

CONTRACEPTION AND RISK OF BACTERIAL VAGINOSIS***Stefan Kovachev**

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ABSTRACT

The aim of this study is to determine the relationship between bacterial vaginosis and the used contraceptive method. **Methods:** In our case-control, single-center study 1450 women used different contraceptive methods with gynecological vulvo-vaginal complaints were included, where the clinical and microbiological studies indicated presence or absence of bacterial vaginosis, other vaginal infections or normal vaginal flora. The used contraceptive method was determined anamnestically. **Results:** Of 1450 (100%) women enrolled in our study 500 (34.4%) women drop out for different reasons and only 995 (68.6%) were included in. From these 995 (100%) included women: 107 (10.7%) used intrauterine devices (IUD), 343 (34.5%) combined oral contraception (COC), 10 (1%) spermicides and 535 (53.8%) condoms. Bacterial vaginosis was determined clinically and

microbiologically in 591 (59.4%) women enrolled in the study, and 404 (19.6%) had normal vaginal flora. There was a statistically significant relationship only between the use of IUD, condoms and the development of bacterial vaginosis ($p \leq 0.05$). The remaining contraceptive methods used by women in our study did not indicate such a relationship ($p \geq 0.05$).

Conclusions: The use of a IUD and condoms can be regarded as a risk factor for disorders of the microbiological balance in the vaginal ecosystem and can lead to the development of bacterial vaginosis. The remaining contraceptive methods used by women in our study did not reveal statistically significant relation to the development of bacterial vaginosis.

KEYWORDS: contraception; bacterial vaginosis; combined oral contraceptives; intrauterine devices; condoms.

INTRODUCTION

Bacterial vaginosis (BV) today is the most common infection in women.^[1] Some contraceptive methods can affect the vaginal microbial eco-balance and lead to development of bacterial vaginosis.^[1,2] Therefore, the choice of contraceptive method is very important for those women who often suffer from vaginal infections, especially bacterial vaginosis.^[2,3] Retention or disturbance of vaginal eco-balance and its consequences depends on the type of contraception used. IUD seriously affects the normal vaginal flora, while oral contraceptives have minimal effects on vaginal microbes.^[2,3] Many data support the hypothesis that intrauterine contraceptive devices may change the cervico-vaginal environment, and that women using such devices have a higher risk of bacterial vaginosis.^[2,3]

Condoms and spermicides have contradictory effects on the vaginal flora, according to various authors and studies. Using condoms treated with spermicide gel can cause more profound changes in the vaginal flora than unprotected sex, because of decreasing of vaginal lactobacilli. This can be a reason for developing bacterial vaginosis.^[4-6] Non-use of condoms on the other hand, greatly increases the risk of the sexually transmitted diseases.

Women using hormonal contraceptives have a low risk for bacterial vaginosis.^[7] Estrogens contained in contraceptive preparations stimulate vaginal epithelial cells to produce more glycogen.^[1] This creates favorable environment for the development and replication of lactobacilli, and they in turn prevent colonization of pathogens.^[1] In these women, higher risk for chlamydial infection or vaginal Candida infections is reported.^[7]

The choice of a contraceptive method, as evidenced by the cited studies, affects the vaginal microbial environment. Retention or disturbance of bacterial vaginal eco-balance may depend on the type of contraception used. Its preservation, without infringing the freedom of patient's choice of type of contraception, sometimes requires specialized microbiology and medicated therapy.

The aim of this study is to establish the relationship between bacterial vaginosis and the contraceptive method used.

MATERIALS AND METHODS

Study cohort

The study is a case-control, open-label, single-center, and was conducted in our gynecology department over the period 2013-2016. 1450 women aged between 16 to 50 years used different contraceptive methods who visited our outpatient clinic with complaints of increased genital fluorine (not always with a bad smell) and subjective sensation of burning, itching, stinging, dysuria, and dyspareunia were enrolled in the study. The patients had either clinically and microbiologically identified bacterial vaginosis, normal vaginal flora or various vaginal infections. Information about the purposes of the study and the entry requirements was provided to the patients. We had an informed consent of each patient. Ethics committee approval (№ 2375/2013), was received for this study from the regional hospital ethics committee.

