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Abstract

BACKGROUND: In the female genital tract, up to 30% of Papanicolaou (Pap)-stained cervicovaginal smears of intrauterine device (IUD) users are positive for actinomyces-like organisms (ALOs). Many clinicians believe that no therapeutic intervention is necessary if women with ALOs are without symptoms. However, there are no recommendations for the procedure in ALO-positive women with need for a routine IUD exchange. STUDY DESIGN: In this retrospective study, the incidence of ALOs was compared in ALO-positive women with a routine IUD exchange according to two new procedures: Group 1 (n=19), insertion of a new IUD immediately after removal of the index device, and Group 2 (n=19) IUD removal and reinserion after 3-5 days. A Pap smear was obtained at intervals of 6 weeks and 12, 24 and 36 months after reinserion. RESULTS: The cytological examination carried out after 6 weeks proved to be negative for ALOs in all cases. After 36 months, smears were more often positive for ALOs in women with immediate IUD exchange (73% vs. 33%; p<.17). CONCLUSION: Our results indicate that in ALO-positive women, IUD reinserion immediately after removal or after an interval of 3-5 days is safe. The interval reinserion might be of advantage on a long-term basis.
Comparison of two procedures for routine IUD exchange in women with positive PAP smears for Actinomyces-like organisms

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Abstract

Background: In the female genital tract up to 30% of Papanicolaou-stained (PAP) cervicovaginal smears of intrauterine device (IUD) users are positive for actinomyces-like organisms (ALOs). Many authors hold the view, that no therapeutic intervention is necessary, if women with ALOs are without symptoms. However, there are no recommendations for the procedure in ALOs positive women with need for a routine IUD exchange.

Study design: In this retrospective study the incidence of Actinomyces-like organisms (ALOs) was compared in ALOs positive women with a routine IUD exchange according to two new procedures: Group 1 (n=19): insertion of a new IUD immediately after removal of the index device; group 2 (n=19) IUD removal and reinsertion after 3-5 days. A PAP smear was obtained at intervals of 6 weeks, 12 months, 24 and 36 months after reinsertion.

Results: The cytological examination carried out after 6 weeks proved to be negative for ALOs in all cases. After 36 months smears were more often positive for ALOs in women with immediate IUD exchange (73% vs. 33%; p<0.17).

Conclusion: Our results indicate that in ALOs positive women IUD reinsertion immediately after removal or after an interval of 3-5 days are safe. The interval refit might be of advantage on a long-term basis.
**Introduction**

Actinomyces species are a gram-positive, non-acid fast anaerobic bacteria that exhibit branching filamentous growth (1). The organism does not cross mucosal barriers unless there is tissue injury (2). In the female genital tract up to 30% of Papanicolaou-stained (PAP) cervicovaginal smears of intrauterine device (IUD) users are positive for actinomyces-like organisms (ALOs) (2-4). The rate is lower with the levonorgestrel-releasing device and increases with the duration of use (2, 5). Although actinomyces have been recognized as a commensal of the vagina in women, most authors found non-IUD wearers to be actinomyces-free (6, 7).

In symptomatic ALOs positive IUD users consistently IUD removal and antibiotic treatment are recommended (2, 8, 9). The management of ALOs in the absence of significant symptoms however is difficult and controversial. Therapeutic recommendations range from observation and controlling for the appearance of symptoms to the removal of the device with or without antibiotic treatment (2, 8, 10-13).

No recommendations exist for the treatment of asymptomatic ALOs positive women, who need a routine exchange of their IUD after the approved lifespan. In our family planning clinic we used to remove the IUD during menstruation, performed a PAP smear 6 weeks later and inserted a new device if this smear was negative for ALOs. In accordance with many authors we found in all cases the PAP smear to be negative 6 weeks after IUD removal (14, 15). However, although we spend a lot of time to instruct women for contraception during the two months interval without IUD several pregnancies occurred. Therefore we discussed the risks of the option to exchange the IUD immediately. Because pelvic actinomycotic abscess is rare we held the view that an immediate exchange or a shorter interval between removal and reinsertion should not put women on an increased risk, to develop pelvic actinomycosis, if disappearance of ALOs is checked by a PAP smear six weeks after reinsertion. From April
2000 on we offered to ALOs positive IUD carriers, who came for the exchange of their device, to directly reinsert an IUD or perform reinsertion after 3-5 days. In the present article we report the results of these two procedures, which we supposed to be more comfortable for the women and to be safe for the protection from pregnancies.
Material and methods

