

Effects of intrauterine device and oral contraceptive on vaginal flora and epithelium

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ABSTRACT

Objectives: To investigate the microbial and cytopathological changes and genital symptoms in oral contraceptive pill (OCP) and intrauterine contraceptive device (IUCD) users.

Methods: Included in the study were 34 women using OCP and 34 women using IUCD for 24 to 36 months period and 34 women as control group. We conducted the study between March to September 2005 in Antakya Maternity Hospital, Turkey. Vaginal discharge was subjected to wet mount examination, gram staining, and culture. Cervical smears were examined and reported using the Bethesda system as reference.

Results: In the IUCD group, women with intermediate score was 20.6%, while those with bacterial vaginosis was 11.7%. In the OCP group however, women with intermediate score was 8.8%, while those with bacterial vaginosis was 5.9%. Compared to the control group, these rates were 2.9% for those with intermediate score and 2.9% for those with bacterial vaginosis. *Escherichia coli* vaginal colonization increased by 5-fold in the IUCD users ($p < 0.05$). Cervical erosion was found in 14.7% of the women using IUCD as compared to the other groups ($p < 0.05$). *Actinomyces* like organisms was detected in 11.7% of the IUCD users ($p < 0.05$).

Conclusion: The use of IUCD clearly alter the normal vaginal flora, although OCP appears to have minimal effects on the vaginal microbial flora. The data support the hypothesis that IUCD might change cervico vaginal environment, and suggests that women with IUCD may be at a higher risk for vulvovaginal infection.

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The normal vaginal ecosystem is recognized as an important host defense mechanism. Alteration of the *Lactobacillus* dominant flora has been associated with an increased risk of bacterial vaginosis (BV).^{1,2} The vaginal flora can be disrupted by several factors, including antimicrobial and contraceptive use and douching.^{3,4} In the past years, many authors investigated the relationship between contraceptives and BV. As risk factors may be very different, it is difficult to compare users with non-users for a specific contraceptive method.

The intrauterine contraceptive device (IUCD) is a commonly used form of reversible contraception world-wide. It is also the most popular modern method in Turkey, and 19.8% of married women were reported using IUCD.⁵ The IUCD generally has shown to be safe and effective but tend to have some side effects. Reproductive tract infection is one of the major complications caused by prolonged usage of an IUCD.^{6,7} Several studies have demonstrated a higher prevalence of BV and pelvic inflammatory disease among IUCD users in different countries.⁸⁻¹⁰

Few studies have been performed to investigate a possible association between BV and oral contraceptives.¹⁰ Oral contraceptive pill (OCP) inhibits gonadotropin and ovarian hormone synthesis, induce anovulation and enhance the cervical mucus barrier to sperm. Some studies have been reported that the effect of OCP use on the vaginal flora is minimal.^{10,11}

The IUCD has been reported to produce inflammation and changes in the cervical cytopathology.^{12,13} Vaginal epithelium might have minimal change in the OCP users.^{14,15} The aim of this study was to investigate the microbial and cytopathological changes and genital symptoms in OCP and IUCD users.

Methods. This study included 102 women visiting the family planning clinic for follow up in Antakya Maternity Hospital, Hatay, Turkey over a

period of 6 months from March to September 2005. The local ethical committees approved this study.

The subjects of this study were comprised of 34 women using IUCD (median duration: 32±3.4 months) and 34 women using OCP (median duration: 31±3.2 months) for 24 to 36 months period. Thirty-four control subjects were women who did not have any gynecological complaint and were attending the Family Planning Clinic. Women were eligible for the study if they were between 17 and 42 years old. The demographic data, sexual performance, contraceptive and detailed gynecologic history, including current genital symptoms were collected on standardized forms at enrollment. Women with chronic illness such as diabetes, use of antibiotic and vaginal suppository or douching in the past month, previous history of urinary tract infection in the past month were excluded. Vaginal and cervical examination was carried out in all women in the study. The type of IUCD used was Copper T (TCU 380 A, SMB Corporation, India) while the OCP used by these women contained ethinyl estradiol 0.03mg + levonor gestrel 0.15 mg (Microgynon 21 tablet, Schering, Germany).

Vaginal discharge was collected from the posterior fornix for Gram staining and wet mount. The amount of vaginal discharge was qualitatively assessed and was recorded. The Nugent's criterion was used for the BV diagnosis, and the flora were scored as normal (Nugent scores 0-3), intermediate (Nugent scores 4-6), or consistent with BV (Nugent scores 7-10). The use of Nugent's criterion and procedure is describe elsewhere.¹⁶

Wet mount smear was examined within 15 minutes of collection for *Trichomonas vaginalis*. Vaginal cultures were collected by inserting a sterile cotton swab into the vagina, and were transported to the laboratory in Amies transport medium, and were performed in blood agar, saboraud dextrose agar and eosin methylene blue agar within 6 hour by using standard laboratory methods. The organisms were identified by colony morphology and biochemical tests.

