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Impact of vulvovaginal atrophy on sexual health and quality of life at postmenopause

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ABSTRACT

Vulvovaginal atrophy (VVA) or atrophic vaginitis is a medical challenge because it is under-reported by women, under-recognized by health-care providers and, therefore, under-treated. More or less 50% of postmenopausal women experience vaginal discomfort attributable to VVA. Very recent surveys suggest health-care providers should be proactive in order to help their patients to disclose the symptoms related to VVA and to seek adequate treatment when vaginal discomfort is clinically relevant. Women are poorly aware that VVA is a chronic condition with a significant impact on sexual health and quality of life and that effective and safe treatments may be available. Indeed, female sexual dysfunction and genitourinary conditions are more prevalent in women with VVA. That being so, it is very important to include VVA in the menopause agenda, by encouraging an open and sensible conversation on the topic of intimacy and performing a gynecological pelvic examination, if indicated. According to very recent guidelines for the appropriate management of VVA in clinical practice, it is essential to overcome the vaginal 'taboo' in order to optimize elderly women's health care.

INTRODUCTION

By the year 2025, there will be 1.1 billion women older than the age of 50 years in the world with specific needs to enter active and healthy aging[1]. Among the variety of conditions associated with menopausal transition with a potential impact on disease activity[2], vulvovaginal atrophy (VVA) or atrophic vaginitis is a medical challenge because it is under-reported by women, under-recognized by health-care providers (HCPs) and, therefore, under-treated[3]. In spite of the evidence that more or less 50% of postmenopausal women experience vaginal discomfort attributable to VVA[4,5], we believe that the issue of vaginal health at midlife and beyond is overlooked for many reasons, mostly related to the lack of understanding on how much VVA may impact the sexual health and the quality of life of women and their partners. Very recent surveys[6–10] suggest the need of ending the silent suffering of women and indicate that HCPs should be proactive in order to help their patients to disclose the symptoms related to VVA (dryness, itching, irritation, burning, and dyspareunia) that may negatively influence well-being and partnership. Even other urinary symptoms eventually associated with VVA, such as increased frequency, urgency, dysuria, and recurrent urinary tract infections, as well as urinary incontinence resulting mainly from pelvic floor relaxation, should be uncovered[6–10]. During menopausal consultation, women are often uncomfortable to report intimate symptoms spontaneously, whereas they may find it easier to talk about hot flushes, weight changes, joint pain or mood swings, and other preventive health topics such as cancer risk, bone loss, high blood pressure or 'bad' cholesterol[11–13]. Moreover, the poor awareness that effective and safe treatments may be available also contributes to postmenopausal women's reluctance to discuss symptoms associated with VVA[8,9,14]. On the other hand, the International Vagina Dialogue Survey[15] confirmed that even young women agree that society's taboos surrounding the vagina contribute to women's ignorance and there is a strong need to overcome misconceptions and get reliable information on vaginal and sexual health.

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We will briefly report the reasons why it is of vital importance to consider VVA in the menopause agenda, by including a gynecological pelvic examination, if indicated by symptoms and circumstances. In addition, we aim to encourage an open and sensible conversation on the topic of intimacy which seems essential to optimize elderly women's health care, as indicated by very recent guidelines for the appropriate management of VVA in clinical practice[16–18].

VULVOVAGINAL ATROPHY AS A CHRONIC CONDITION AT MENOPAUSE

In European countries, natural menopause occurs between 51 and 52 years of age and the increased life expectancy means that most women will spend at least one-third of their life in the postmenopausal period, an hypoestrogenic state[19]. Menopausal syndrome is a multidimensional phenomenon in which biological variables are modulated by intrapersonal and interpersonal factors varying according to the sociocultural environment and the health-care system[19].

VVA is one of the many changes occurring after menopause as a consequence of the loss of estrogen production by the aging ovaries[20–22]. It may occur as a consequence of other hypoestrogenic states but this is less common[23]. Unlike hot flushes that usually resolve over time, VVA has a chronic progressive nature throughout the menopausal transition and beyond. The presence and severity of symptoms are variable, from mild discomfort to great impairment[4,5], depending also on age, time and type of menopause, parity and vaginal delivery, frequency of coital activity, cigarette smoking and certain medical conditions/medications[24–28].

