

NEW HORIZONS IN THE DIAGNOSIS OF VAGINITIS AND VAGINOSIS: MOLECULAR TECHNOLOGIES AND PROBIOTIC THERAPIES

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ABSTRACT

Introduction: Vaginal discharge remains one of the main gynecological complaints, characterized or not by associated symptoms such as leucorrhea, pruritus, dyspareunia, and unpleasant odor. However, due to excessive, unnecessary prescriptions and limited guidance on daily care, it is necessary to develop new diagnostic approaches, like *propaedeutics*, to prevent treatment resistance, which can render therapies ineffective when needed. Thus, the present study compiled information on the most up-to-date diagnostic methods for the treatment of vaginitis and vaginosis. **Methodology:** An integrative review was conducted using data from the PubMed and SciELO databases to identify studies on diagnostic techniques. Eleven articles were selected and analyzed according to inclusion and exclusion criteria. **Results:** Vaginitis caused by microorganisms such as *Gardnerella vaginalis*, *Candida spp.*, and *Trichomonas vaginalis* is classified as specific. Vaginitis associated with imbalances in the vaginal microbiota, with proliferation of aerobic bacteria, is classified as nonspecific. Modern diagnostics include molecular methods, such as RT-PCR and NGS, which offer greater accuracy. The *Immuno Quantex* test assesses the local inflammatory response. Intravaginal devices containing hexylresorcinol and herbal extracts are effective in treating vaginal conditions. Probiotics, especially *Lactobacillus crispatus*, show promise in maintaining the microbiota and preventing infections, while new approaches to mixed vaginitis are under development to improve treatment and diagnostic efficacy. **Conclusion:** The combination of traditional treatments with new therapies, including probiotics and innovative medical devices, may provide a more comprehensive and effective solution for women experiencing recurrent vaginitis and other vaginal conditions.

Keywords: Clinical diagnosis; Gynecology; Treatment.

INTRODUCTION

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The vagina is a dynamic organ lined with stratified squamous epithelium. It is protected by secreted fluids that play an essential role in defending against infections. These secretions, which harbor more than 200 different types of microorganisms, must be in balance to ensure the health of the vaginal canal. The predominance of *Lactobacillus spp.* is crucial for maintaining an acidic pH (between 3.8 and 4.2), which serves as a natural protective barrier. However, when this balance is disrupted, either by infectious causes such as candidiasis, trichomoniasis, or bacterial vaginosis; or by non-infectious factors such as hormonal changes, irritation, or allergies, complications may arise that can significantly impact women's quality of life (Linhares *et al.*, 2019; Kissinger *et al.*, 2022).

Vaginal discharge is one of the most common manifestations of these imbalances and can range from physiological to pathological. Physiological discharge is typically clear or whitish, odorless, and it may also vary in consistency. Abnormal discharge, on the other hand, may indicate infections such as vulvovaginal candidiasis, which affects millions of women annually, or trichomoniasis, one of the most prevalent sexually transmitted infections worldwide. (Carvalho *et al.*, 2021; Rodrigues *et al.*, 2022).

Vaginitis refers to inflammation of the vaginal mucosa, which may be of infectious or non-infectious origin. *Vaginosis* is a type of vaginitis, caused either by excessive bacterial proliferation or by a reduction in the protective vaginal microbiota. Thus, this study explores emerging diagnostic techniques and novel therapeutic approaches for the management of vaginitis and bacterial vaginosis.

METHODOLOGY

An integrative literature review was conducted, focusing on new diagnostic techniques for vaginitis and vaginosis. The guiding question was: "What are the new methods for diagnosing and treating the most prevalent gynecological infections?" The PubMed and SciELO databases were consulted to collect scientific production in indexed journals. A total of 305 articles published between 2018 and 2024 were identified, of which 176 were excluded based on title and abstract analysis. After that, 28 duplicates were removed, and 101 articles were examined based on the PECO

strategy. Finally, 11 articles that fully addressed the theme were selected. The search terms used were 'Vaginitis,' 'Clinical Diagnosis,' and 'Treatment,' in both English and Portuguese. The electronic search took place between July and August 2024.

The inclusion criteria were: original studies, published in the last 4 years, available in full, and addressing new techniques or advances in techniques already available for diagnosis. Incomplete articles or those not available in full (fee required for access), studies in the project or pilot phase, and those whose focus did not correspond to the research question were excluded.

