ORIGINAL RESEARCH ARTICLE

The effects of intrauterine device on cervico-vaginal smears with liquid-based cytology technique: A North-Eastern Anatolia region study in Turkey

DOI: 10.29063/ajrh2022/v26i1.5

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Abstract

Intrauterine device (IUD), is one of the most efficient methods of contraception. The aim of study to investigate the effects of intrauterine device in cervicovaginal smears with liquid based cytology technique in our patient population. Cervicovaginal smears of 5492 patients who sought the services of the pathology department in a sixmonth period were reviewed retrospectively. Samples were prepared with liquid based cytology technique. The patients using IUD as contraceptive method (n= 562 cases) were included in the study. The samples taken with the conventional method were excluded from the study. The results were categorized according to the Bethesda system. The age range of the patients was 18-61 years (mean age: 34.6). The most common diagnosis was "negative for intraepithelial lesion or malignancy" (97.2%). In 307 patients (54.6%) there were infection and only in 93 out of them (30.2%) a specific agent was detected. *Actinomyces* (11%) were recorded as the most common infectious agent, followed by *Gardnerella vaginalis* (2.8%) and Candida species (2.4%). There were reactive changes in 134 cases (23.8%). In 13 cases (2.3%) epithelial cell abnormalities were detected. The most common cytopathologic diagnosis was ASC-US (atypical squamous cells of undetermined significance) in patients who had epithelial cell abnormalities (2.1%). In conclusion, IUDs increase the frequency of genital infection by disrupting the genital flora. In our study the most frequent agent was Actinomyces, and this rate was higher than some studies. This high rate for Actinomyces may be associated with IUDs that are frequently used for contraception in Erzurum province with long term uses. *(Afr J Reprod Health 2022; 26[1]: 47-52).*

Keywords: IUD, cervico-vaginal smear, liquid based cytology, PAP test

Résumé

Le dispositif intra-utérin (DIU), est l'une des méthodes de contraception les plus efficaces. Le but de l'étude est d'étudier les effets du dispositif intra-utérin dans les frottis cervico-vaginaux avec une technique de cytologie à base de liquide dans notre population de patients. Les frottis cervico-vaginaux de 5492 patientes qui ont sollicité les services du service de pathologie au cours d'une période de six mois ont été revus rétrospectivement. Les échantillons ont été préparés avec une technique de cytologie à base de liquide. Les patientes utilisant le DIU comme méthode contraceptive (n= 562 cas) ont été incluses dans l'étude. Les échantillons prélevés avec la méthode conventionnelle ont été exclus de l'étude. Les résultats ont été classés selon le système Bethesda. La tranche d'âge des patients était de 18 à 61 ans (âge moyen : 34,6). Le diagnostic le plus fréquent était « négatif pour une lésion intraépithéliale ou une malignité » (97,2 %). Chez 307 patients (54,6%) il y avait une infection et seulement chez 93 d'entre eux (30,2%) un agent spécifique a été détecté. Les actinomyces (11 %) ont été enregistrés comme l'agent infectieux le plus courant, suivis de Gardnerella vaginalis (2,8 %) et des espèces de Candida (2,4 %). Il y avait des changements réactifs dans 134 cas (23,8%). Dans 13 cas (2,3%) des anomalies des cellules épithéliales ont été détectées. Le diagnostic cytopathologique le plus courant était l'ASC-US (cellules squameuses atypiques de signification indéterminée) chez les patients présentant des anomalies des cellules épithéliales (2,1 %). En conclusion, les DIU augmentent la fréquence des infections génitales en perturbant la flore génitale. Dans notre étude, l'agent le plus fréquent était Actinomyces, et ce taux était plus élevé que certaines études. Ce taux élevé d'Actinomyces peut être associé aux DIU qui sont fréquemment utilisés pour la contraception dans la province d'Erzurum avec des utilisations à long terme. *(Afr J Reprod Health 2022; 26[1]: 47-52).*

Mots-clés: DIU, frottis cervico-vaginal, cytologie en milieu liquide, test PAP

Introduction

Intrauterine devices (IUDs), used by millions of women worldwide, is one of the most efficient methods of contraception. The most serious disadvantage of intrauterine devices is creating a potential risk for cervical and uterine infections[1,2]. An IUD has a "body" which rests in the uterine cavity, a small "neck" which occupies the endocervical canal and a "tail" that may be seen or felt at the external os. With its tail IUD creates a foreign body reaction and by forming a solid surface for bacterial colonization it plays an important role in changing the flora of the women genital tract[2-4]. IUDs may result intense inflammatory response in epithelial cells and various reactive cytological changes with its' local irritation and pressure effects[3,4]. Liquid base cytology (LBC) is the first major change in preparation method for cervical screening samples for more than 50 years. It is a better alternative to conventional smear because of lower rate of unsatisfactory smears. Furthermore, it has advantages such as HPV DNA testing can perform in residual LBC samples[5,6]. We want to investigate effects of IUD on cervical epithelial cells and flora in cervicovaginal smear (CVS)s which prepared with LBC technique.

