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Prevention of IUD-related pelvic infection: the efficacy of prophylactic doxycycline at IUD insertion

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Abstract

It is believed that much of the small increased risk for developing pelvic inflammatory disease (PID) associated with the use of an intrauterine device (IUD) appears to be caused by bacterial contamination of the endometrial cavity at the time of insertion. Previous research suggests that use of prophylactic antibiotics immediately prior to IUD insertion may reduce the risk of developing PID. This paper presents results from a randomized clinical trial of 1485 women in Ibadan, Nigeria evaluating the effectiveness of 200 mg of doxycycline (versus placebo) given orally at the time of IUD insertion in reducing the incidence of PID during the first three months of IUD use. Rate of PID infection in the doxycycline-treated group was not significantly lower than that in the placebo-treated group. The rate of unscheduled IUD-related visits to the clinic also was not significantly lower among the doxycycline-treated group. However, the incidence of PID was low (21 cases) for both study groups. Aseptic conditions during IUD insertion, follow-up visits with short intervals to monitor health, and treatment of opportunistic infections may have reduced the potential of PID within this population.

Introduction

Pelvic inflammatory disease (PID) is a gynecologic condition usually indicating an inflammation caused by an infection in the upper genital tract [1–3]. Infections resulting in PID include endometriosis, salpingitis, oophoritis, myometritis, parametritis and/or infection of the pelvic peritoneum. Acute PID is primarily a polymicrobial infection that is often caused by organisms ascending from the vagina and cervix along the mucosa of the endometrium and then infecting the mucosa of the oviduct [3]. Bacterial organisms commonly linked to the development of PID include *Neisseria gonorrhoeae, Chlamydia trachomatis*, endogenous aerobic and anaerobic

bacteria, and, occasionally, genital *Mycoplasma* species [3–6]. PID may cause chronic pelvic pain, infertility or ectopic pregnancy, while the social, psychological and economic consequences can be significant. With the growing epidemic of sexually transmitted diseases in the developing world, the potential increase in the incidence of PID among young, sexually active women is becoming a major public health concern.

An association between PID and the use of an intrauterine device (IUD) has been suggested in previous studies [4,7–9]. Much of the increased risk for developing PID associated with IUD use appears to be caused by bacterial contamination of the endometrial cavity at the time of IUD insertion. A number of studies have found the risk of PID to be inversely related to the duration of IUD use, with the highest rate of infection occurring from one to three months postinsertion [10–13]. Others have cultured bacteria from the uterine cavity without any apparent relationship to the time elapsed since IUD insertion [14].

In a population with a high prevalence of intracervical sexually transmitted pathogens, the risk of IUD-related PID may be correspondingly increased. Previous research has found that the use of prophylactic antibiotics for induced abortion appears to reduce the risk of subsequent infectious morbidity by about 50% [1,2,15]. These results suggest the possibility that prophylactic antibiotic administration immediately prior to IUD insertion may reduce the risk of developing PID. The main objective of this study was to evaluate the efficacy of a single 200 mg antibiotic doxycycline dose (capsule) given orally at the time of IUD insertion in preventing PID during the first three months of IUD use among IUD acceptors in Nigeria. This study is a companion to a joint FHI/CDC study conducted in Kenya [15].

Patients and methods

Patient recruitment

From July 1986 through June 1988, all women requesting an IUD at the University College Hospital, University of Ibadan, Ibadan, Nigeria, who were currently menstruating and who were between 20 and 44 years of age were candidates for inclusion in the study. Volunteers were not admitted into the study if they: had a history of ectopic pregnancy; had been pregnant within 42 days prior to study recruitment; had leiomyomata of the uterus; had active PID; had a cervical or endometrial malignancy; had a known hypersensitivity to tetracyclines; had used any antibiotics within the past 14 days or were on long-lasting injectable penicillin; had an impaired response to infection; lived outside the city of Ibadan or did not have a sufficient address for follow-up, or were unwilling to return for follow-up. Informed written consent was obtained before entry into the study.

The study protocol required a study size of at least 1800 patients (900 per group). Due to difficulties encountered in recruiting eligible patients, a total of 1485 women were admitted into the study.

