

THE ASSOCIATION OF CANDIDA INFECTION WITH INTRAUTERINE CONTRACEPTIVE DEVICE

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SUMMARY

In order to analyse the relationship between intrauterine contraceptive device (IUCD) usage and *Candida* infection, we planned to examine cytologically the cervico-vaginal smears of 600 patients stained with Papanicolou method.

Among 56 IUCD users 8 women had *Candida* infection (14%) while 44 of 544 non-users (8%) were infected by this fungus. Our detailed analyses indicated that the prolonged usage of Cu-IUCD may predispose the cervico-vaginal flora for *Candida* especially for the infectious "hyphae" form although statistically the correlation between IUCD usage and candidiasis was not significant ($p>0.05$).

These findings imply the importance of controlled IUCD usage against *Candida* infection and its removal for treatment if necessary. Because retained IUCD may cause serious clinical complications especially in pregnant women such as "fetal candidiasis" which may lead to miscarriage, premature labor or ectopic pregnancy. For these reasons, the possibility of candidiasis should be considered in patients wearing IUCD for a long period.

Key words: *Candida*, IUCD, hyphae, cervico-vaginal smears

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INTRODUCTION

IUCD is an effective, safe and economic way of contraception (1). Despite the notorious history of old-fashioned "Dalkon shield", new devices (Copper-T, hormone releasing IUCD, medicated IUCD) are fairly safe and reliable. IUCDs have a long past but neither their ways of action nor the effects they have on the endometrium and cervico-vaginal microflora have been fully understood.

There are several theories about the action mechanisms of IUCD for preventing pregnancy one of which emphasizes the role of macrophages attracted by this giant antigen (2, 3). The other suggests the induction of matrix metalloproteinases (MMPs) in endometrium by IUCD (4) or the alteration of carbohydrate metabolism and secretory functions of endometrial cells by this device (5). But the role of copper ions is definitely important for this kind of contraception devices not only for their effects on estrogen receptors (5) and reducing pregnancy rate (6) but also for the protective role of copper ions against microorganisms (7).

It's well known that the presence of a foreign body like IUCD alters the vaginal microflora in favor of anaerobes (1), disturbs vaginal ecobiocenosis, reduces *Lactobacilli* population and prepares the environment especially for *Actinomyces* and other enterobacteria (*Gardnerella*, *Staphylococcus*, *Candida*) (8). Although there is abundant data in literature focused on the relationship between IUCD usage and *Actinomyces*, *Gardnerella* spp. and *Trichomonas vaginalis*, the interaction of *Candida* cells with this device is not well studied.

Candida is a dimorphic yeast like opportunistic organism

causing vulvovaginal candidiasis particularly in immunocompromised and debilitated patients (9). The major sign of a *Candida* infection is a thick, curdy and white vaginal discharge (10) which may be cheese-like in the presence of more infectious "hyphal" form (11). The virulence of *Candida* mostly depends on the filamentation and adherence to host cells. This fungus was identified as a normal vaginal flora microorganism; when the conditions are in favor of this opportunistic yeast, the blastospores increase in number and begin filamentation and hyphael forms of *Candida* dominate exhibiting the pathogenic pattern. The pH of the flora is mostly responsible for this colonization since this microorganism survives when the pH is acidic.

While we were examining the literature we have encountered a number of cases reporting "fetal candidiasis" in women having retained IUCD despite pregnancy. Although vaginal colonization with *Candida* is frequent during pregnancy, its transmission to fetus is rare (12–22). This transmission was conducted by a IUCD in all cases.

For these reasons we planned this study to elucidate the possible interaction of candidiasis with IUCD which may cause serious complications particularly in long-term usage. We also discussed our results by the help of literature.

