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Systemic atherosclerosis and voiding symptom

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ABSTRACT

Objective: To evaluate the effect of atherosclerosis on the storage and voiding symptoms of the bladder in women with overactive bladder (OAB).

Study design: We retrospectively reviewed the charts of women with OAB who were evaluated between 2013 and 2015 in our urogynecology unit. Charts were assessed for history, examination findings, urinary diary, quality of life (QOL) questionnaires, urodynamic studies (UDSs), and four main risk factors for atherosclerosis: hypertension, diabetes mellitus, smoking, and hyperlipidemia. In a previous study, these were defined as vascular risk factors. Cases were excluded for insufficient data, diabetes mellitus with dysregulated blood glucose, or prolapse greater than 1 cm to avoid confusing bladder outlet obstruction. We included 167 eligible cases in this study. We evaluated storage and voiding symptoms such as frequency, nocturia, residual urine volume, and voiding difficulties and UDS findings such as maximum bladder capacity, first desire, strong desire, detrusor overactivity, and bladder contractility index. The vascular risk score was categorized as "no risk" if the woman did not have any of the four risk factors and "at risk" if she had any of the factors. Independent sample *t*-test and chi-square tests were performed for analyses.

Results: Among the participants (n = 167), 71.9% had at least one vascular risk factor. Those who were at risk were facing significantly more wet-type OAB (p = 0.003) and nocturia (p = 0.023). Moreover, mean age (p = 0.008) and mean gravidity (p = 0.020) were significantly higher in the at-risk group, whereas mean total nocturia QOL questionnaire scores (p = 0.029) were significantly lower.

Conclusion: Our findings suggest that aging and atherosclerosis may be associated with severe OAB and poorer QOL. Nocturia and related parameters of poor quality can be explained by impaired bladder neck perfusion. Future trials need to assess vascular and molecular changes in women with OAB.

Introduction

Overactive bladder (OAB) is defined as urinary urgency, usually accompanied by daytime frequency, and nocturia, with or without urgency urinary incontinence, in the absence of a urinary tract infection or other obvious disease [1]. Although the mechanisms are unclear, recent trials reported that aging, oxidative stress, ischemia, and inflammation may be important contributors to the development of molecular and structural changes associated with OAB [2,3]. On the basis of results from animal studies, mild to moderate ischemia damages the bladder, resulting in the storage symptoms manifested in OAB; it is defined as compensation status. If bladder ischemia becomes severe, it causes voiding symptoms due to decreased bladder compliance [4–6]. Systemic atherosclerosis as a result of decreased bladder perfusion may trigger oxidative stress and ischemic processing in the bladder wall and may play a role in lower urinary tract symptoms (LUTS). Vascular risk factors for atherosclerosis such as diabetes mellitus, hypertension, smoking, and hyperlipidemia or increased carotid intima media thickness as a marker for atherosclerosis were investigated for LUTS. There is some evidence of a relationship between systemic atherosclerosis and LUTS [7,8]. Markedly decreased bladder neck perfusion was associated with the pathophysiological characteristics of LUTS in aging individuals [9]. We aimed to evaluate the effect of atherosclerosis on the storage and voiding symptoms of the bladder in women with OAB.

Materials and methods

The study was conducted after receiving the approval of the local ethics committee. We retrospectively reviewed the charts of

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women who were evaluated between 2013 and 2015 in our urogynecology unit. Charts were assessed for history, examination findings, urinary diary, quality of life (QOL) questionnaires, and urodynamic studies (UDS). Women with OAB were identified by using urinary diaries according to the International Continence Society definition [1]. Cases were excluded for insufficient data or for prolapse greater than 1 cm to avoid confusing bladder outlet obstruction. Patients with diabetes mellitus with dysregulated blood glucose were also excluded.

We included 167 eligible cases in this study. The routine urogynecological protocol was performed before urodynamic testing. This included a comprehensive urogynecological history, pelvic examination, 3-day urinary diary, and no urinary infection. Sociodemographic characteristics such as age, weight, height, smoking, parity, gravidity, menopausal status, and previous medication or surgery were provided by the charts. Body mass index (BMI) was calculated as weight in kilograms divided by height in meters squared. Obesity was defined as a BMI of 30 or more. Pelvic examination consisted of a cough stress test, residual volume measuring, Q-tip test, and Pelvic Organ Prolapse Quantification staging [10,11]. The storage and voiding symptoms and findings such as frequency, nocturia, residual urine volume, and voiding difficulties were identified according to the urinary diaries. Frequency (eight voids per day), nocturia (two voids per night), and symptomatic incontinence (OAB wet at least once a day or OAB dry, respectively) were determined. UDS were performed in accordance with the criteria established by the International Continence Society. The presence or absence of DOA and leakage during UDS were determined. UDS findings such as maximum bladder capacity (MBC), first desire (FD), strong desire, detrusor overactivity (DO), and bladder contractility index (BCI) were evaluated. BCI was calculated using the formula $BCI = P_{detQmax}$ (detrusor pressure at peak flow rate) + 5_{Qmax} [12].

