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REVIEW ARTICLE

Etiopathogenic Bases and Therapeutic Strategies in Recurrent Candidal Vulvovaginitis

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ABSTRACT

Introduction: recurrent vulvovaginal candidiasis currently constitutes a serious problem that affects women's quality of life.
Objective: to identify the predisposing etiology and therapeutic alternatives for recurrent vulvovaginal candidiasis.
Methods: an exhaustive literature search was conducted, consulting 27 sources from various databases, with prior compliance to the selection criteria of the analyzed sources. After reviewing the selected sources, an analysis of the available information was carried out, which allowed establishing a clear and updated overview of the existing scientific evidence.
Development: recurrent vulvovaginal candidiasis is a multifactorial gynecological infection, where genetic, immunological, hormonal, and environmental factors converge, favoring its persistence. Antifungal resistance, especially to azoles, complicates treatment, although fluconazole is recognized as first-line therapy. However, repeated use generates resistance, so combined and prolonged regimens, as well as alternatives and new drugs, are recommended.
Conclusions: the etiopathogenic bases of the disease were described, identifying the predisposing factors for its development, as well as its therapeutic management.

Keywords: Candida Albicans; Candidiasis, Vulvovaginal; Drug Resistance, Multiple, Fungal.

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INTRODUCTION

Yeasts of the genus Candida are opportunistic pathogens that can generate infections, although they may be present in up to 20 % of the normal microbiota of some women without causing symptoms. Approximately 75 % of women may experience an episode of vaginal candidiasis in their lifetime, and about 50 % on several occasions,[1] it is considered that candidal vaginitis is recurrent when 4 or more episodes occur per year, affecting around 4-10 % of patients.[2]

Generally, this type of infection occurs in 90 % of cases due to a single Candida species, which is usually albicans, but it can be mixed, associating C. albicans and C. glabrata in up to 10 % of cases, although infections by non-C. albicans Candida also exist. In women with recurrent episodes, strains of C. albicans resistant to conventional treatments are usually found due to previous exposure to these, and in the case of non-albicans strains, efficacy is reduced, which requires dose and medication adjustment.[3]

Vulvovaginal candidiasis is not considered a sexually transmitted disease; its main symptoms are pruritus, erythema, dyspareunia, dysuria, and leukorrhea.[4] The causes of recurrent candidal vulvovaginitis have various etiologies ranging from diseases such as diabetes, use of contraceptives, personal hygiene habits, sexual activity, among others; several studies indicate that an important predisposing factor is the alteration in the balance of the vaginal ecosystem, which facilitates the overgrowth of pathogens, influencing the development of complex vaginal infections.[2,5]

The management of these infections includes the elimination of risk factors, symptomatic relief, pathogen elimination, and prevention of recurrence; however, currently an important problem is resistance to conventional treatments, which makes this infection a challenging disease in the long term. Recurrent vulvovaginal candidiasis (RVVC) decreases women's quality of life and is also associated with high healthcare costs and morbidity.[3] With the above expressed, the present work seeks to identify the predisposing etiology and therapeutic alternatives for recurrent vulvovaginal candidiasis.

METHODS

A bibliographic review was conducted, focused on the systematic collection of scientific articles available in the PubMed, Redalyc, Cochrane Library, SciELO, and Elsevier databases. The search strategy included specific terms related to the topic, such as: Candida albicans, vulvovaginal candidiasis, recurrent candidiasis, recurrent vulvovaginitis, and treatments for vaginal candidiasis.

Inclusion criteria contemplated studies published between January 2010 and May 2025 in English and Spanish. Research with comparative design, evaluation studies, meta-analyses, cross-sectional and prospective studies that addressed clinical, therapeutic, or epidemiological aspects of vulvovaginal candidiasis were selected. Case reports, studies without a control group, publications on websites not endorsed by the scientific community, as well as research conducted in special populations such as pregnant women, immunosuppressed patients, or those with chronic diseases were excluded, with the objective of maintaining the homogeneity of the analysis.

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The selection of articles was oriented to guarantee the currency and relevance of the evidence, prioritizing studies published in the indicated period, with rigorous methodological approach and clinical relevance for the management of recurrent vulvovaginal candidiasis.

