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SELF-REPORTED ESTROGEN USE AND NEWLY-INCIDENT URINARY INCONTINENCE AMONG POSTMENOPAUSAL COMMUNITY-DWELLING WOMEN

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Abstract

OBJECTIVE—To examine the relationship between self-reported estrogen use and newly-incident urinary incontinence (UI) among community-dwelling postmenopausal women.

METHOD—A population based longitudinal survey of postmenopausal women who did not report UI in 1993 and for whom complete data were available. Women were classified as having newly-incident UI if they reported uncontrolled urine loss within 12 months of the 2004 interview. Condition-specific functional loss secondary to UI was assessed by questions on participants' inability to engage in certain activities due to UI. Duration of hormone therapy containing estrogen was obtained in 1993 using a structured questionnaire.

RESULTS—Among 167 postmenopausal women who did not report UI in 1993, 47 (28.1%) reported newly-incident UI and 31 (18.6%) reported newly-incident UI with condition-specific functional loss in 2004. Of the 167 postmenopausal women, 46 (27.5%) reported ever using hormone therapy containing estrogen and 14 (8.3%) women reported using hormone therapy containing estrogen for 5 years or more in 1993. Estrogen use for 5 years or more was significantly associated with newly-incident UI with condition-specific functional loss compared to estrogen use for less than 5 years or no reported history of estrogen (adjusted relative odds (RO) = 3.97, 95% confidence interval (CI) [1.02, 15.43]) in multivariate models controlling for potentially influential characteristics.

CONCLUSIONS—Postmenopausal community-dwelling women with a history of estrogen use for 5 years or more were more likely to report newly-incident UI with condition-specific functional loss after 10 years of follow-up.

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Keywords

Urinary incontinence; estrogen; hormone therapy; menopause; epidemiology

INTRODUCTION

Urinary incontinence (UI) is common in women and may be disabling. The incidence of UI increases with age and after menopause.[1] Emerging evidence suggests that postmenopausal hormone therapy is associated with an increased risk of UI,[2-7] although the biological mechanisms for this increased risk are unclear. Prior randomized controlled trials have indicated that the use of hormone therapy worsens UI symptoms or increases the risk of developing UI.[2, 3, 5] Results from the Women's Health Initiative demonstrated that postmenopausal women randomized to receive either estrogen plus progestin or estrogen only were at increased risk of experiencing worsening UI symptoms or developing incident UI after one year.[5] These findings were observed for both stress and urge UI. Other observational studies showed a relationship between current use of postmenopausal hormone therapy and incident UI during follow up.[6, 7] However, many of these studies examining the use of hormone therapy and UI were conducted in largely homogeneous populations with few co-morbid health conditions or select co-morbid health conditions, thus limiting the generalizability of the findings.

Despite evidence linking postmenopausal hormone therapy and the risk of developing UI, it remains important to further delineate the characteristics of women at highest risk for developing UI leading to a loss in functioning which may limit both social and physical activities. To that end, the role of hormone use duration and subsequent UI requires further study in diverse populations. Understanding the temporal relationships between estrogen use and UI is important to practitioners counseling women with diverse reproductive histories regarding their risk of developing UI with condition-specific functional loss. Our investigation differs in several ways from prior work examining the association between UI and postmenopausal hormone therapy. We employed standardized interviews in an ethnically diverse community based sample of women initially reporting no UI. Our sample is from an ongoing prospective observational study allowing for the examination of temporal effects in disease causation over approximately a decade of follow-up, more than twice the length of follow-up reported by other studies.[6, 7] Our study design allows us to estimate the temporal relationship between the duration of self-reported estrogen use at baseline and the development of UI at follow-up. Importantly, our data also include variables for the assessment of self-imposed functional loss resulting from lifestyle modifications related to UI, thus allowing for the assessment of disease severity associated with estrogen use. We recognize the exploratory nature of our analyses but took the opportunity afforded by the Epidemiologic Catchment Area (ECA) Program conducted by the National Institute of Mental Health to probe the association of self-report of estrogen use at baseline and the incidence of UI after 10 years of follow up.

