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Vitamin D and Incident Urinary Incontinence in Older Adults

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Abstract

Objective—To determine if vitamin D status is associated with incident urinary incontinence (UI) among community-dwelling older adults.

Methods—The University of Alabama at Birmingham Study of Aging is a prospective cohort study of community-dwelling Medicare enrollees. Standardized assessment of UI using the validated Incontinence Severity Index. Analysis of 25-hydroxyvitamin D (25(OH)D levels was performed on stored baseline sera. UI was assessed every 6–12 months for up to 42 months. Analyses included multivariable logistic regression and Cox proportional hazard models.

Results—Of 350 participants (175 male, 147 black, mean age 73.6 ± 5.8), 54% (189/350) were vitamin D deficient [25(OH)D < 20 ng/mL] and 25% (87/350) were vitamin D insufficient

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Conflict of Interest

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[25(OH)D 20 ng/mL to < 30 ng/mL]. Among the 187 subjects with no UI at baseline, 57% (107/187) were vitamin D deficient and 24% (45/187) were vitamin D insufficient. 175 of the 187 subjects had follow-up evaluation for incident UI over 42 months and incident UI occurred in 37% (65/175). After adjustment cumulative incident UI at 42 months was associated with baseline vitamin D insufficiency (p=0.03) and demonstrated a trend association with deficiency (p=0.07). There was no association between baseline vitamin D status and time to incident UI.

Conclusions—These preliminary results support an association between vitamin D and incident UI in community-dwelling older adults. Future studies may target specific at risk groups, such as men with BPH or women with pelvic floor disorders for evaluation of the impact of vitamin D supplementation on urinary symptoms.

INTRODUCTION

The prevalence of urinary incontinence (UI) is increased among older adults and is associated with poor quality of life, social isolation, falls, and depression(1–4). Treatment is usually multifactorial involving lifestyle, behavioral and often pharmacologic therapies(5). Drug therapy for UI is associated with the potential for adverse events and, may have significant cost; thus adherence is often maintained for only a few months(6, 7). Additional treatment modalities are needed in order to maximize the impact of multicomponent therapy and reduce the potential for adverse events.

Recent studies have suggested a relationship between vitamin D and conditions increasing the risk of UI among both men and women. Vitamin D receptors are present in the bladder and striated muscle of the pelvic floor musculature(8, 9). Additionally, prostatic cells express 1α-hydroxylase and can synthesize 1,25-di-hydroxyvitamin D (the active form of vitamin D)(10). Low vitamin D levels are associated with increased prevalence of pelvic floor disorders among women and moderate-to-severe UI in men(11–13). However, these studies are based on cross-sectional data. One randomized controlled trial demonstrated treatment with a vitamin D analog reduced prostate enlargement in the setting of benign prostatic hyperplasia(14).

Evaluation of data assessing the longitudinal relationship between vitamin D and incident UI would allow for additional insights and provide next steps in determining the need for interventional studies. Thus, our aim was to evaluate the association of low vitamin D with incident UI in a cohort of community-dwelling older adults.

METHODS

Subjects

The University of Alabama at Birmingham Study of Aging (SOA) is a longitudinal cohort study of community-dwelling older adults designed to assess factors associated with changes in mobility. Between 1999 and 2001 the study recruited 1,000 individuals 65 years of age and older from five counties in west central Alabama, including 3 rural counties and 2 urban counties. Individuals were randomly selected from Medicare beneficiary lists stratified by race and gender so that the cohort included equal numbers of men and women, black and white, and urban and rural residence. Exclusion criteria included: inability to understand the

recruiter, residing in nursing homes, or inability to independently coordinate an appointment for the baseline, in-home interview. The institutional review board at the University of Alabama at Birmingham approved the study and written informed consent was obtained prior to beginning study procedures.

At baseline and in 2004, a two-hour, in-home assessment was performed, which included a medical history, cognitive screening test, screening for depression, assessment of activities of daily living, and questions regarding multiple facets of functional status. Eligibility for the in-home follow-up in 2004 was the same as the baseline evaluation with 624 of 733 (85.1%) of surviving participants agreeing to the in-home assessment in 2004(15). These 624 participants were offered the opportunity to have a blood test obtained, and 408 (65.4%) agreed to the lab test. Blood samples were used to measure multiple laboratory assays, but not vitamin D levels. Serum samples were stored in −70 degree freezers for future use. Vitamin D analyses were completed in 2013 for 350 of the 408 (85.8%) participants who had a blood sample obtained and had sufficient serum available for the vitamin D assays.

Of these participants with vitamin D data available, 187 /350 (53.4%) did not have UI in 2004. Follow-up incident UI data were available on 175/187 (94.6%) of these participants. Thus, prevalence of vitamin D deficiency and insufficiency was assessed using 350 participants; while the 175 participants without UI in 2004 and with follow-up incident UI data were the focus of the current analysis. Every six to twelve months, participants were contacted by phone to complete a questionnaire including information about UI.

