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Symptom severity and quality of life in the management of vulvovaginal atrophy in postmenopausal women

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ABSTRACT

Objectives: To evaluate the association between treatments for vulvovaginal atrophy (VVA) and symptom frequency and severity, quality of life (QoL) and sexual functioning in postmenopausal women.
Study design: Cross-sectional survey conducted in postmenopausal women aged 45–75 years. Data on demographic and clinical variables, as well as vaginal, vulvar and urinary symptoms were collected. The EuroQoL questionnaire (EQ5D3L), the Day-to-Day Impact of Vaginal Aging (DIVA), the Female Sexual Function Index (FSFI) and the Female Sexual Distress Scale - revised (FSDS-R) were filled out.
Main outcome measures: Association between treatments for VVA and symptom frequency.
Results: Women on VVA treatment presented with more severe symptoms. The sexual function score was higher in the treated women (FSFI: 15.6 vs 16.7; $p = 0.010$), as was the score for sexual distress (FSDS-R: 9.2 vs 12.3, $p < 0.0005$). The systemic hormone group presented with fewer VVA symptoms, lower vaginal impact (DIVA), and better sexual function (FSFI and FSDS-R) and vaginal health. The rates of sexual distress and vulvar atrophy were higher in the non-hormonal treatment group. No significant differences were found according to treatment duration.
Conclusions: Postmenopausal women with VVA receiving treatment complained of more severe symptoms than those untreated. Women on systemic treatment had fewer and milder VVA symptoms and presented with better vaginal and vulvar health than women on other treatments. Many women request effective local treatment too late, when VVA symptoms are already severe. Our data suggest that VVA treatments should ideally be initiated when symptoms commence and cause distress, rather than later, when symptoms may have become more severe and even a cause of intolerable distress for the woman.

1. Introduction

Vulvovaginal atrophy (VVA) is a common condition of menopause which leads to symptoms in approximately 50% of postmenopausal women [1,2]. Symptoms of VVA include vaginal dryness, dyspareunia, vulvar and vaginal irritation and/or itching, dysuria and post-coital bleeding [3]. Women often do not report the symptoms of VVA because they feel it is a natural part of ageing or due to embarrassment. Also, women's perceptions seem to vary across countries attending the possibilities of the healthcare systems, especially in relation to communication with professionals [4]. This leads to underreporting by women, underdiagnosing and often undertreatment by healthcare providers, despite a significant impact of VVA symptoms on interpersonal relationships, daily activities and sexual function [5] and on quality of life (QoL) of postmenopausal women [6,7].

The main therapeutic goal of treatment is the relief of symptoms [8,9] as well as to restore the vaginal physiology [8]. Non-hormonal treatments, like vaginal moisturizers and lubricants, and vaginal estrogens are considered the standard of care. Systemic estrogens are only recommended if other postmenopausal symptoms are present, requiring systemic estrogen treatment (e.g. vasomotor symptoms) [3,10]. Recent, evidence-based therapies for VVA include ospemifene, a selective

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estrogen receptor modulator [11–13], and prasterone, a DHEA (dehydroepiandrosterone) based vaginal insert [14]; even more recently, the vaginal application of energy based devices like laser or radiofrequency, although there is still a lack of robust data regarding the efficacy and (long term) safety of these devices [15].

Insufficient symptom relief, poor compliance and inconvenience have been cited as major limitations of some vaginal treatments [5]. An appropriate management of VVA in postmenopausal women appears essential to minimize its impact in patients and partners.

The European Vulvovaginal Epidemiology Survey (EVES) study is a large cross-sectional survey of women visiting a gynecologic or menopause clinic in two European countries (Spain and Italy). Apart from evaluating VVA symptomatology, QoL, lifestyle and therapies, this study has unique characteristics as there was a physical examination to confirm VVA [16]. In that study, a 67% of women with confirmed VVA showed a very low to moderate satisfaction with treatment for VVA. Up to 61% reported no relief to moderate relief of treatment. Reasons for not being satisfied were mainly that they considered treatment not effective enough (41.3%) or messy (18.5%) [16]. Despite the available therapeutic options, the relief of symptoms of VVA in postmenopausal women and satisfaction with current treatments can be improved by development of both healthcare provider- and patient-based educational programs as previously suggested [17]. A better knowledge of the association between different management options and symptom/QoL outcomes will help to improve VVA-related healthcare [16,18].