The purpose of this paper was to carefully examine the temporal relationships between self-reported postmenopausal estrogen use, UI, and condition-specific functional loss related to UI among an ethnically diverse community-based sample of postmenopausal women. We hypothesized that postmenopausal women with a longer duration of self-reported history of estrogen use would be more likely to report newly-incident UI with condition-specific functional loss.

METHOD

The Baltimore Epidemiologic Catchment Area Program follow-up

The Epidemiologic Catchment Area (ECA) Program conducted by the National Institute of Mental Health (NIMH) was a survey of psychiatric disorders in the general population between 1980 and 1984 at five university-based sites in the United States. The Baltimore site of the ECA Program[8] probabilistically sampled 175,211 adult household residents in Eastern Baltimore in 1981, selecting 4,238 participants for participation. Among persons selected, 3,481 completed household interviews (82% of persons selected by random sample).[9] In 1982, a second wave of interviews was conducted among 2,768 participants interviewed in 1981 (79.5%). Between 1993 and 1996, 1,920 of participants interviewed in 1981 (69.4%) were interviewed again[10] (Since most interviews were conducted in 1993 this wave is referred to as '1993'). Between 2004 and 2005, 1,071 participants interviewed in the prior wave (1993-1996) were interviewed again (55.8%) (Since most interviews were conducted in 2004 this wave is referred to as '2004'). Data collected in 1993 and in 2004 are included in our analysis. UI was not assessed between 1981 and 1982 and therefore data from this wave are not included in our analysis. ECA data was obtained through highly structured interviews in a private place, usually the participant's home. At the baseline interview participants gave permission for future follow-up. The ECA study design and methods have been described in detail elsewhere.[11] In the current study, we took advantage of the existing ECA data set on postmenopausal women to explore the role of self-reported prolonged estrogen use in 1993 and incident urinary incontinence in 2004 given the long duration of follow-up. The original protocol was approved by the Committee on Human Research of the Johns Hopkins University Institutional Review Board.[8] The present investigation was also approved by the Institutional Review Board at the University of Pennsylvania.

Urinary incontinence

The symptom of UI was assessed by the question: "Have you ever had any difficulty in controlling your water, that is, losing your urine or having trouble getting to the bathroom on time?" which conforms to the current definition of the symptom of UI provided by the International Continence Society.[12] Postmenopausal women reporting any uncontrolled urine loss within the 12 months prior to the interview were classified as having UI. Women denying uncontrolled urine loss within the 12 months prior to the interview were classified as continent.

Urinary incontinence and condition-specific functional loss

Four questions assessed condition-specific functional loss associated with UI.[13, 14] Participants were asked if their UI resulted in: "avoiding social gatherings, visiting friends, going to church";" avoiding traveling"; "not going shopping"; and "avoiding physical activities." UI was the only condition in the ECA assessing condition-specific functional loss. Participants with a positive response to any of these questions were categorized as having condition-specific functional loss due to UI.

Estrogen use and reproductive history

The questionnaires contained detailed questions regarding prior hormone therapy including estrogen as well as other questions about reproductive history. All responses were recorded in 1993. The questionnaire included questions that asked, after menopause, "Have you ever taken estrogen pills for any reason?" and "How long did you take estrogen pills?" Duration of estrogen use in 1993 was characterized into 3 broad categories (never use, estrogen use < 5 years, estrogen use ≥ 5 years) consistent with Hendrix et al.[5] Additional information in

1993 was obtained by standard questions about parity, menopausal duration, and type of menopause (surgical versus nonsurgical).[15]

Covariates

Educational attainment, self-identified ethnicity, and marital status were assessed in 1993 using structured questionnaires. Activities of daily living (ADLs) were assessed by standard survey items on using the toilet, knife or fork to cut up food, getting to bed by oneself, dressing and undressing, and taking a bath or shower. Instrumental activities of daily living (IADLs) were assessed by standard survey items on keeping track of money and bills, being able to get together with friends, preparing meals, cleaning house, and using the telephone. Consistent with previous ECA reports[16, 17] individuals were characterized as having ADL or IADL impairment in 1993 if they were unable to perform at least one activity without help. Participants were asked if they had ever had diabetes, heart trouble, arthritis, stroke and cancer. A positive response to any of these conditions in 1993 was considered a medical comorbidity. Smoking status was based on report of smoking within 7 days of the 1993 interview. Body mass index (BMI) was calculated as the weight in kilograms divided by the squared height in meters in 1993. Consistent with the definition for obesity,[18] body mass index (BMI) was dichotomized as equal to or greater than 30 and less than 30.

