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CERVICAL CYTOLOGIC AND COLPOSCOPIC CHANGES IN CASES USING IUDs FOR A LONG TIME

BulatAytek Şık¹, Mehtap Şentürk², Serkan Kumbasar³, Elif Sumer⁴, Yolda Arzu Aba⁵, Özlem Dülger¹

¹Reproductive Endocrinology and Infertility Clinical, Şişli Kolan International Hospital, Istanbul, Turkey

²Department of Gynecology and Obstetric, Bakırköy SadiKonuk Education and Research Hospital, Istanbul, Turkey

³Department of Gynecology and Obstetric, Sakarya Education and Research Hospital, Sakarya, Turkey

⁴Department of Gynecology and Obstetric, Gaziosmanpaşa-Taksim Education and Research Hospital, Istanbul, Turkey.

⁵Bandırma Onyeddi Eylül University Health Science Faculty, Balıkesir, Turkey

Corresponding author; E-mail: yaba@bandirma.edu.tr

ABSTRACT

The present study aims to examine cervical cytologic and colposcopic changes in patients using IUDs for a long time. Our study is a cross-sectional study that enrolled 188 cases. 62 monogamous patients without a history of sexually transmitted infection, and using an IUD for 5 years or more were included in the study group (Group 1). 126 patients without a previous anamnesis of IUD use and patients in whom IUDs were not detected during the examination were enrolled in the control group (Group 2). All patients underwent a colposcopic examination and a smear was obtained. Patients with a history of HPV were excluded from the study. Smear test results and findings of colposcopic examination of the study and control groups were compared. Gravida, Parity, Number of Births, age at first coitus were determined through the patients' histories. The mean age of the patients in Group 1 was 38.67, age at first coitus was 19.49, and the mean age in Group 2 was 39.11 and age at first coitus was 18.95 years. There was a significant difference detected in the comparison of Gravida ($p=0.03$), while parity and NSD parameters were not found significantly different ($p=0.15$, $p=0.14$). Rates of mild ectopy in Group 1 and Group 2 were 25.8% and 19.18%, moderate ectopy were 25.8%, 28.6%, severe ectopy were 11.3% and 23.8%, respectively. Polyp detection rate was found 16.7% in Group 1, while it was 40.9% in Group 2. On the other hand, leukoplakia detection rate was 8.3% in Group 1, while it was found 18.2% in Group 2. no statistically significant difference was detected between the two groups. F. Mosaic rate in patients using IUDs was found significantly lower ($\chi^2= 3.74$ $p= 0.05$). As a result of our study, no significant difference could be shown in NTZ, ATZ, Asetowhite, C.Mosaic, F.Punction, C.Punction, Atypical Vascularization, and Schiller rates.

Keywords: Cervical smear, Colposcopy, Inflammatory changes

1. Introduction

Intrauterine devices are reversible, long-lasting, and the most commonly used birth control method worldwide [1, 2]. It is still unclear how IUDs work. It is believed that it has various effects on sperm, ovum, fertilization, implantation, and endometrium [3]. The optimal time for IUD insertion is the menstrual period [1, 2, 3]. Postpartum IUD insertion can be performed during the postpartum control visits 4-8 weeks after delivery [2, 4]. Studies could not prove the fact that IUDs increased the risk of pelvic infection and caused an ectopic pregnancy. Of all other female genital organ cancers, cervical cancer is the most common cancer type for women worldwide. Cervical cancer, with an ever-increasing incidence rate in younger females worldwide, has been one of the major causes of morbidity in women below 40 years of age [5]. Cervical cancer is seen at lower rates in developed countries where the public health is improved, while it is more prevalent in less developed countries [6]. Although Israel is not a developed country; women have the lowest incidence rates of cervical cancer since sexual behaviors, circumcision, and hygiene habits have an important place in the etiological causes [5, 7].

Cervical cancer doesn't progress suddenly and remains as precancerous lesions over the course of many years. This allows for an early diagnosis through some methods of cytologic and clinical diagnosis and creates a window of opportunity for a curative treatment [5, 6, 8]. Cytology and colposcopy are the most advantageous techniques used in the diagnoses of cervical cancer and pre-invasive lesions [5]. However; cytology doesn't provide the last finding of the disease, it is a screening method that should be performed with others for further examination (Colposcopy, Histo-Pathology). It is acknowledged that colposcopy and cytology are mutually complementary methods [9]. Cytology examines exfoliated cells, while colposcopy examines the changes occur in the vascular structure of the cervix [10]. According to some research, endocervical curettage (ECC) should be performed routinely in all cases with abnormal cytologic findings [8, 11]. ECC is performed when colposcopic examination is unsatisfactory or fails to provide any finding that explains the abnormal cytology during a colposcopic examination [8]. Patients with an abnormal pap smear result or patients with a suspicious-looking cervix even they had a (-) pap smear should be evaluated by colposcopy and colposcopy directed biopsy [12, 13, 14]. The false-negative rate of the Pap smear test is about 20%-40%. These rates also cover the patients diagnosed with cervical cancer shortly after a normal cytology [15].