The vagina and surrounding urogenital tissues require estrogen stimulation to maintain normal structure and function. Estrogen receptors (both α and β) are widely present in the vagina, vulva, musculature of the pelvic floor, endopelvic fascia, urethra, and bladder trigone during reproductive life, decline with menopause and may be restored by estrogen treatment[5]. The absence of estrogen stimulation contributes to the loss of mucosal elasticity by inducing fusion and hyalinization of collagen fibers and fragmentation of elastin fibers. Even mucosal hydration is reduced in the dermal layer, with a reduction of intercellular acid mucopolysaccharide and hyaluronic acid. The vagina loses its rugae, the epithelial folds that allow for distensibility, and there is a shortening and narrowing of the vagina. The mucosa of the vagina, introitus, and labia minora becomes thin and pale and the significant reduction of vascular support induces a decrease of the volume of vaginal transudate and of other secretions. Over time, there is a progressive dominance of parabasal cells with fewer intermediate and superficial cells as a marker of a deprived estrogen vaginal squamous epithelium which becomes friable with petechiae, ulcerations, and eventually bleeding after minimal trauma. With thinning of the vaginal epithelium, there is also a significant reduction of glycogen and, therefore, of the population of lactobacilli, causing an increase in vaginal pH (between 5.0 and 7.5) and a decrease of vaginal hydrogen peroxide that allow the growth of other pathogenic bacteria, including staphylococci, group B streptococci, and coliforms. Similar anatomical and functional changes in the vulva, as well as in the pelvic floor and within the urinary tract, occur, resulting in an impairment of the neurovascular and neuromuscular substrates of the pelvic area[26,28–33]. That being so, VVA is a chronic condition during the postmenopausal years and it cannot regress unless adequately treated.

EVIDENCE OF THE IMPACT OF VVA ON SEXUALITY

Sexual health is an essential right of human beings[34] and staying sexually active later in life is a key element of successful aging[35]. Indeed, the experience of sexual dysfunction is more likely among women and men with poor physical and emotional health and it is highly associated with negative experiences in sexual relationships and overall well-being[36]. In spite of the frequency of sexual intercourse declining with age[37], a considerable proportion of postmenopausal women are still sexually active. The National Survey of Sexual Health and Behavior reported that nearly 20% of women over 70 had vaginal intercourse within the previous year in the US[38]. In the Global Study of Sexual Attitudes and Behaviors, the majority of women (76%) from 29 countries agreed with the statement 'a satisfactory sex life is essential to maintain a relationship' and 57% disagreed with the statement 'older people no longer want sex'[39]. Moreover, the majority of postmenopausal European women (71%) reported that it was important to them to maintain an active sex life[40].

A true epidemiology of VVA is difficult to determine because most of the data rely on self-reported symptoms and the severity of symptoms (from mild to severe) is rather subjective. The perception of women is, indeed, far more relevant than the objective signs of VVA and women may not report symptoms because they are self-treating, feel the symptoms are not important enough, or are embarrassed[41]. The FDA-recommended metric of the most bothersome symptom is a major step forward in standardizing measurement of self-assessed VVA symptom changes to validate potential new treatments[42]. However, evaluation of change in individual symptoms remains an important, unbiased primary analysis of efficacy in VVA studies[42]. It is also relevant to point out that the type of symptoms reported by women is influenced mainly by age and sexual activity[24]. Dyspareunia is generally less reported later in life mainly because older women are less likely to still have a spousal or other intimate relationship[43] and sexually related personal distress declines with age[44]. In addition, cognitive, affective and interpersonal factors may be implicated in pain ratings[45].

Not all women exhibiting signs of VVA are highly symptomatic from a sexual standpoint. In the hormone therapy (HT) trials of the Women's Health Initiative (WHI), VVA at

baseline correlated with sexual inactivity, but, among those women (69%) having physical evidence of VVA upon clinical examination, only 10% reported moderate to severe symptoms[46]. A cross-sectional analysis in postmenopausal women ($n = 98\ 705$, age range: 50–79 years) enrolled in the US-based WHI observational study and clinical trials showed the prevalence of self-reported urogenital symptoms: dryness (27.0%), irritation or itching (18.6%), discharge (11.1%), and dysuria (5.2%)[47]. About 20% of elderly women non-institutionalized showed evidence of bacteriuria and up to 17% experienced recurrent urinary tract infections[48]. Women with VVA (mean age 60.2 years) have a greater risk of genitourinary conditions compared to those without[49].