Trial design

The study was a double-blind, randomized clinical trial of the efficacy of a 200 mg oral dose of prophylactic doxycycline (Pfizer Limited, Sandwich, England) versus placebo given at the time of IUD insertion in preventing PID. The study was approved by the institutional review boards of FHI and the University of Ibadan. Patients were randomized only after admission criteria were met on the scheduled day for IUD insertion, and when eligibility had been assured by the physician. Patients had an equal probability of assignment to either treatment group. No exclusions of women were allowed after randomization and IUD insertion.

The doxycycline and placebo were in capsule form and were identical in appearance. They were prepackaged in bottles and consecutively numbered for each patient according to a computer-generated randomization schedule. The patients were randomized by assigning a patient order number and administering the capsules in the corresponding prepackaged bottle.

The randomization code was kept in the United States and entered on the patient's study admission form by FHI project staff. All administration and evaluation of study project was blinded to treatment assignment, and investigators and patients were blinded to the ongoing results of the study.

Regimen

Both the doxycycline and placebo were supplied in capsule form (two capsules of 100 mg each). The physician administering the treatment at the time of randomization closely observed that the capsules were ingested to assure compliance. The therapies were administered at least one hour before IUD insertion to allow for systemic absorption of the drug.

Choice of IUDs inserted was at the discretion of the study investigator and the patient, but almost all were the Copper T380A. Antibiotics or other treatments for PID were not to be prescribed at the study facility unless PID was diagnosed. However, patients enrolled in the study were treated for other illnesses that occurred during the follow-up period.

Endocervical cultures

Cultures of the endocervix were taken for both *N. gonorrhoeae* and *C. trachomatis* prior to insertion of the IUD. For the gonorrhea (GC) culture, a cotton-tipped swab was used to inoculate Thayer-Martin medium. Plates were incubated at 35°C in candle jars and examined at 48 and 72 h. Colonies typical of *N. gonorrhoeae* were confirmed by Gram stain appearance and oxidase positivity. For the *Chlamydia* (CT) culture, a second, dacron-tipped, metal or plastic swab was rotated in the endocervical canal for 5–10 s. The swab was placed into 2-SP transport medium and held at 4°C until being transported to the laboratory, where it was kept at −80°C until being

inoculated onto cycloheximide-treated McCoy cells and centrifuged at 2800 *g* for one hour. Cells were incubated for 72 h and stained with fluoresceinated monoclonal antibody (Syva Company, Palo Alto, California).

Measurement of outcomes

Patients were scheduled to be seen at the clinic at 1 and 3 months after IUD insertion. Complete information, including evaluation for PID, was recorded at these visits for returning patients. Throughout the study, an evaluation for PID was performed on all patients returning for unscheduled IUD-related visits.

The clinical evaluation for PID was performed by the gynecologist responsible for admitting and evaluating all patients in the study. The primary outcome variable of interest was the incidence of PID during the three months following insertion. An important secondary outcome variable was the incidence of an unscheduled visit for an IUD-related problem. The criteria used for diagnosis of PID were those suggested by the Infectious Disease Society for Obstetrics and Gynecology in the United States [16]. To be diagnosed as having PID, a woman had to have all three of the following criteria present: direct abdominal tenderness; tenderness with motion of cervix and uterus; and adnexal tenderness. If all three of the tenderness criteria were present, then at least one of the following criteria also had to be present for a confirmed diagnosis of PID: Gram stain of endocervix, positive for Gram-negative intracellular diplococci; oral temperature greater than 38°C; leukocytosis greater than 10 000 wbc/mm^3; purulent material from peritoneal cavity by culdocentesis; or pelvic abscess or inflammatory complex on bimanual examination.

Statistical analysis

Fisher's exact test was used for one-tailed comparisons of prophylactic doxycycline patients with placebo patients on dichotomous outcome variables such as incidence of PID, number of patients with at least one unscheduled IUD-related follow-up visit, and number of patients with any PID-related complaint (adnexal, abdominal, or cervical tenderness, etc.) [17–20]. Chi-square tests were used for the two-tailed comparisons of type of contraceptive used in the past and type of IUD inserted. Logistic regression was used to test for differences in incidence of PID between the two study groups. The two-sample *t*-test was used for comparisons of interval-scaled variables including age, parity, education, number of spontaneous or induced abortions. Life-table analysis was used to compare the distributions of PID over time in the two study groups, and the Wilcoxon test was used to compare the event rates between two groups. The Wilcoxon test was chosen because it places more emphasis on early events, which was more appropriate for this data. Cox's proportional hazards model was used to test for differences in time to event (PID) between the groups when education, age, number of live births, number of different sexual partners in the month preceding study enrollment, and average number of acts of intercourse per week in the month prior to enrollment entered into the model simultaneously.

