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Association of diuretic use and overactive bladder syndrome in older adults: a propensity score analysis

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Abstract

Diuretics use and overactive bladder syndrome are common in older adults. However, the relationship between the two has not been well studied. Data were collected by self-administered questionnaires including the Urge Urinary Distress Inventory (Urge-UDI) and the Urge Incontinence Impact Questionnaire (Urge-IIQ), and by outpatient chart abstraction. Patients (n = 172) had a mean age of 79 ± 7.5 (± S.D.), 76% were women, and 48% were African Americans; 76% had hypertension, 32% had heart failure, and 66% were receiving diuretics (57% loop diuretics). Overall, 72%, 68%, and 73% of patients respectively reported urinary frequency, urgency and urge incontinence. Diuretic use was associated with increased frequency (81% versus 55% non-diuretic; odds ratio = OR = 3.48; 95% confidence interval = CI = 1.73–7.03) and urgency (74% versus 57% non-diuretic; OR = 2.17; 95% CI = 1.11–4.24) but not with incontinence (OR = 1.74; 95% CI = 0.87–3.50). When adjusted for propensity scores, diuretic use had independent associations with frequency (adjusted OR = 3.09; 95% CI = 1.20–7.97) and urgency (adjusted OR = 2.50; 95% CI = 1.00–6.27). In addition to frequency and urgency, loop diuretic use was also associated with incontinence (OR = 2.54; 95% CI = 1.09–5.91), which lost significance after propensity adjustment (adjusted OR = 1.88; 95% CI = 0.57–6.17). Overall summary mean Urge-IIQ score was 1.83 ± 0.85 (±S.D.) with 1.75 ± 0.86, 1.68 ± 0.76, and 2.03 ± 0.88, respectively for no-diuretic, non-loop, and loop-diuretic patients (one-way ANOVA p = 0.063). Overactive bladder symptoms were common among ambulatory older adults and were associated with diuretic use, and had stronger associations with loop diuretic use.

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Keywords

Diuretic use; overactive bladder; quality of life; propensity score; older adults

1. Introduction

The overactive bladder syndrome, characterized by urinary urgency, frequency, nocturia and/or urge incontinence, is common in older adults and may be negatively associated with quality of life (Hampel et al., 1997; Brown et al., 1999; Lubeck et al., 1999; Brown, 2002; Abrams et al., 2003; Odeyemi et al., 2006). Diuretic use is also common in older adults as the prevalence of hypertension and heart failure increases with age (Donahue et al., 1990; Fried et al., 1998). By causing diuresis or increased formation of urine by kidneys, diuretics increase urinary frequency and may cause urinary urgency and incontinence. However, whether diuretic use is associated with symptoms of overactive bladder and worsening quality of life has not been well studied (Ouslander et al., 1987; Diokno et al., 1991; Fitzgerald et al., 2007). The objective of this study was to evaluate the relationship between diuretic use and symptoms of overactive bladder syndrome and to evaluate the impact of diuretics on overactive bladder symptoms' related quality of life among ambulatory older adults.

2. Subjects and methods

2.1. Study design

This study is a cross-sectional survey of older adults attending an academic geriatric medicine clinic between 2002 and 2005. Data on demographic variables, Urge-UDI and Urge-IIQ were collected by self-administered questionnaires. The Urge-UDI was used to assess the presence of overactive bladder symptoms and how much the symptoms bother the patients, while the Urge-IIQ was used to evaluate the impact of overactive bladder on quality of life. These measures have been validated in diverse populations of patients with urge urinary incontinence and have been found to have excellent test-retest reliability. Scores range from 0–4 on the Urge-UDI and 0–5 on the Urge-IIQ with higher scores indicating more severe bother and poorer quality of life (Brown et al., 1999; Lubeck et al., 1999). Data on comorbidity, Mini Mental State Examination (MMSE) score, Geriatric Depression Scale (GSE) score, and medications were obtained by chart abstraction.

2.2. Study patients

Ambulatory older adults, 65 years and older, attending an academic, Geriatric Medicine outpatient practice and who could read and respond to a written, English Language questionnaire were eligible to participate. Trained study personnel approached patients for participation in the study in the waiting room during routine clinic visits. The study protocol was explained to patients by study coordinators and informed consents were obtained. Patients who consented to participate were categorized into two groups based on use of diuretics, and those receiving diuretics were further classified into taking loop and non-loop diuretics. A total of 176 patients participated in the study. Four patients with incomplete data were excluded from analysis. The protocol was approved by the Institutional Review Board.