RESULTS

Vaginitis can be classified as specific and nonspecific. The specific form is caused by microorganisms such as *Gardnerella vaginalis* (responsible for most cases of bacterial vaginosis), *Candida sp.* (causing candidiasis, the main existing gynecological complaint), and *Trichomonas vaginalis* (responsible for trichomoniasis). Nonspecific, or aerobic, vaginitis results from an imbalance in the vaginal microbiome, characterized by the proliferation of aerobic bacteria such as *Corynebacterium*, *Staphylococcus epidermidis*, *Enterococcus faecalis*, *Escherichia coli*, and streptococci of groups A, B, and D. This type of vaginitis is often misdiagnosed, despite its specific clinical characteristics, such as vaginal inflammation and changes in the composition of vaginal epithelial cells (Toader *et al.*, 2023).

The diagnosis of bacterial vaginosis is still based on the Amsel criteria and the Nugent score, which evaluate clinical and microscopic characteristics (Merchán-Villafuerte *et al.*, 2020). However, new molecular techniques, such as Real-Time Polymerase Chain Reaction (RT-PCR) and next-generation sequencing (NGS), have gained prominence for their ability to accurately identify a wide range of bacteria, including those associated with bacterial vaginosis, which are challenging to culture in laboratory conditions. Nucleic acid amplification tests (NAATs) are also becoming common, allowing for faster and more accurate diagnoses (Savicheva, 2023).

A molecular test called *Immuno Quantex* has been developed to assess the local inflammatory response by measuring levels of specific cytokines (IL-1b, IL-10, IL-18, TNF α , among others) (Budilovskaya, 2020). Studies have shown that vaginal

infections, such as bacterial vaginosis and aerobic vaginitis, have distinct patterns of cytokine mRNA expression, allowing immunological markers to be used for the differential diagnosis of these conditions.

Regarding treatment, one of the intravaginal devices currently used is composed of hexylresorcinol, vegetable collagen, bismuth subgallate, and herbal extracts, formulated in homogeneous ovules and indicated for the treatment of vulvovaginitis, cervical erosion, postoperative bleeding, and restoration of normal vaginal pH and flora. Its components have specific functions: bismuth subgallate promotes healing, while collagen aids in healing. *Calendula officinalis* extract has antimicrobial and antifungal activities, which reduce significant side effects.

From another point of view, colonization by lactobacilli is essential for maintaining a healthy vaginal microbiome, playing an essential role in preventing urogenital diseases and ensuring reproductive success. Imbalances in the vaginal environment caused by external or internal factors affect the vaginal microbiota and lead to a decrease in protective lactobacilli (FEBRASGO, 2018).

Thus, it is known that traditional treatments can cause side effects, drug resistance, and recurrence of infection (Andrade *et al.*, 2022). In this context, the use of probiotics has been widely discussed as a promising strategy to regulate vaginal homeostasis and prevent vulvovaginal candidiasis.

Lactobacillus crispatus is one of the main probiotic species, known for producing lactic acid, hydrogen peroxide, and bacteriocins, which act as pathogen antagonists and immune system stimulators (Zheng *et al.*, 2021). Studies show that both oral and vaginal probiotic capsules are effective in reducing the symptoms of bacterial vaginosis and candidiasis, with vaginal forms demonstrating greater efficacy in maintaining high levels of healthy microorganisms.

Mixed vaginitis, characterized by the presence of multiple pathogens such as *Gardnerella vaginalis*, *Candida* spp., and *Trichomonas vaginalis*, presents therapeutic challenges due to the coexistence of these microorganisms. Although the use of multiple antimicrobials is considered in specific cases, routine polytherapy is not recommended (Carvalho *et al.*, 2021).

Future studies should focus on understanding polymicrobial interactions and mixed biofilms to improve treatment efficacy and laboratory diagnosis, minimizing inappropriate therapies and the chance of reinfection. In addition, approaches such as the use of probiotics in combination with sucrose, which improves recolonization by lactobacilli, have shown promising results, comparable to vaginal metronidazole. Other options under investigation include DNase agents, capable of disrupting biofilms by targeting extracellular DNA, and synthetic antimicrobial peptides, which offer new therapeutic perspectives (Abou Chacra; Fenollar; Diop, 2022).

CONCLUSION

Ongoing research, the development of new medical devices, and probiotic approaches provide broader opportunities for the effective treatment and prevention of vaginitis and vaginosis. The combination of traditional treatments with new therapies, including probiotics and innovative medical devices, may provide a more comprehensive and effective approach for managing recurrent vaginitis or vaginosis, as well as other vaginal conditions.

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