A retrospective study was carried out to review all clinical cases of ALOs positive women with a routine exchange of an IUD according to two different new clinical procedures. Because we aimed to report a follow-up period of three years we included cases attending our Center for Family planning from 2000 up to 2003. From a list of all IUD insertions identified those women with a positive smear for ALOs within 6 weeks before exchange of the device. All women included used the Multiload 375 Copper-IUD (ML 375), which is recommended to be exchanged after five years. The protocol for this analysis has been submitted to the local ethical committee. The following investigations are part of our clinical routine performed 4-6 weeks before IUD exchange: Pelvic examination, PAP smear, endocervical swab for Chlamydia trachomatis, vaginal smear for bacterial vaginosis or trichomoniasis and transvaginal ultrasound. Pathological PAP smears, positive swab for Chlamydia trachomatis or pelvic pain are reasons for IUD removal without reinsertion. The exchange is performed during the next menstruation, if PAP smear and Chlamydia swab are normal and if necessary after treatment of a vaginal infection. Women were included, when the smear 4-6 weeks prior to insertion was positive for ALOs. Depending on the women’s preferences the devices were either refitted immediately (group A) or after an interval of 3-5 days (group B). Sonographic control of the IUD position in the uterus was performed as part of our clinical routine immediately after insertion, 6 weeks later and later on annually. Information was given about the presence of ALOs and about the necessity to obtain a PAP smear after six weeks to test for clearance of the organism. Furthermore women were informed about the incidence of pelvic actinomycosis and the possibility to remove colonisation with ALOs by removal of the device. All women were aware of the importance to report symptoms. Later on annual PAP smears were performed according to our local guidelines.

Each smear was seen by one experienced pathologist. Over the observation period three different pathologists from the same cytological laboratory were involved in the analyses of
the PAP smears. Cytomorphologic characteristics for the cytological diagnosis of ALOs in the PAP-stained smears were the presence of basophilic conglomerates with a dense central part surrounded by intertwined filament-type formations.

The main variable of this retrospective study is the appearance or non-appearance of ALOs in the cytological smear after IUD exchange. Disappearance of ALOs was considered to have occurred, when the cytological report of the post-intervention smear was negative. A further point of interest was the reappearance of ALOs with the two procedures over the observation period of 36 months.

**Statistical Analysis**

Fisher’s exact test was used to test the difference between incidence of ALOs in both groups. Student's t-test was used for comparison of baseline parameters. The level of significance was set at a $p$-value $\leq 0.05$. Baseline data are given as mean (SD). All analyses were performed by using the Statview 4.01 data analyses software (Abacus Concepts, Berkeley, CA, USA).

**Results**

During the follow-up period 461 IUD insertions were performed. Before exchange of the IUD 47 IUD carriers had ALOs positive smears and a device in situ for 5 years. Thirty-eight of these women wished an IUD reinsertion and obtained a follow-up smear 6 weeks after IUD exchange. Incidentally the number of women was identical in both intervention groups (n=19). The mean age of the participants did not differ between groups (direct exchange 37.9 (7.49) years; interval exchange 37.5 (10.5) years). All women were carriers of a Multiload 375 Copper-IUD (ML 375), whereas after exchange one person of each group obtained a Levonorgestrel-releasing device (LNG-IUD). The complete follow-up period of the cohort, was a total of 802 months. No actinomycotic abscess was observed. During the observation
period the number of women with follow-up decreased from 38 after 6 weeks to 20 after 36 months (Table 1). The reasons for drop-out in each group are described subsequently. From 6 weeks to 12 months three women were lost to follow-up, one woman wanted an IUD removal for personal reasons and 4 devices were removed because of partial or complete dislocation in group A. In group B there were 4 persons lost to follow-up during the same interval and three expulsions. Between 12 and 24 months there was one expulsion in group B. IUD dislocations and expulsions were diagnosed by routine vaginal sonogram. The number of participants in group A was higher after 24 months in comparison with the number after 12 months, because one woman who did not attend the clinic after 12 months came for a smear after 24 and 36 months. One expulsion and on IUD removal for personal reasons were the reason for two dropouts after 24 months in group B.