Methods

For a sixmonth period 5492 CVSs was accepted Erzurum Regional Training and Research Hospital, Department of Pathology and prepared with LBC technique. CVSs were reviewed retrospectively. patients which indicated IUD use clinically (n=562) were included the study and evaluated. Conventional samples were excluded from the study. BD Surepath PAP test kit (BD Diagnostics-tripath, Burlington, NC, USA) was used in LBC preparation. Examples in ethanol-based fixative was centrifuged 2 times (1st 2min 15sec, 2nd 10 min 15 sec). Then cellular sample was mixed with a vortex homogeneously. 40 micro liter sample pulled out with micropipette and sample spread as a thin layer in a circular area of microscope slide. Cytopathological evaluation was made according to the Bethesda System[7]. Demographic features of the patients collected from pathology reports. The incidence of epithelial cell abnormalities (ECA), the accompanying reactive changes and identified pathogens were examined. Data analysis was performed using SPSS 20.0 program. In the evaluation of results descriptive statistics was shown in the form of mean ± standard deviation, nominal variables were shown as number of cases and the percentage (%).

Results

The age range of the patients was 18-61 years (mean age: 34.67±7.86). 546 patients (97.2%) were negative for intraepithelial lesion or malignancy. Three (3) cases (0.5%) were reported as unsatisfactory for evaluation. In 307 patients (54.6%) infection was detected. 93 out of 307 patients (30.2%) an infection agent was found. ECA was detected in 13 cases (2.3%). 12 of these cases were ASC-US (atypical squamous cells of undetermined significance) and one of them was AGUS (atypical glandular cells of undetermined significance) (Table 1). In the case series LSIL (low-grade squamous intraepithelial lesion), HSIL (high-grade squamous intraepithelial lesion) and ASC-H (atypical squamous cells cannot exclude HSIL) were not detected. Infection was found in 54.6% of cases. The major cause of infection in agent positive group was *Actinomyces* species (AS) which is followed *Gardnerella vaginalis* (GV) and *Candida species* (CS), respectively (Figure 1a,1b,1c). AS, GV and CS found in 62 cases (11%), 16 cases (2.8%) and 14 cases (2.4%), respectively. However, in a significant number of the cases with infection no agents were specified (Table 1). In 134 cases (23.8%) reactive changes were detected. There were reactive changes due to inflammation in 123 cases, atrophy findings in 3 cases and reactive changes due to the effect of IUD in 8 cases (Figure 1d).

Discussion

IUDs are commonly used contraceptive methods[1,2]. Therefore there are numerous studies about the effects of IUDs, especially on flora. Kalitera *et al*. found specific infectious agents in 29% of IUD (+) patients[1]. In a study specific infectious agent was found 150 out of 300 IUD (+) patients (2). Ferraz do Lago *et al*. found specific infectious agents in 29.1% of IUD users[8]. In our study 30.8% of infection (+)

Table 1: The classification of cases

	Number of cases (n)	Percentages (%)
Unsatisfactory for evaluation	3	0.06%
ECA *	13	2.3%
ASC-US†	12	2.1%
AGUS‡	1	0.2%
Negative§	546	97.1%
Infection	307	54.6%
Agent (-)	214	69.8%
Agent (+)	93	30.2%
Total	562	100.0%

*epithelial cell abnormalities, † Atypical squamous cells of undetermined significance, ‡ Atypical glandular cells of undetermined significance, § Negative for intraepithelial neoplasia or malignancy

patients, a specific agent was detected and the most common infectious agent was AS.

It is estimated that 7-10% of women with an IUD have *Actinomyces* bacteria on their CVS at some stage and the frequency is related to the duration of continuous IUD use. In a small number of cases women with an IUD develop pelvic actinomycosis, usually a tubo-ovarian abscess, presumably through ascending infection[3,9].