MATERIALS AND METHODS

Vaginal smears were collected from 600 patients who attended Gynaecology and Obstetrics Clinics at Hacettepe University. The smears were taken with a wooden spatula and were stained with Papanicolaou stain. All the smears were examined carefully to

Table 1. Number of women according to the presence of IUCD and Candida

	Number of women		Total
	Absence	Presence	
IUCD	544	56	600
Candida	548	52	600

Table 2. The classification of 600 patients according to the presence of IUCD and Candida

Group I	IUCD (-)	Can. (-)	500
Group II	IUCD (-)	Can. (+)	44
Group III	IUCD (+)	Can. (-)	48
Group IV	IUCD (+)	Can. (+)	8

Table 3. Duration of IUCD usage and the number of women having candida according to the cell type

Duration of IUCD usage	Number of women				
	Candida (-)	Candida (+)			
		Hyphae	Spore	Hy.+Sp	
0-1 year	8	-	-	-	8
1-5 year	18	2	1*	1	22
5<year	5	2	-	-	7
Unknown	17	-	-	2	19
Total	48	8			56

*Spores of non-albicans Candida spp.

be able to detect the association between IUCD and Candida. Each smear was examined for the presence of Candida cells (blastospores or hyphae) by using (x10), (x40) and oil objectives. Detailed examinations were performed by using (x40) or oil objectives.

The type of IUCD was a copper-T, Model T Cu 380 A for all women using IUCD (n=56). Each unit of Cu-T wound consisted of approximately 176 mg copper wire. In addition a single copper sleeve is placed on each of the two transverse arms. Each sleeve contains approximately 68.7 mg of copper. The total surface area of copper on the device is $380 \pm 23 \text{ mm}^2$. Statistical analyses were performed by using the χ^2 test and SPSS package programme.

RESULTS

We examined the smears of 600 patients cytologically by light microscopy (Table 1). These patients were separated into four groups according to the presence and the absence of IUCD and Candida cells, but we compared only two groups (Group III and IV) in this study. These 4 groups are given in Table 2. Among IUCD users (n=56) 8 women were diagnosed as having candidiasis (Group IV). The prevalence of this group is 14.3%. Fourty four of 544 non-users (Group II) were also diagnosed as having candidiasis at prevalence of 8%.

The age range of the patients was 23-73 and the mean age

was 39.82 ± 0.4 . The duration of IUCD usage was evaluated and the data were given in Table 3. This data indicate the effect of prolonged Cu-IUCD usage on the growth of Candida cells in the cervico-vaginal flora. We also separated the Candida cells as "hyphae only", "blastospore only" and "both hyphae and blastospore" in Table 3. This findings pointed out the correlation between long-term IUCD usage and presence of more pathogenic hyphael form.

DISCUSSION

In our study we investigated 600 cases among which 56 patients had IUCD in situ and 52 patients were infected by Candida (Table 1). The prevalence of candidiasis among IUCD users (14.3%) was higher than non-users (8%). However the correlation between the presence of Candida cells and IUCD was not significant according to the χ^2 test ($p > 0.05$). But when we analysed the duration of IUCD usage and the presence of Candida cells regarding their dimorphic situation it was obviously seen that as the IUCD usage prolonged the probability of Candida infection increased. Since we couldn't find such a correlation in the literature we would like to discuss the effect of IUCD on the growth and the transmission of Candida cells based on our microscopic observations.

Because of its advantages in birth control in a safe, easy and economic way, Cu-IUCD usage is quite common in Turkey. The small quantity of copper adjuncted to the T-device reduces the pregnancy rate by mechanisms such as altering endometrial milieu, affecting the biochemistry of endometrial and tubal mucosa, changing the characteristics of cervical mucus, interacting with estrogen receptors and spermatozoa (5, 6). Beside these local effects of Cu^{2+} ions, they also protect the cervico-vaginal microflora against microorganisms better than plastic devices via weak antibacterial and antifungal action of copper salts (7). Copper release from the device which is decreased during the second year, shows variability among women depending on several factors like uterine secretions, amount of surface area of copper and the quantity of the solvent (23, 24). Furthermore degenerative changes and calcification of the surface begin as early as after 12 weeks and IUCD becomes more irregular, cobblestoned and accumulates deposits as the usage prolongs (1). For these reasons the controlled usage of IUCD and the necessity of its removal if required is very important because IUCD serves as a passage between vaginal cavity and uterine cavity assisting the descent of uterine contents to posterior fornix and the ascent of vaginal microorganisms to uterus (1). Also IUCD may modify or destroy the cervical mucus which serves as a powerful barrier for ascending infections (15).