This analysis of the EVES study evaluates the association of treatment vs no treatment, including differences between treatment options and duration of treatment, and symptom frequency and severity, menopause-specific QoL and sexual function in postmenopausal women with VVA.

2. Materials and methods

2.1. Design and patients

The EVES study is a cross-sectional survey among postmenopausal women (> 12 months after the last menstrual period) aged 45–75 years old attending menopausal centres or gynaecological clinics in Italy and Spain. The study was conducted in accordance with the Declaration of Helsinki and was approved by the Institutional Review Board of the participant centres. All patients provided written informed consent before study entry. From a total population of 2412 women initially enrolled, 2160 were evaluable for all parts of the study and form the core population in this analysis. From these, 1242 were untreated and 918 were treated for VVA symptoms (see Fig. 1). The data presented include an analysis of the association between the type (non-hormonal treatment, hormonal local and systemic) and duration (< 1 week, 1–4 weeks, 1–3 months, > 3 months) of VVA treatments on quality of life and symptomatology in these patients.

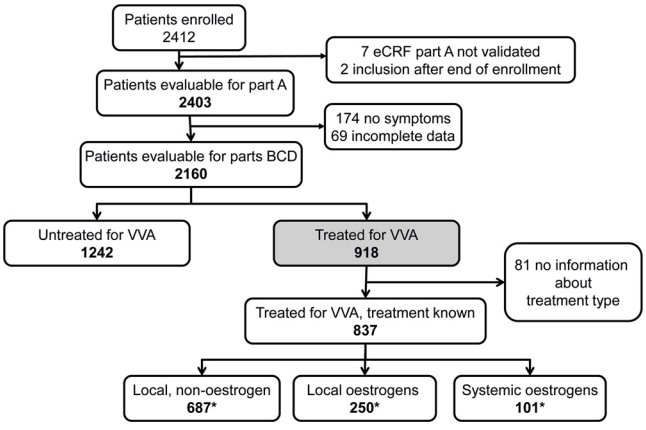

Fig. 1. Diagram flow of the study.

2.2. Study procedures

The study procedures have been reported elsewhere [16]. The study consisted of 4 parts assessing demographic and menopause and VVA-related data and included the following QoL/sexual functioning data: the EuroQoL questionnaire (EQ5D3L) [19] (measuring the impact of VVA on QoL), a Visual Analog Scale (VAS) for today's health status, the Day-to-Day Impact of Vaginal Aging (DIVA) [20] the Female Sexual Function Index (FSFI) [21] and the Female Sexual Distress Scale - revised 2005 (FSDS-R) [22]. A gynaecological examination was also carried out in accordance with routine clinical practice. The Vaginal Health Index [23] and Vulva Health Index [24] were also calculated. In the case of the EQ-5D3L, the VAS score, the FSFI and the Vaginal Health Index, a higher score means better status and more preserved function (e.g. a score < 15 in the Vaginal Health Index corresponds to vaginal atrophy). In the case of the symptom severity score, the DIVA, the FSDS-R and the Vulva Health Index, a higher score means worse status and function loss (e.g. a score > 8 points or a score of 3 [severe] in any category of the Vulva Health Index indicates vulvar atrophy).

2.3. Statistical analyses

In order to obtain a sufficiently representative sample size, we planned to recruit approximately 1000 patients for each country (Italy and Spain). A final sample of 1094 Spanish women and 1066 Italian women were recruited. For continuous variables, descriptive statistics include means, standard deviation (SD) and median. Categorical variables were to be summarized as percentages. Comparisons of categorical variables between different groups were performed by Chi-Square test while Student *t*-test was used to compare quantitative variables. Some of the patients reported more than one treatment, so statistical comparisons were not performed in terms of treatment type.