Study sample

In all, 299 women responded “yes” to the question “Have your menstrual cycles stopped permanently?” in 1993. In order to examine the onset of UI directly, we excluded 103 postmenopausal women because they indicated that they had UI in the 1993 interview. These exclusionary criteria allowed us to begin the observation interval with a cohort of postmenopausal women who did not have UI. In addition, 29 people were excluded because they did not have complete data for other variables in our analysis, leaving a sample size of 167 for this analysis (Table 1).

Analytic Strategy

The analytic plan proceeded in three phases. The first phase consisted of calculating appropriate means and frequencies for each variable for participants with and without newly-incident UI in 2004. Comparisons between groups of participants were made using χ^2 or t-tests as appropriate for categorical data or continuous data. Bivariate associations between UI, estrogen use, and other important variables were examined. The second phase consisted of examining the age-adjusted relationship between duration of estrogen use in years reported in 1993 and newly-incident UI with and without condition-specific functional loss reported in 2004. Lastly, multivariable logistic regression models were developed to assess the relationship of duration of estrogen use to newly-incident UI. Multivariable models adjusted for age, education level, ethnicity, activities of daily living impairment, instrumental activities of daily living impairment, chronic health conditions, body mass index, current smoking status, parity, and type of menopause. Data analysis was performed using SPSS version 12 (SPSS, Chicago, IL).

RESULTS

Baseline Characteristics

The mean age ± standard deviation of the study sample was 57.1 ±12.4 years. The self-identified ethnicity of participants was 94 whites (56.3%), 64 African Americans (38.3%), 5 American Indians (3.0%), 2 Asians (1.2%), 1 Hispanic (0.6%), and 1 Pacific Islander (0.6%). Among 167 postmenopausal women who did not report UI in 1993, 47 (28.1%) reported having UI within one year of 2004 and 31 (18.6%) reported having UI with

condition-specific functional loss within one year of 2004. Of the 167 postmenopausal women, 46 (27.5%) reported ever using hormone therapy containing estrogen and 14 (8.3%) women reported using hormone therapy containing estrogen for 5 years or more in 1993.

Sociodemographic characteristics, functional status, health status, type of menopause, and duration of postmenopausal estrogen use were compared between women with and without newly-incident UI in 2004 (Table 1). Postmenopausal women with and without newly-incident UI were similar in BMI, current smoking status, parity, ethnicity, functional status, chronic medical conditions, and type of menopause. Postmenopausal women with newly-incident UI were significantly older than postmenopausal women without newly-incident UI ($p = 0.03$). Postmenopausal women without newly-incident UI trended towards shorter duration of estrogen use, higher education level, and less impairment of instrumental activities of daily living although these differences approached but did not reach significance (all $p \geq 0.07$).

Estrogen Use and Urinary Incontinence

In multivariate models, estrogen use for 5 years or more was significantly associated with newly-incident UI compared to estrogen use for less than 5 years or no reported history of estrogen (adjusted RO = 3.99, 95% CI [1.21, 13.10]) (Table 2). In multivariate models, estrogen use for 5 years or more was also significantly associated with newly-incident UI with condition-specific functional loss compared to estrogen use for less than 5 years or no reported history of estrogen (adjusted RO = 3.97, 95% CI [1.02, 15.43]). The final multivariate models controlled for potentially influential covariates including age, education level, ethnicity, activities of daily living impairment, instrumental activities of daily living impairment, chronic health conditions, body mass index, current smoking status, parity, and type of menopause.