Results

A total of 1485 patients were admitted into the study: 741 were randomly assigned to receive placebo and 744 doxycycline. A total of 1199 patients (80.7%) returned for both follow-up visits (590 placebo and 609 doxycycline). Of the remaining 286 women in the study, 88 returned for only the first follow-up visit (44 placebo and 44 doxycycline), 142 returned for only the second follow-up visit (74 placebo and 68 doxycycline) and 56 did not return for follow-up after treatment (33 placebo and 23 doxycycline).

Table 1 Sociodemographic characteristics of patients by treatment group: Nigeria PID-IUD antibiotic trial

Characteristic	*Placebo (n = 744)*	*Doxycycline (n = 741)*	*p level*[a]
Age (mean ± SD)	31.3 ± 6.1	30.5 ± 4.9	0.01
Education (mean ± SD)	6.1 ± 4.8	6.1 ± 4.6	0.90
Live births (mean ± SD)	4.5 ± 1.8	4.3 ± 1.8	0.03
Spontaneous abortions (mean ± SD)	0.4 ± 0.8	0.4 ± 0.8	0.74
Induced abortions (mean ± SD)	0.4 ± 0.9	0.4 ± 0.8	0.70
Coital frequency/week (mean ± SD)	1.6 ± 1.0	1.6 ± 1.0	0.47
Contraceptive method used in month prior to study (*n*, (%))			0.55[b]
None	574 (77.2)	582 (78.5)	
Pill	70 (9.4)	72 (9.7)	
Condoms	62 (8.4)	47 (6.3)	
Withdrawal	24 (3.2)	23 (3.1)	
Other	14 (1.8)	17 (2.4)	
Currently married (*n*, (%))	730 (98.1)	728 (98.2)	0.85[c]
More than one sexual partner in last month (*n*, (%))	64 (8.6)	68 (9.2)	0.72[c]

[a] Two-tailed T-tests for two groups
[b] Chi-square test of significance
[c] Fisher's exact test (two-tailed)

Table 1 presents data on the sociodemographic characteristics of the women participating in the trial. Both groups were similar in years of education, weekly coital frequency, number of different sexual partners in the last month, and in the incidence of spontaneous and induced abortion. Women in the doxycycline group were, on average, younger than women in the placebo group ($p = 0.01$). However, the difference was less than one year, overall, and therefore not considered meaningful. Doxycycline users also had slightly more live births than did placebo users ($p = 0.03$), although the average difference of 0.2 children was not meaningful. There were no differences between the two groups in the contraceptive method used in the month prior to the study or in marital status.

With few exceptions, women were fitted with Copper T380A IUDs (Table 2). Few women experienced a failed insertion or perforation at the time of IUD insertion. Slightly over 1% in each study group had a positive gonorrhea test at screening. The occurrence of *Chlamydia* was around 7% among both study groups. Actinomycosis was twice as likely to be diagnosed in the placebo group as in the doxycycline group. However, none of these differences was statistically significant.

Table 2 Percentage of patient characteristics by treatment group: Nigeria PID-IUD antibiotic trial

Characteristic	*Placebo (n = 744)*		*Doxycycline (n = 741)*		*p level*[a]
	n	%	*n*	%	
Type of IUD inserted					0.69[b]
Lippes Loop	11	1.5	14	1.9	
Copper T380A	726	97.7	723	97.6	
Failed insertion	7	0.8	4	0.5	
Perforation	3	0.4	2	0.3	0.69
Positive *Gonorrhea*	8	1.1	9	1.3	0.81
Positive *Chlamydia*	50	6.7	50	6.8	0.51
Positive *Actinomycosis*	16	2.2	8	1.1	0.15

[a] Fisher's exact test (two-tailed)
[b] Chi-square test of significance

Table 3 presents data for the 1289 women who returned for the first scheduled follow-up visit (at least 30 days postinsertion). Incidence of PID was low, with 1.11% of the placebo users and 1.22% of the doxycycline users having a confirmed diagnosis ($p = 0.53$). Doxycycline users were less likely to have an unscheduled IUD-related visit than were placebo users, but this difference was not significant. The number of unscheduled visits was very low for both study groups, respectively. The occurrence of PID-related complications (pain during sexual intercourse, abdominal, cervical and adnexal tenderness, chills or fever) was low for both study groups, as was the use of antibiotics during the study. None of these differences was statistically significant.