A spatula was used to take scrapings from cervix for cytologic specimens. Cervical smear were stained using Papanicolaou's staining. The pathologist examined the smears for any cytological abnormality and reported using the Bethesda system as reference.¹⁷

Statistics. Statistical analysis was performed using chi-square test, fisher exact tests and one way analysis of variance test. The *p* values less than 0.05 were considered statistically significant. Statistical Package for Social Sciences version 10.0 software was used for the data analyses.

Results. The groups were similar in all demographic characteristics examined (Table 1). All women had

sexual activity and 100% of them were married. The distribution of age, residence, number of parity, education levels were not statistically different among groups (*p*>0.05). Vaginal discharge, backache, external genital pruritis were observed in a significant number of the women with IUCD. Complaints of backache in IUCD, OCP users and control group were found to be 29.4%, 14.7%, 8.8%, respectively (*p*<0.05). Total vaginal discharge were 76.4% in IUCD, 55.8% in OCP, 38.2% in the control group (*p*<0.05). While there was no a significant difference between the OCP users and the control group for backache and amount of vaginal discharge (*p*>0.05), there was a significant difference between the IUCD users and the control group (*p*<0.05). Cervical erosion in the IUCD users was significantly higher compared to the OCP and the control groups (*p*<0.05). Table 2 shows a detailed specific characteristics of the studied groups.

Gram stain findings of the vaginal discharge were different among the groups (*p*<0.05). Although the OCP group showed little changes in Gram stain findings, there was a higher changes in the IUCD group. *Lactobacilli* were the dominant organism in the group using OCP and control (*p*>0.05).

A score with normal flora (Nugent score 1-3) was present in 67.6% of IUCD group, 85.3% of OCP group, and 94.1% of the control group. The rates of the women with intermediate scores or bacterial vaginosis

Table 1 - Baseline characteristics of women enrolled in the study.

Variables	No. of patients (%)			P
	IUCD group	OCP group	Control group	
Age				
Range	16 - 42	17 - 41	16 - 42	
Mean*	30.9 ± 7.0	28.2 ± 6.8	27.9 ± 6.6	>0.05
Residence				>0.05
Urban	23 (67.6)	26 (76.5)	22 (20.8)	
Rural	5 (14.7)	6 (17.6)	7 (6.6)	
Urban stums	6 (17.6)	2 (5.9)	5 (4.7)	
Literacy				>0.05
Literate	30 (88.2)	34 (100)	32 (94.1)	
Illiterate	4 (11.8)	-	2 (5.9)	
Parity				>0.05
1	12 (35.3)	20 (58.8)	12 (35.3)	
2	11 (32.6)	9 (26.5)	11 (32.6)	
3	4 (11.8)	1 (2.9)	4 (11.8)	
> 4	5 (14.7)	1 (2.9)	4 (11.8)	
Married	34 (100)	34 (100)	34 (100)	>0.05
Period of married **	8.34 ± 5.6	7.8 ± 4.2	8.34 ± 4.3	>0.05

*values are mean ± SD, **years, IUCD - intrauterine contraceptive device, OCP - oral contraceptive pill

by Gram stain were 20.6% and 11.7% in the IUCD group, 8.8% and 5.9% in the OCP group, 2.9% and 2.9% in the control group, respectively. There was a significant difference between the IUCD group and the OCP or the control groups ($p < 0.05$).

The proportion of women growing *Escherichia coli* (*E. coli*) in vaginal discharge bacterial culture in the IUCD users, OCP users and the control group were found to be 14.7%, 2.9%, 0%, respectively ($p < 0.05$). There was 5-fold increased risk for vaginal *E. coli* colonization in the IUCD users. The women with *E. coli* colonization were significantly more likely to have an abnormal Nugent score. None of the other organisms isolated in the vaginal culture changed significantly among the groups ($p > 0.05$).

The prevalence of the women with *Candida* species in the OCP, IUCD and control groups were found to be 14.7%, 11.8% and 5.9%, respectively ($p > 0.05$). *Trichomonas vaginalis* in vaginal discharge in the IUCD users was higher than in those in the OCP and control group, but the difference was not statistically significant ($p > 0.05$). Table 3 shows a more detailed laboratory findings of the studied groups.

Cytological findings were predominantly inflammatory with a significant difference among groups. Four cases of actinomyces-like organisms were detected in the IUCD users, which were statistically different among groups ($p < 0.05$). While low grade squamous intraepithelial lesion (LGSIL) was present in 5.9% of the IUCD users, the OCP and control groups had no positivity of LGSIL ($p > 0.05$). No case

of high grade squamous intraepithelial lesion (HGSIL) was detected in groups. None of the study subjects had malignant cytological changes.