2.3. Outcome variables

The primary outcomes were symptoms of overactive bladder including urinary urgency, frequency, nocturia, and urge incontinence. Patients were asked to answer 'yes' or 'no' if they experience any of these symptoms based on the Urge-UDI questionnaire. Secondary outcomes were summary and domain-specific Urge-IIQ scores. The summary and domain-specific Urge-IIQ scores were used to evaluate the overall impact of overactive bladder symptoms on quality

of life and on the six domains of quality of life that may be affected by overactive bladder (activities, travel, physical activities, feelings, relationships, and sexual function). The mean Urge-UDI score was used to assess the severity of the symptoms of overactive bladder. Higher scores on these measures indicate more severe bother and poorer quality of life.

2.4. Statistical analysis

We first compared baseline characteristics of patients receiving and not receiving diuretics using Pearson's chi-square and Student t-tests as appropriate. We then estimated propensity scores for diuretic use for every patient by using a multivariable logistic regression model in which diuretic use was the dependent variable (Ahmed et al., 2006, 2007a,b; Ahmed, 2007). The propensity score for diuretic use for a patient is the conditional probability of receiving a diuretic given that patient's baseline characteristics (Rosenbaum and Rubin, 1983, 1984; Rubin, 1997, 2001, 2004). Baseline patient characteristics included in the model were age, gender, race, education, employment status, marital status, living status, diabetes, coronary artery disease, heart failure, hypertension, urinary tract infection (UTI), use of angiotensin-converting enzyme (ACE) inhibitors, beta blockers, angiotensin receptor blockers (ARB), and serum creatinine. The propensity score, the composite single covariate representing all measured baseline covariates used in the propensity score model, can be used to reduce selection bias in observational studies.

The association between diuretic use and symptoms of overactive bladder was then assessed using separate logistic regression models in which diuretic use was the predictor variable and individual symptoms of overactive bladder were dependent variables. Each model was adjusted for by raw propensity scores for diuretic use. We then repeated our analysis using traditional multivariable logistic regression model that included key baseline covariates (age, gender, race, education, employment status, marital status, living status, diabetes, coronary artery disease, heart failure, hypertension, UTI, use of ACE-inhibitors, beta blockers, ARB and serum creatinine). We also examined the association between the type of diuretic used and symptoms of overactive bladder using loop and non-loop diuretics as dummy variables. One-way analysis of variance test was used to estimate the differences between no diuretic, non-loop diuretic, and loop diuretic use and the domain and overall mean scores of the Urge-IIQ and the Urge-UDI. All tests were two-tailed, and a p-value of 0.05 or less was considered statistically significant. All statistical analyses were conducted using the Statistical Package for the Social Sciences (SPSS 14; SPSS Inc., Chicago, IL).

3. Results

3.1. Patient characteristics

Patients (n = 172) had a mean age of 79 ± 7.5 years, 76% were women, 48% were African Americans, 76% had hypertension, 32% had heart failure, and 66% were receiving diuretics. Overall, 72%, 68%, 73%, and 82% of patients respectively, reported urinary frequency, urgency, urge incontinence, and nocturia, with an overall mean Urge-IIQ summary score of 1.83 ± 0.85. Baseline characteristics of patients by diuretic use are displayed in Table 1. Patients on diuretics were more likely to be women and African Americans, and more likely to have diabetes, coronary artery disease, heart failure, and hypertension.

3.2. Association of diuretic use with overactive bladder

Urinary frequency was reported by 55% of no-diuretic and 81% of diuretic patients (odds ratio = OR = 3.48; 95% confidence interval = CI = 1.73–7.03; $p < 0.0001$). The association remained significant after adjustment for propensity scores (adjusted OR = 3.09; 95% CI = 1.20–7.97; $p = 0.020$; Table 2) and in the multivariable model (adjusted OR = 3.56; 95% CI = 1.29–9.82; $p = 0.014$). Urinary urgency was reported by 57% of no-diuretic and 74% of diuretic patients

(OR = 2.17; 95% CI = 1.11–4.24; p = 0.024). The association, however, lost its signi-ficance after adjustment for propensity scores (adjusted OR = 2.50; 95% CI = 1.00–6.27; p = 0.051; Table 2). Diuretic use was not associated with urinary incontinence or nocturia (Table 2).