Sexual dysfunction almost doubles with advanced menopause status[50] and, in the Study of Women's Health Across the Nation (SWAN), women reporting vaginal dryness were more likely to also report dyspareunia and lower arousal[51]. In addition, the prevalence of specific symptoms differs by race/ethnicity, with Japanese and Chinese women reporting less symptoms compared with non-Hispanic Caucasians[52]. Vaginal dryness was reported significantly more frequently by African-American than by Caucasian women, whereas Hispanic women reported vaginal dryness more frequently than did non-Hispanic Caucasian women[52]. Vaginal dryness has been connected with the menopausal transition, ranging from 3% at premenopause to 47% at 3 years postmenopause[52]. Indeed, the Melbourne Women's Midlife Health Project found a significant decrease in women's desire, arousal, orgasm and frequency of sexual activity and a significant increase in vaginal dryness, poor lubrication and dyspareunia, with a rate of sexual dysfunction that ranged from 42% to 88% throughout the menopausal transition[53,54]. Both age and declining estradiol levels had significant detrimental effects on sexual functioning, desire, and sexual responsiveness (arousal, sexual pleasure and orgasm), as well as mood changes and the nature of partnership (general and sexual health of the partner, feelings for the partner)[54–56]. However, different cultures and religious practices should be taken into account when discussing the impact of VVA on sexuality, because data from a population-based, national-level, family health sample survey in India (age range 15–49 years) indicated that sexual pain is more prevalent in younger newly married women[57]. Indeed, women's attitudes to menopause influence their symptom experience and the use of standardized, culturally sensitive measures is needed in future studies[58].

A cross-sectional, population-based study of 1480 sexually active US postmenopausal women (40–65 years) reported that 55% of sexually active women experienced female sexual dysfunction (FSD) and 57% VVA[59]. Interestingly enough, those women with positive scores for FSD were almost four times more likely to have VVA in comparison with those women not reporting sexual symptoms[59]. A similar prevalence of FSD (56.8%), mostly related to poor vaginal lubrication, was found in middle-aged Latin American women (age range 40–59 years) with a wide range of variability depending on different populations[60].

Dyspareunia may be accompanied by postcoital bleeding and secondary vaginismus triggered by avoidance, anxiety and loss of sexual desire because of the anticipation of coital pain[29,32]. That being so, whenever a postmenopausal woman reports sexual dysfunction in clinical practice, an accurate pelvic examination should be performed to recognize the signs of VVA[61,62]. Tissues may be easily traumatized and irritated and a gentle approach is mandatory in the most severe cases. As already comprehensively described[16–18], the inspection includes the tissues of the vulva, vestibule, vagina, and urethra, and clinical scales may be used in an attempt to quantify VVA[63,64]. Organ prolapse and the muscle tone of the pelvic floor should also be noted, as well as other disorders that can cause symptoms similar to those of VVA[65,66]. Although VVA is typically a clinical diagnosis, other laboratory tests may be used to support the diagnosis, such as an evaluation of vaginal pH and the vaginal maturation index, which describes the relative proportion of parabasal, intermediate, and superficial vaginal epithelial cells[67].

However, the potential burden of VVA should be considered also in women who abstain from sexual activity because they may suffer even more of the long-term consequences of estrogen deprivation, especially vaginal and introital stenosis, fusion of the labia minora to the labia majora, and other urogenital conditions[26,66,68]. Special care should be also devoted to women with breast cancer and other gynecological malignancies who are at very high risk of VVA and FSD as a consequence of endocrine chemotherapy, surgery and radiation[69]. Finally, severe VVA may be a barrier to adequately assess both cytologic and colposcopic findings to prevent cervical cancer, and it is a very common reason for urgent referral to exclude endometrial cancer and other malignancies after an episode of postmenopausal bleeding[70]. Vaginal occlusion is uncommon[71] but may cause vaginal synechiae and hematocolpos, impeding early diagnosis of cancer[72,73].

