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Voiding characteristics and related hormonal changes in peri-menopausal and post-menopausal women: A preliminary study

Jong Kyu Kwon[a], Jae Heon Kim[b,*], Hoon Choi[c], In Ho Chang[a], Bo Ra Park[d], Soon-Sun Kwon[e], Eun Sil Lee[d], Gyu Yeon Choi[d], Jeong Jae Lee[d], Im Soon Lee[d]

[a] Department of Urology, Chung-Ang University Hospital, Urological Science Institute, Chung-Ang University College of Medicine, Seoul, South Korea
[b] Department of Urology, Sooncheonhyang University Hospital, Suncheonhyang University College of Medicine, Seoul, South Korea
[c] Department of Urology, Korea University Hospital, Korea University College of Medicine, Ansan, South Korea
[d] Department of Obstetrics and Gynecology, Sooncheonhyang University Hospital, Sooncheonhyang University College of Medicine, Seoul, South Korea
[e] Medical Research Collaborating Center, Seoul National University Bundang Hospital, Seongnam, South Korea

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ABSTRACT

Objectives: To characterize voiding symptoms during the peri- and post-menopausal periods and to investigate related hormonal changes.
Methods: We enrolled a total of 55 patients between February 10, 2013, and August 15, 2013, to participate in this cross-sectional study. To characterize patients' voiding symptoms, we administered voiding questionnaires, including the International Prostate Symptom Score (IPSS), Overactive Bladder Symptom Score (OABSS), and Sandvik Severity Index. Measured hormones included E2, FSH, TSH, prolactin, progesterone, and testosterone.
Results: In the univariate analysis, there were significant intergroup differences for all of the hormones except progesterone. Among the voiding symptoms, straining (IPSS question 1), frequency (IPSS question 2), and SUI were significantly different between the two groups ($p = 0.039$. 0.010, and 0.017, respectively). In the multivariate analysis, frequency (IPSS question 2) and SUI were significantly different between the two groups ($p = 0.020$ and 0.011, respectively). Among the hormones, only testosterone was marginally different between the two groups ($p = 0.059$).
Conclusions: During the transition to menopause, voiding symptoms, such as frequency, can potentially worsen in the peri-menopausal period, and SUI is more prevalent in the post-menopausal period. Additionally, testosterone may have a role in voiding changes that occur during the menopausal transition.

1. Introduction

Menopause means the "end of monthly cycles," which is an event that signals the end of fertility and typically occurs during a woman's late 40s or early 50s. Menopause can also be described as the permanent cessation of the primary function of the ovaries [1,2]. Women usually experience a peri-menopausal period before menopause, which is known as the menopausal transition (MT). The MT can last for several years, ends 12 months after the last menstrual period, and is accompanied by many symptoms related to hormonal changes [3]. Many symptoms increase in frequency in midlife, both before and after the last menstrual period, including vasomotor symptoms, vaginal dryness, sexual dysfunction, and lower urinary tract symptoms (LUTS) [4].

As the aging population steadily increases, LUTS are commonly encountered and cause considerable morbidity among menopausal women. Nevertheless, voiding symptoms in older women have received relatively little attention, with few studies on this subject in the literature. The prevalence of female LUTS increases with advancing age, particularly by the time a woman enters the peri-menopausal period [5]. Therefore, LUTS can be considered a phenomenon of the menopausal transition. Urogenital atrophic changes are more prevalent in post-menopausal women and increase with duration of estrogen deficiency, and these changes are also associated with urinary symptoms, such as frequency, urgency, nocturia, urinary incontinence, and recurrent urinary tract infections [6]. Furthermore, peri-menopausal patients frequently report menopausal symptoms and symptoms of relative androgen

* Corresponding author Tel.: +82 2 709 9378; fax: +82 2 709 9378.
E-mail addresses: piacekjh@hanmail.net, piacekjh@schmc.ac.kr (J.H. Kim).

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deficiency (RAD), most of which are not related to estradiol levels [7,8]. Testosterone replacement therapy in menopausal women is effective for the relief of hormone deficiency symptoms in both pre- and post-menopausal patients [9].

To date, it remains unclear whether the increasing prevalence of LUTS is due to changes in sex hormones that occur during the menopausal transition or is due to advancing age. There are no reports directly investigating the relationship between hormonal factors and symptoms using combined symptom-scoring questionnaires administered simultaneously in this population. Previous reports about LUTS in this population have largely focused on stress urinary incontinence.

The specific aim of our study was to evaluate overall voiding symptoms among peri- and post-menopausal women and to assess how multiple sex hormones affect LUTS. We used the International Prostate Symptom Score (IPSS), Overactive Bladder Symptom Score (OABSS), and Sandvik Severity Index (SSI), which are representative and well-validated self-administered questionnaires for evaluation of female voiding symptoms.

2. Materials and methods

The Soonchunhyang University Hospital Institutional Review Board granted approval of this cross-sectional study. Between February 10, 2013, and August 15, 2013, hormone treatment-naive peri- and post-menopausal women between the ages of 45 and 60 years who presented to the Urologic Clinic at Soonchunhyang University Hospital for evaluation of LUTS were invited to participate in the study.

