.85	1.74	1.97
Medications						
Diuretics	2.83	2.62	3.06	1.80	1.65	1.96
Beta-blockers	2.24	1.96	2.56	1.55	1.35	1.79
Antibiotics	0.62	0.44	0.87	0.43	0.30	0.61
Insulin	2.10	1.83	2.40	1.32	1.14	1.52
Laxatives	2.24	2.08	2.42	1.28	1.18	1.39

UTI: urinary tract infection, CVA: cerebral vascular accident, COPD: chronic obstructive pulmonary disease, DM: diabetes mellitus, CHF: congestive heart failure

We further analyzed the risk of hypokalemia in UTI patients (Table 3). Recurrent UTI was associated with an increased risk of hypokalemia. The ORs were 1.32 (95% CI: 1.22–1.42) in univariable logistic regression and 1.14 (95% CI: 1.05–1.23) in multivariable logistic regression. CVA, COPD, HTN, and CHF

were independently associated with hypokalemia in UTI patients, but DM was not. The OR for CVA, COPD, HTN, and CHF were 1.16 (95% CI: 1.08–1.24), 1.49 (95% CI: 1.39–1.59), 1.41 (95% CI: 1.30–1.53), and 1.41 (95% CI: 1.30–1.52), respectively. Diuretics, steroid, laxatives were also associated with hypokalemia and Beta-blockers, insulin was associated with a lower risk of hypokalemia in UTI patients.

Table 3
Risk of hypokalemia among patients with urinary tract infection

Factors	Univariable			Multivariable		
	OR	95%	CI	OR	95%	CI
Recurrent UTI	1.32	1.22	1.42	1.14	1.05	1.23
Age	1.02	1.02	1.03	1.01	1.01	1.01
Comorbidity						
CVA	1.71	1.61	1.83	1.16	1.08	1.24
COPD	2.09	1.96	2.22	1.49	1.39	1.59
DM	1.39	1.31	1.48	1.06	0.99	1.14
HTN	2.22	2.07	2.37	1.41	1.30	1.53
CHF	2.18	2.02	2.34	1.41	1.30	1.52
Medications						
Diuretics	1.72	1.54	1.93	1.26	1.12	1.42
Beta-blockers	0.93	0.76	1.14	0.75	0.61	0.93
Insulin	0.94	0.74	1.20	0.72	0.56	0.93
Steroid	1.59	1.34	1.88	1.29	1.08	1.53
Laxatives	1.81	1.66	1.98	1.32	1.20	1.45

UTI: urinary tract infection, CVA: cerebral vascular accident, COPD: chronic obstructive pulmonary disease, DM: diabetes mellitus, CHF: congestive heart failure

Discussion

In this case-control study, we demonstrated an association between UTI and hypokalemia. This is supported by the increased OR of hypokalemia in the univariable and multivariable logistic regressions when comparing UTI patients to patients hospitalized for other reasons. Recurrent UTI is also associated with hypokalemia in UTI patients. The increased risk of hypokalemia in UTI may partially explain the cardiac arrest following infectious disease in a previous study [14]. Patients hospitalized for UTI were selected in this study because the serum potassium was more likely to be measured among inpatient.

Less 1% of UTI in outpatient measured serum potassium in the dataset. We suspected that UTI may lead to hypokalemia through an increased urinary potassium loss because renal parenchyma is damaged in UTI [15, 16]. Our clinical observation supported the increased urinary potassium loss because urine potassium creatinine ratio was increased during UTI and returned to basal levels after treatment of UTI. Other possible causes of hypokalemia include medications such as diuretics [17], increased gastrointestinal loss such as vomiting, or decreased potassium intake such as poor intake [4, 11, 18, 19]. We analyzed medications that may be related to hypokalemia and these medications include diuretics, beta-blockers, insulin, and laxatives. We found these medications were independently associated with an increased risk of hypokalemia.

Because hypokalemia may be related to multiple comorbidities, we also analyzed comorbidities that may be associated with both UTI [19, 20] and hypokalemia [21]. Among these comorbidities, CVA, COPD, DM, HTN, and CHF were independently associated with hypokalemia. Hyperkalemia is a well-known complication of CKD and therefore the chance hypokalemia may be decreased in CKD patients [22]. But we did not find an association between CKD and hypokalemia in both univariable and multivariable logistic regression.

The limitations to the study include: First, nausea/vomiting symptoms were rarely recorded in the LHID, we are not able to further analyze if vomiting is responsible for the hypokalemia in UTI patients. Second, the serum potassium readings and symptoms associated with hypokalemia were not available in the LHID, we were not able to report the severity of hypokalemia in this study. In our clinical practice, most of the hypokalemia was asymptomatic and potassium replacement was rarely acquired. Third, we hypothesized that the renal parenchyma injury in UTI may be responsible for the development of hypokalemia. Therefore, acute pyelonephritis (ICD-9-CM 590.1) may be associated with more severe renal parenchyma injury than lower UTI and therefore more likely to develop hypokalemia. However, we did not find a significant association between acute pyelonephritis and hypokalemia. It is likely that many of the patients with acute pyelonephritis were coded as UTI in the LHID. Fourth, the diagnosis of UTI and hypokalemia was obtained based on the code on discharge. The causal relationship is difficult to be determined. Some of the recurrent UTI may be caused by the hypokalemia that results in the elaboration of alkaline urine, bladder dysfunction, and urinary stasis [23].

Conclusions

Urinary tract infection is associated with an increased risk of hypokalemia and measurements of serum potassium should be considered in clinical practice. UTI and hypokalemia are associated with multiple chronic diseases and medications. The association of hypokalemia and UTI is independent of comorbidities and medications.

Declarations

Ethics approval and consent to participate

The dataset is a de-identified secondary data and is released to the public for research purposes. A review of the institutional review board is not required in conducting this study.

Consent for publication

Not applicable

Availability of data and material

The datasets 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 competing interests

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Authors' contributions

HL and HC analyzed and interpreted the data. YF and CY made substantial contributions to the conception. CY have drafted the work. AL substantively revised the work. All authors read and approved the final manuscript.

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