2. Method:

Our study aims to investigate cervical cytologic and colposcopic changes in patients using IUDs for a long period of time. The present study is a cross-sectional study enrolling 188 cases who presented to Istanbul Bakırköy Sadi Konuk Hospital, Department of Gynecology and Obstetrics, Gynecology Clinic. The study group (Group 1) included 62 monogamous patients without a history of sexually transmitted infection and using an IUD for 5 years or more. On the other hand, the control group (Group 2) included 126 patients without a previous anamnesis of IUD use and patients in whom IUDs were not detected during the examination. All cases underwent a colposcopic examination performed by the same gynecologist with the same colposcopic device (LEICA CLS 150 XC MS5, Germany) and a smear was obtained from all patients. Cases with a history of HPV were excluded from the study. Smear test results and colposcopic examination findings of the study and control groups were compared. Age, Gravida, Parity, Number of births, age at first coitus were determined through the patients' histories. A smear was obtained prior to the examination. The cervix was examined with the naked eye before applying

Acetic Acid (AA) and the presence of displaced endocervical epithelium (Ectropion or Ectopy) was noted. Ectropion and/or ectopy was classified as mild (Periorificial), moderate, and severe (reaching to Fornix zone) according to the area occupied in the cervix.

Previously, the presence or absence of atypical vascularization was recorded using a green filter by wiping the cervix with serum physiologic. Following this procedure, cervical mucus was removed with a 3% of AA solution and after waiting for about a minute, Squamocolumnar Junctions (SCJ) and Transformation Zone (TZ) were observed. The response of the cervix to AA was evaluated as mild and dense according to the severity of whitening. Mosaic and punctuation patterns were described as coarse and fine. Colposcopy was considered satisfactory in cases where SCJ could be observed clearly and continuously and the entire TZ and any extent of a lesion, if present, were visible. On the other hand, colposcopy was considered unsatisfactory in cases where SCJ weren't observed clearly and TZ couldn't be seen fully and in cases with a lesion extending into the cervix canal where the upper limit could not be seen clearly. ECC was performed with the Novak curette in patients with unsatisfactory colposcopy in order to determine the treatment protocols and to examine the endocervical canal, as well. Punch biopsy was performed on mild-dense Aceto-White (AW) areas, Schiller positive areas and areas with fine or coarse mosaics and punctuations. Before obtaining the cytology and histo-pathology results, IUDs were not removed from any of the patients, including those diagnosed with lesions. Biopsy specimens fixed in 10% formaldehyde were sent to pathology. After a routine histo-pathological examination, 5-micron tissue sections stained with Hematoxylin Eosin were examined under a light microscope at 40x, 100x, and 400x magnifications.

2.1. Statistical Analysis

Statistical analysis of the results was performed using a SPSS 11.0 (Chicago_USA) package program. Chi-square test was employed for comparing the classified variables of the groups, and t test was used in independent samples to compare the continuous variables. Alternatively, Mann-Whitney U test was performed in the case of a different variations or a low number of subjects. $p < 0.05$ was considered statistically significant. Classified variables were presented as number (n) and percentage (%) in the table.

3. Findings

The mean age of the cases in Group 1 and Group 2 were 38.67 years and 39.11 years, respectively. The mean age at first coitus in Group 1 and Group 2 were 19.49 years and 18.95 years, respectively. No significant difference was found between the two groups regarding age and age at first coitus ($t=0.36$, $p=0.72$; $t=0.91$ $p=0.36$). There was a significant difference found in the comparison of Gravida ($p=0.03$); while parity and NSD parameters were not significantly different ($p=0.15$, $p=0.14$). Demographic characteristics of the patients are shown in Table 1.

Table 1. Demographic Characteristics of the Patients

	Group I (n:62) Mean±SD	Group II (n:126) Mean±SD	t	p
Age*	39.1±6.4	38.7±10.1	0.36	0.72
Age at first coitus*	18.9±2.8	19.5±4.2	0.91	0.36
Gravida**	4.12	3.59		0.03
Parity**	3.016	2.74		0.15
NSD**	2.62	2.61		0.14

* Student - T Test , **Mann Whitney – U Test

Cross Table Ectopy results in Group 1 and Group 2 were as follows; Detection rates of Mild Ectopy in Group 1 and Group 2 were found as 25.8% and 19.18%, Moderate ectopy as 25.8% and 28.6%, Severe ectopy as 11.3% and 23.8%, respectively. No statistically significant difference was found between the two groups regarding the ectopy rates before colposcopy (Table 2).