DEVELOPMENT

RVVC is not only a public health problem; it also has socioeconomic, psychological, and even sexual well-being repercussions for women in general, with a perception of lower satisfaction in their lives. This gynecological infection is characterized by its high incidence and recurrence.[6] Between 85-90 % of this pathology is caused by the fungus Candida albicans,[7] and worldwide, it affects approximately 138 million women annually, with a global annual prevalence of 3,871 per 100,000 women; it is estimated that, in addition to being experienced by up to 75 % of women, about 50 % have presented recurrent episodes, predominantly in women of reproductive age. In some cases of this pathology, there are no evident predisposing conditions or factors in patients, which could have a genetic and immunological basis.[8,9]

RVVC is currently understood as a multifactorial condition in which host factors, factors related to the responsible fungus, and the vaginal environment converge. Genetic predisposition and certain immunological alterations present in women favor the persistence of infection. To this are added hormonal factors, since elevated estrogen levels during fertile age facilitate fungal colonization, while comorbidities such as diabetes mellitus or prolonged antibiotic use alter the vaginal microbiota.[4]

Among the causative agents, the most prevalent type of infection is Candida albicans, followed by C. glabrata. In the case of the former, it possesses virulence mechanisms such as hyphal formation, biofilms, and proteolytic enzymes that allow it to adhere and resist treatment, in addition to the possibility of developing resistance to antifungals, especially azoles. Finally, the vaginal environment also plays a key role: the decrease in lactobacilli reduces the production of lactic acid and hydrogen peroxide, which weakens the natural defense against Candida proliferation. External factors such as humidity, tight clothing, or the use of irritating products may contribute to recurrence.[10,11,12,13]

This type of infection has economic repercussions due to multiple treatments and medical visits, physical repercussions with the discomfort of symptoms in acute phases, and decreased enjoyment of sexual activity.[8] VVC is characterized by vulvodynia, pruritus, excoriation, fissure formation, dysuria, vulvar edema, and vulvar maceration.[13,14]

Without timely treatment, RVVC can trigger consequences such as pelvic inflammatory disease, infertility, abortions, pelvic abscesses, among others; hence the importance of prevention, diagnosis, and standardized and timely treatment.[6] In view of this, there are different alternative treatment presentations for vulvovaginal candidiasis, either systemic or local. Evidence suggests that clinical and mycological cure is similar with different treatment routes both in the short and long term, being slightly higher by 5-10 % with the oral route compared to the local route.[14,15,16]

One of the drugs most commonly used in the treatment of VVC is fluconazole, but the sensitivity of all strains to this medication has decreased significantly due to recent and repeated exposure to fluconazole; it should be noted that after discontinuing its use, resistant strains return to their susceptibility over time; therefore, the use of local medication to treat recurrent VVC would be beneficial, limiting resistance to systemic medications.[13]

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One of the reasons for antifungal medication resistance is the indiscriminate use of medications, which makes it difficult to treat recurrent infections, leading to consumption of more antimycotic treatments and generating a vicious cycle; added to this, we have incomplete or erroneous diagnoses and treatments.[17]

Standardized therapies for RVVC include azole antifungal medications such as clotrimazole, fluconazole, voriconazole, itraconazole, ketoconazole, and miconazole. In particular, fluconazole and clotrimazole have various therapeutic doses and regimens for the treatment of VVC, but other approved treatment alternatives also exist.[13,18]

Since 2004, fluconazole has been accepted as first-line treatment, but resistance to it and a high recurrence rate after treatment cessation have been generated. Currently, there are guidelines that recommend the use of 150 mg of fluconazole on the first and fourth day; another regimen recommended by the American College of Obstetricians and Gynecologists recommends the use of 150 mg of fluconazole every 72 hours for a total of two or three doses in acute phases, and for the maintenance phase, a dose of fluconazole 150 mg weekly for six months is recommended; however, there are no specific differences in efficiency between regimens, although it is important to consider that its use has a higher mycological cure rate compared to three-dose clotrimazole.[8,13]

