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Positive Testing for *Neisseria gonorrhoeae* and *Chlamydia trachomatis* and the Risk of Pelvic Inflammatory Disease in IUD Users

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Abstract

Background: Unintended pregnancies are a major public health problem in the United States, and intrauterine devices (IUDs) are among the most effective reversible birth control methods available. Historically, there have been concerns about IUD use and infection among young and/or high-risk women that may increase the risk of pelvic inflammatory disease (PID) and subsequent infertility.

Methods: The Contraceptive CHOICE Project (CHOICE) was a prospective cohort study of over 9,000 women 14–45 years of age residing in the St. Louis area who were interested in initiating a new form of reversible contraception. At enrollment, participants were counseled regarding long-acting contraceptive methods with the goal of increasing awareness of all reversible methods available. Participants were also tested for *Neisseria gonorrhoeae* (GC) and *Chlamydia trachomatis* (CT) during enrollment and were provided with contraception at no cost for 2–3 years.

Results: We estimate the frequency of self-reported PID in new IUD users compared with women using other contraceptive methods. Among both new IUD users who tested positive for GC and/or CT and those who tested negative, the PID rate was 1% or below.

Conclusions: Our results demonstrate that IUD use is safe for all women, including women at high risk for sexually transmitted infections.

Introduction

THE INTRAUTERINE DEVICE (IUD) is one of the most effective reversible birth control methods available to women.¹ Yet, less than 8% of women in the United States use an IUD, making the rate of IUD use in the U.S. lower than many other countries.^{2,3} The low rate of use among U.S. women can be attributed, in part, to clinician and patient concerns regarding IUD use and infection, especially among young and/or high-risk women. In a national survey of 811 practicing obstetrician-gynecologists, nearly 33% responded that IUD use increases the risk of pelvic inflammatory disease (PID).⁴ Similarly, in a survey of 250 obstetrician-gynecologists in the St. Louis region, 29% reported that an IUD causes an increased risk of PID, 38% stated that IUDs were inappropriate for nulliparous women, and 67% would not provide IUDs to adolescents.⁵

The Dalkon Shield, an intrauterine device available in the 1970s, was associated with increased risk of infection due to its braided, polyfilament tail. Many clinicians still associate any IUD with an elevated risk of infection and resulting infertility. However, modern IUDs, such as the Copper T380A IUD (Cu-IUD) and levonorgestrel intrauterine system (LNG-IUS), have monofilament tails and have been shown to have relatively low rates of infectious complications.⁶

Several international studies have found the PID rate in IUD users to be no different than nonusers after the first 20 days following insertion.^{7–10} A meta-analysis by the World Health Organization found the overall rate of PID in IUD users to be 1.6 per 1,000 women-years of use among studies with up to 8 years of follow-up.¹¹ The authors found that PID risk was more than 6 times higher during the 20 days after insertion than during later times; and reported an unadjusted rate for PID risk of 9.7 per 1,000 woman-years for the first 20

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days after insertion. A study in Kenya of 615 participants found that among women without cervical infection at the time of IUD insertion, 0.4% were diagnosed with PID compared with 3.1% among women with a cervical infection.¹² Another study reported 2 of 29 women with *Chlamydia trachomatis* infection at the time of IUD insertion developed PID.¹³ Data from studies done in multiple African countries estimate the risk of PID attributable to IUD to be 0.15% (1.5 per 1,000).^{14,15} Finally, the annual rate of PID among privately insured women in the U.S., regardless of birth control method, was 236 per 100,000 enrollees (2.36 per 1,000) in 2005.¹⁶

The presence of mucopurulent cervicitis or current *Neisseria gonorrhoeae* (GC) and/or *Chlamydia trachomatis* (CT) infection are considered to be contraindications to IUD insertion. In fact, the Centers for Disease Control and Prevention (CDC) U.S. Medical Eligibility Criteria describes this scenario as category 4, representing an “unacceptable health risk.”¹⁷ Data on modern IUD users and infectious morbidity in the U.S. are scarce, especially from large cohort studies using contemporary IUDs with systematic follow-up. The Contraceptive CHOICE Project is one of the largest cohorts of modern IUD users in the U.S., with over 5,000 IUD users. The objective of this report is to estimate the rate of self-reported PID in new IUD users. We compared the PID rate in women testing positive for GC and/or CT to women testing negative for both infections, and made the same comparison in women using other contraceptive methods. We hypothesized that the PID rate in IUD users was low, even among women testing positive for STIs at baseline.

