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Short communication

The role of probiotics in the vaginal microbiome

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Introduction

Probiotics, according to the WHO are live microorganisms which when administered in adequate amounts confer a health benefit on the host. They are successfully used as an adjunct to traditional antibiotic therapy for bacterial vaginosis, to improve the cure rate, and to prevent the recurrence of the disease through their ability to supplement the reduced concentration of lactobacilli strains (Vujic et al., 2013).

Exogenously applied lactobacilli have been shown to persist on the mucosal surface and aid in the establishment of a normal microbiome in bacterial vaginosis (Martínez-Peña et al., 2013; Ravel and Brotman, 2016). Daily intake of probiotics with food means the use of fermented products, while the intake of probiotic supplements means the use of pharmaceutical products with probiotics and prebiotics as dietary supplements. Oral intake of lactobacilli may play a role in modeling the structure of the vaginal microbiome. These orally enter bacteria probably reach the vagina through not very clear mechanisms, which involve transition through the anus, perineum, and vulvar skin (Reid and Hammond, 2005). It is believed that capsules, ie suppositories containing Lactobacillus crispatus inserted into the vagina can help regulate the flora (Ma et al., 2013). The protective role of *Lactobacillus crispatus* has been confirmed and identified in numerous studies. The role of *Lactobacillus iners* is unclear, as it is detected in normal conditions as well as in vaginal dysbiosis and BV. It is considered that they contribute to the onset and maintenance of vaginal dysbiosis, as well as they are a risk factor for a negative pregnancy outcome.

Materials and methods

Prospective cross-sectional study of 110 reproductive age women. The inclusive criteria were signed informed consent appropriately obtained from all participants. The exclusive criteria were pregnancy, menstrual or other types of uterine or vaginal bleeding, antibiotic treatment within the previous month, sexual intercourse within the previous three days, use of vaginal tablets, capsules, or gels within the previous three days, transvaginal interventions within the previous month.

In addition to the routine gynecological examination, two vaginal swabs were collected, for obtaining the Nugent score and divided the women into three groups according to the score: normal flora (NF) (0-3); intermediate for bacterial vaginosis (IMBV) (4-6) and bacterial vaginosis (BV) (7-10). The second swab was immediately frozen at -20°C and thus transported to the Laboratory at the

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Academy of Sciences and Arts of Republic of North Macedonia. A total of 93 samples were selected randomly for molecular analysis of *Lactobacillus spp*. Identification was done by amplification of 16S rRNA genes. The complete 16S rRNA gene (1.5 kb) was amplified by PCR using primers and sequenced. To identify the isolates, obtained sequences of the 16S rRNA of Lactobacilli, which are hypervariable, were compared with the DNA database of the BLAST algorithm (www.ncbi.nlm.nih.gov). Identification is considered to be confirmed at 99-100% homology to the type of strain sequence.

Results and discussion

Most of the women from the NF group, N=40 (61.5%) consume probiotics with food daily, followed by 37.5% from the IMBV group and only 4.8% from the BV group. The difference registered between the groups in terms of intake of probiotics with food is statistically significant, between the NF and BV group (61.5% vs 4.8%), the IMBV and BV group (37.5% vs 4.8%), and the NF and IMBV group (61.5% vs 37.5%) for $p < 0.05$ (Difference test, $p = 0.0000$, $p = 0.0085$, $p = 0.0434$).

Most of the women taking probiotics with supplements were from the NF group (12.3%), vs 4.2% from the IMBV group and none of the BV group, but the difference registered between the groups was statistically insignificant for $p > 0.05$.

Only 10.8% of the NF group reported the use of lactic acid and probiotics containing products for vaginal use, and no such habits were registered in the other two groups.

The most frequently identified species among women who consume probiotics with food daily, were *Lactobacillus iners* (42.0%), *Lactobacillus crispatus* (32.0%) and *Lactobacillus casei* (30.0 %) with other lactobacilli. Among women taking supplements with probiotics, *Lactobacillus crispatus* and *Lactobacillus casei* in combination were identified in 55.5% and *Lactobacillus iners* in 33.3%.

In women who apply probiotics vaginally, the molecular analysis identified *Lactobacillus crispatus* and *Lactobacillus casei* in combination in 4 out of 7 (57.1%) and *Lactobacillus iners* in only one women.

Conclusion

According to the existing data, the determination, manipulation, and recovery of the vaginal microbiome with probiotics orally and vaginally is considered to have a great potential for improving women's reproductive health and preventing disease (Lewis et al., 2017; Ravel and Brotman, 2016). The development of the exact targeted pharmaceutical products containing specific protective species of *Lactobacilli* for oral and vaginal use for prevention of disturbance as well as improving the healthy vaginal microbiome is of great importance. But much research is needed to develop effective strategies.

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