3. Results

3.1. Demographics and treatments used

Table 1 compares main demographic characteristics between untreated and treated women for VVA. The most relevant finding was the time since menopause, which was significantly higher in women treated for VVA (mean ± SD of 10.3 ± 7.0 vs 9.5 ± 7.1, p = 0.009). Supplementary Table 1 shows the main demographic characteristics by type of treatment (local non-hormonal, local and systemic hormonal). Women on systemic hormonal treatment were younger and had a shorter period since menopause than the other two populations. There were no significant differences in demographics between the patients receiving local hormonal treatment by duration of treatment (Supplementary Table 2).

Table 2 shows the number and type of treatments used. 42.5% of women used at least one treatment, with 8.9% two or more. The most common treatment type used was non-hormonal therapy applied vaginally (31.8%), followed by hormonal therapy (estrogen-containing) applied vaginally (11.6%). Systemic hormonal therapy was used by 4.7% of the population. Among the women who reported at least one treatment (N = 918), a total of 753 (82.0%) had an evaluation of treatment satisfaction for the first treatment. Of these, 488 (64.8%) indicated very low to moderate satisfaction with the first treatment.

3.2. VVA symptom frequency

The most prevalent VVA symptom was vaginal dryness (inside), which was more prevalent in the treated population than the untreated population (89.9%% vs 79.1%, p < 0.0005), followed by vaginal dryness (outside) (81.9% vs 70.8%, p < 0.0005) and dyspareunia

Table 1
Demographics and presence of main VVA symptoms: untreated vs treated women for VVA.

	Non-treated (N = 1242)	Treated for VVA (N = 918)	P
Age (years), mean ± SD (median)	58.8 ± 6.8 (58)	59.1 ± 6.7 (59)	0.308
Weight (Kg), mean ± SD (median)	66.4 ± 11.8 (65)	65.3 ± 11.4 (64)	0.030
Height (cm), mean ± SD (median)	160.6 ± 6.2 (160)	160.3 ± 6.4 (160)	0.273
BMI (Kg/m^2), mean ± SD (median)	25.8 ± 4.6 (25.2)	25.5 ± 4.4 (24.9)	0.127
Time since menopause (years), mean ± SD (median)	9.5 ± 7.1 (8)	10.3 ± 7.0 (9)	0.009
VVA Symptoms, %			
Dryness inside	79.1%	89.9%	< 0.0005
Dryness outside	70.8%	81.9%	< 0.0005
Pain inside	53.9%	71.8%	< 0.0005
Pain during intercourse/penetration	73.5%	56.4%	< 0.0005
Pain during exercise	20.5%	26.1%	0.002
Bleeding during intercourse	13.8%	19.9%	< 0.0005
Bleeding during sexual contact	11.0%	14.2%	0.029
Burning or irritation inside	50.1%	60.7%	< 0.0005
Burning or irritation outside	48.5%	58.1%	< 0.0005
Itching inside	35.8%	40.4%	0.031
Itching outside	43.9%	50.2%	0.004
Vaginal discharge	32.7%	32.9%	0.963
Urinary incontinence	38.5%	36.1%	0.261
Urinary urgency	42.4%	41.0%	0.624
Urinary frequency	50.7%	54.3%	0.098
Urinary difficulty	12.4%	14.3%	0.222
Recurrent urinary tract infections	19.3%	27.8%	< 0.0005
Postcoital cystitis	13.4%	19.8%	< 0.0005
Abdominal pain	26.0%	27.2%	0.522

SD: standard deviation; VVA, vulvovaginal atrophy. Different missing values across the variables and groups.

Table 2
Treatments used to relieve VVA symptoms.