Methods

This is a secondary analysis of data collected in the Contraceptive CHOICE Project (CHOICE), which sought to promote the use of long-acting reversible contraception, including LNG-IUS, Cu-IUD, and subdermal implant, and to reduce the number of unintended pregnancies in the St. Louis region. The project was an observational cohort study of 9,256 women that removed access, education, and financial barriers to contraception. CHOICE provided each participant with reversible contraception of her preference at no cost for 2–3 years. The Washington University in St. Louis School of Medicine Human Research Protection Office approved the CHOICE protocol before participant recruitment began. A detailed description of the CHOICE methods was previously reported.¹⁸

The study population enrolled in CHOICE was a convenience sample of women who met the following inclusion criteria: (1) aged 14–45 years; (2) resident of the St. Louis region; (3) English or Spanish as a primary language; (4) sexually active with a male partner in the past 6 months or anticipated sexual activity in the next 6 months; (5) did not desire pregnancy in the next year; and (6) not currently using a contraceptive method or interested in starting a new reversible contraceptive method.

CHOICE recruited participants between August 2007 and September 2011 from community health centers, private medical providers, newspaper reports, study flyers, and word of mouth. The recruitment sites consisted of university-affiliated clinics and providers, two facilities providing

abortions services, and community clinics providing family planning, obstetric, gynecologic, and primary care. During enrollment, participants were provided standardized contraceptive counseling by research assistants. After written informed consent was obtained, participants completed a structured survey and were screened for CT, GC, and *Trichomonas vaginalis* (TV).

Because all women in CHOICE were offered GC and CT testing at the time of enrollment, positive test results implied an infection was present at IUD insertion. Participants who tested positive were treated with a CDC-approved antibiotic regimen with the IUD in place. Most women began the antibiotic regimen within 2–3 weeks of testing, and all were offered screening for reinfection after treatment. The one exception to the above was if mucopurulent cervicitis was present at the time of initial planned insertion. In these rare cases, women were first treated for GC and/or CT and returned after treatment for IUD insertion.

Telephone interviews were conducted at 3 and 6 months and every 6 months post enrollment for the duration of study participation. We collected data regarding method use, clinical signs and symptoms, STI diagnosis, and pregnancy. At each interview, participants were asked, “[s]ince we last spoke, have you been told by a health care provider that you had pelvic inflammatory disease (PID) (or an infection of the tubes, ovaries, or uterus)?” Because the investigators were aware of additional PID cases that may have occurred in participants that did not respond to the 3- or 6-month survey, we also reviewed the CHOICE adverse event log for women calling or presenting with signs or symptoms of infection.

We reviewed the available medical records of all patients who self-reported PID in the 3- or 6-month telephone survey or cases discovered from the adverse event log. If a patient was seen at an outside clinic or emergency department, we attempted to obtain medical records from the visit for confirmation of the diagnosis. Medical records were reviewed by two physicians (TM and JP) and rated as “likely PID,” “possible PID,” or “not PID.” Cases were considered “likely PID” if medical records documented abdominal or pelvic pain and/or tenderness on exam and a positive STI or other findings (e.g., tubo-ovarian abscess) that indicated a high likelihood of PID. Any participant presenting with signs and/or symptoms of pelvic infection (e.g., abdominal pain, pelvic tenderness, abnormal vaginal discharge, etc.) and no other obvious etiology was considered “possible PID.” Medical records could not be obtained in four cases, and these participants were considered “possible PID.” If no pelvic tenderness was noted on exam or the evaluating clinician communicated to the study team that the patient did not have PID, we considered these cases as “not PID.” Evaluation discrepancies were discussed, and a consensus was reached regarding PID classification.

For this analysis, we included participants for whom we had baseline GC and/or CT test results and survey follow-up data at 3 or 6 months. We included all women who started their baseline chosen method within the first 9 weeks of enrollment; 93% of participants started their chosen method within 4 weeks of enrollment. We calculated the self-reported rate of PID reported in the 3- and 6-month surveys among IUD users (LNG-IUS and Cu-IUD) and stratified this group by whether their baseline test for GC and/or CT was positive. We also compared these rates with the rate in non-IUD users

(oral contraceptive pill [OCP], contraceptive patch, vaginal ring, implant, and depot medroxyprogesterone acetate [DMPA]). Only women who started their non-IUD contraceptive method within the first 9 weeks of their enrollment were included in the non-IUD category; therefore, women using no method were excluded. The PID rate was calculated using the number of PID cases divided by the number of users.