In both groups all smears obtained 6 weeks after IUD exchange were negative for ALOs. Follow-up data for both groups are presented in Table 1. After 12-36 months there is a high rate of recolonisation with ALOs (table 1). Although more ALOs positive cases were observed after three years in the group with direct exchange this difference is not statistically significant. The 36 months smear of one woman with a LNG-IUD was ALOs negative. After exchange of the IUD all ALOs positive smears persisted to be positive during the whole follow-up period.
Discussion

In the present study the incidence of ALOs reappearance after routine IUD exchange in ALOs positive women was investigated. The devices were inserted according to two clinical procedures. Both, IUD removal with immediate or interval refitting resulted in ALOs negative smears at the first cytological examination carried out after 6 weeks. At first sight this suggests, that immediate and interval IUD refitting is a good option for carriers of ALOs with need for a routine exchange. However, during longer follow-up we observed a trend to more ALOs positive smears in the group with direct IUD exchange, which increased with the duration of use (Table 1). Although the recolonisation rate is not significantly different after 36 months, we suppose, that with longer follow-up the difference between groups might be relevant. The incidence of 73% ALOs positive smears three years after direct device exchange is very high in comparison with ML 375 users after interval exchange (33%), whereas the incidence after interval exchange is similar to that of users without a previous history of ALOs, which was reported to be 27% in our clinic after 36 months and 32.9% independent of duration of use. (5, 16) Other authors found a colonisation rate of 17% after 25-36 months of use, when inert and copper IUDs where included into the analysis (3). In carriers of the LNG-IUD the incidence of ALOs positive smears is extremely low with 2.9%. Because in both groups only one person wished the insertion of an LNG-IUD, whereas all other women received a ML 375 device, variety in IUD-types between groups can not account for the distinct difference in ALOs recolonisation in the present study. However, before drawing clinical consequences of our results the following aspects have to be considered. Cytological diagnosis of actinomyces is difficult and the clinical significance of ALOs positive PAP smears is still uncertain (2, 7, 9, 17). Several authors report a lack specificity of PAP smears in identifying actinomycetes (9, 18). False – positive identification can occur in the presence of Candida, Leptothrix, Aspergillus and Eubacterium nodatum (4, 19). Therefore the term ALOs is preferable to actinomyces in reporting a PAP smear (2). ALOs positive smears
reflect colonisation but not necessarily infection. Under ordinary conditions Actinomyces do not cross mucosal barriers (2). However, if the mucosa is disrupted actinomycosis can result. On the other hand the diagnosis of severe pelvic actinomycosis is often delayed, because symptoms are modest in relation to the extensive disease (4, 20). Furthermore the low incidence of actinomycotic abscesses in comparison with the high number and low precision of positive smears makes the management of ALOs positive IUD carriers difficult. In cases of IUD removal or exchange the high risk of pregnancy has to be balanced against the low risk for potential infection in future. Although today most authors agree to leave the IUD in situ if women do not develop symptoms, there are no recommendations for the procedure in cases of routine IUD exchange (7, 8, 10, 13, 16). One author reported seven cases of an immediate IUD exchange in ALOs positive women (15). All of these women were found to be ALOs negative six to twelve months later. The disappearance of ALOs after the removal of the device is in accordance with the idea that ALOs are normally confined to the IUD and the superficial layers of the endometrium and may be shed in the menstrual cycle once the foreign body is removed (15, 17). Although ALOs positive PAP smears are not very specific and pelvic actinomycosis is rare, our results indicate that interval refit is of advantage for routine IUD exchange in ALOs positive women. In contrast to other authors we never observed spontaneous disappearance of ALOs in the smear during follow-up (16).

An important strength of our study is the long observation period, which allowed us to recognise that in spite of the fact that 100% of the smears obtained after 6 weeks were ALOs negative, ALOs may reappear more often, if there is no interval between removal and reinsertion. Our results are limited by the high dropout rate. The most common reason for dropout was IUD dislocation, which occurred in seven cases during the first year after insertion. The dislocation rate was in the range reported previously for copper devices (21,22). The observation that most dislocations occurred during the first year is in accordance with data of other authors. (21,22).
In conclusion at the end of the lifespan immediate IUD exchange as well as removal and reinsertion after 3-5 days are sufficient to eliminate ALOs. The rate of ALOs reoccurrence may be higher with immediate exchange. Both procedures are more safe and convenient than a 6 week IUD-free interval.

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Requests for reprints:

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Table 1

Actinomyces-like organisms (ALOs) in PAP smears of ALOs positive IUD users after exchange of the device according to two different procedures

<table>
<thead>
<tr>
<th>Interval since IUD exchange</th>
<th>Immediate exchange Group A</th>
<th>Reinsertion after 3-5 days Group B</th>
<th>p – value</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Number of women</td>
<td>ALOs positive (%)</td>
<td>Number of women</td>
</tr>
<tr>
<td>6 weeks</td>
<td>19</td>
<td>0 (0)</td>
<td>19</td>
</tr>
<tr>
<td>12 months</td>
<td>10</td>
<td>4 (40)</td>
<td>12</td>
</tr>
<tr>
<td>24 months</td>
<td>11</td>
<td>7 (64)</td>
<td>11</td>
</tr>
<tr>
<td>36 months</td>
<td>11</td>
<td>8 (73)</td>
<td>9</td>
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