Table 2. The Rates of Ectopy Detected with the Naked Eye before Colposcopy

	ECTOPY			
	Absent	Mild	Moderate	Severe
Group 1 (%)	37.1	25.8	25.8	11.3
Group 2 (%)	27.8	19.8	28.6	23.8

Smear results of Group 1 and Group 2 were as follows; the rates of unsatisfactory smear were 0.0% and 1.6%, colocyctosis rates were %1.6, %4.9, inflammation were 29.3%, 32.8%, chronic cervicitis were 31.7%, 29.5%, ASCUS were 4.9%, 1.6%, LGSIL were 6.5%, 4.9%, HGSIL were 1.6%, 0.0%, Squamous CA were 2.4% and 0.0%, respectively. No significant difference was detected between the patient and control groups regarding smear test results (Table 3).

Table 3. Smear results of the Groups

Smear results	Group 1(%)	Group 2(%)
Normal	22	24.6
Unsatisfactory Smear	0	1.6
Coilocytosis	1.6	4.9
Infection	29.3	32.8
Chronic Cervicitis	31.7	29.5
ASCUS	4.9	1.6
LG SIL	6.5	4.9
HG SIL	1.6	0
Squamous CA	2.4	0

Colposcopic examination results of the patients were as follows; in Group 1 and Group 2, polyp rates were found as 16.7% and 40.9%, leukoplakia as 8.3% and 18.2% respectively. No statistically significant difference was found between the two groups. F.Mosaic rate was detected significantly lower in patients using an IUD ($\chi^2 = 3.74$ p= 0.05) (Table 4).

Table 4. Colposcopic Examination Results of the Patients

Colposcopy Findings	Group 1(%)	Group 2(%)
Unsatisfactory Colposcopy	33.4	18.2
Polyp	16.7	40.9
Leukoplakia	8.3	18.2
Condyloma	25	0
Specific Infection	8.3	0
Cervix CA	8.3	13.6
Erosion	0	9.1
F Mosaic n, (%)	3 (4.8%)	18(14.3%)

In ECC results of Group 1 and Group 2, chronic cervicitis rate was 10% in patients with IUDs, while it was found 6.9% in the control group. HG SIL detection rates were 1.7% and 3.4 in Group 1 and Group 2, respectively. There was no statistically significant difference observed between the two groups.

The biopsy results in Group 1 and Group 2 were as follows: LGSIL; 13.3% , 16.4%, HGSIL; 0%, 3.3%, Squamous CA; 1.7% ,3.3%, Coilocytosis; 11.7% , 6.6% , Endometriosis; 0.0%, 0.8%, respectively. No statistically significant difference found between the two groups (χ^2 : 6,18 p=0,52) (Table 5).

Table 5. Colposcopic biopsy results of the patients

Biopsyresults	Group 1(%)	Group 2(%)
Chronic Cervicitis	23.3	28.7
LG SIL	13.3	16.4
HG SIL	0	3.3
Squamous CA	1.7	3.3
Coilocytosis	11.7	6.6
Erosion	0	8
Endometriosis	0	0.8

4.Discussion

IUDs are one of the most efficient and the simplest contraception method used in patients selected very carefully. Non-specific, non-infectious, namely; the development of sterile vaginitis are observed more frequently during the use of an IUD when compared to the other contraceptive methods. In gynecology, studies investigating the relationship between malignancies and IUD use could not reach a conclusion on the possible carcinogenic potential of IUDs. As a result of IUD use, cytologic atypia are commonly observed in the squamous and columnar epithelium of the cervix. Nuclear atypia in the squamous epithelium are generally mild, but the severity may increase in the columnar epithelium. In fact, this atypia changes to a severe atypia that supports adenocarcinoma in situ and adenocarcinoma [15]. In a study carried out by Fiore et al. [16], cervical pathologies developed as a result of contraceptive methods were compared in women using IUDs and women using combined oral contraceptives. Cervical smear results revealed that mild dyskaryosis rate was 17.6% in women using an IUD, while it was found 10.53% in women using steroid OCs [16]. In another study performed by Howard et al. [17], the relationship between contraceptive methods, cervical dysplasia and carcinoma in situ was investigated. In this study, when the group using an IUD and the other group using OCs were compared, carcinoma in situ rate was found to be 1.4 times higher in the OC group, however; it was concluded that this rate was not statistically significant. In the recent years, a great success has been achieved in gynecology thanks to screening tests allowing for an early diagnosis and the treatment of cervical pre-invasive lesions. Nevertheless, unnecessary interventions may take place due to the low positive predictivity of the screening tests. In addition, even the high false negative rate of the screening tests affects their reliability, they are still of a great value as being the simplest and the most commonly used tests that can be performed widely.

