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The most bothersome symptom of vaginal atrophy: Evidence from the observational AGATA study

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ABSTRACT

Objectives: Vaginal atrophy (VA) is a chronic medical condition. It is managed unsatisfactorily, despite its high prevalence and negative impact on female quality of life. In order to meet their needs, it would be useful to know what women perceive to be the most bothersome symptom (MBS) of VA.
Study design: Cross-sectional, multicenter study of 913 postmenopausal women consulting 22 gynecological outpatient services.
Main outcome measures: Prevalence of the MBS perceived by postmenopausal women of different age and vaginal condition.
Results: Vaginal dryness was the most prevalent MBS (54.4%), followed by dyspareunia (17.6%), itching (7.8%), dysuria (5.9%) and burning (2.0%). The prevalence of vaginal dryness as the MBS increased with years since menopause, while that of itching, dysuria and burning remained approximately constant over time. The prevalence of dyspareunia as the MBS was 26.2% in the first 6 years after menopause and declined thereafter, to 8.8%.
Conclusions: Among all postmenopausal women vaginal dryness per se, independent of dyspareunia, is the most commonly reported MBS. In each woman, the identification of the MBS may help to define more appropriate VA management.

1. Introduction

1.1. Background/Rationale

Vaginal atrophy (VA), which is now considered a component of the genitourinary syndrome of the menopause, is a chronic and progressive condition associated with the post-menopausal withdrawal of circulating estrogens [1,2]. Its prevalence evaluated in different population by web surveys or interviews ranges from 27% to 59%, with value that reach 79% in the AGATA study, where both objective and subjective signs where considered in a population of women attending outpatient gynecological services [3–8].

Anatomical changes related to VA increase with time since the menopause [8,9], are associated with an increase of vaginal pH [1,8–11] and an increased risk of infection [1,8,11]. Vaginal dryness and dyspareunia are the most prevalent symptoms [6,8–10,12–20]. Symptoms are believed to impact female quality of life [3,12], sexual activity, and partner relationship [13–18]. Recent data indicate that the management of VA is highly inefficient, with a diagnosis performed in no more than 50% of individuals [21], and a therapeutic management highly unsatisfactory [22]. In order to improve the approach to VA and its treatment, physician have to learn how to meet women's needs, to understand which signs or symptoms they should focus on, and to provide specific remedies for those symptoms that women, depending on their status and age, feel as the most bothersome.

1.2. Objectives

The aim of this investigation was to evaluate the prevalence of the most bothersome symptom (MBS) among all VA symptoms perceived

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[1] Results from the Atrophy of the vaGina in womAn in posT – menopause in itAly (AGATA) study for the Italian Society for the Menopause (SIM). Participants: M. Bongiolatti (Gallarate); L. Cipolla (Garbagnate); R. Chionna (Milano); G.M Donvito (Peschiera del Garda); M. Bertezzolo (Conegliano Veneto); C. Schrettenbrunner, S. Messini (Bolzano); P. Mancino, A. Carrone, L. Riganelli, P. Benedetti – Panici (Roma); R. Lorefice, A. Di Francesco (Chieti – Lanciano); M. Torella (Napoli); A. Chiacchio (Lagonegro); F. Zullo (Catanzaro); A. Cianci (Catania); R. Daguati, I. Baini (Milano); P. Villa, C. Moruzzi, L. Vacca, E. Tempestilli (Roma); C. Demetrio (Ferrara); A. Cagnacci (Udine), F. Palma, C. Romani, A. Volpe (Modena); A. Becorpi, Z. Tredici (Firenze); N. Surico, D. Surico, S. Zorzetti Cigna, L. Leo (Novara); C. Di Carlo (Napoli); P.G. Zampi, C. Pellegrini, F. Quaglia (Brescia); M. Ciammella (Seriate), A. Gambera (Brescia).

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by women, depending on their age and clinical condition.

2. Methods

2.1. Study design

This study is part of the AGATA study a multicenter cross-sectional study performed on the prevalence of VA signs and symptoms in Italy. Complete details on the AGATA study design have been previously reported [8,9,21,22].

2.2. Setting

Women were recruited between December 2013 and March 2014, from 22 public outpatient gynecological services during their routine gynecological examination.

2.3. Participants

Eligible participants were white Italian women of any age, in postmenopause, defined as the presence of amenorrhea for at least 12 months. Written informed consent was obtained prior to enrolment in accordance with the Ethical Committee approval in all the involved centers. No financial incentive was offered to any of the participants.

2.4. Variables, measurements and bias

Each woman underwent a medical interview where basic demographic, personal and family history, and co-morbidity information were collected.

