



Maintenance of Female Genital Tract Micro Ecology in Association of Dominated Gram Positive Bacilli

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Abstract

Although the effect of gram positive bacilli on the health of the female reproductive tract is still disputed, they have been widely used to treat intestinal diseases. Lactobacillus is the most bountiful and dominated gram positive bacteria in the vagina, which is connected with the vaginal mucosal hindrance. Lactobacillus can compete with pathogens to prevent their colonization by adhering to the vaginal epithelium. Bacteriocin and hydrogen peroxide (H₂O₂), two Lactobacillus-produced factors, can keep the vagina's low pH level and prevent the growth of pathogenic microorganisms. Probiotic supplementation is the essential source of huge range of gram positive bacteria specially lactobacillus for preventing cervical cancer from spreading, strengthening the immune system, and preserving the stability of the vaginal microenvironment. In order to provide a basis for further exerting the role of Different Lactobacillus species in women's health, we review the research progress of probiotics represented by Lactobacillus in gynecological diseases like Human Papilloma Virus (HPV) infection, Bacterial Vaginosis (BV), and Genitourinary Syndrome of Menopause (GSM).

Keywords: Intestinal diseases, Microorganism, Vaginal mucosal hindrance, Bacteriocin, Cervical cancer

INTRODUCTION

The normal flora in the vagina, endocrine regulation, and the mucosal epithelial barrier make up the vaginal microenvironment. In healthy women's vagina, a variety of microorganisms colonize, with Lactobacillus playing a major role (95 percent). There are five distinct community state types (CSTs) based on the various species of a given Lactobacillus. CST I, II, III, and V are primarily composed of *L. crispatus*, *L. gasseri*, *L. iners*, and *L. jensenii*, respectively. It is addressed by the decrease of lactic corrosive microscopic organisms and there are completely anaerobic species, for example, *Gardnerella sp.*, *Megasphaera sp.* and *Prevotella sp.* *L. crispatus*, *L. gasseri*, and *L. jensenii*, among others, are able to produce lactic acid and H₂O₂, acidify the vaginal environment to a pH below. Under the influence of estrogen and progesterone, the cells that make up the vagina undergo periodic changes. Lactobacillus grows on the energy provided by the glycogen produced in this process. Through competitive rejection, lactobacillus can also prevent invasive pathogens from adhering to the vaginal

epithelium. Pathogenic bacteria are able to easily invade and reproduce in women who enter menopause because of the decrease in estrogen levels, glycogen content in epithelial cells, and Lactobacillus numbers. Probiotics are a sort of dynamic microorganisms that colonize the human digestive system and conceptive parcel and are valuable to the host. Numerous studies have demonstrated that oral probiotics can treat a wide range of digestive system conditions. The vaginal micro ecological balance can be maintained or altered by lactobacillus, the most prevalent bacterial species in the microenvironment. In this audit, we center on the job of probiotics in keeping up with vaginal wellbeing in ladies (Mei Z, 2022).

Probiotics associated to cervical cancer cells

About 300,000 women are diagnosed with cervical cancer each year, which is the first malignant tumor of the female reproductive tract. When contaminated with HPV, it can annihilate the vaginal micro ecological balance, diminish the quantity of Lactobacillus what's more, and increment the grip and colonization of strange vegetation. This further prompts

the up guideline of HPV protein articulation, advances the development of Cervical Intraepithelial Neoplasia (CIN), and even prompts the event of cervical malignant growth. A systematic evaluation of the relationship between the vaginal microbiota and HPV infection. They discovered that the vaginal microbiota of HPV-positive women had a different composition and diversity of bacteria. A review demonstrated for the first time that oral *Lactobacillus curlicus* has the ability to alter the state of CST and boost HPV clearance. Changes in the cervical microenvironment and persistent high-risk HPV infection encourage the development of cervical precancerous lesions (Champer M et al., 2018).