DISCUSSION

In our longitudinal study, community-dwelling postmenopausal women with a history of estrogen use for 5 years or more were more likely to report newly-incident UI with condition-specific functional loss after 10 years of follow-up compared to women who reported estrogen use for less than 5 years or no history of estrogen use. In routine clinical practice, women are asked to report their reproductive history including age at menopause and prior use of menopausal hormone therapy. Our results suggest that among an ethnically diverse community-dwelling sample, a self-report of prior estrogen use for 5 years or more at baseline may be associated with an increased risk of incident UI during the subsequent 10 years, especially when incontinence was associated with condition-specific functional loss. Our findings may be useful for counseling women interested in postmenopausal hormonal therapy.

Our study is consistent with prior research that showed postmenopausal estrogen use is associated with worsening or incident urinary incontinence. Our study augments prior work by studying a more ethnically diverse group of community-dwelling postmenopausal women. In a cohort of older postmenopausal women in the Women's Health Initiative (WHI), women randomized to receive estrogen with or without progestin, had an increased risk of developing urge and stress UI after 1 year.[5] Another randomized controlled trial including older postmenopausal women with cardiac disease, the Heart Estrogen/progestin Replacement Study (HERS Trial), also demonstrated an increased risk of developing stress and urge UI during 4 years of follow up.[2] In addition, postmenopausal women in this trial with baseline UI were noted to have worsening symptoms during the same follow up period.[3] Although our study did not specifically determine the dose of estrogen taken or if progesterone was also used, our data similarly suggests that postmenopausal estrogen use is

associated with urinary incontinence and functional loss. In the Nurse's Health Study I, older postmenopausal female health professionals (aged 50-75) enrolled who reported taking postmenopausal hormones at baseline had a 34-68% increased risk of incident UI after 4 years compared to women who had never taken hormones irrespective of the type and route of hormone therapy which is similar to our findings.[7] Comparable results were shown in younger postmenopausal women (aged 37-54) from the Nurse's Health Study II where there was a 39% increased risk of UI among current hormone therapy users after 2 years compared to never users of hormone therapy.[6] In addition, Grodstein and colleagues showed a significant trend toward decreasing risk of incident UI after participants self-reported stopping postmenopausal hormone therapy for 10 years to that equivalent to women who had never taken hormones suggesting that duration of discontinuation of estrogen may also play a role in the risk of UI.[19]

Our findings join a growing body of literature that suggests that postmenopausal hormone therapy increases the risk of developing UI. However, the role of estrogen use for urinary symptoms is still unclear because of data from small clinical trials that suggest there may be a benefit of local estrogen therapy on irritative voiding symptoms in women.[20] In addition, a study in postmenopausal women randomized to receive vaginal estrogen or placebo demonstrated that vaginal estrogen improves blood flow to the bladder neck and proximal urethra,[21] but did not report a difference in UI symptoms. Nevertheless, the available data supports the hypothesis that oral estrogen worsens UI symptoms or increases the risk of developing UI.

Our study has several limitations that deserve comment. First, only recently have several validated questionnaires that measure type (urge, stress, or mixed) and severity of UI been published.[22-24] Because we were not able to use one of these instruments in 1993, our measure of UI is limited. For example, estrogen use has been found to be associated with incident stress incontinence.[5] However, utilizing these instruments in 2004 when they were available would have meant significant measurement changes and a loss in the ability to make individual longitudinal comparisons between 1993 and 2004. Furthermore, a crude examination of all types of urinary incontinence together would likely reduce the chance of finding an association with incident UI, and would have biased our results toward the null (i.e. no effect of prolonged estrogen use on incident UI). In addition, the symptom of UI as measured by the Baltimore site of the ECA is consistent with the current International Continence Society definition.[12] Therefore, the symptom of UI in our study would be expected to be comparable with other published studies that also report UI based on this same definition. In addition, condition-specific functional loss serves as a marker of severity.[12] Second, examining incident urinary incontinence in the preceding 12 months in 2004 may have missed women who developed urinary incontinence during the intervening 10 years and were either successfully treated or had spontaneous remission of their UI resulting in misclassification bias. However, misclassification of some individuals with UI would likely lead to a conservative bias toward the null. Third, there is the potential for all the sources of error associated with self-report interview data including imperfect recall and response bias (e.g., socially desirable responding). We attempted to mitigate these biases by limiting recall of UI to the previous 12 months. In addition, the self-report of UI among community-dwelling adults has been found to be reliable.[25] Fourth, while the initial study was drawn from a community sample, follow-up data consisted of people that could be found and re-interviewed. However, studies based on the ECA follow-up data have shown little influence of baseline factors on loss to follow-up.[26] Fifth, we recognize there is the potential role of chance due to the small number of participants in some sub-groups. Our results therefore should be interpreted with caution, and we cannot make any broad conclusions or clinical recommendations based on our data. Finally, we confined our

analysis to the self-report of oral estrogen use only. We are not able to determine the specific risk associated with the combined use of estrogen and progesterone.