WHAT WOMEN THINK ABOUT THE IMPACT OF VVA ON SEXUAL HEALTH AND QUALITY OF LIFE

Very recently, qualitative research[74] conducted in an international sample of postmenopausal women who had symptoms of VVA confirmed the results of previous surveys[6–10] indicating that VVA is not recognized as a medical condition. Women's reactions to their VVA varied according to personality, and those discussing VVA symptoms with their HCPs felt their concerns were dismissed as a normal part of aging, without receiving any counseling about treatment options[74]. HCPs tended not to take a proactive approach to sexual health management in the middle and later life age groups, mainly because of inadequate training, constraints of time, personal attitudes and beliefs that sex is not a priority for older patients[35]. This is surprising in light of the evidence that VVA has a significant impact on sexual health and quality

of life of postmenopausal women[3]. The 'women's voices in the menopause' international survey used computer-assisted web interviews among 4246 women aged 55–65 years, living in Sweden, Finland, the United Kingdom, the United States and Canada, and was conducted to provide a general insight into issues surrounding VVA in Western countries[9]. Overall, 98% of survey respondents were postmenopausal and 39% of them had experienced VVA with country-specific differences in attitudes and knowledge, probably reflecting the different sociocultural environment. The Global Survey of Sexual Attitudes and Practices administered to 6725 women from 11 countries[75] has already shown that women from different cultural backgrounds differ substantially in their experiences, concerns, and reports of vaginal dryness/sexual pain, as well as in their familiarity with personal lubricants as a treatment. In the 'women's voices in the menopause' international survey[9], symptoms were described as being moderate or severe by 55% of the interviewees. A high proportion of women reported moderate or severe symptoms in the United States (63%), the United Kingdom (62%) and Canada (55%), whereas both in Finland and Sweden only 41% of women reported moderate or severe symptoms. However, VVA was deemed to impact on quality of life by a higher proportion of women in Finland and Sweden ($\geq$60%) in comparison with women in the United Kingdom, the United States and Canada ($\leq$50%). Seventy-seven percent of the interviewees believed that women were uncomfortable discussing the condition. Among women with vaginal discomfort, 40% declared that VVA had a negative consequence for sex life. In spite of this, 63% of women who had experienced VVA had never been treated, while 67% of those who had been treated reported positive effects, including improvements in everyday life (28%), sex life returning to normal (27%) and better quality of life (26%). The 'Vaginal Health: Insights, Views & Attitudes (VIVA)' online survey[8] was conducted in Europe and North America to further explore women's knowledge regarding vaginal health and confirmed the need for a country-specific approach, even though the proportion of US women who experienced vaginal symptoms (48%)[76] mirrored that of the overall VIVA population (45%)[8]. Out of 3520 postmenopausal women aged 55–65 years, only 4% of women attributed symptoms of vaginal discomfort to VVA, and 63% failed to recognize VVA as a chronic condition. Overall, 75% said that VVA would have a negative impact on various aspects of life in general, 65% considered that it would have negative consequences on a woman's sex life, 40% thought that it would have negative consequences on marriage or relationships, 36% felt that it would lower quality of life, 31% stated that it would make them feel old, 26% thought that it would have negative consequences on self-esteem, and 13% felt that it would be detrimental to a woman's social life. The areas of a woman's life thought most likely to be negatively impacted by VVA were sexual intimacy (64%), having a loving relationship with a partner (32%), overall quality of life (32%), feeling healthy (21%), and feeling attractive (21%). Most women used over-the-counter products for VVA symptoms, but specific means of treating the underlying cause were less well known; 55% of women who had experienced VVA reported having symptoms for 3 years or longer and only half of the survey participants said that they would feel comfortable discussing VVA with their HCPs. The REVIVE (REal Women's VIews of Treatment Options for Menopausal Vaginal ChangEs) online survey[7] conducted in 3046 postmenopausal women with VVA symptoms in the United States confirmed the negative impact on enjoyment of sex (59%). Moreover, 56% of participants had ever discussed VVA symptoms with their HCP and 40% currently used VVA-specific topical treatments (vaginal over-the-counter products (29%) and vaginal prescription therapies (11%)). Insufficient symptom relief and inconvenience were cited as major limitations of over-the-counter products and concerns about side-effects and cancer risk limited use of topical vaginal prescription hormone therapies.