In the literature, the incidence of AS in IUD (+) patients is variable. In a study from Malasia the researchers examined results of CVS of 350 IUD (+) women the incidence of AS was found as 2%[4]. In another study from Philadelphia, USA, AS was found 11.4% of 1540 IUD (+) patients[10]. In a study 20390 cervical smears of Korean women were examined for two years and actinomyces-like organisms were found in 52 cases (0.26%) that 42 out of 52 cases were IUD users[11]. In studies from Turkey the incidence of AS is variable, too. In studies from Mardin and Ankara provinces AS was found 4% in IUD (+) patients[2,12]. Ocak S *et al.* found AS in 11.7% of IUD users in Antakya province which is a South Anatolia Region of Turkey[13]. In our study the incidence of AS in IUD (+) patients was detected as 11%. This rate is similar to some studies in the literature while it is quite higher than others. This height for AS may be associated with that IUDs were frequently used contraceptive methods in Erzurum province, long term and continuous use of them.

In the study of Pillary *et al.* the most common cervicitis factors in IUD (+) patients were GV 42%, CS 28% and *Actinomyces-like* organisms 2%, respectively[4]. Madden *et al.* found the incidence of GV was 37.0% among IUD users[14]. In studies from Turkey the rates of GV 7%, 12%, 20.6%, 26%[2,12,13,15]. In studies from Turkey the rates of CS were 6.4%, 7.3%, 12%[2,12,15]. In our study the rates of GV and CS found as 2.8% and 2.4%, respectively. We did not detect *Trichomonas Vaginalis* (TV). Our rates for GV and CS were lower than most of the studies. The differences about these infectious agents from the literature can be associated with socio-economic status of the region and regional differences such as monogamy tradition of women. In addition, it may associate with frequent use of antibiotics before taken smears and differences in experiences of pathologists. Also, the work was performed with liquid based cytology techniques. In CVSs which are taken with conventional technique the thickness of smears and accompanying of leukocytes and erythrocytes make some difficulties for evaluation. These disadvantages sometimes can cause misdiagnosis or over diagnosis especially for GV and TV. In LBC erythrocytes and some leukocytes are eliminated by density centrifugation and in addition the LBC smears are thinner than conventional smears[9].

In addition to the alterations in the microbial environment and *Actinomyces* infection, usage of the IUD is associated with cellular changes occurring in the various genital tract epithelium[3]. The reactive changes in CVSs related with IUD are giant balloon cells with cytoplasmic vacuoles, large and irregular nucleus, increase in nucleocytoplasmic ratio, cells mimicking HSIL (IUD cells) and atypical glandular cells[2,3,4,7]. Also amorphous calcified bodies, squamous metaplasia and multinuclear giant cells detected more often in CVSs of IUD (+) patients[16]. In our study 1.4% out of cases various reactive changes due to the effect of IUD were detected.

Common findings in literature showed that development of squamous atypia is unrelated to the presence of IUD[2,4,17]. However, some studies showed that the IUDs are significant factors for the development of ASC-US[2,15,18]. In a study which examined CVSs of 9009 IUD (+) patients 622 women (6.9%) had LSIL and ASC-US and 128 women had (1.46%) HSIL[14]. In a different study researchers found ECAs more frequent in patients that used other contraceptive than intrauterine