CONCLUSION

In summary, newly-incident UI with condition-specific functional loss is associated with estrogen use for 5 years or more among a sample of community-dwelling postmenopausal women. Our study design is similar to how we obtain historical data clinically in women presenting for care. Most women are able to approximate the duration of use, and duration among those self-reporting use influences the risk of incident UI and women's inability to engage in certain activities due to their UI. Future research is required to confirm a causal relationship between prolonged estrogen use and incident urinary incontinence. In addition, more research is needed to further understand the biology of how hormone therapy affects bladder and urethral function to promote UI and to identify other therapies that will treat menopausal symptoms without the side effect of UI.

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Table 1

Incident urinary incontinence in 2004 by sociodemographic variables, functional status, health status, type of menopause, and estrogen use among menopausal women in 1993 (n=167).

	No urinary incontinence (n=120)	Incident Urinary Incontinence (n=47)	P-Value
Sociodemographic			
Age in years, n (s.d.)	55.7 (12.3)	60.5 (12.2)	0.03
Education less than high school, n (%)	38 (31.7%)	22 (46.8%)	0.08
White, n (%)	68 (56.7%)	26 (55.3%)	>0.99
Functional status			
Activities of daily living status impaired, n (%)	3 (2.5%)	2 (4.3%)	0.62
Instrumental activities of daily living impaired, n (%)	7 (5.8%)	7 (14.9%)	0.07
Health status			
Chronic health conditions, mean (s.d.)	1.38 (.49)	1.30 (.46)	0.34
Body Mass Index (BMI) = 30, n (%)	37 (30.8%)	19 (40.4%)	0.28
Smoking within last 7 days, n (%)	35 (29.2%)	12 (25.5%)	0.71
Nulliparous, n (%)	17 (14.2%)	9 (19.1%)	0.48
Type of menopause			
Surgical menopause, n (%)	61 (50.8%)	24 (51.1%)	>0.99
Estrogen use			
Estrogen use ever, n (%)	35 (29.2%)	11 (23.4%)	0.56
Estrogen use ≥ 5 year, n (%)	7 (5.8%)	7 (14.9%)	0.07

Note: Data gathered from the Baltimore, Maryland Epidemiologic Catchment Area Program Follow-up, 1993 and 2004. P-values given for comparison groups with χ^2 or t-test as appropriate.

Table 2

Association between length of estrogen use in 1993 and incident urinary incontinence with and without functional loss in 2004 among menopausal women (n=167).

	Age- adjusted RO [95% CI]	Multivariable* RO [95% CI]
Incident urinary incontinence		
≥ 5 years of estrogen use	3.01 [0.96, 9.42]	3.99 [1.21, 13.10]
< 5 years of estrogen use or no estrogen use	1.00	1.00
Incident urinary incontinence with functional loss		
≥ 5 years of estrogen use	3.24 [0.91, 11.52]	3.97 [1.02, 15.43]
< 5 years of estrogen use or no estrogen use	1.00	1.00
Incident urinary incontinence without functional loss		
≥ 5 years of estrogen use	2.94 [0.52, 16.60]	4.34 [0.69, 27.32]
< 5 years of estrogen use or no estrogen use	1.00	1.00

Note: Data gathered from Baltimore, Maryland Epidemiologic Catchment Area Follow-up, 1993 and 2004.

RO=relative odds; CI=confidence interval.

*Adjusted for age, education level, ethnicity, activities of daily living impairment, instrumental activities of daily living impairment, chronic health conditions, body mass index, current smoking status, parity, and type of menopause.