Exclusion criteria

Patients below 16 and over 50 years of age were excluded from the study. Patients with identified *Neisseria Gonorrhoeae*, *HSV*, *HPV*, *Chlamydia Trachomatis*, *HIV*, *Candida* and different from BV vaginal infections were also excluded from the study. Pregnant women and those who were on therapy with corticosteroids, antibiotics, imidazoles, and probiotics, or had used vaginal agents within the last month were not enrolled in the study. Immunocompromised patients, women with autoimmune and endocrine diseases or diabetes were not enrolled in the study either. Patients with identified malignancies also were excluded from the study.

Clinical and laboratory tests

At study entry, medical history was recorded, gynecological examination and microbiological tests were performed for all women. Patients were questioned about the type of contraception they used. Data was entered in an outpatient card. During the gynecological examination inspection of the vaginal discharge (often defined by the patients as fluorine) was assessed based on the following characteristics: amount; viscosity; color; odor, and they were recorded in the outpatient card. Again during this inspection from the posterior vaginal fornix with a dry sterile swab, a vaginal content for microbiological testing was taken. To determine the diagnosis of bacterial vaginosis (BV) the following clinical criteria were used (introduced in modern gynecological practice by Amsel et al.1983):

- Profuse gray-white discharge

- Vaginal Ph > 4.5.
- Testing native preparation in which "clue cells" are found.
- Positive amino test of vaginal discharge when dripping 10% KOH.^[8]

The presence of three of the four criteria is considered sufficient when determining a diagnosis.^[8] Indicator strips (Merck KGaA, Darmstadt, Germany), range of 4 to 7, were used to measure pH, and the values of pH above 4.5 were reported as pathological. The aminotest of vaginal discharge taken from the posterior vaginal fornices was reported as positive when an unpleasant smell was released. For the native preparation normal saline (0.9% NaCl) was added to the vaginal discharge and applied on a microscope slide. The preparation was inspected under a light microscope. BV diagnosis was made in the presence of "clue cells". Clue cells > 20% on light field is considered a positive sign for BV. Not all patients enrolled in the study showed expressed clinical symptoms. In many of them, bacterial vaginosis was asymptomatic, and the diagnosis was determined through microscopic examination of Gram-stained preparations of vaginal discharge. The Gram-stained preparations were evaluated for the following morphotypes in observing with immersion (x1000): large, Gram-positive rods (morphotype of lactobacilli); small, Gram-variable rods (*G. vaginalis* morphotype); small Gram-negative rods (*Bacteroides* spp. morphotype); curved Gram-variable rods (*Mobiluncus* morphotype) and Gram-positive cocci. The ten-point (0-10) system for evaluation of microscopic preparations introduced by Nugent et al. 1991 was used.^[9] Levels 0 and I were detected in women with preserved vaginal microbial balance.^[9] The second degree is intermediary. It is not found in women with dominant anaerobic strains satisfying the criteria of Amsel.^[9] The third degree is typical for women with clinically definite BV.^[9] IV degree also occurs in BV.^[9]

Data analysis

The data obtained were analyzed by using Chi-Square tests (χ^2) to evaluate the results. Statistical significance was assumed at $p < 0.05$. For statistics calculation we used computer software - Calculation for the chi-square test: An interactive calculation tool for chi-square tests of goodness of fit and independence [Computer software]. Preacher K. J. Vanderbilt University, Nashville, Tennessee, USA 2001, April; available from <http://quantpsy.org>.^[10]

RESULTS

Of 1450 (100%) women enrolled in our study 500 (34.4%) women drop out for different reasons (exclusion criteria) and only 995 (68.6%) were included in. Most of the excluded

women have different from BV vaginal infections. Of 995 (100%) women enrolled in our study that used various contraceptive methods, bacterial vaginosis was determined clinically and microbiologically in 591 (59.4%) women and 404 (19.6%) had normal vaginal flora. From these 995 (100%) included women: 107 (10.7%) used intrauterine devices (IUD), 343 (34.5%) combined oral contraception (COC), 10 (1%) spermicides and 535 (53.8%) condoms.