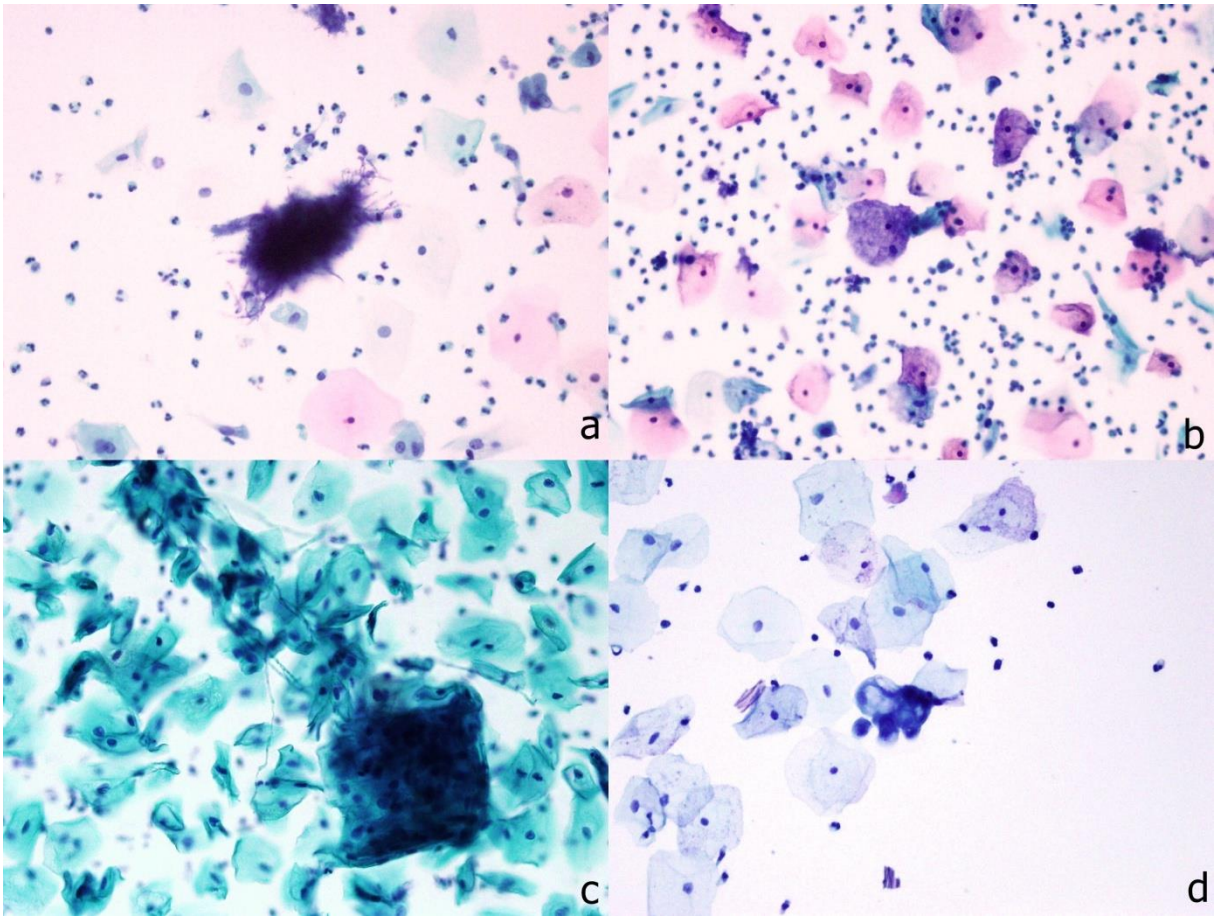

Figure 1: a- *Actinomyces species* that flamentous organisms, with angle branching, like "cotton ball" clusters (PAPx400). b- Squamous cells are covered by a layer of coccobacilli called "clue cells" and there are no lactobacilli in GV infection (Bacterial vaginosis flora) (PAPx400). c- Pseudohyphae, formed by cytoplasmic extension of budding yeasts of *Candida* (PAPx400). d- Reactive cytological changes associated with IUD: The cell cluster have cytoplasmic vacuole that displace the nucleus, creating a signet-ring appearance (PAPx400).

copper device[19]. In our study, ECA was found in 2.3% of IUD users. ASC-US was found in 2.1% of cases and it was the most common ECA in IUD (+) patients. Our results for ECA were similar to literature.

Conclusion

LBC smears can provide useful information about flora, infectious diseases and ECA in the cervicovaginal region. IUDs increase the frequency of genital infection by disrupting the genital flora. In Erzurum province which is a North-Eastern Anatolia region of Turkey the most frequent agents were AS, and this rate was higher than some studies. The variety of results from literature may be associated with socio-economic status of the region and regional, cultural differences. These differences that can affect frequency of medical controls and may explain long-term use of IUDs.

Acknowledgments

This research was presented as an oral presentation at 25th National Congress of Pathology and 6th National Congress of Pathology, in 11-17 October 2015, in Bursa/Turkey and published as an abstract in the congress book.

Conflict of interest

The Authors have no conflict of interest. No support was received from any source for the study.

Contribution of authors

Senay Erdogan-Durmus made substantial contributions to conception, data curation, methodology, analysis, and data interpretation, wrote the final manuscript, and managed the overall progress of the study. Sevilay Ozmen and Ilknur Calik helped in providing and analysing data and checked the final version of the article. Ali Kurt and Hilal Balta conceptualized the study design, analysed and interpreted the data, edited the final version of the article. Yusuf Can and Mehmet Esref Kabalar helped in providing and analysing data, literature research. All authors approved the final version of the manuscript.

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