	N = 2160
None	56.1%
At least 1 treatment used	42.5%
Number of treatments used	
1	33.6%
2	8.1%
3	0.8%
Non-hormonal therapy applied vaginally	31.8%
Moisturizer (liquids, gels or ovules, water based, to improve vaginal hydration)	19.3%
Lubricant (applied to the vagina at the time of sexual activity to reduce pain during sex)	11.6%
Phytoestrogen tablets	0.9%
Hormonal (estrogen-containing) therapy applied vaginally)	11.6%
Cream	8.2%
Ovule	2.2%
Tablet	1.0%
Ring	0.2%
Hormonal (estrogen-containing) therapy taken non-vaginally	4.7%
Oral tablet	3.3%
Transdermal patch/gel	1.4%

VVA, vulvovaginal atrophy.

(inside) (71.8% vs. 53.9%, p < 0.0005). In global terms, most of the VVA symptoms were more prevalent in the treated group. Within the three treatment groups, the most prevalent VVA symptom was vaginal dryness, followed by pain during intercourse (Table 3). Among the different treatment populations, women using a systemic hormonal treatment presented with fewer VVA symptoms than those on local hormonal or those using non-hormonal treatment.

Moderate or severe symptom frequency by duration of local hormonal and non-hormonal treatments is indicated in Supplementary Figs. 1 and 2, respectively. Apart from vaginal dryness, there was no a clear duration-related pattern in symptom frequency within the local hormonal group, but more than 3 months treatment resulted in a lower frequency of moderate or severe symptoms. There were no significant differences in symptom frequency based on treatment duration in women using local non-hormonal therapy.

3.3. VVA symptom severity

Table 3 demonstrates vulvovaginal discomfort by severity of symptoms, from absent to severe and Fig. 2 the mean score for each symptom by group (treated vs non-treated, higher score means worse). Most of the symptoms were significantly worse in the treated population whilst using their therapy (ies).

Supplementary Table 3 shows the frequency of moderate or severe VVA symptoms by treatment group and Supplementary Fig. 3 the mean score for each symptom by treatment type. Frequency and severity of symptoms were higher for most in the non-hormonal and local hormonal treatment populations compared to the systemic treatment population.

The severity score was significantly higher in the treated group as compared with the non-treated group for vaginal and vulvar symptoms as well as for the total symptom score (p < 0.0005) (Table 4). The severity score was consistently higher in the non-hormonal and local hormonal treatment groups as compared to the systemic hormonal treatment group for vaginal, vulvar and urinary symptoms, as well as for the total symptom score (Supplementary Table 4).

3.4. Quality of life and sexual function

In terms of QoL, the EQ5D3L score showed no differences between treated and non-treated women, whilst the EQ-VAS score was slightly better in treated women (71.0 vs 72.6, p = 0.021) (Supplementary Table 5). Within the different dimensions of the EQ5D3L, pain/discomfort was more prominent in the treated women (p = 0.007) as also seen in the assessment of individual symptoms. Supplementary Table 6 provides the QoL information by treatment type. The EQ5D3L overall score was slightly higher in the systemic hormonal treatment; however, the EQ-VAS score was highest in the local hormonal treatment population.

The DIVA score demonstrated a statistically significantly worse overall score for the treated vs the untreated population (p < 0.0005) which was statistically significant in three out of the four dimensions (emotional well-being p = 0.039, sexual functioning p < 0.0005 and self-concept and body image p < 0.0005), see Supplementary Table 7.

Table 3
Vulvovaginal discomfort (severity of symptoms): untreated vs treated women for VVA.

