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Oral probiotics and vaginal microbiome in post-menopause women: an opinion for the improvement of natural therapies in gynecology

Virginia Franco Silva[1*], Paulo Refinetti[1], Franco Vicariotto[2], Edmund Chada Baracat[3], Jose Maria Soares Junior[3]

The vaginal microbiota represents an intricate and multifaceted biome that directly modulates female health. It refers to the community of microorganisms, including bacteria, fungi, and viruses, which reside in the vagina[1]. This complex ecosystem plays a crucial role in female health and a potential role in reproductive fitness. The vaginal microbiome's composition varies among individuals and can be influenced by numerous factors such as age, racial factors, hormonal changes, sexual activity, and the use of contraceptives or antibiotics. In many healthy individuals, the vaginal microbiome is often dominated by bacteria from the *Lactobacillus* genus. These bacteria produce lactic acid, helping to maintain a low pH in the vagina and thus providing a natural defense against the colonization of pathogenic microbes. However, an imbalance or dysbiosis in the vaginal microbiome can lead to various health issues such as bacterial vaginosis, yeast infections, or increased susceptibility to sexually transmitted infections[2].

Disruptions in this microbiome, particularly during the menopausal transition, are caused especially by the lack of estrogen and can lead to an array of deleterious conditions such as atrophic vaginitis, recurrent urinary tract infections, and susceptibility to sexually transmitted diseases. Climacterium is a phase marked by profound endocrine transitions impacting various facets of women's health, including the vaginal microbiome. Concomitant with the decrease in estrogen levels, there is an alteration in the vaginal microbiome composition and a decline in the predominant *Lactobacillus* species, which are fundamental for vaginal health homeostasis[3]. This state augments female susceptibility to an array of health diseases. Consequently, probiotics have been spotlighted as a promising intervention to assist in the reconstitution and maintenance of the vaginal microbiome. When administered in appropriate quantities, these viable microorganisms provide health benefits to the host. The capacity of probiotics to colonize the gastrointestinal and vaginal milieu and foster *Lactobacillus* recolonization may provide a natural and efficient strategy for managing vaginal health during the menopausal transition[4]. This editorial explores the intricate relationship between the vaginal microbiota, menopause, and the application of probiotics, placing emphasis on prospective strategies for enhancing vaginal health in postmenopausal women.

From a regulatory perspective, oral probiotics are generally recognized as safe by many health authorities and their use is widespread in various forms, from supplements to fortified food products[5]. This contrasts with vaginal probiotics, which can be subject to more stringent regulations given their route of administration[6].

A well-designed randomized, double-blind, placebo-controlled study published by Petricevic et al.[4] presents promising findings regarding the use of orally administered probiotic strains, *Lactobacillus rhamnosus* GR-1 and *Lactobacillus reuteri* RC-14, in postmenopausal women to improve the quality of their vaginal flora. The study demonstrated a significant improvement in the Nugent scores, with 60% of the intervention group showing a reduction of at least two grades compared to only 16% in the control group. The median difference in Nugent scores further emphasized the effectiveness of the probiotic intervention. These results suggest a compelling alternative approach to restoring healthy vaginal flora in postmenopausal women through the targeted use of specific probiotic strains administered orally[4].

Another study focused on the positive advantages of oral probiotics for vaginal microbiome eubiosis in adult women aged from 18 to 45 years, significant findings emerged regarding the impact of probiotic intake, specifically involving *Lactobacillus paracasei* LPC-S01. The study employed statistical analysis to assess changes in bacterial taxa. Notably, the analysis revealed that while the placebo had no discernible effect, probiotic intake led to a substantial decrease

[1]YONI Solutions SA – Monthey, Switzerland.
[2]"San Pio X" Nursing Home, Gynaecology Unit – Milan, Italy.
[3]Universidade de São Paulo, Faculty of Medicine, Clinical Hospital, Department of Obstetrics and Gynecology, Structural and Molecular Gynecology Laboratory (LIM-58), Gynecology Discipline – Sao Paulo (SP), Brazil.
*Corresponding author: virginia.franco@yonisolutions.ch
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in the presence of the genus *Gardnerella* (p=0.049). Furthermore, there was a notable increase in the amount of *L. gasseri* (p=0.078). This shift in microbial composition suggests that oral probiotics containing *Lactobacillus paracasei* LPC-S01 can play a pivotal role in promoting vaginal microbiome eubiosis. It is worth mentioning that these positive changes in microbial balance were further confirmed through qPCR analysis, using *G. vaginalis*-specific primers on DNA extracted from vaginal swabs.

Indeed, while our focus has primarily been on postmenopausal women, it is imperative to recognize the observed reduction in the prevalence of *Gardnerella* and the concurrent increase in health-associated *Lactobacillus* species, following the interventions like oral probiotics in reproductive-age women, since those interventions could potentially restore a balanced vaginal microbiota by reducing pathogenic elements and promoting the proliferation of beneficial *Lactobacillus* species[7], thereby mitigating the adverse effects of dysbiosis, particularly in the postmenopausal, a phase characterized by a marked decline in estrogen levels, when the vulnerability to *Gardnerella* colonization becomes more pronounced.