Table 1: Distribution of all women enrolled in our study.

All women in the study	Excluded women n/%	Women with BV n/%	Women with healthy vaginal flora n/%	Total n/%
All women enrolled in the study n -1450	500/34.4	591/40.7	404/27.9	1450/100
Women met inclusion criteria of the study	0/0	591/40.7	404/27.9	995/68.6

*BV - bacterial vaginosis

Table 2: Patients using combined oral contraceptives (COCs), intrauterine devices (IUD), spermicidal gel and condoms in the groups with bacterial vaginosis and in the healthy women of the control group.

All women included in study (n -995 /100%) Contraceptive methods			Women (n-591/100%) with BV n /%	Women (n-404/100%) without BV n /%	P - value
COC n /%	Yes	343 /34.5	273 /46.2	202 /50.0	P = 0.23
	No	652 /65.5	318 /53.8	202 /50.0	
IUD n / %	Yes	107 /10.7	99 /16.8	8 /2.0	P = 0.00001
	No	888 /89.3	492 /83.2	396 /98.0	
Spermicides n / %	Yes	10 /1.0	9 /1.5	1 /0.2	P = 0.47
	No	985 /99.0	582 /98.5	403 /99.8	
Condoms n/%	Yes	535 /53.8	210 /35.5	193 /47.8	P = 0.0001
	No	460 /46.2	381 /64.5	211 /52.2	

*Data are presented with N and % for categorical variables. **Data was available for 995 subjects. ***A p value ≤ 0.05 was considered statistically significant. ****BV - bacterial vaginosis; COC – combined oral contraceptives; IUD – intrauterine devices.

Our data show that women with an IUD have a statistically higher risk of bacterial vaginosis than others ($p \leq 0.05$). This is confirmed by the data of other studies about. The same risk ($p \leq 0.05$) we find out for the group of women using condoms for contraception. Of 995 (100%) women having bacterial vaginosis included in the study 343 (34.5%) used combined oral

contraceptives (COCs). Of 404 (100%) healthy women included in the study, 202 (50%) used combined oral contraception.

In our study, we did not find a statistically significant influence of the factor combined hormonal oral contraceptives (COCs) for the development of bacterial vaginosis ($p \geq 0.05$) and also of the risk factor spermicidal gel for the development of bacterial vaginosis, which can be explained with the small number of women (10) using this method of contraception.

DISCUSSION

The most commonly used spermicide gel is nonoxynol-9.^[4,6] In addition to its spermicidal effect, it also has microbicidal effect, therefore in addition to spermatozooids it also kills other microorganisms.^[4,6] Many studies show how detergent spermicides such as nonoxynol-9 not only do not protect against STI, but also lead to inflammation of the vagina, kill lactobacilli, create conditions for the development of dysbacteriosis, and make it more susceptible to STI.^[4-6] Other researchers such as Schreiber et al. 2006 do not find a similar effect of the spermicidal gel on the vaginal flora when it is used durably.^[11] Modern developments in this area are related to the discovery of non-detergent spermicides with lower toxicity compared to the lactobacilli.^[12] Harmless to the vaginal flora are condoms processed only with lubricant that does not contain spermicidal gel.^[12] They protect against STI and do not disturb vaginal eco-balance. Tracking 871 women at high risk of STI for a period of three years by Hutchinson et al. studying the vaginal discharge including the 6th, 12th, 24th and 36th month showed a close correlation between the use of a condom (lubricant) and the percentage reduction of the cases of bacterial vaginosis.^[13] The assessment by Nugent shows preservation of normal flora and lactobacilli in 95% of women used a condom in every sexual contact.^[13] The risk of distorting the vaginal microbial balance and bacterial vaginosis when a practicing safe sex using condom is minimal, the author's state.^[13] The direct import of pathogens in the vagina and the semen factor with all its negative effects on the vaginal flora are avoided.^[13] A similar study of Ma et al. 2013 of 164 women shows preservation of normal flora in 93.1% of patients in the group using condoms and 75.4% in the group using an IUD.^[14] The prevalence of H₂O₂-producing lactobacilli was significantly higher in the condom group (82.3%) than in the IUD group (68.2%), ($p=0.016$).^[14] Another study of Yotebieng M et al. 2009 of 563 women conclude that consistent condom use was associated with reduced BV prevalence at 6 months for women who were BV-negative at baseline, but had no effect among women who were BV-positive at baseline.^[15] A study of Smart et al. 2004 clarifies