Results

The baseline characteristics of the 7,611 CHOICE participants who responded to PID questions during the 3 or 6-month telephone survey and had baseline GC and/or CT results are presented in Table 1. Half (48.8%) of the participants self-identified as black and 43.5% as white. The mean age of participants was 25.2 years. More than half of the participants (56.1%) reported receiving government support (food, stamps, Women, Infants, and Children Supplemental Nutrition program, welfare, and/or unemployment) or having trouble paying for food, transportation, healthcare, and/or housing. A history of STI was common among our cohort: 3,046 (40.0%) of participants reported a history of STI, and 552 (7.3%) tested positive for an STI (GC, CT, or TV) at the baseline enrollment visit. Over one-third (35.4%) reported a history of abortion. The median total lifetime sex partners was 6, and 410 (5.5%) of the participants reported having more than one male sex partner in the past 30 days at enrollment. Approximately one-quarter (23.1%) reported current smoking, and 19.3% reported drug use in the past 30 days at enrollment.

Table 1 also provides baseline characteristics by baseline chosen method, IUD ($n=4,371$) versus non-IUD users ($n=3,240$). The mean age was higher among IUD users (26.4 years) than non-IUD users (23.7 years, $p<0.01$). Although IUD users were equally likely to be black or white, non-IUD users were more likely to be black. Participants who chose an IUD reported more total lifetime sex partners than non-IUD users: median of 6 versus 5 ($p<0.01$). IUD users were more likely to report never using condoms than non-IUD users (41.9% vs. 29.7%; $p<0.01$), and less likely to report using condoms every time (33.8% vs. 40.0%; $p<0.01$). IUD users were more likely to report a history of STI than non-IUD users (41.2% vs. 38.4%; $p=0.01$), being a current smoker (24.1% vs. 21.8%), and receiving government support or having trouble paying for basic necessities (57.0% vs. 54.7%).

We identified 33 PID cases among the 7,611 participants included in this analysis. Upon subsequent review, 10 did not have PID. Of the 23 remaining participants, we categorized 6 as “likely PID” and 17 as “possible PID.” Table 2 shows the rate of PID by IUD use, and also stratified by baseline GC/CT status. We found both the self-reported rate of PID among IUD and non-IUD users in the first 6 months to be near or below 1%. The self-reported PID rate by 6 months was 0.46% among all IUD users (95% confidence interval 0.26%–0.66%) and 0.09% among all non-IUD users (95% confidence interval 0%–0.20%). We were conservative in our approach and included the “possible PID” and “likely PID” cases as PID. If we only include “likely PID” cases, the rate of PID in IUD users would decrease from 0.46% to 0.14%.

Among participants who tested positive for GC and/or CT at baseline, the PID rate among IUD users and non-IUD users

were 1.10% and 0% respectively ($p=0.42$). Among patients with negative baseline GC and CT tests, the PID rates in IUD and non-IUD users were 0.44% and 0.10% respectively ($p=0.008$).

Discussion

We found that the rate of PID was higher in the IUD group than the non-IUD group. However, the occurrence of PID in both IUD and non-IUD users was rare. The rates of PID in IUD and non-IUD users who had tested positive for GC and/or CT at baseline were 1% or less. The low rate of PID among women testing positive for GC and/or CT may be attributed to their prompt antibiotic treatment. Among participants who tested negative for GC and/or CT at baseline, both IUD and non-IUD users reported rates of PID that were well below 1%.

A World Health Organization (WHO) meta-analysis of 12 randomized studies comparing two or more types of IUDs found the overall rate of PID to be 1.6 per 1,000 woman-years.¹¹ The meta-analysis included 22,908 IUD insertions and reported 81 cases of PID (0.35% of insertions) with 51,339 woman-years of follow-up. After the first 20 days post insertion, the PID incidence was 1.4 per 1,000 woman-years; however, the PID rate within the first 20 days of insertion was 9.7 per 1,000 woman-years. If we convert the observed 0.46% of IUD users who were diagnosed with PID by 6 months to a rate per 1,000 woman-years, it would approximately be 9.2 per 1,000 woman-years. This is very similar to the findings from the WHO meta-analysis.