Event outcomes for the 1334 women who returned for the scheduled 90-day follow-up visit are presented in Table 4. The incidence of PID was less than 1% for both doxycycline and placebo users ($p = 0.35$). None of the placebo users had an unscheduled IUD-related follow-up visit during this follow-up interval, compared to less than 0.5% of the doxycycline users (not significant). Few women in either group experienced PID-related complications or used antibiotics during their time in the study (not significant).

Table 3 Percentage of patients reporting event at first follow-up visit, 30 days after IUD insertion and treatment: Nigeria PID-IUD antibiotic trial

Event	*Placebo (n = 632)*		*Doxycycline (n = 657)*		*p level*[a]
	n	*%*	*n*	*%*	
PID	7	1.11	8	1.22	0.53
Abdominal pain	9	1.42	8	1.22	0.47
Pain during sex	1	0.16	4	0.61	0.20
Chills or fever	9	1.42	4	0.61	0.12
Abdominal tenderness	5	0.79	7	1.06	0.41
Cervical tenderness	7	1.10	8	1.22	0.53
Adnexal tenderness	10	1.58	10	1.52	0.56
Antibiotics taken	3	0.47	3	0.46	0.64
Unscheduled visits	5	0.79	2	0.30	0.21

[a] Fisher's exact test (one-tailed)

Table 4 Percentage of patients reporting event at second follow-up visit, 90 days after IUD insertion and treatment: Nigeria PID-IUD antibiotic trial

Event	*Placebo (n = 664)*		*Doxycycline (n = 670)*		*p level*[a]
	n	*%*	*n*	*%*	
PID	2	0.30	4	0.60	0.35
Abdominal pain	5	0.75	4	0.60	0.49
Pain during sex	0	0.00	2	0.30	0.25
Chills or fever	0	0.00	2	0.30	0.25
Abdominal tenderness	3	0.45	4	0.60	0.50
Cervical tenderness	2	0.30	4	0.60	0.35
Adnexal tenderness	2	0.30	6	0.89	0.15
Antibiotics taken	13	1.96	8	1.19	0.18
Unscheduled visits	0	0.00	2	0.30	0.25

[a] Fisher's exact test (one-tailed)

Data were analyzed comparing the percentage of women ($n = 1429$) ever reporting any of these events at any time during observation (Table 5). More women in the doxycycline group (12 cases, 1.66%) had a confirmed diagnosis of PID than in the placebo group (9 cases, 1.27%). However, this difference was not statistically significant ($p = 0.35$). The incidence of unscheduled follow-up visits throughout the trial was low ($p = 0.49$). No significant difference in the incidence of PID-related complications or use of antibiotics during the trial was noted.

Table 5 Percentage of patients ever reporting* event after IUD insertion and treatment: Nigeria PID-IUD antibiotic trial

Event	*Placebo (n = 708)*		*Doxycycline (n = 721)*		*p level*[a]
	n	*%*	*n*	*%*	
PID	9	1.27	12	1.66	0.35
Abdominal pain	14	1.98	12	1.66	0.40
Pain during sex	1	0.14	6	0.83	0.06
Chills or fever	9	1.27	6	0.83	0.29
Abdominal tenderness	8	1.13	11	1.53	0.34
Cervical tenderness	9	1.27	12	1.66	0.35
Adnexal tenderness	12	1.69	16	2.22	0.30
Antibiotics taken	16	2.26	11	1.53	0.21
Unscheduled visits	5	0.71	4	0.55	0.49

* Excludes 56 patients who did not return for follow-up after study admission
[a] Fisher's exact test (one-tailed)

No significant difference in the occurrence of PID between the doxycycline and control groups was found when education, age, number of live births, number of different sexual partners in the month preceding study enrollment, and average number of acts of intercourse per week in the month prior to enrollment were simultaneously controlled for in a logistic regression analysis. Identical nonsignificant results were found at each follow-up interval as well as for the overall study period.