As in a previous study, four main risk factors for atherosclerosis were identified: hypertension, diabetes mellitus, smoking, and hyperlipidemia [7]. The vascular risk score was categorized as “no risk” if the woman did not have any of the four risk factors and “at risk” if she had any of the factors. For determination of hyperlipidemia, laboratory test results were evaluated. These data were obtained from charts and our hospital database.

Questionnaires

The data for the study were obtained using questionnaires that were divided into three parts. Part- 1 was the Urogenital Distress Inventory short form (UDI-6) and the Incontinence Impact Questionnaire short form (IIQ-7). The IIQ-7 and UDI-6, consisting of 7 and 6 questions, respectively, were reported to have a high degree of correlation with longer forms that were developed to measure the effect of incontinence in women’s lives by Shumaker et al. [13]. The IIQ-7 and UDI-6 were validated in Turkish by Cam et al. [14]. UDI-6 scores range from 0 to 18, with higher scores indicating poorer QOL. The IIQ-7 assesses the adverse effects of urinary incontinence on QOL in terms of physical activities, household chores, recreation, traveling, social activities, emotional health, and feelings of frustration. IIQ-7 scores range from 0 to 21, with higher scores indicating poorer QOL.

Part 2 was the Overactive Bladder Symptom and Health-related Quality of Life Questionnaire Short Form (OABq-SF), which was developed by Coyne et al. [15] and validated in Turkish by Acquadro et al. [16]. It has two parts; the first part is a scale that measures symptom severity, and the second part is a scale (Health-related Quality of Life Questionnaire Short Form [HRQOL]) that measures health-related QOL. The OABq-SF subscale scores were transformed into a scale from 0 to 100 points as follows: (actual raw score–lowest possible raw score)/possible raw score range $\times 100$. Higher scores on the former scale indicated increasingly problematic symptoms, but higher scores on the latter scale indicated a better HRQOL. HRQOL was also transformed to 100-point scale as follows: (highest possible score−actual raw score)/possible raw score range $\times 100$. Minimum and maximum scores for symptom severity range from 6 to 36 and for HRQOL from 13 to 78. For the subscale analyses, if 50% or fewer of the scale items were missing, the scale was retained, and the mean scale score was used to impute a score for the missing items. If more than 50% of the items were missing, a scale score was not calculated, and the subscale score was considered missing.

Part 3 was the Nocturia Quality of Life (N-QOL) questionnaire. The N-QOL questionnaire was developed by Abrahams et al. [17] and validated in Turkish by McKown et al. [18]. The N-QOL questionnaire is a 13-item questionnaire that consists of 3 domains or subscales: a sleep/energy domain consisting of six items (items 1–5 and 7), a bother/concern domain consisting of 6 items (items 6 and 8–12), and a global QOL domain consisting of 1 item. The global QOL item (question 13), however, was removed from the N-QOL and scored separately from the core 12 items. We used a five-item Likert scale scoring a minimum of 0 to a maximum of 4 points, with minimum and maximum score ranges from 0 to 48 for each domain. The domain scores were transformed into a scale from 0 to 100 points, with 0 representing the lowest QOL and 100 representing the highest QOL, as follows: (actual raw score–lowest possible raw score)/possible raw score range $\times 100$ [17]. The total score was independent of the subdomain scores; therefore, the participants were allowed to miss up to one question.

Statistical analysis

Data were analyzed using SPSS 15.0 software. Continuous variables were presented as mean $\pm$ 1 SD, and classified variables were shown as percentages. Independent sample *t*-test and chi-square tests were performed for analyses, and $p < 0.05$ was considered to indicate statistical significance.

Results

We included 167 women with OAB in this study. Mean age was 57.12 $\pm$ 10.53 years (range, 26–86), and mean BMI was 29.45 $\pm$ 4.99. Among the participants, 18.0% had diabetes mellitus, 39.5% had hyperlipidemia, 36.5% had hypertension, and 21.0% were smokers. In total, 71.9% (n = 120) had at least one vascular risk factor and were categorized as being at risk. Mean age and mean gravidity were significantly higher in the at-risk group. N-QOL-1 scores were poorer in the at-risk group, meaning those who were at risk had a lower QOL. Moreover, the ones who were at risk had significantly more wet-type OAB ($p = 0.003$) and nocturia ($p = 0.023$). There were no significant differences in terms of BMI, parity, frequency, and residual urine or in results from the other questionnaires such as the IIQ-7, HRQOL, and N-QOL-2 (Table 1). MBC, FD, DO, and BCI were evaluated by means of UDS, and there were no significant differences between the two groups (Table 2).

Comment

We evaluated four major factors for systemic atherosclerosis—hypertension, hyperlipidemia, smoking, and diabetes mellitus—in women with OAB to test the link between atherosclerosis and storage and voiding symptoms of the bladder. The Framingham Heart Study, based on 38 years of follow-up data, identified that these four factors increase the risk of atherosclerosis by a factor of 1.2–2.6 and that each increase of 10 years in age increases this risk by a factor of 1.5 [19]. Our findings suggest that aging and having at least one major risk factor for developing atherosclerosis may be