In accordance with this, different alternatives are being studied, recommending double treatment with oral medication with fluconazole 150 mg daily for 3 days or itraconazole 200 mg daily for 10 days, and vaginal with clotrimazole 200 mg daily for 12 days or 500 mg of clotrimazole or sertaconazole weekly for 2 weeks or fenticonazole 600 mg daily for 3 days; triple initial treatment: itraconazole 200 mg oral daily for 10 days plus clotrimazole 500 mg weekly for 2 weeks and clotrimazole cutaneous application daily for 2 weeks. Regarding the maintenance dose, it is recommended to use vaginal topical with clotrimazole or sertaconazole 500 mg weekly for 6 to 12 months or fenticonazole 600 mg vaginal weekly for 5 to 12 months or oral with fluconazole 150 mg weekly for 6 to 12 months or itraconazole 100 or 200 mg postmenstrual for 6 to 12 months or ketoconazole 100 mg daily for 6 to 12 months.[3,6,10]

On the other hand, in women with non-albicans Candida such as glabrata or other species, therapy with azoles is usually not as effective. In view of recent resistance to fluconazole, the regimen of clotrimazole 200 mg vaginal daily for three doses remains a good alternative for clinical and mycological cure. Thus, an alternative in recurrent cases is advised to prolong treatment for 14 days and also the administration of Lactobacillus.[8,10,13]

Similarly, due to the resistance presented to different treatments with azoles, treatment alternatives have been investigated, such as the intravaginal use of boric acid with 600 mg intravaginally for a period of 10 to 14 days; it could also be used for maintenance between 300 and 600 mg once or twice a week, but its safety with long-term use is still unknown. In general, treatments range from single doses to 14-day treatments as initial treatments, and their maintenance ranges from six to twelve months.[1,19]

Taking into account the above, it is understood that currently, there is no approved antifungal as the choice for treating RVVC. However, oral or topical antifungals may decrease clinical symptomatic recurrence of VVC compared to placebo, but there is no greater difference between dose, duration, or route of administration regarding their effectiveness; however, oral treatment has a slight advantage in mycological cure in the short and long term and is also preferred for use due to its convenience.[1,8,13]

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Similarly, currently, treatments are being developed as options to counteract the resistance generated to conventional treatments, among which Ibrexafungerp stands out, which was approved by the FDA in 2021, having a clinical cure rate comparable to fluconazole in non-resistant Candida; this drug is used once monthly to prevent recurrence of VVC; the population that may benefit from this drug are those with azole allergies, non-albicans albicans species or azole-resistant, or other contraindications of azoles such as drug interactions.[20,21]

Likewise, in 2021, the FDA approved the use of oteseconazole with its monthly oral use and effectiveness comparable to fluconazole in non-resistant strains, which could be an alternative for treating these patients.[22,23] On the other hand, there are alternatives such as vaginal suppositories of boric acid 600 mg that have acceptable cure rates, although they are not yet approved by the FDA and are marketed as homeopathic products.[24,25]

Probiotics can also be used as an alternative for the management in treatment and prevention of VVC; they seem to improve vaginal health and reduce symptoms; by themselves, they do not have greater efficiency than antifungal treatment such as fluconazole, but the combination of both seems to reduce recurrence and significantly improve symptoms.[26]

Regarding side effects with the use of vaginal treatments, local reactions occur with the topical route, and with oral treatments, systemic reactions such as gastrointestinal symptoms and headache occur, in addition to hepatotoxicity and allergies. For this reason, treatment alternatives such as phytotherapy with the use of herbs such as turmeric, garlic, among others, are being developed, but there is still a lack of evidence to prove their efficacy.[7,13,27]

CONCLUSIONS

Recurrent vulvovaginal candidiasis is the most common gynecological infection affecting many women of reproductive age, which decreases women's overall quality of life. The predisposing factors for this range from immunological conditions, chronic diseases, alterations of the vaginal microbiota, use of drugs, to sexual and hygiene practices; therefore, it is important to identify risk factors to carry out treatments and avoid recurrences. Among the treatments used are conventional ones such as the use of oral and vaginal azoles alone or in combination, as well as the development of new drugs and homeopathic therapy, which are used from single doses to long periods of time ranging between six and twelve months.

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