3.3. No diuretic versus non-loop and loop diuretic use

Compared to patients not using diuretics, use of loop diuretic was associated with increased urinary frequency (OR = 6.62; 95% CI = 2.58–16.94; p = <0.0001) and urgency (OR = 4.09; 95% CI = 1.75–9.59; p = 0.001). These associations remained significant after adjustment for propensity scores (Table 3). Loop diuretic use was also associated with increased urge incontinence (OR = 2.54; 95% CI = 1.09–5.91), but the association was no longer significant after adjustment for propensity scores. Use of non-loop diuretic was not associated with overactive bladder symptoms (Table 3).

3.4 Diuretic use and quality of life

The mean Urge-IIQ summary scores for patient not using diuretics, and those using non-loop and loop diuretics were respectively 1.75 ± 0.86, 1.68 ± 0.76, and 2.03 ± 0.88, one-way ANOVA p = 0.063 (Table 4). The mean Urge-IIQ domain-specific scores for patients' not using diuretics, and those using non-loop and loop diuretics are displayed in Table 4. Patient characteristics and summary Urge-IIQ scores for patients from this study and two studies of relatively younger patients with known overactive bladder syndrome (Brown, et al., 1999;Lubeck, et al., 1999) are displayed in Table 5.

4. Discussion

4.1. Key findings

Findings from the current study demonstrate that symptoms of overactive bladder were common among community-dwelling older adults attending a university-based geriatric clinic, and that these symptoms had a strong negative impact on their quality of life. We also observed that use of diuretics was associated with symptoms of overactive bladder, and these associations were stronger with the use of more potent loop diuretics. To the best of our knowledge this is the first report of an association of diuretic use with symptoms of overactive bladder and its impact on quality of life of ambulatory older adults using Urge-UDI and Urge-IIQ and a propensity score method. Loop diuretics are often needed for control of fluid volume in heart failure, however they can activate neurohormones and cause electrolyte imbalance (Ahmed et al., 2006; Ahmed et al., 2007c). Our findings demonstrate another, and often under-reported adverse effect of these useful drugs among a population for which they are commonly prescribed (Burgio et al., 1994).

4.2. Possible explanation of study findings

The high prevalence of overactive bladder symptoms in our study is likely due to aging and use of diuretics. Data from laboratory animals and human overactive bladder suggest that age-related functional, neuro-pharmacological, and morphological changes in the bladder may predispose older adults to develop overactive bladder syndrome (Ordway et al., 1986; Inadome et al., 1998; Yoshida et al., 2001, 2004). Diuretic-induced rapid production of urine may add urgency to diuretic-associated frequency by triggering detrusor overactivity in the aging bladder (Diokno et al., 1991; Steele et al., 1999). The lack of an association of diuretic use with urinary incontinence in our study was likely due to the fact that a large number of these patients were receiving non-loop diuretics for hypertension. This notion is supported by the fact that use of more potent loop diuretics was associated with urge urinary incontinence. Despite a reduction in the magnitude of the association and statistical significance after multivariable adjustment, likely due to covariates such as age and comorbidities such as diabetes and heart

failure, and the relatively small sample size, the association remained positive and strong. Interestingly, in the subgroup receiving no diuretics, urge incontinence was more prevalent than urinary frequency (Table 2). This may be due to age-related decrease in bladder sensation resulting in incontinence without frequency (Griffiths et al., 2007). In contrast, in the group receiving diuretics, urinary frequency was more prevalent than urinary incontinence, likely due to increased urine volume from diuresis.

4.3. Comparison with other studies in the literature

Studies that evaluated symptoms of overactive bladder and diuretic use and its effect on quality of life, particularly among non-institutionalized elderly population are scarce. Available studies only assessed the symptoms of nocturia (Fitzgerald et al., 2007) and urinary incontinence with diuretic use without consideration for symptoms of overactive bladder, impact on quality of life, and the type of diuretics used (Ouslander et al., 1987; Diokno et al., 1991). The impact of overactive bladder symptoms on quality of life in our study population of community-dwelling older adults was high (Table 4 and Table 5) and comparable to those reported by other investigators among younger patients with a diagnosis of overactive bladder and urinary incontinence (Brown et al., 1999; Lubeck et al., 1999).