Affecting the cervico-vaginal microflora by reducing Lactobacilli and predisposing the flora for anaerobes, the presence of IUCD shows correlation with some infectious agents. Actinomycosis (1, 7, 25) is the most related case of IUCD, second most frequent infection seen in IUCD employing women is "bacterial vaginosis" (26). Trichomoniasis is the third most common infection related with IUCD (25, 27, 28, 29). All of this three agents prefer basic pH and anaerobic conditions and moreover it was shown that their presence in the microflora and relation with IUCD mostly depends on the long-term usage of IUCD

(27). The reduction of Lactobacilli may help the colonization of these microorganisms by increasing the pH and decreasing the protective products of Lactobacilli such as metabolic inhibition products and bacteriocin-like substances (30).

But in the case of *Candida*, reduction of Lactobacilli, basic pH and anaerobic conditions are not convenient for colonization unless there is another predisposing factor like hormone usage, antibiotic usage or accidental pregnancy. Because of these reasons *Candida* infection in women employing IUCD is not as frequent as in the other women although *Candida* is a flora microorganism. Consistently we found that women with IUCD less than 1 year ($n=8$) had no *Candida* infection. On the other hand 4 patients who had used IUCD 1–5 years and 2 patients who had used IUCD more than 5 years were infected by this microorganism. Moreover 2 patients were *Candida*(+) in whom IUCD usage duration was unknown. This group can be evaluated as “more than 5 years IUCD usage” category since the patients were not sure about the date because of long time usage. Surprisingly we encountered the fact that the dominant form of this dimorphic fungus found in the patients using IUCD more than a year was the pathogenic “hyphae” form demonstrating the progressing infection (see Table 3).

Since the intermediate cells of mucosa reserving glycogen dominate during pregnancy, carbohydrate utilizing Lactobacilli population grow producing lactic acid and lowering the pH. This acidic condition is very suitable for *Candida* colonization of lower genital tract. This interaction between Lactobacilli, intermediate cells and *Candida* was shown by Demirezen in 2002 (30). It's well known that the prevalence of candidiasis among pregnant women is very high, but transmission of *Candida* cells to uterus and fetus is only restricted by the presence of a foreign body like retained IUCD in the literature. In order to be able to prevent the entrance of *Candida* cells to uterine cavity from vagina by the help of IUCD, it should be removed immediately after the pregnancy is diagnosed or the patient should be checked regularly for vaginal yeast (15).

In conclusion we observed that *Candida* infection is a frequent problem of women and also its prevalence is relatively high in IUCD users although the correlation between *Candida* and IUCD is not significant according to the χ^2 test. Since this fungus is an opportunistic normal cervico-vaginal flora microorganism, it will overgrow and begin filamentation as soon as the conditions are favorable for *Candida*. According to our data these conditions are obtained by the long-term usage of IUCD which supported the expansion of more pathogenic “hyphae” form. This result indicates that when the usage of IUCD exceeds 1 year, probably the effects of Cu^{2+} ions decrease and Lactobacilli population grows better increasing the possibility of *Candida* infection. In addition pregnant women retaining their IUCD bear the risk of fetal *Candida* invasion through the device if vaginal yeast is already present or colonization takes place during pregnancy. Therefore the use of IUCD must be under control, its duration must be limited and possible infections like “moniliasis” should be checked regularly during usage to prevent serious complications.

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