	Non-treated (n = 1242)					Treated for VVA (n = 918)					
VVA Symptoms, %	Absent	Mild	Moderate	Severe	Mean ± SD	Absent	Mild	Moderate	Severe	Mean ± SD	P
Vaginal dryness (inside)	20.9%	26.9%	36.6%	15.7%	1.47 ± 0.99	10.1%	23.3%	39.1%	27.5%	1.84 ± 0.94	< 0.0005
Vaginal dryness (outside)	29.2%	26.6%	32.0%	12.2%	1.27 ± 1.01	18.1%	26.9%	37.1%	17.9%	1.55 ± 0.98	< 0.0005
Pain during intercourse (inside)	46.1%	18.3%	21.3%	14.3%	1.04 ± 1.12	28.2%	22.0%	25.2%	24.6%	1.46 ± 1.14	< 0.0005
Pain during intercourse at penetration	43.6%	19.7%	21.0%	15.7%	1.09 ± 1.13	26.5%	20.8%	25.5%	27.2%	1.53 ± 1.15	< 0.0005
Pain during exercise	79.5%	12.6%	6.5%	1.4%	0.30 ± 0.65	73.9%	14.7%	8.7%	2.7%	0.40 ± 0.76	0.001
Bleeding during intercourse	86.2%	9.2%	4.0%	0.6%	0.19 ± 0.52	80.1%	13.9%	3.8%	2.2%	0.28 ± 0.64	< 0.0005
Bleeding during sexual contact	89.0%	6.5%	3.8%	0.6%	0.16 ± 0.50	85.8%	8.8%	3.7%	1.6%	0.21 ± 0.58	0.032
Burning or irritation (inside)	49.9%	27.4%	16.8%	5.9%	0.79 ± 0.93	39.3%	27.8%	23.9%	9.0%	1.03 ± 1.00	< 0.0005
Burning or irritation (outside)	51.5%	26.2%	17.2%	5.1%	0.76 ± 0.91	41.9%	29.1%	21.8%	7.2%	0.94 ± 0.96	< 0.0005
Itching (inside)	64.2%	22.1%	11.0%	2.7%	0.52 ± 0.79	59.6%	23.6%	12.1%	4.7%	0.62 ± 0.87	0.005
Itching (outside)	56.1%	26.6%	13.4%	3.9%	0.65 ± 0.86	49.8%	29.6%	14.8%	5.8%	0.77 ± 0.91	0.002
Vaginal discharge	67.2%	21.8%	8.8%	2.2%	0.46 ± 0.75	67.1%	25.7%	5.3%	1.9%	0.42 ± 0.68	0.203
Urinary incontinence	61.5%	21.7%	13.4%	3.4%	0.59 ± 0.85	63.9%	23.5%	10.0%	2.5%	0.51 ± 0.78	0.025
Urinary urgency	57.6%	23.3%	15.1%	4.0%	0.66 ± 0.88	59.0%	24.0%	13.1%	3.9%	0.62 ± 0.87	0.294
Urinary frequency	49.3%	24.0%	22.1%	4.7%	0.82 ± 0.93	45.6%	26.4%	22.8%	5.2%	0.88 ± 0.94	0.140
Urinary difficulties	87.6%	7.8%	3.9%	0.8%	0.18 ± 0.51	85.7%	9.7%	3.8%	0.8%	0.20 ± 0.53	0.376
Recurrent urinary tract infections	80.7%	11.5%	6.0%	1.8%	0.29 ± 0.66	72.2%	16.0%	8.5%	3.3%	0.43 ± 0.78	< 0.0005
Postcoital cystitis	86.6%	8.9%	3.6%	0.8%	0.19 ± 0.52	80.2%	11.1%	6.2%	2.5%	0.31 ± 0.70	< 0.0005
Abdominal pain	74.0%	16.9%	8.1%	1.0%	0.36 ± 0.67	72.8%	16.9%	9.0%	1.3%	0.39 ± 0.71	0.313

SD: standard deviation; VVA, vulvovaginal atrophy. Different missing values across the variables and groups.