4.4. Clinical implications

Diuretics are commonly used in older adults as prevalence of chronic medical conditions such as hypertension and heart failure, which require diuretic therapy is high in these patients. Urinary frequency and urgency may lead to urge incontinence in those with delayed reaction time to micturition sensation, particularly among older adults with impaired mobility. Frequency and urgency may lead to rushing to the bathroom to avoid urge incontinent episodes, thus increasing the risk of falls in older adults (Brown et al., 2000). Also, due to incontinence or fear thereof, older adults may skip their medication if they need to go outside of the home, which may affect compliance with diuretics. Although, taking loop diuretics at night might interfere with sleep, taking them in mid afternoon can provide morning and early afternoon time free of increased frequency and urgency.

Non-loop, thiazide-type diuretics are recommended by the current Joint National Committee as the initial drug therapy for most patients with uncomplicated hypertension (Chobanian et al., 2003). However, other antihypertensive drugs may be preferred initially when certain comorbidities such as diabetes, chronic kidney disease, coronary artery disease and heart failure, coexist (Chobanian, 2007). Because of high prevalence of these comorbidities in older adults, use of non-diuretic anti-hypertensive drugs in these patients may reduce the symptoms of overactive bladder and its negative impact on quality of life. Loop diuretics are essential to control fluid volume in heart failure (Hunt et al., 2005). However, by using the lowest possible dose needed to achieve and maintain euvolemia, it may be possible to minimize the untoward effect of diuretics on overactive bladder.

4.5. Strengths and limitations

Cross sectional surveys are limited by recall bias. However, data on diuretic use and other comorbidity were obtained from chart abstraction in this study. Lack of data on diuretic doses and adherence is also a limitation of our study. Lastly, the cross-sectional design of the study precludes any causal inference between diuretic use and overactive bladder symptoms.

5. Conclusions

The prevalence of symptoms of overactive bladder was high among ambulatory older adults attending a university-based geriatric clinic and was associated with use of diuretics, especially

with the use of loop diuretics. Clinicians should routinely ask their patients on diuretics about symptoms of overactive bladder and offer treatment when feasible and appropriate.

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Table 1

Comparison of baseline characteristics of patients by diuretic use

n (%), mean ± S.D.	All (N=172)	No diuretic (n=59)	Diuretic (n=113)	p
Socio-demographics,				
Age, year	78.8 ± 7.5	77.2 ± 7.6	79.6 ± 7.4	0.049
Female	131(76.2)	39(66.1)	92(81.4)	0.037
African American	83 (48.3)	18 (30.5)	65 (57.5)	0.001
Education ≤high school	99 (57.6)	31(52.5)	68 (60.2)	0.336
Not actively employed	160 (93.0)	51(86.4)	109 (96.5)	0.014
Married	63 (36.6)	33 (55.9)	30 (26.5)	<0.0001
Living alone	69(40.1)	21 (35.6)	48 (42.5)	0.382
Co-morbid conditions				
Heart failure	55 (32.0)	5 (8.5)	50 (44.2)	<0.0001
Hypertension	130(75.6)	30 (50.8)	100(88.5)	<0.0001
Diabetes	57(33.1)	9(15.3)	48 (42.5)	<0.0001
Coronary artery disease	44 (25.6)	8(13.6)	36(31.9)	0.009
UTI in the past 4 weeks	5 (2.9)	3(5.1)	2(1.8)	0.340
Medication use				
ACE inhibitors	84 (48.8)	15 (25.4)	69(61.1)	<0.0001
ARB	33 (19.2)	7(11.9)	26 (23.0)	0.078
Beta-blockers	72 (41.9)	17 (28.8)	55 (48.7)	0.012
Others				
MMSE score	26.0 ± 4.3	26.6 ± 4.2	25.7 ± 4.4	0.313
GDS score	3.7 ± 3.0	4.3 ± 3.6	3.5 ± 2.7	0.190
Serum creatinine, mg/dl	1.20 ± 0.51	1.10 ± 0.27	1.25 ± 0.59	0.059

Table 2

Association of overactive bladder symptoms with diuretic use

	All N (%)	No diuretic N (%)	Diuretic N (%)	Absolute difference	p	Unadjusted OR (95% CI)	Adjusted[1] OR (95% CI)
Frequency	122 (72%)	32 (55%)	90 (81%)	26%	<0.0001	3.48 (1.73–7.03)	3.09 (1.20–7.97)
Urgency	116 (68%)	33 (57%)	83 (74%)	17%	0.022	2.17 (1.11–4.24)	2.50 (1.00–6.27)
Incontinence (urge)	124 (73%)	38 (66%)	86 (77%)	11%	0.117	1.74 (0.87–3.50)	1.29 (0.50–3.35)
Nocturia	137 (82%)	47 (84%)	90 (81%)	−3%	0.651	0.82 (0.35–1.93)	1.19 (0.38–3.70)