Life-table analysis was used to determine the distributions of PID and unscheduled IUD-related clinic visits over time (Table 6). Although the study protocol required follow-ups at one and three months postinsertion, approximately 10% of the patients returned from five to ten months after study admission for scheduled end-of-study visits. Life-table rates (per 100 women) were therefore calculated through ten months postinsertion to assess the true effect of time on the incidence of PID. The ten-month life-table rate for PID in the placebo group was 12.7 per 100 women, compared to 10.36 per 100 women in the doxycycline group (not significant). Although the number of reported cases of PID was greater among the doxycycline group, the higher ten-month life-table rate among placebo users is a result of two cases of PID reported at seven and eight months postinsertion. As a result, these rates should be interpreted with caution. Ten-month life-table rates for unscheduled IUD-related clinic visits were 1.19 and 0.63, in the placebo and doxycycline groups, respectively (not significant).

Cox proportional hazards modeling was used to adjust for education, age, number of live births, number of different sexual partners in the month preceding study enrollment, and average number of acts of intercourse per week in the month prior to enrollment. Identical to the earlier Fisher's exact test results and the life-table results, no significant difference between the study was found at the 0.05 level or lower.

Table 6 Gross cumulative life-table rates for PID and unscheduled follow-up visits: ever-reported cases: Nigeria PID-IUD antibiotic trial*

Event	*Placebo Rate ± SE*	*Doxycycline Rate ± SE*	*p value*[a]
PID	12.71 ± 7.96 (n=708)	10.36 ± 6.80 (n=721)	0.608
Unscheduled visits	1.19 ± 0.70 (n=634)	0.63 ± 0.37 (n=659)	0.873

* Excludes 56 patients who did not return for follow-up after study admission
[a] Wilcoxon rank tests (1 d.f.)

Discussion

Current information suggests that the risk of PID among users of IUDs most likely is caused by a bacterial contamination of the endometrial cavity at the time of IUD insertion. While previous studies propose that prophylactic antibiotics taken at the time of IUD insertion may offer some protective effect, our data do not support these findings [15]. A 200 mg dose of doxycycline at the time of insertion was not associated with a reduced likelihood of PID in the present study. Interestingly, the crude incidence of PID was 23% higher in the doxycycline group than in the placebo group. Although this percentage increase seems high at first glance, the number of women with PID in this study was small (9 placebo and 12 doxycycline) and differences in the overall incidence rates between study groups when controlling for time were not found to be statistically significant. Likewise, the incidence of unscheduled IUD-related follow-up visits was not significantly different between the two groups.

These results do not support those of a similar study of 1800 women in Kenya jointly sponsored by FHI and the Centers for Disease Control [15]. In that study, a 31% decrease in both the incidence of PID and of unscheduled IUD-related follow-up visits was noted for women who received a 200 mg dose of doxycycline at the time of IUD insertion. Even though these differences were not statistically significant, it is unlikely that our findings were affected by confounding factors, since our study design replicated the Kenya study and controlled for the potential biases that have hampered previous IUD-PID studies. We used a computer-generated randomization procedure to control for selection biases that have occasionally affected STD prophylactic research. Uniform data collection procedures and blind-study protocol for study participants, physicians and laboratory personnel controlled for ascertainment bias.

The comparatively low incidence of PID-related complaints in both study groups indicates that this population was at a lower risk for PID or IUD-related complications than previously thought. IUD exclusion criteria during patient selection and aseptic conditions when IUDs were inserted could effectively reduce the risk of

bacterial contamination and subsequent PID without the use of prophylactic antibiotics. As in the Kenya study, the lower incidence of PID among these women suggests that the use of intrauterine devices in Nigeria may not significantly increase the risk of IUD-related PID [15].

Cumulative life-table rates for PID in this study were 12.71 per 100 women in the placebo group and 10.36 per 100 women in the doxycycline group at ten months ($p = 0.61$). These rates should be interpreted with caution due to the erratic follow-up behavior of patients in this trial. Although the study protocol required follow-up visits at one and three months postinsertion, approximately 10% of our subjects returned to the clinic anywhere from five to ten months postinsertion for follow-up. While the crude incidence of PID was somewhat greater among doxycycline users, two cases of PID in the placebo group were diagnosed at seven and eight months postinsertion, resulting in a higher life-table rate for placebo users when the actual number of cases diagnosed indicated otherwise. These rates likely reflect the occasional occurrence of PID among few women returning late for follow-up.

The early occurrence of PID in this trial is consistent with findings in other studies and suggests that most most IUD-related morbidity occurs around the time of IUD insertion [10–12]. Fifteen of the 21 PID cases (71.4%) were diagnosed within one month postinsertion, with seven occurring among the placebo users and eight among the doxycycline users.