Activities of probiotics on cervical cancer cells

In addition to acidifying the vaginal environment, stabilizing the vaginal flora, enhancing the function of vaginal epithelial cells, and killing cervical cancer cells, *Lactobacillus* is a type of vaginal probiotic. The vaginal epithelium is occupied by lactobacilli, which adsorb and prevent the aggressive pathogenic bacteria that cause cancer from adhering (Abdolalipour E et al., 2020). By releasing peptidoglycan and exopolysaccharides, lactobacillus can stop cancer cells from growing. The body's immune system is primarily enhanced, cytokine production is encouraged, and monocyte proliferation is inhibited by probiotics. Recent research has demonstrated that probiotics like *Lactobacillus casei* and *Lactobacillus rhamnosus* activate the maturation of NK cells and dendritic cells, which in turn helps fight cancer (Li Y et al., 2020). *Lactobacillus* can likewise influence cell and humoral resistance, advance the multiplication and separation of thymus inferred cells, and further advance the resistant acknowledgment and multiplication of bone marrow-inferred cells (Medina Contreras O et al., 2020). In expansion, probiotic metabolites additionally cytotoxically affect cervical disease cells. It was discovered that *Lactobacillus spp.* was connected with the reduction of the discovery pace of high-risk subtype HPV contamination, cervical intraepithelial neoplasia and disease (Wang H et al., 2019).

Probiotics in association of reducing radiotherapy induced consequences

One of the main methods for treating cervical cancer is radiotherapy. However, there are many side effects, the most common of which is Radiotherapy Induced Diarrhea (RID), which makes patients' lives more difficult (Hombrink J et al., 2020)(Jahanshahi M et al., 2020). A study with 228 patients with stage IIIB cervical malignant growth showed that patients getting probiotics as adjuvants had longer endurance than patients getting radiotherapy alone (Okawa T et al., 1993). The preparation was safe for the local administration of cisplatin, according to histopathological studies. More research, particularly clinical preliminaries, is expected to comprehend the explicit instruments by which probiotics can mitigate the side impacts of radiation treatment for cervical disease.

Significance of probiotics containing *Lactobacillus* therapy instead of vaccine therapy in HPV

The HPV vaccine can effectively prevent high-risk HPV infection, but it cannot enhance the efficacy of cervical cancer treatment. As a result, researchers are currently concentrating on developing vaccines that are therapeutic (Werner J et al., 2012). The bacteria-based vaccine is one of them that are widely used. Transgenic *Lactobacillus* has been shown in numerous preclinical studies to be relatively safe, capable of delivering recombinant antigens, eliciting humoral and cellular immunity in the host, and further eliminating HPV virus (Taghinezhad SS, 2021). The bacteria-based vaccine is one of them that is widely used. Transgenic *Lactobacillus* has been shown in numerous preclinical studies to be relatively safe, capable of delivering recombinant antigens, eliciting humoral and cellular immunity in the host, and further eliminating HPV virus (Das S, 2022). E7-specific mucosal immune response induction efficiency was found to be linked to the level of E7 molecule expression. The HPV16 E6 protein expressed on *Lactobacillus casei* was administered orally to mice and they discovered that the vaccine could induce the production of E6-specific serum IgG and IgA (Park YC et al., 2019).

Antibiotic vs. *Lactobacillus* probiotic therapy in bacterial vaginosis

For the treatment of vaginal infections like BV and VVC, antibiotics like fluconazole, metronidazole, and clindamycin are frequently used. Despite the fact that these antibiotics stimulate the activation of intravaginal bacteria and anaerobes that cause vaginal infections, their use is fraught with danger due to antibiotic resistance, side effects, and recurrences. In the case of metronidazole or clindamycin, BV recurrence rates were as high as 80% among patients who showed an initial response, and initial cure rates were in the range of 10% to 15%. Antibiotic resistance and the persistence of BV-inducing microorganisms result from prolonged or repeated antibiotic exposure, resulting in high rates of recurrence. Hence, lactobacilli probiotics have as of late been bit by bit supplanting anti-toxin treatment for the treatment and counteraction of vaginal contaminations such as BV (Senok AC, 2009). "Live microorganisms that confer a health benefit on the host when administered in adequate amounts" is how probiotics are defined (Rome, 2006). Regarding the health of the vagina, probiotics maintain the normal lactobacilli microbiota in the vagina to improve the therapeutic outcome in women with vaginal infections. As a result, it plays a crucial role in maintaining a vaginal environment that is more resistant to harmful microorganisms by producing lactic acid and lowering the intravaginal pH level to 3.5 to 4.5.5. Indirectly, probiotics contribute to the treatment of BV and VVC by preventing the recurrence and spread of the infections. Numerous studies have demonstrated that by positively altering the composition of the intravaginal microbiota, probiotics are effective in the treatment of vaginal infections like BV and