[1] Adjusted for propensity score

Table 3

Unadjusted and adjusted odds ratio of association of overactive bladder symptoms with loop and non-loop diuretic use

	No diuretic (n=59)	Non-loop diuretic (n=49)	Loop diuretic (n=64)
	Reference	OR (95% CI); p =<	OR (95% CI); p =<
Frequency			
Unadjusted	1.00	1.92 (0.85–4.31); p = 0.117	6.62 (2.58–16.94); p < 0.0001
Adjusted[1]	1.00	1.79 (0.65–4.93); p = 0.263	5.60 (1.61–19.45); p = 0.007
Urgency			
Unadjusted	1.00	1.17 (0.53–2.52); p = 0.714	4.09 (1.75–9.59); p = 0.001
Adjusted[1]	1.00	1.30 (0.49–3.49); p = 0.601	6.10 (1.83–20.23); p = 0.003
Incontinence (urge)			
Unadjusted	1.00	1.16 (0.51–2.62); p = 0.725	2.54 (1.09–5.91); p = 0.031
Adjusted[1]	1.00	1.04 (0.37–2.94); p = 0.940	1.88 (0.57–6.17); p = 0.301
Nocturia			
Unadjusted	1.00	0.93 (0.33–2.65); p = 0.897	0.75 (0.29–1.92); p = 0.550
Adjusted[1]	1.00	1.28 (0.35–4.68); p = 0.711	1.45 (0.40–5.32); p = 0.574

[1] Adjusted for propensity score

Table 4

Comparing mean scale scores for the Urge-Incontinence Impact (U-IIQ) and Urge Urinary Distress Inventory (U-UDI) by type of diuretic use

Mean ± S.D.	All (N=172)	No diuretic (n=59)	Non-loop diuretic (n=49)	Loop diuretic (n=64)	p = (overall)
U-IIQ					
Activities	2.11 ± 1.10	2.04 ± 1.12	2.00 ± 0.95	2.25 ± 1.17	0.405
Travel	2.16± 1.15	1.97 ± 1.09	1.91 ± 1.09	2.52 ± 1.16	0.006
Physical activities	1.49 ± 0.86	1.45 ± 0.78	1.46 ± 0.86	1.55 ± 0.96	0.866
Feelings	1.65 ± 0.96	1.58 ± 0.95	1.51 ± 0.95	1.82 ± 0.96	0.177
Relationships	1.53 ± 1.03	1.44 ± 0.96	1.51 ± 1.08	1.63 ± 1.06	0.581
Sexual function	1.95 ± 1.36	1.20 ± 0.63	2.70 ± 1.57	2.88 ± 1.65	0.030
Mean summary score*	1.83 ± 0.85	1.75 ± 0.86	1.68 ± 0.76	2.03 ± 0.88	0.063
Urge-UDI					
Urge symptoms	2.20 ± 0.90	2.09 ± 0.95	1.91 ± 0.87	2.50 ± 0.79	0.001

* for comparison of no diuretic versus non-loop diuretics p = 0.660, no diuretic versus loop diuretics p = 0.080 and non-loop versus loop diuretics p = 0.031

Table 5

Comparison of Urge-IIQ and Urge-UDI among three studies

	Brown et al. (1999)	Lubeck et al. (1999)	Our study
	83	**257**	**172**
% or mean ± S.D.			
Age, years	63.8 ± 11.6	59.6 ± 13.9	78.9 ± 7.5
Non-white	37	8	48
Female	100	91	76
Incontinence treatment	100	100	14.0
Urge-IIQ			
Activities	2.8 ± 1.4	2.12 ± 1.14	2.11 ± 1.10
Travel	2.9 ± 1.6	2.26 ± 1.34	2.16 ± 1.15
Physical activities	2.7 ± 1.5	2.24 ± 1.33	1.49 ± 0.86
Feelings	2.4 ± 1.3	1.74 ± 1.33	1.65 ± 0.96
Relationships	1.7 ± 1.1	1.07 ± 1.22	1.53 ± 1.03
Sexual function	1.8 ± 1.4	1.28 ± 1.38	1.95 ± 1.36
Man summary score	2.40 ± 1.4	1.77 ± 1.68	1.83 ± 0.85
Urge-UDI			
Urge symptoms	2.4 ± 1.0	2.37 ± 0.79	2.20 ± 0.90