Urinary Incontinence Assessment

Participants provided information about the presence of UI using the validated two-item Incontinence Severity Index, which correlates well with UI measured with 24-hour pad weights and UI frequency on bladder diaries(16). Participants were asked, *Have you ever leaked even a small amount of urine?* and *How often does that occur?* Incident UI was classified as an affirmative response to the first question and a response to the second question of at least monthly UI.

Vitamin D Assessment

Analysis of serum concentrations of 25-hydroxyvitamin D [25(OH)D] was performed on stored sera using an IDS-iSYS analyzer. To ensure quality control of the vitamin D assay, the laboratory participates in the vitamin D external quality assessment scheme every 3 months and in the NIST/NIH Vitamin D Metabolites Quality Assurance Program semi-annually. For the purposes of this evaluation, vitamin D deficiency was defined as a serum 25-hydroxyvitamin D level < 20 ng/mL and vitamin D insufficiency as a 25-hydroxyvitamin D level from 20 ng/mL to < 30 ng/mL.

Statistical Analysis

Descriptive statistics were used to analyze baseline characteristics of the subsample (n=350) of UAB Study of Aging participants for which sera were available for vitamin D assays in 2004 and the 175 participants who were included in the incident UI analysis. Multivariable logistic regression and Cox proportional hazard models adjusted for age, gender, and race/

ethnicity were utilized to evaluate the relationship between vitamin D status and incident UI among those participants reporting no UI at baseline. All analyses were conducted using SAS 9.2 (SAS Institute, Cary, NC).

RESULTS

Of the 350 participants who had serum samples available for vitamin D assays in 2004 (the baseline year for this analysis) (Table 1), 54% were vitamin D deficient [25(OH)D < 20 ng/mL] and 25% were vitamin D insufficient [25(OH)D 20 ng/mL to < 30 ng/mL] (Table 1). Among the 187 subjects with no UI at baseline, 57% (107/187) were vitamin D deficient and 24% (45/187) were vitamin D insufficient. For these 187 subjects, the mean baseline 25(OH)D level was 20.5 ng/mL ± 9.7.

Mean length of follow-up was 34.5 months (range 6 – 42). For the 175 of the 187 subjects who had follow-up evaluation for incident UI over 42 months, incident UI occurred in 37% (65/175, 37% of women and 38% of men). These 175 participants generally reflected the demographic distribution of the original SOA cohort and those included in a previous analysis of incident UI(17). Among those with vitamin D deficiency, 37/97 (38%) developed UI and among those with vitamin D insufficiency, 20/44 (45%) developed UI. This compared to 8/34 (23%) of those with sufficient levels of vitamin D. However, there was no statistically significant difference in the proportion of individuals developing incident UI during the study period by vitamin D status (p=0.13).

After adjustment for age, gender and race/ethnicity, cumulative incident UI at 42 months was associated with vitamin D insufficiency status at baseline [aOR 3.18 (95%CI 1.14–8.87), p = 0.03]. There was a trend toward association between baseline vitamin D deficiency and incident UI [2.47 (95%CI 0.93–6.53), p=0.07]. However, there was no association between vitamin D insufficiency or deficiency and time to incident UI in unadjusted (Log-rank p=0.19) or adjusted analyses (Cox model overall test of significance, p=0.14).

DISCUSSION

These results suggest a potential association between vitamin D and the development of UI among a racially diverse cohort of older men and women. An evaluation of the longitudinal association between vitamin D status and incident UI among older adults is novel. Previous cross-sectional data have suggested an association between low vitamin D status and lower urinary tract symptoms in men and women; however, these studies are limited because they cannot evaluate for causality(11, 12). The University of Alabama at Birmingham SOA is unique among longitudinal studies of aging populations because the study population is racially diverse, validated questionnaires were used to assess urinary symptoms, and stored serum samples were available.

There are several mechanisms by which vitamin D could exert influence on lower urinary tract function. Vitamin D receptors are present in the bladder and striated muscle of the pelvic floor musculature(8, 9). Skeletal muscle control and strength are vital for the voluntary control of the urethral sphincter and pelvic floor muscles and likely a significant

factor in achieving continence. A vitamin D analog was evaluated as a potential adjuvant treatment with tolterodine and demonstrated improved bladder capacity in an animal model of bladder outlet obstruction(18). Additionally, prostatic cells express 1α-hydroxylase and can synthesize 1,25 di-hydroxyvitamin D (the active form of vitamin D)(10). A recent study found a specific polymorphism of the vitamin D receptor uniquely linked to a protective effect for the development of lower urinary tract symptoms in men(19).

Current treatment guidelines for UI care recommend lifestyle changes and behavioral therapy as a first step followed by bladder relaxant drug therapy(5). Older adults are more susceptible to the anticholinergic adverse events from bladder drug therapy (constipation, reflux, cognitive changes, xerostomia), which occur frequently with the most commonly prescribed bladder relaxants. Additionally, these drugs can be costly and many patients discontinue drug therapy after a few months(6, 7). Vitamin D is a low cost, well-tolerated supplement and could provide an adjuvant treatment to currently recommended exercise-based behavioral therapy.