potential sexual and non-sexual risk factors for BV.^[1] 890 women with BV and 890 controls were studied.^[1] In this study women with BV were significantly less likely to have used hormonal contraception (OR = 0.60, 95% CI: 0.51 to 0.81) or to have used condoms consistently (OR = 0.5, 95% CI: 0.31 to 0.71) than controls.^[1] In our study we find statistical significance of the risk factor condom use for the development of bacterial vaginosis ($p \leq 0.05$), even we don't know how often and what kind of condoms with or without spermicides woman included used.

A study of Ocak et al. 2007 examined the microbial and cytopathological changes and genital symptoms in women using oral contraceptives and intrauterine contraceptive devices (IUD).^[3] In the group of patients with an IUD, after examination and evaluation of vaginal discharge, the authors find intermedium changes of vaginal flora in 20.6% and bacterial vaginosis in 11.7%.^[3] In the group using oral contraceptives (COCs), 8.8% of women have intermedium changes of vaginal flora, and 5.9% have bacterial vaginosis.^[3] In women in the control group, these rates are respectively 2.9% intermedium changes and 2.9% BV.^[3] The authors conclude that IUD seriously affects the normal vaginal flora, while oral contraceptives have minimal effects on vaginal lactobacilli.^[3] IUD use, especially in female patients with frequent episodes of bacterial vaginosis, should be carefully précised.^[3] The data support the hypothesis that intrauterine contraceptives may change the cervico-vaginal environment and that women using such devices have a higher risk of vaginal infections. Ferraz do Lago et al. 2003 find cervicovaginal infections in 29.1% of all 223 women with IUD included in the study, where the highest is the frequency of bacterial vaginosis - 19.7%.^[16] Similar results are also published by Agarwal et al. 2004 after examining the vaginal medium of women with IUD.^[17] They recommend regular clinical examinations and follow-up of women with IUD for early diagnosing of impaired vaginal medium and preventing bacterial vaginosis.^[17]

Women using hormonal contraceptives have a lower risk of BV. A prospective study of Riggs et al. 2007 included 3077 women of reproductive age who used hormonal contraceptives did not find disturbances in the vaginal microenvironment and increased risk of BV.^[18] The authors found more frequent episodes of BV in women taking hormone injections and implants.^[18] A Bulgarian study of Batashki et al. 2006 also did not find an increased risk of developing bacterial vaginosis in women who use oral contraceptives.^[19] A prospective study of Gupta et al. 2000 examined the effect of contraceptive methods on the

vaginal flora.^[2] Study enrolled 331 women used oral contraceptives, spermicides or cervical cap.^[2] Vaginal flora tracking (by Nugent criteria) in this study showed partial or complete loss of lactobacilli in the groups who used spermicides and cervical cap.^[2] In women with oral contraception in this study, no changes were found in the normal vaginal flora.^[2]

CONCLUSIONS

Many risk factors for bacterial vaginosis have been described, however, clear and robust scientific explanation cannot be found for all of them. The high incidence of this infection in all countries in the world is explained with them. It is a cause of morbidity number one among women of reproductive age and often leads to lengthy and unpleasant health disorders. This requires consideration of possible risk factors, among which is the used method of contraception. In our study, we found a statistically significant dependence between IUDS and condoms using and the development of bacterial vaginosis ($p \leq 0.05$). Other contraceptive methods used by women in our study did not show such dependence ($p \geq 0.05$).

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