In a study conducted by Risse et al. [18], cytologic and histological findings developed as a result of IUD use were investigated. Rates of inflammatory changes were detected as 85.9% in the group with IUDs, and as 75.3% in the control group, however; there was no significant difference found in the comparison of infection rates between the control group and the group using IUDs. In a series of 400 cases conducted by Fahmy et al., a statistically significant difference was found when the infection rates of the group using IUDs and the control group were compared ($p < 0.05$) [19]. In our study, infection rates were detected as 29% in women using IUDs, and as 32% in the control group. This difference was not found statistically significant ($p = 0.46$).

In a study by Usha et al. [15] conducted in 2603 patients using an IUD for 5 years, smear results obtained before IUD use and after a 5-year IUD use were compared. Dysplasia rate was found as 2.5% in smear results obtained before IUD use, and as 4.2% , 1.6% , 3.8% , 0.9%, and 3%, respectively, in smear results of a 5-year follow-up. According to the smear results obtained prior to IUD use, no change was detected during a 5-year follow-up of women with negative smear results or presenting inflammatory changes. Over the course of a 5-year follow-up, none of these women diagnosed with dysplasia before an IUD insertion developed carcinoma in situ. As a result of this study, it was concluded that the use of IUDs did not pose a risk of cervical dysplasia or cancer development. Additionally, a study by Risse et al. [18] expressed that a long term use of IUDs did not entail a risk of moderate or severe dysplasia or development of carcinoma in situ, and that even atypical squamous metaplasia and mild dysplasia might be detected in patients using IUDs, they could regress in time when the IUD was removed.

HSu et al. [20] published a wide series of studies reporting that there was no association between the long term use of IUDs and uterine malignancies at all. A study published by Pike et al. [21] increased the reliability of IUDs by revealing that IUDs containing progesterone in particular had a reducing effect on the incidence of endometrial cancer. In our study, ASCUS, LGSIL, and HGSIL rates were detected as 1.6%, 4.9%, 0.0%, respectively. When these results were compared with those of the control group, no statistically significant difference was found ($p = 0.46$). A wide series of studies performed by Lassise et al. [22], enrolling a total of multicentric 1268 patients, investigated the association of cervical cancer with the types of IUDs and the duration of IUD use. It was concluded that using a copper IUD reduced the risk of cervical cancer significantly, while mechanical IUDs had no effect on cervical cancer development. It was also concluded that a long term IUD use had no positive protective effect on invasive cervical cancer development. In our study, there wasn't any squamous cancer case found in patients using an IUD. Yet, randomly selected patients in the control group were detected with squamous cancer at a rate of 2.4%. This, indeed, has once again proved the importance of a smear test that is used for screening.

In a study by Fahmy et al. [19], 100 patients with an IUD were compared with the control group

in terms of specific infection, dyskaryosis, and CIN and as a result, no significant difference was found ($p>0.05$). On the other hand, our study has found the fine mosaic rates significantly lower in patients with IUD than those in the control group ($p=0.05$). There was no significant difference detected in other colposcopic findings ($p=0.08$). In a study by Fahmy et al. [19], a statistically significant finding could not be found in fine mosaics. No significant difference was detected in Aceto-White areas, leukoplakia, punctuation and atypical vascularization ($p>0.05$), however; inflammatory colposcopic changes showed a significant difference in both Lippes loop group and Cu T200 (with copper) group ($p<0.05$). Similar to other studies conducted to date, our study could not find any association between IUD and invasive cervical cancer. Nonetheless, as in other studies [23], we cannot suggest that the copper IUD use has a protective effect on invasive cancer. There is a difference between our study and a study carried out by Engineer et al.[23] in finding an increased dysplasia rates in patients with copper IUDs.

4. Results

After obtaining smear test results, we performed colposcopy in patients using IUDs for more than 5 years. We investigated cervical changes that might be caused by >5 years of IUD use. As a result of our study; no significant difference could be detected in NTZ, ATZ, Aceto-white, C.Mosaic, F.Punction, C.Punction, Atypical Vascularization, and Schiller rates. To conclude, cervical changes that may result from a long term IUD use still remains a topic needing further investigation.

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