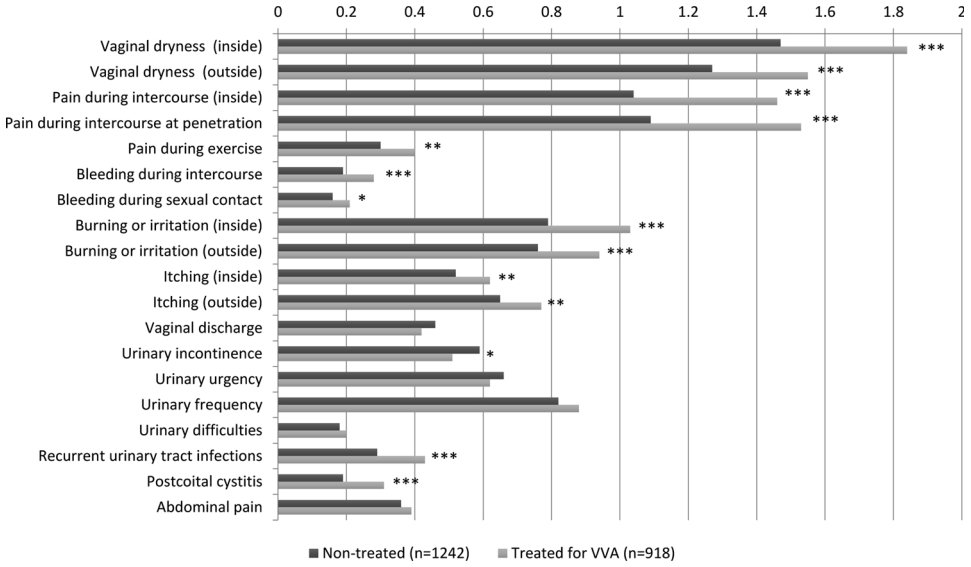

Fig. 2. Mean score for each VVA symptom by group: treated vs non-treated women. Statistically significant differences are presented (*P < 0.05; **P < 0.005; ***P < 0.001).

In global terms, women using a systemic hormonal treatment showed lower vaginal impact vs non-hormonal and local hormonal treatment (DIVA scores, Supplementary Table 8).

Whilst there was a small, statistically significant difference between the untreated and the treated population in FSFI score, in favour of a better score for the latter (p = 0.010), there is very little or no difference in the domains of lubrication (2.5 vs. 2.6 respectively, p = 0.246) and pain (2.7 for both, p = 1.000). In contrast, the FSDS-R score shows significantly worse sexual distress in the treated vs. the untreated population (12.3 vs. 9.2 respectively, p < 0.0005) with a significantly higher percentage of treated women displaying sexual dysfunction (defined as a score ≥11, 45.0% vs 31.3% respectively, p < 0.0005) (see Supplementary Table 9). Sexual function was better in patients using systemic hormonal treatment than local treatment (Supplementary Table 10).

Table 4
Symptoms severity total scores: untreated vs treated women for VVA.

	Non-treated (n = 1242)	Treated for VVA (n = 918)	P
Vaginal symptoms total score, mean ± SD (median)	5.7 ± 4.4 (5)	7.4 ± 4.5 (7)	< 0.0005
Vulvar symptoms total score, mean ± SD (median)	3.0 ± 2.6 (2)	3.7 ± 2.6 (3)	< 0.0005
Urinary symptoms total score, mean ± SD (median)	2.7 ± 2.9 (2)	2.9 ± 3.0 (2)	0.098
All symptoms total score, mean ± SD (median)	11.8 ± 8.2 (10)	14.4 ± 8.2 (13)	< 0.0005

SD: standard deviation; VVA, vulvovaginal atrophy. Different missing values across the variables and groups.

3.5. Vaginal and vulvar atrophy

The mean Vaginal Health Index was significantly lower (=worse) in treated vs untreated women (12.7 vs 13.1, p = 0.011) and as expected, vaginal atrophy was more prevalent in this group (72.2% vs 67.7%, p = 0.026). The mean Vulva Health Index was also worse in treated women (10.1 vs 9.1, p < 0.0005,) as well as the prevalence of severe vulvar atrophy (64.5% vs 54.1%, p < 0.0005) (Supplementary Table 11).

When considered by treatment type, the mean Vaginal Health Index was higher (=better) in women on systemic treatment and overall vaginal atrophy was more prevalent in the other two groups (non-hormonal treatment: 74.7% and local hormonal treatment: 79.4% vs. 48.5%). The mean Vulva Health Index was higher (=worse) in women on non-hormonal and local hormonal treatment (10.3 and 10.9, vs. 8.2) as well as the prevalence of severe vulvar atrophy (66.1% and 70.3%, vs. 45.5%) (Supplementary Table 12).