Vitamin D deficiency is highly prevalent. The results from the Study of Aging showing more than half of participants were deficient in vitamin D and more than 80% were insufficient or deficient are consistent with population-based estimates(20). Vitamin D has been implicated in multiple health conditions and the Institute of Medicine has called for additional studies to provide information about the role of vitamin D(21). Longitudinal studies evaluating vitamin D replacement rarely include outcomes related to bladder health(22, 23). The current results add to the growing body of literature focused on the potential for vitamin D status to impact the health of older adults.

There are limitations to this study. The assessment of the association of vitamin D deficiency with UI may have been limited by the small number of persons with a baseline serum 25-hydroxyvitamin D level of 30 ng/mL or greater (n=34). The Cox proportional hazard analyses are limited because UI was reported every 6–12 months, which could lead to left censoring. We were not able to ascertain if participants received interval non-pharmacologic treatments for their bladder symptoms during the 6–12 month assessments. The UAB Study of Aging was designed to assess factors impacting social mobility among community-dwelling older adults and did not query a comprehensive set of factors that might impact the development of incontinence in this population. Lastly, vitamin D could be a marker of better health and physical activity, which was not controlled for in this analysis.

CONCLUSION

Urinary incontinence is a burdensome condition with significant impact on quality of life for many adults as they age. Treatment strategies for geriatric conditions such as UI are often multicomponent; however, current drug therapy is limited because of the potential for adverse events and cost. These results add to a growing body of literature suggesting physiologic mechanisms, cross-sectional association studies, and now preliminary longitudinal research demonstrating a potential association between vitamin D and optimal pelvic floor function. Vitamin D offers a low cost, well-tolerated option that warrants further

evaluation in an interventional trial, particularly focused on a population of older adults with vitamin D insufficiency.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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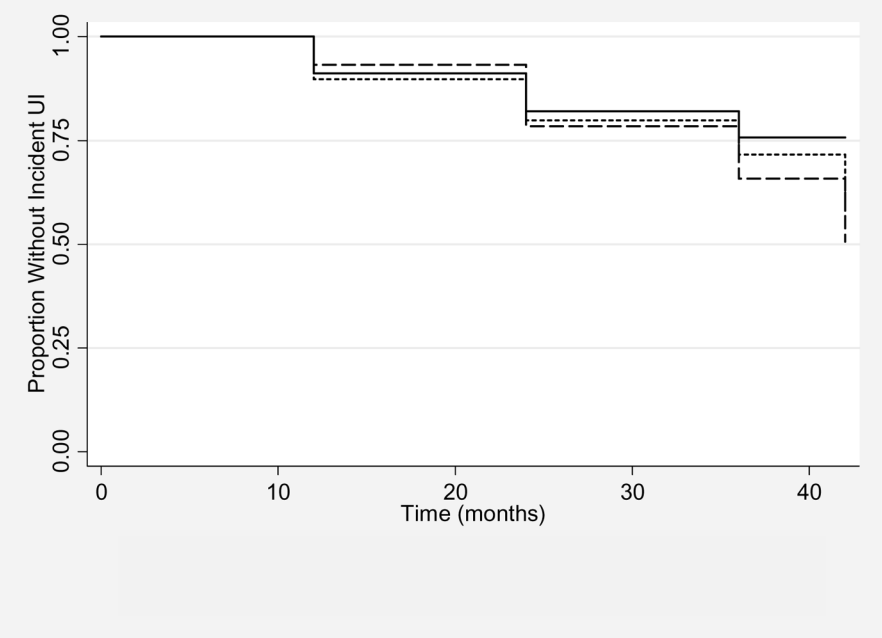

Figure 1. Incident UI among Vitamin D Sufficient, Insufficient, and Deficient Participants (n=175)

Key:

Sufficient Vitamin D (≥ 30 ng/mL)_____

Insufficient Vitamin D (20 to < 30 ng/mL)_ _ _ _ _ _ _ _ _ _

Deficient Vitamin D (< 20 ng/mL)----------

Log-Rank p-value = 0.19

Table 1

Baseline Characteristics of UAB Study of Aging Participants with Serum Samples (n=350) and Subgroup with Incident UI Evaluation(n=175)

Characteristic[a]	Serum Sample available (n=350)	Incident UI Evaluation (n=175)	P value[b]
Age (mean ± SD)	73.6 ± 5.8	74.8 ± 6.0	0.03
Gender			0.03
Female	175 (50)	98 (56)	
Male	175 (50)	77 (44)	
Ethnicity			<0.001
Black	147 (42)	91 (48)	
White	203 (58)	84 (52)	
Vitamin D status			0.91
Deficient (< 20 ng/mL)	189 (54)	97 (55)	
Insufficient (20 – < 30 ng/mL)	87 (25)	44 (25)	

[a] Number (%) unless noted)

[b] Chi-square or t-test