After obtaining informed consent, we immediately used a standard medical history questionnaire and additional specialized voiding symptom questionnaires, including the International Prostate Symptom Score (IPSS), Overactive Bladder Symptom Score (OABSS), and Sandvik Severity Index (SSI). Women were excluded if they had any of the following: gynecologic malignancy; need for urologic surgery; history of hysterectomy, myomectomy, or pelvic inflammatory disease; symptomatic or asymptomatic urinary tract infection; pelvic floor complaints, including symptomatic pelvic organ prolapse; psychiatric problems requiring psychotropic medication; depressive mood disorder; or other problems that were not considered eligible for participation. Because we were focused on recruiting appropriate patients to constitute a more valid and reliable cohort, one-on-one interviews were conducted with each patient under the supervision of an experienced interviewer with sufficient time (15.2 min on average) to assess menopause-related symptoms. Determination of menopausal status for each patient was conducted according to the definition given by the Stages of Reproductive Aging Workshop (STRAW) [3]. Approximately 260 women were initially offered participation in this study. After review of histories and symptoms, 117 women met inclusion criteria, and of these women, 59 women were initially enrolled. Four women were subsequently excluded because of withdrawal of consent for private reasons, resulting in a total of 55 women enrolled in the peri- ($n = 24$) and post-menopausal ($n = 31$) groups.

The IPSS is a widely used representative questionnaire for evaluating symptom severity in male LUTS patients with benign prostatic hyperplasia, and it has also been used to survey female patients with LUTS. Many urologists use the IPSS in their daily practice and research on female patients with LUTS [10,11]. OABSS is an objective diagnostic tool that was recently developed and has gained acceptance for assessment of the severity of overactive bladder (OAB) and for evaluating treatment outcomes among various symptom scores for OAB [12]. Additionally, SSI is used for a more detailed assessment of stress urinary incontinence [13]. All three questionnaires used in our survey have proven feasibility for use in female patients. We acquired translation and linguistic validation of the Korean version of the questionnaires [14–16]. In order to obtain more precise data on voiding symptoms, one-on-one interviews were conducted with each patient under the supervision of an experienced interviewer. Each patient enrolled in our study completed the three questionnaires in order after a detailed description of the purpose of the study.

Serum hormones related to the menopausal transmission were also evaluated in all eligible patients and included follicle-stimulating hormone (FSH), luteinizing hormone (LH), thyroid-stimulating hormone (TSH), and prolactin. In addition to the general methods used for the hormone tests, we used radioimmunoassay (RIA) for estradiol, progesterone, and testosterone as a direct measurement method to avoid the disadvantages of the day-counting indirect measurement method, which can be inaccurate in the context of irregular menstrual cycles and low hormone levels.

Descriptive statistics included comparative measurements of age, BMI, hormonal parameters, and symptom scores between the peri- and post-menopausal groups. Spearman correlation analysis was also performed to investigate correlations among age, BMI, hormonal parameters, and symptom scores. Comparisons of hormonal parameters and urinary symptom scores were conducted using logistic regression analysis between the peri- and post-menopausal groups. All data were analyzed using Statistical Package for Social Science (SPSS) software, version 18.0 (Chicago, IL, United States), and significance was indicated at a p value less than 0.05.

3. Results

Overall mean age, BMI, hormonal parameters, and urinary symptom scores from each questionnaire are presented in Table 1. A total of 55 women completed the study, and the mean age and BMI were 51.52 ± 3.48 (41–60) and 22.44 ± 2.25 (17.29–27.29), with ranges of 41–60 and 17.29–27.29, respectively. Units for the hormone levels are detailed in the tables. There were no differences in age or BMI between the peri- and post-menopausal groups (Table 2).

Comparing hormone levels of the peri-menopausal and post-menopausal women, FSH and LH levels were significantly increased in the post-menopausal women, and prolactin, estradiol, progesterone, and testosterone levels were significantly decreased in the post-menopausal women (Table 2). TSH levels did not differ between the groups. In the comparison of symptom scores on the IPSS between the two groups, Q1 (incomplete emptying) and Q2 (frequency) were significantly different (1.63 ± 1.58 vs 0.81 ± 1.08 and 2.33 ± 1.76 vs 1.16 ± 1.13, respectively) ($p < 0.01$) without differences in other symptom scores. SUI was significantly increased in the post-menopausal group on the SSI (0.25 ± 0.44 vs 0.58 ± 0.50, respectively). There were no differences in OABSS between the two groups (Table 2).

Table 3 shows a similar trend for testosterone, estradiol, Q1 and Q2 on the IPSS, and SUI in the logistic regression analysis, with results as described above. Q1 and Q2 on the IPSS had a negative B value as did testosterone, and Odd ratio were all positive and statistically significant ($p < 0.05$ for testosterone and Q1 on IPSS, and $p < 0.01$ for Q2 on the IPSS).

In multivariate analysis, frequency (IPSS question 2) and SUI were significantly different between the groups ($p = 0.020$ and 0.011, respectively). Among the hormonal factors, only testosterone was marginally different ($p = 0.059$) (Table 3).

For investigation of correlations between hormonal parameters and urinary symptom scores, Spearman correlation analysis was performed and the results are shown in Table 4. FSH was