Medical confirmation of the presence of VVA confirmed by gynaecological clinical assessment among treated women was slightly higher compared to the non-treated women (91.8% vs 89.5%, p = 0.064).

3.6. Population comparison by country

The data in Supplementary Table 13 indicate the differences between the Spanish and Italian populations regarding the main baseline demographic and clinical characteristics. The only statistically significant differences in terms of demographics were height and consequently BMI. With regards to VVA symptoms, Spanish women reported a higher prevalence than Italian women for 70% of all VVA symptoms. In general, the Spanish population indicated a higher use of concurrent treatments to relieve VVA. Non-hormonal therapies applied vaginally were the most reported treatments in both countries (see Supplementary Table 14). There was no significant difference in the reported use of hormonal non-vaginal approaches between the two populations.

4. Discussion

The current cohort analysis of the EVES study shows that in a Southern European population of postmenopausal women with at least one symptom of VVA, up to 57.5% were not using any form of treatment. Spanish and Italian women were similar in terms of baseline demographics and time since menopause. However, VVA symptoms were more prevalent in the Spanish population as was the use of concurrent VVA treatments. Overall, the most common treatment was local non-hormonal therapy (31.8%), followed by local estrogen-containing treatment (11.6%). Only a small percent of women used systemic hormonal therapy (4.7%). These results are similar to other surveys like the European REVIVE where 45.2% of women who complained of one or more VVA symptoms currently used some form of treatment [25]. In this study, 36% used a local non-hormonal treatment and 14.2% a prescription treatment, usually a local estrogen. In contrast, treatment was more common (70%) in a recent published cohort of Spanish postmenopausal women [26].

Treated postmenopausal women with VVA had a longer duration since menopause and demonstrated a higher prevalence of VVA, confirmed by gynaecological clinical assessment, compared to non-treated women.

Women on treatment had more frequent and severe VVA symptoms than those not using treatment. This was confirmed in the more objective assessment of VVA like the Vaginal Health Index where the treated women scored worse than the untreated population. Although the Vulvar Health Index is not yet validated, the significantly higher prevalence of severe vulvar atrophy in treated women shows a similar trend, an observation that may be indicative of clinically meaningful differences. The comparison of treated vs. untreated women for QoL are less clear, with the EQ-VAS showing better QoL in the treated population, the EQ5D3L showing no difference and the DIVA score showing poorer QoL in the treated population. The results for sexual functioning are also inconsistent, with the FSFI score better in treated women and the FSDS-R score worse in the same population. This may be due to the fact that neither questionnaire was specifically developed for postmenopausal women with no specific sexual problems. The FSFI was designed to measure female sexual arousal and other relevant domains of sexual functioning in women with emphasis on Female Sexual Arousal Disorder (FSAD) [21] whereas the FSDS-R was designed as an instrument to measure sexual distress in women with hypoactive sexual desire disorder (HSDD) [22]. Finally, it is worth noting that in the treated population, almost 2/3 of women were not entirely satisfied with the treatment.

As for the findings between different treatment groups, the population using systemic estrogen treatment consistently had fewer, and less severe VVA complaints than the local treatment populations, a better EQ5D3L and DIVA score, a better FSFI and FSDS-R score and better vaginal and vulvar health indices. It is however unlikely that this resulted from better efficacy of systemic treatment compared to local estrogen treatment, but probably more related with an early use of systemic hormone replacement therapy (HRT) during the transition that is preventing VVA symptoms, as suggested by the significantly younger age of participants using systemic hormonal treatment.

All large societies of professionals involved in treating postmenopausal women recommend that systemic HRT should not be used for VVA alone [8–10,27]. Although not specifically enquired about, it is probable that systemic HRT users had vasomotor complaints in addition to their vaginal discomfort. This is also suggested by the fact that systemic HRT users were somewhat younger than the users of local treatments as vasomotor symptoms tend to occur earlier in postmenopause [28].