VVC (Falagas M, 2006). *Lactobacillus spp.*, *Enterococcus spp.*, *Streptococcus spp.* are all examples of probiotics. The *Lactobacillus* genus contains the most well-known beneficial probiotic species for intravaginal use. Lactic acid bacteria generate lactic acid and CO₂ to decompose carbohydrates and maintain an acidic intravaginal microflora. This keeps harmful microorganisms like *Enterobacteria spp.*, *E. coli*, *Candida*, and *G. vaginalis* from colonizing the vagina and growing there (Cadioux P et al., 1940). After taking probiotics, 51.1 percent of the women in the Intervention Group (IG) had a normal composition of *G. vaginalis*, fungi, mixed flora, *Trichomonas*, mycosis, and lactobacilli, whereas only 20.8% of the women in the Control Group (CG) had a normal composition (Ya W, 2010). Long haul anti-toxin organization for BV was related with unfriendly impacts, counting a high likelihood of BV repeat due to antibiotic obstruction got from rehashed openness to anti-toxins, though transient organization joining anti-infection agents with probiotics diminished the quantity of destructive intravaginal microorganisms. This implies that co-treatment with probiotics and anti-microbials was more powerful in BV treatment also, repeat counteraction than was anti-microbial administration alone (Anukam K et al., 2006) (Heczko PB et al., 2015).

Lactobacillus probiotics in bacterial vaginosis

A mixed infectious disease known as Bacterial Vaginosis (BV) is characterized by an increase in anaerobic bacteria, particularly *Gardnerella* and *Prevotella*, and a decrease in *Lactobacillus* in the vagina (Onderdonk AB et al., 2016). Metronidazole and other antibiotics are the standard course of treatment. In point of fact, the rate of BV recurrence following oral metronidazole treatment is extremely high, and systemic antibiotic use has significant adverse effects (Muzny C A et al., 2020). Probiotics have the potential to improve vaginal flora, increase beneficial bacteria, decrease harmful bacteria, and further support the environment's stability (Ling Z et al., 2013). The link between cancer and chronic inflammation is supported by experimental studies conducted on humans and animals. Increased gene mutation rates, cancer development, and tumor metastasis are all consequences of chronic inflammation. In the treatment of inflammation, probiotics and antibiotics play an important role together.

Vaginal microbial reorientation

In addition to achieving remarkable results, Fecal Microbiota Transplantation (FMT) has gained increasing attention for the treatment of digestive system diseases. In recent years, there has also been a growing interest in Vaginal Microbial Transplantation (VMT) (Korpela K et al., 2020) (Wang J et al., 2021). Using a vaginal dysbiosis model, one study examined how VMT affected vaginal dysbiosis (Chen T et al., 2021). Transplanted the feces of female mice with intact and productive ovaries into the feces of ovariectomized mice and discovered a significant reduction in vaginal epithelial

atrophy and a significant alteration in the intestinal flora (Huang J et al., 2021). In a randomized controlled trial, the gut microbiota of infants born by caesarean section was evaluated at two hours, one month, and three months following oral administration of maternal vaginal microbes, in contrast to the previous studies (Wilson BC et al., 2021).

CONCLUSION

There is a relationship between an exceptionally different vaginal microbiota and female conceptive plot wellbeing. Probiotics are very important for keeping the female reproductive tract healthy, getting rid of gynecological diseases, and making the vagina's local immunity stronger. Preventing the progression of CIN, treating BV, and alleviating senile vaginitis symptoms are all improved by probiotics or VMT treatment. The development of 16SrRNA sequencing technology has the potential to aid in the identification of microbial markers and the implementation of personalized disease prevention and treatment. Probiotics' effect on cervical cancer is still poorly understood at this time. Larger-scale clinical studies and longitudinal tracking are required in the future. To fully comprehend the connection between the host, vaginal microbes, and disease, multi-omics analysis and combination immunotherapy are also required.

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