Our study results suggest that the use of a systemic antibiotic at the time of IUD insertion did not significantly reduce PID or unscheduled IUD-related clinic visits among this population. While it is not clear why this occurred, it may be due to a combination of factors, including, but not limited to: effective screening out of women who are at risk for PID, a population at lower risk for sexually transmitted diseases which often lead to the onset of PID, attention to sterile insertion procedures, expert medical care during both the insertion procedure and follow-up visits, and prompt follow-up of patients within one month postinsertion.

The prophylactic administration of systemic antibiotics may not offer the most cost-efficient method to reduce the risk of pelvic inflammatory disease among IUD acceptors at lower risk of developing PID. One alternative may be the judicious screening and selection of appropriate candidates for IUD use [21]. Another could be recruiting women in stable monogamous relationships who generally are at low risk of sexually transmitted diseases. Risk of PID also has been found to be only minimally increased after IUD insertion among women in stable monogamous relationships [5]. The use of disinfectant and sterile insertion conditions may also be important factors since the potential for bacterial infection can be eliminated. These programmatic intervention strategies may prove to be a more cost-effective and reliable option for controlling the incidence of IUD-related PID in developing countries, such as Nigeria, where the use of expensive prophylactic therapies at the time of IUD insertion may not be cost-effective. Further study on the cost–benefit ratios for these programs is necessary before decisions on policy can be made.

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Resumé

On pense qu'un bon nombre des légers risques de contracter une affection pelvienne inflammatoire liée à l'utilisation d'un dispositif intra-utérin est sans doute dû à une contamination bactérienne de la cavité utérine au moment de l'insertion. Les recherches précédentes semblent indiquer que l'administration d'antibiotiques à titre prophylactique immédiatement avant l'insertion d'un DIU peut réduire le risque de telles inflammations. Ce document présente les résultats d'un essai clinique randomisé sur 1485 femmes effectué à Ibadan (Nigéria) en vue d'évaluer l'efficacité de 200 mg de la doxycycline (comparée à un placebo), administrés par voie buccale au moment de l'insertion du DIU, pour réduire l'incidence des affections pelviennes inflammatoires pendant les trois premiers mois d'utilisation d'un DIU. Le pourcentage d'infection dans le groupe des femmes traitées à la doxycycline n'étaiet pas significativement moins élevé que celui du groupe traité au placebo. Le pourcentage de consultations imprévues à la clinique pour des raisons liées au DIU n'étaient pas non plus significativement moins élevé pour le groupe traité à la doxycycline. Toutefois, l'incidence d'affections pelviennes inflammatoires étaiet faible (21 cas) pour les deux groupes étudiés. Il est possible que les conditions d'aseptie pendant l'insertion du DIU, les visites de suivi à intervalles rapprochés pour contrôler l'état de santé, ainsi que le traitement d'infections intercurrentes aient réduit l'eventualité de telles affections inflammatoires dans cette population.

Resumen

Se piensa que una gran parte de los pequeños riesgos de contraer una afección pélvica inflamatoria relacionada con la utilización de un dispositivo intrauterino parece haber sido causada por una contaminación bacteriana de la cavidad uterina en el momento de la colocación. Las investigaciones anteriores parecen indicar que la administración de antibióticos a título profiláctico inmediatamente antes de la colocación de un DIU reducir el riesgo de tales inflamaciones. En este documento se presentan los resultados de un ensayo clínico al azar realizado con 1,485 mujeres de Ibadán, Nigeria, a los efectos de evaluar la eficacia de 200 mg de doxiciclina (en comparación con un placebo) administrada por vía oral en el momento de colocar el DIU, para reducir la incidencia de afecciones pélvicas inflamatorias durante los primeros tres meses de utilización de un DIU. El porcentaje de infección en el grupo de mujeres tratadas con doxiciclina no era significativamente menos elevado que en el grupo tratado con un placebo). El porcentaje de consultas imprevistas en la clínica por motivos relacionados con el tampoco era significativamente menos elevado en el caso del grupo tratado con doxiciclina. Sin embargo, la incidencia de afecciones pélvicas inflamatorias era baja (21 casos) en los dos grupos estudiados. Es posible que las condiciones de asepsia durante la colocación del DIU, las visitas de seguimiento a intervalos cortos para controlar el estado de salud, así como el tratamiento de infecciones intercurrentes, hayan reducido la posibilidad de tales afecciones inflamatorias en esta población.