All women underwent a physical examination where signs of VA such as thinning of vaginal rugae, mucosal dryness, pallor of the mucosa, mucosal fragility, presence of petechiae and vaginal pH were evaluated. All women completed a self-assessment questionnaire of VA symptoms, which consisted of questions about the severity of each of five individual symptoms of VA such as vaginal dryness, itching, burning, dysuria and dyspareunia. VA diagnosis was performed by the concomitant presence of a pH $>$ 5, the subjective sensation of vaginal dryness and the presence of at least one of the five clinical signs considered [8,9]. Each woman was requested to define among all those perceived, which VA symptom, if any, she rated as the MBS. During the compilation of each auto-administered questionnaire there was no interaction between the woman and the investigator.

2.5. Study size calculation

This is a secondary analysis of the AGATA study that was designed to obtain a reliable estimated of VA. The AGATA study was designed assuming a prevalence of VA of 40.3%. On that basis it was calculated that 753 women were necessary to obtain a reliable estimate of VA [8].

2.6. Variables and statistical methods

All signs and symptoms were collected in an anonymous medical record and then transferred to a computer database. Descriptive statistic was used for statistical analyses.

The prevalence of each MBS of VA was stratified into categories of years since menopause.

Logistic regression analysis was used to define the prediction of each MBS by independent variables. Uni-variable logistic regression analysis was used to identify the factors related to the MBS.

Collinearity among the covariates was tested through a uni-variable regression analysis and was accepted with a coefficient of regression of more than 0.7 [23]. Multi-variable logistic regression models were constructed with the MBS as the dependent variable, and all those parameters found to be related or more related (in case of collinearity) to the MBS, as independent variables.

Covariates included in the models were both categorical variables such as objective vaginal pH $>$ 5 (yes/no), mucosal dryness (yes/no), vaginal thinning (yes/no), fragility (yes/no), pallor of the mucosa (yes/no), presence of petechiae (yes/no), type of menopause (medical, surgical, physiological), lifestyle (sedentary or not), use of alcohol (yes/no), smoking (yes/no), recent (within 3 months) or actual presence (yes/no) of vaginal infections, and continuous variables such as age, weight, years since menopause.

For each regression model, the R squared is provided as a measure of the quality of the model. R squared indicates the proportion of the dependent variable's variability that is explained by the independent variables [23].

Analyses were performed by the statistical package StatView5.01 (SAS Institute Inc., Cary, NC). All results are expressed as the means and standard deviations. A p value $<$ 0.05 was considered as statistically significant.

3. Results

913 out of 927 eligible women were enrolled into the study. They had a mean age of 59.3 $\pm$ 7.4 years and were in physiological (83.3%) surgical (10.1%) or premature or early (6.6%) menopause since 10.3 $\pm$ 8.8 years. Almost all women (99%) were white non-Hispanic. A sedentary lifestyle was reported by 55%, use of alcoholic beverages by 15% and smoking by 18.5% of women, with former smokers being 17.6%. Only 274 (30%) of women had a previous diagnosis of vaginal atrophy, and among these 9.8% did not receive any therapy, 9.2% were treated with systemic hormone, 44.5% with local hormonal and 36.5% with local non-hormonal therapy. At the time of our investigation 266 of them (97.1%) still had vaginal atrophy. More detailed information is reported in previous articles [8,9,22].

3.1. Subjective symptoms and objective signs of VA

In the full cohort (n = 913), sensation of vaginal dryness was present in 746 women (81.7%). It was the most frequent symptom of VA, followed by dyspareunia (64.4%), burning and itching (48%) and dysuria (31.4%). Stratification of symptoms according to severity graded from 0 (none) to 3 (severe) is presented in Fig. 1a.

Upon objective evaluation, the sign most frequently detected by gynecologists was dryness of vaginal mucosa (82.5%), pallor of the mucosa and thinning of vaginal rugae (about 80%). Mucosal fragility and presence of petechiae were detected in 59.5% and 37.6% of women, respectively (Fig. 1b).

A pH $>$ 5 was detected in 91.0% of participants.

3.2. The most bothersome symptom

The symptom most frequently reported as the MBS was vaginal dryness (54.4% of subjects), followed by dyspareunia (17.5%), none (12.2%), itching (8.9%), burning (3.8%), and dysuria (3.2%) (Fig. 2).

Prevalence of the MBS varied when considering women with different years since menopause (Fig. 3). Vaginal dryness was identified by 49.1% of women 1 year after menopause, value that increased above 55.5% in women who had 10 or more years after menopause. Dyspareunia was identified by 26.2% of the women up to 6 years since the menopause, but the rate decreased to about 8.8% in women having 20 years of menopause. Vaginal itching, burning and dysuria were identified as the MBS less frequently and with a prevalence rather stable in time (from 2.0% to 7.8% in women 1 year since menopause to values of 1.7–12.3% in those having 20 years after menopause) (Fig. 3).