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Spanish consensus on vulvar disorders in postmenopausal women

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ABSTRACT

Introduction: The consequences of vulvar disorders in terms of health, sexuality, and quality of life are usually undervalued, with disparities in the conceptual, diagnosis and treatment criteria.
Aim: The objective of this guide will be to analyse the factors associated with the diagnosis and treatment of vulvar disorders and to provide recommendations for the most appropriate diagnostic and therapeutic measures.
Methodology: A panel of experts from various Spanish scientific societies related to sexual health (Spanish Menopause Society [SMS] and the *Asociación Española de Patología Cervical y Colposcopia* [AEPCC]) met to reach a consensus on these issues and to decide the optimal timing and methods based on the best evidence available.
Results: We recommend a biopsy of all vulvar lesions with an uncertain diagnosis, especially with asymmetry, irregular borders, variegated and irregular colour and diameter >6 mm. For vulvodynia, we recommend the use of lubricants or topical treatments with lidocaine or bupivacaine, amitriptyline, baclofen or triamcinolone. For vulvar epithelial disorders, we recommend beginning with topical corticosteroids of moderate to high potency. For sexual dysfunction, a multidisciplinary approach is the best management strategy in these patients.

1. Introduction

Vulvar disorders are more common after menopause, often due to hypooestrogenism or immune factors that damage the vulvar tropism. Regardless, the consequences of vulvar pain in terms of health, sexuality, and quality of life are usually undervalued among patients who suffer from these disorders. The disparity regarding vulvar disorders can be observed in their definition, diagnosis and treatment, which reflect the shortage of meta-analyses and systematic reviews, and in the difficulty of creating clinical practice guidelines on this subject [1].

Because a high percentage of women report disorders related to vulvar health during menopause, a panel of experts from the Spanish Menopause Society (SMS) and the *Asociacion Española de Patología Cervical y Colposcopia* (AEPCC) met to review the conditions that determine vaginal pathophysiology and the recommendations for preventing or treating this class of diseases.

2. Methods

A panel of experts from various Spanish scientific societies related to POI (*Spanish Menopause Society, Spanish Fertility Society, Spanish Contraception Society and Spanish Medical-Oncologic*

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Society) met to reach a consensus on these issues. Each society chose participants who would be responsible for reviewing and drafting each part of this guide. All of the authors participated in the statement and approved the final version of the manuscript. The consensus considers it appropriate to develop its own recommendations based on the GRADE (*Grading of Recommendations Assessment, Development and Evaluation)* system to elaborate clinical practice guidelines and to classify the quality of the evidence and the strength of the recommendations [2].

3. Anatomy and physiology

Vulvar structures have an embryological origin from the urogenital sinus and are anatomically constituted by the pubis, labia majora and minora, and perineum, each with different epithelial characteristics that are relevant to their different disorders. The inner side of the labia majora has no hair, while the outer side is cover by hair; the labia minora are free of hair and contain several sebaceous glands and sensitive nervous endings. One special area is the vestibule, which is perforated by the urethra, vagina and Bartholin's glands' orifices. In addition, there are several smaller glands such as Skene's and the paraurethral glands leading the vestibule.

The vulva is innervated by the pudendal, ilioinguinal, genitofemoral and femoral cutaneous nerves. The sympathetic innervation derives from the hypogastric nerves, which produce vasoconstriction and muscular contraction. Parasympathetic innervation derives from the splanchnic nerves, which produce vasodilatation and inhibit contraction. The rich innervation explains the complex and diverse symptomatology that accompanies vulvar disorders.

During puberty, the vulva undergoes significant changes, such as the growth of the structures, becoming covered with hair, and gland secretions. Sexual response appears in parallel with women's behaviour. The endocrine milieu, particularly of the sex steroid hormones, is critical in the maintenance of vulvar tissue structure and function. During the post-menopausal period, the declining levels of oestrogens and androgens are associated with dramatic alterations in the vulva, including anatomic atrophy with attenuated genital blood flow and lubrication, hair loss, and reduced innervation. Furthermore, sex steroid hormone deficiency is associated with reduced expression of sex steroid receptors, increasing the vicious circle [3].