Collectively, these surveys indicate that HCPs should proactively raise the topic of vaginal health, help patients to understand that VVA is a chronic condition, and discuss treatment options as appropriate, so that more women can receive timely and effective therapy. Indeed, after the publication of the WHI studies, attitudes to the management of urogynecological and sexual health have significantly changed[77] and an open dialogue between women and doctors is needed in order to individualize the most suitable strategy for VVA according to the personal risk–benefit profile[32,78,79].

WHAT COUPLES THINK ABOUT THE IMPACT OF VVA ON SEXUAL HEALTH AND QUALITY OF LIFE

The definition of FSD comprises the presence of sexual symptoms associated with personal and relational distress[80], underlining the importance of considering sexual health in the context of the couple. Symptoms of VVA are strongly associated with FSD because painful sex (dyspareunia, secondary vaginismus, and non-coital pain) may prevent women from desiring, initiating or responding sexually to their partner[59]. It is also true that the sexual performance of the partner may affect the clinical relevance of FSD and vice versa[26,81,82]. The CLOSER (CLarifying Vaginal Atrophy's Impact On SEx and Relationships) Survey[6] is the first multinational (UK, Finland, Norway, Sweden, Denmark, Italy, France, Canada, and the USA) research study in postmenopausal women coping with VVA in which an equal number of men whose female partners suffer from VVA (4100 females and 4100 males) shared their feelings and the impact of this condition on intimacy. The CLOSER survey revealed that 28% of women did not tell their partners when they first encountered vaginal discomfort, mainly because they felt 'it was just a natural part of growing older' (52%), or due to 'embarrassment' (21%). Eighty-two percent of male respondents wanted their partner to share their experiences of VVA; males were also more comfortable discussing VVA than females (68% vs. 58%, respectively). Having sex less often (women: 58%, men: 61%);

less satisfying sex (women: 49%, men: 28%); and putting off having sex (women: 35%, men: 14%) were the main effects of VVA on the sexual aspect of a couple's relationship. Intimacy avoidance was attributed to painful sex (women: 55%, men: 61%), and women's reduced sexual desire (women: 46%, men: 43%). Interestingly enough, significant differences were evident in Northern and Southern Europe[83]. For example, Southern European women were generally more worried about the long-term effects of vaginal discomfort on their relationship with their partner and were more likely to avoid intimacy because of vaginal discomfort. Accordingly, Southern European women were more likely to report benefits in terms of their relationship with their partner after treatment for VVA. Sociocultural peculiarities were also evident in samples from the UK[84] and in North America[85]. As far as the dialogue with HCPs was concerned, more women were likely to discuss erectile dysfunction of their partners then men were likely to discuss VVA of their partners[6].

Collectively, the CLOSER survey indicates that evaluation of men's attitudes regarding VVA affecting their postmenopausal partners may lead to better understanding of the impact of VVA on sexual intimacy and may help couples to address the consequences of vaginal discomfort with their HCPs. This will not only enhance the physical quality of life experienced by postmenopausal women, but will also help to restore their self-esteem and their sexual and emotional well-being by removing barriers to intimacy between women and their partners.

CONCLUSION

VVA is a chronic, age-dependent condition resulting from estrogen deficiency and may worsen without appropriate treatment, leading to the vicious cycle of worsening FSD and urogynecological consequences. Early recognition and effective treatment of VVA may enhance sexual health and the quality of life of women and their partners. HCPs have to proactively raise the subject of VVA in midlife medical practice to encourage postmenopausal women to overcome the vaginal 'taboo' by openly discussing urogenital symptoms. Unfortunately, due to the complexity of FSD etiology[86], there is still no gender equality in the availability of effective treatments[87,88], but recent guidelines for the management of VVA[16–18] and forthcoming new pharmacological agents for FSD[89,90] might fill this gap and give postmenopausal women and their partners some hope of better care.

Conflict of interest During the past 2 years, Dr Nappi has had financial relationships (lecturer, member of advisory boards and/or consultant) with Bayer-Schering Pharma, Eli Lilly, Gedeon-Richter, HRA Pharma, Merck Sharpe & Dohme, Novo Nordisk, Pfizer Inc, Shionogi Limited, TEVA/Theramex. Dr Palacios has had financial relationships (lecturer, member of advisory boards and/or consultant) with Amgen, Bayer-Schering Pharma, Eli Lilly, Gedeon-Richter, Sandoz, Novo Nordisk, Pfizer Inc, Pierre-Fabre, Shionogi Limited.

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