Discussion. Choice of contraceptive methods may have important effects on the vaginal microbial flora. The insertion of IUCD and OCP use is prevalent and an effective reversible methods of contraception worldwide.^{11,18} It is generally recognized that the usage of IUCD results in quantitative and not qualitative alterations in the normal vaginal bacterial flora. Increase risk of pelvic inflammatory disease has been reported

Table 3 - The laboratory findings of the IUCD, OCP and control groups.

Variables	No. of patients				P
	IUCD group	OCP group	Control group		
Bacterial vaginosis					< 0.05
Nugent score 0-3	23 (67.6)	29 (85.3)	32 (94.1)		
Nugent scores 4-6	7 (20.6)	3 (8.8)	1 (2.9)		
Nugent scores 7-10	4 (11.7)	2 (5.9)	1 (2.9)		
Gram stain of vaginal discharge					< 0.05
Gram positive cocci	4 (11.7)	2 (5.9)	1 (2.9)		
Gram negative cocci	4 (11.7)	1 (2.9)	1 (2.9)		
GPGN coccus bacilli	2 (5.9)	2 (5.9)	1 (2.9)		
Yeast cells	4 (11.7)	4 (11.7)	2 (5.9)		
Pus cells	6 (17.6)	2 (5.9)	1 (2.9)		
Vaginal discharge culture					
<i>Escherichia coli</i>	5 (14.7)	1 (2.9)	-		< 0.05
<i>Klebsiella</i> species	-	1 (2.9)	-		
<i>Pseudomonas pyocyanus</i>	1 (2.9)	1 (2.9)	-		
<i>Staphylococcus aureus</i>	3 (8.8)	1 (2.9)	1 (2.9)		
CONS	2 (5.9)	2 (5.9)	2 (5.9)		
<i>Streptococcus fecalis</i>	2 (5.9)	1 (2.9)	1 (2.9)		
<i>Enterobacter</i> spp.	2 (5.9)	1 (2.9)	1 (2.9)		
More than one type	2 (5.9)	-	-		
<i>Candida</i> spp.	4 (11.8)	5 (14.7)	2 (5.9)		> 0.05
Total	20 (58.8)	13 (38.2)	7 (20.5)		< 0.05
Sterile	14 (41.2)	21 (61.7)	27 (79.4)		
Wet mount examination					
<i>Trichomonas vaginalis</i>	6 (17.6)	3 (8.8)	2 (5.9)		> 0.05
Cytological findings					
Inflammatory					< 0.05
Minimal	-	22 (64.7)	31 (91.2)		
Moderate	12 (35.3)	9 (26.5)	3 (8.8)		
Copious	22 (64.7)	3 (8.8)	-		
Actinomyces like organisms	4 (11.7)	-	-		< 0.05
LGSIL	2 (5.9)	-	-		> 0.05
HGSIL	-	-	-		

LGSIL - low grade squamous intraepithelial lesion,
HGSIL - high grade squamous intraepithelial lesion,
CONS - coagulase negative *Staphylococcus*, IUCD - intrauterine contraceptive device, OCP - oral contraceptive pill

Table 2 - Clinical examination and complaints data of women in the groups

Variables	No. of patients (%)			P
	IUCD group	OCP group	Control group	
Speculum examination				
Erosion around cervix	5 (14.7)	-	-	< 0.05
Vaginal discharge				
Minimal	6 (17.6)	7 (20.6)	4 (11.8)	
Moderate	15 (44.1)	8 (23.5)	7 (20.6)	
Profuse	5 (14.7)	4 (11.8)	2 (5.9)	
Total	26 (76.4)	19 (55.8)	13 (38.2)	< 0.05
Backache	10 (29.4)	5 (14.7)	3 (8.8)	< 0.05
Dyspareunia	3 (8.8)	1 (2.9)	1 (2.9)	> 0.05
Dismenorrhea	6 (17.6)	3 (8.8)	3 (8.8)	> 0.05
Increased menstrual flow	4 (11.7)	5 (14.7)	5 (14.7)	> 0.05
Decreased menstrual flow	5 (14.7)	4 (11.7)	3 (8.8)	> 0.05
External genital pruritis	9 (26.5)	5 (14.7)	3 (8.8)	> 0.05

IUCD - intrauterine contraceptive device, OCP - oral contraceptive pill

among IUDC users.^{12,18} On the other hand, Beerthuis et al¹⁹ reported that IUCD users, selected for low risk of sexually transmissible disease, do not have excess pelvic inflammatory disease (PID) but there is a higher risk shortly after insertion, so limiting IUCD replacements will reduce the incidence of PID.