4. Vulval semiology

The conditions related to vulvar tropism were called "vulvar dystrophies" for more than 50 years, but the preferred term to refer to any type of skin disease at present is dermatosis. However, some structures of the vulva that are in intimate contact with the vagina acquire diseases similar to vaginal diseases. Additionally, the differential diagnoses are difficult because vulvar diseases are more prevalent in post-menopausal women, and they coincide with the body's physiological changes during this period. As a result, this organ is given very little attention during the gynaecological exam; it is only examined if there is adequate light, and vulvoscopy or biopsy is only performed if indicated. In fact, when the diagnostic methods for vulvar lesions are analysed, there is evidence to support carrying out a biopsy on all lesions with uncertain diagnoses, generally using a punch biopsy with local anaesthesia and utilising silver nitrate or ferric subsulfate for haemostasis [4].

Within vulvar semiology, itching and pain are highlighted due to their high prevalence and consequences. Approximately 70–90% of women who consult for vulvar–vaginal disorders have itching and irritation [5]. The presence of itching is a clue to identifying the aetiology as infectious, inflammatory or neoplastic so as to find an adequate treatment for each case. In situations where the cause of the itching is not found, a systematic review analysed several therapeutic strategies, ranging from hygienic-dietary measures (washing with mild soap, seated baths, loose underwear made of natural material, a diet without stimulants), oral antihistamines (dexchlorpheniramine or hydroxyzine), topical corticosteroids, and even tranquilisers (benzodiazepines, antidepressants and gabapentin), although mixed results were reported [6,7] (see Algorithm 1).

Pain (*vulvodynia*) is present in up to 8% of women after menopause [8]. At present, we classify this pain as a function of whether it is localised or general and if it is spontaneous or provoked. As such, the most frequent form of vulvar pain is *localised provoked vulvodynia* (LPV), characterised by a zone (erythematous or not) that is painful to the touch or to pressure. This area is commonly in the vulvar vestibule zone (previously vulvar vestibulitis), although it can also be observed in the clitoris and in other foci of the vulva. LPV is associated with fungal infections and interstitial cystitis/painful bladder syndrome [9]. Its diagnosis is made clinically after excluding other causes (dermatological, neurological, musculoskeletal or psychosexual), and biopsy is not needed. For treatment of LPV, several systematic reviews and some therapeutic guidelines include the use of lubricants or prepared topical agents with anaesthetics (lidocaine, bupivacaine), antidepressants (amitriptyline), muscle relaxants (baclofen) or corticosteroids (triamcinolone). When these treatments are not effective, the use of oral antidepressants, anticonvulsants, or electric stimulation of the pelvic floor muscles is recommended (see Algorithm 2). Surgical treatment (vestibulectomy) is normally reserved for when a patient does not respond to any of these measures [10–12].

5. More prevalent vulvar conditions

5.1. Alterations in vulvar pigmentation

Vitiligo, a degenerative skin disease in which melanocytes disappear, can be observed in the vulva more than any other cutaneous zone. Vitiligo, however, does not present any complications beyond aesthetic complications.

Conversely, pigmented lesions of the vulva (vulvar nevus, vulvar lentigo, melanosis, vulval warts, seborrheic keratoses, human papillomavirus [HPV]-related lesions) are present in 10–12% of white women, and approximately 2% of them are nevocellular nevi. These lesions are mainly benign and, except for the nevus, can be successfully treated with cryotherapy. Perhaps more interesting is the differential diagnosis of vulvar melanoma, which is an uncommon tumour in this location and has a difficult diagnosis and a worse prognosis. Thus, if the lesion's pigmentation is uncertain, performing a biopsy following the ABCD criteria is recommended (asymmetry, irregular borders, variegated and irregular colour and diameter >6 mm) [13,14].

5.2. Infections

After menopause, vulvar infections are usually sexually acquired, and they are less common than prior to menopause. Among viral infections, those caused by herpes simplex virus and HPV are the most noteworthy. Herpes infections after menopause are more commonly caused by recurrences than by initial infections, and treatment is the same as for younger women. Oral antivirals active against herpes virus are recommended (aciclovir, famciclovir, valaciclovir) together with localised care of any lesions to avoid bacterial infection [15].

HPV infection has a prevalence of approximately 10% in climacteric women, but a third will present positivity at least once during a