In essence, these findings advocate for the application of oral probiotics as a viable and beneficial strategy to optimize vaginal health and microbial balance, not only in postmenopausal women but also across a wider spectrum of individuals who may be susceptible to vaginal dysbiosis, offering a promising alternative to traditional interventions.

Oral probiotics as an alternative to vaginal probiotics present numerous potential advantages in postmenopausal women, especially considering regulatory hurdles in some countries and patient compliance[8]. Oral probiotics are typically easier to regulate, given their wide usage and established safety profile in various demographic cohorts. Furthermore, they may be integrated into routine dietary habits, fostering long-term compliance and adaptation among women (Figure 1). However, further studies are necessary to evaluate the benefits of oral probiotics on the women health.

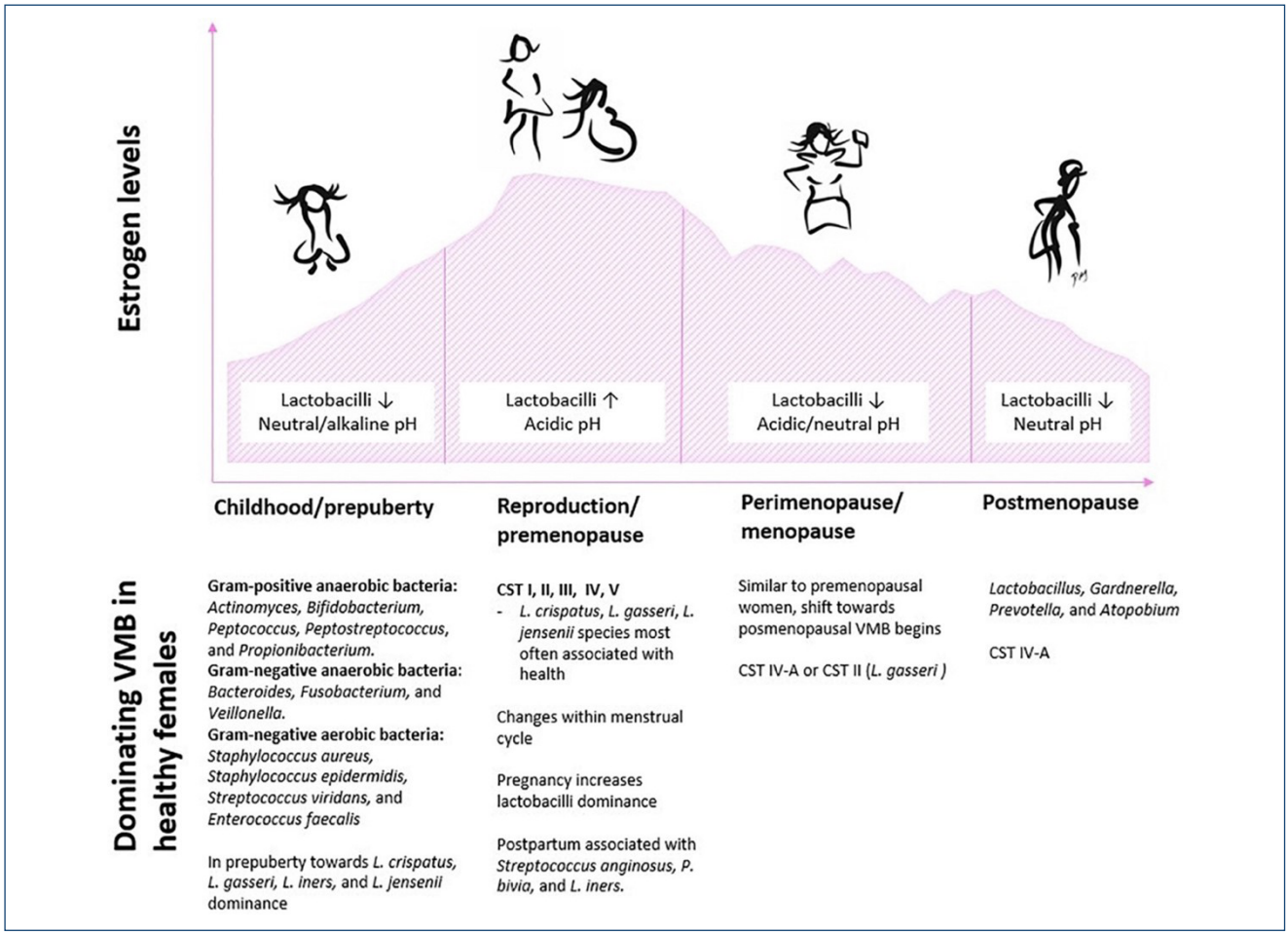

Figure 1. The composition of the vaginal microbiome undergoes significant changes throughout a woman's life, from childhood through puberty, reproductive years, pregnancy, and into menopause and post-menopause. As a result, it is essential to explore tailored probiotic solutions that match each life stage's unique vaginal microbiome needs[9].

AUTHORS' CONTRIBUTIONS

PR: Conceptualization, Data curation, Formal Analysis, Project administration, Resources, Software, Validation, Visualization. **JMSJ**: Conceptualization, Investigation, Methodology, Supervision, Writing – review & editing. **VFS**: Data curation, Project administration, Visualization, Writing – original draft. **ECB**: Funding acquisition, Resources, Supervision. **FV**: Writing – review & editing.

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