Interestingly, there was a trend towards symptom reduction in the local estrogen population by treatment time, but non-hormonal local treatment showed deterioration associated with long-term use, supporting the hypothesis that non-hormonal treatment only alleviates symptoms, but does not treat the underlying condition. Our findings suggest that women seek and receive effective treatment relatively late in their VVA disease when symptoms are severe. This interpretation seems the most plausible when, even with current treatment, FSFI scores continued to reflect dysfunction and distress (FSDS-R) was still high according to our results. It has repeatedly been recommended that women with VVA should seek help and be treated early rather than late, before symptoms are severe, considering the progressive nature of the disease, which usually does not resolve spontaneously [8,29].

Better communication between women and their healthcare providers, and attention to both physical as well as psychological needs [30] should help achieve therapeutic goals earlier before the distress that symptoms cause become intolerable for women.

There are some limitations to this study. The cross-sectional nature of the EVES survey means that we were not able to capture the real effect of treatment as the baseline data are unknown. Even the data on “duration of treatment” cannot be interpreted as real effect of treatment as the lack of baseline data cannot exclude serious confounding factors. In addition, some of the sub-populations are too small to be considered representative of the entire population. Finally, the results were collected in Italy and Spain in clinical settings, which may not be representative of the average population and/or postmenopausal women in other countries because of biological heterogeneity as well as ethnic and cultural differences; for example, those observed between Northern and Southern European countries.

5. Conclusions

Vulvovaginal atrophy, a common but underreported condition, occurs in women who experience a reduction in estrogen levels. We found

that postmenopausal women with VVA already using a treatment have more and worse symptoms than those not using treatment. The most plausible interpretation of these results might be that women only seek or commence treatment when symptoms have already become so distressing that they cannot tolerate them any longer.

Early treatment of VVA may prevent further deterioration of symptoms that may not be easily reversible [29]. Thus, treatment should start as early as possible as the first symptoms of VVA appear and should be maintained as long as required without arbitrary limits on duration of use [31].

Contributors

Nick Panay participated in the study design, and wrote the manuscript with writing and editorial support from a third party.

Santiago Palacios participated in the study design and critically revised the manuscript.

Nico Bruyniks critically revised the manuscript.

Martire Particco critically revised the manuscript.

Rossella E. Nappi participated in the study design and critically revised the manuscript.

All authors developed the methodology, supervised the collection of data managed by a third party, reviewed the data analysis managed by a third party, and gave final approval of the version to be published.

Conflict of interest

Nick Panay has received honoraria for lecturing and acting in an advisory capacity for a number of pharma companies, including Abbott, Bayer, Besins, Mithra, MSD, Mylan, Novo Nordisk, Pfizer, SeCur and Shionogi.

Santiago Palacios has financial relationships (as a lecturer, member of advisory boards and/or consultant) with Pfizer, Servier, Amgen, MSD, Preglem, Gynea, Sandoz, Procare Health, Bayer, MSD, Serelys and Shionogi. He has also been a symposium speaker or advisory board member and has received research grants and/or consulting fees from Servier, Pfizer, GSK, Abbott, Ferrer, Bioiberica, Shionogi, Amgen, Novo Nordisk, Teva, Bayer Healthcare, Serelys and Gedeon Richter.

Nico Bruyniks was a consultant for Shionogi Ltd.

Martire Particco is an employee of Shionogi Ltd.

Rossella E. Nappi has financial relationships (as a lecturer, member of advisory boards and/or consultant) with Bayer-Schering Pharma, Endoceutics, Exceltis, Gedeon-Richter, HRA Pharma, Merck Sharp & Dohme, Novo Nordisk, Pfizer Inc., Shionogi Limited and Teva Women's Health Inc/Theramex.

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Ethical approval

The study received the approval of the pertinent ethics committee at all participating centres, centralised by the University of Pavia (Italy) and the Palacios Institute of Women's Health (Spain).

Provenance and peer review

This article has undergone peer review.

Research data (data sharing and collaboration) The authors have no authorization to share data, mainly because the sharing of the database would involve patient data protection issues.

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Appendix A. Supplementary data

Supplementary material related to this article can be found, in the online version, at doi:https://doi.org/10.1016/j.maturitas.2019.03.013.

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