The extent and type of microbial alteration may likely depend on a combination of additional factors, such as literacy, socio cultural status. Age, number of parity, rate of rural residence, number of illiterate were higher in the IUCD users than OCP and the control groups ($p>0.05$). We observed that the IUCD users had lower socio economic levels. Backache, vaginal discharge were more frequently complained among IUCD users as compared to OCP and control groups ($p<0.05$). These complaints could be related to the changes in the vaginal and cervical flora or other reasons.

Several studies reported that BV frequency is higher in women using IUCD than in those using other contraceptive methods.^{5,10,18,20} The H_2O_2 produced by *Lactobacilli* may inhibit or kill other vaginal flora, particularly flora that lack or have low levels of H_2O_2 -scavenging enzymes. *Lactobacilli* use glycogen to produce lactic acid, which helps maintain both the low pH and the dominance of *Lactobacilli* and other acidophilic bacteria in the vagina.^{3,11} The loss of *Lactobacilli* may play a role in the pathogenesis of both BV and *E. coli* vaginal colonization.^{2,3,11} Several studies documented a higher prevalence of BV with abnormal Nugent score among IUCD users than among other contraceptive users.^{10,20} Our data also showed that IUCD users had elevated Nugent scores and had an increased risk for BV (Table 3).

In the present study, it was shown that IUCD use was associated with vaginal colonization with *E. coli*, as well as with an elevated Nugent score. The association between BV and *E. coli* vaginal colonization has been reported among women who use cervical cap and other spermicide. Gupta et al¹¹ reported that the use of spermicidal contraception was associated with an abnormal Nugent score, colonization with *E. coli*, *Enterococcus* species and anaerobic gram-negative rods. Similarly, this study also showed that IUCD users had a significant increased risk for *E. coli* vaginal colonization. Five-fold increased rate of *E. coli* vaginal colonization was found in the IUCD group as compared with the OCP group ($p<0.05$).

It has been reported that the use of OCP have little effect on the vaginal flora.^{11,21} Similarly, we also found the little effect of OCP on the vaginal flora. The OCP use had a slight effect on vaginal *E. coli* and other microorganism ($p>0.05$).

It has been reported that OCP users are more likely to develop vaginal yeast than non-users.^{22,23} In

our study, the prevalence of *Candida* among groups in the vaginal cultures were found to be 11.8%, 14.7%, 5.9%, respectively. The isolation rate of vaginal yeast in the OCP users did not reach the values found in the previous studies. It was found that vaginal yeast in the OCP users was higher than the IUCD users and control group, but there was no statistically significant difference ($p>0.05$).

Krishna et al¹² and Nayer et al²⁴ reported the rates of cervical erosion among IUCD users as 13.5% and 20%, respectively. Similarly, in the current study, cervical erosion was found in 14.7% of the women using IUCD ($p<0.05$). Cervical erosion were not detected in the OCP and control groups. According to this finding it could be considered that IUCD may be responsible for cervical erosion.

Significant increase in the inflammatory smear among IUCD users have been reported.^{12,25,26} In the present study, increased incidence of inflammatory smear in the IUCD group was found compared to that in the OCP and control groups, which was statistically significant ($p<0.05$). The OCP group had slight increase in the incidence of inflammatory smear ($p>0.05$). The incidence of dysplasia in the present study is comparable to that in the general population.^{12,13,25} Kaplan et al²⁶ reported that there was no difference in the rates of cervical squamous intraepithelial lesions in the IUCD user as compared with non-users. We found that LGSIL was present in 2 (5.9%) of the IUCD users. The other groups had no LGSIL. This finding is not in agreement with Kaplan et al.²⁶ One of 2 cases with LGSIL had also cervical erosion.

In this study, 100% of the participants were married, infection with *Neisseria gonorrhoeae* was not found. The prevalence of trichomoniasis in the IUCD, OCP and control groups were found as 17.6%, 8.8%, 5.8% ($p>0.05$). It has been reported that IUCD users are more likely to develop trichomonas infection.^{13,20,27,28} Our results also showed that trichomoniasis was frequent in the IUCD users, but not in the OCP and control groups.

It has been reported that IUCD users are more likely to develop actinomyces infection as compared with other contraceptive methods.^{29,30} On the other hand, Krishna et al¹² did not found a relation between actinomyces infection and IUCD use. In our study, actinomyces-like organisms were found in 11.7% of cervical smears in the IUCD users, but not in the OCP and control groups ($p<0.05$). All women with actinomyces-like organisms had profuse or moderate vaginal discharge and 2 of them had backache. The results suggest that the use of IUCD might act as a factor for actinomyces infection.

In conclusion, IUCD use clearly alter the normal vaginal flora although OCP method of contraception appears to have minimal effects on the vaginal microbial flora. The results of this study suggest that women with IUCD may be at a higher risk for cervico-vaginal infections.

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