Because PID rates are not consistent over time after IUD insertion, we should consider the duration of follow-up time when comparing rates from different studies. Several other international studies have found the incidence of PID in IUD users to be statistically similar to that in nonusers after the first 20 days following insertion.^{7–10} In our study, when analyzed by type of IUD, the rate of PID for the Cu-IUD was 0.58 per 1,000 woman-years (with 2,795 insertions), and there were no PID cases in women using the LNG-IUS (1,552 insertions). A meta-analysis of studies done in multiple African countries with high STI prevalence estimated the risk of PID attributable to IUD to be 1.5 per 1,000 women at high-risk of STI.^{14,15} The same meta-analysis cited a smaller study that estimated the risk of symptomatic PID after IUD insertion during CT and/or GC infection to be 3.1%.¹²

The Contraceptive CHOICE Project contains the largest prospective cohort of IUD users in the U.S. Thus, strengths of this study include the large number of IUD users and the systematic, prospective assessment. Our analysis relied on a combination of data sources to capture PID cases: (1) self-reported PID by study participants in response to a survey question; (2) unscheduled calls to study staff to report PID or signs/symptoms of infection; or (3) during a visit to the study clinic. However, we attempted to assess false positive cases by reviewing participant medical records, when available. We used a liberal case definition for PID and therefore may have included cases that were not truly PID. In addition, we had four cases of self-reported PID for which we could not locate supporting medical record documentation. We were conservative in our approach and included these “possible PID” cases as PID. Thus, our rate is most likely an overestimate of the true rate of PID among IUD users.

TABLE 1. PARTICIPANT BASELINE CHARACTERISTICS BY BASELINE CHOSEN METHOD

	<i>Total (n=7,611)</i>		<i>Non-IUD (n=3,240)</i>		<i>IUD (n=4,371)</i>		<i>p^a</i>
	<i>Mean</i>	<i>SD</i>	<i>Mean</i>	<i>SD</i>	<i>Mean</i>	<i>SD</i>	
Age	25.2	5.9	23.7	5.4	26.4	5.9	<0.01
	<i>Median</i>	<i>Range</i>	<i>Median</i>	<i>Range</i>	<i>Median</i>	<i>Range</i>	
Total lifetime sex partners	6	0–308	5	0–308	6	0–215	<0.01
	<i>n</i>	<i>%</i>	<i>n</i>	<i>%</i>	<i>n</i>	<i>%</i>	
Race							<0.01
Black	3713	48.8	1730	53.4	1983	45.4	
White	3310	43.5	1249	38.6	2061	47.2	
Others	587	7.7	260	8.0	327	7.5	
History of STI ^b							0.01
No	4565	60.0	1996	61.6	2569	58.8	
Yes	3046	40.0	1244	38.4	1802	41.2	
Any STI at baseline ^c							0.01
No	7059	92.7	2964	91.5	4095	93.7	
Yes	552	7.3	276	8.5	276	6.3	
Ever abortion at baseline							<0.01
No	4920	64.6	2195	67.7	2725	62.3	
Yes	2691	35.4	1045	32.3	1646	37.7	
Gravidity							<0.01
No	2432	32.0	1326	40.9	1106	25.3	
Yes	5179	68.0	1914	59.1	3265	74.7	
More than 1 partner in last 30 days							0.02
No	7106	94.5	2979	93.9	4127	95.0	
Yes	410	5.5	195	6.1	215	5.0	
Condom use with all partners in last 30 days ^d							<0.01
Every time	1997	36.4	917	40.0	1080	33.8	
Almost every time	623	11.4	303	13.2	320	10.0	
Sometimes	537	9.8	245	10.7	292	9.1	
Almost never	309	5.6	148	6.5	161	5.0	
Never	2019	36.8	680	29.7	1339	41.9	
Public support or trouble paying for basic necessities							0.04
No	3345	43.9	1467	45.3	1878	43.0	
Yes	4266	56.1	1773	54.7	2493	57.0	
Health care in last 12 months							<0.01
Yes	5977	89.1	2520	87.8	3457	90.1	
No	732	10.9	351	12.2	381	9.9	
Cervical cancer screening in the last year							0.13
No	932	13.2	401	13.9	531	12.7	
Yes	6124	86.8	2475	86.1	3649	87.3	
Currently smoker							0.02
Yes	1756	23.1	706	21.8	1050	24.1	
No	5837	76.9	2529	78.2	3308	75.9	
Any drug use ^e							0.01
No	6104	80.7	2554	79.3	3550	81.7	
Yes	1463	19.3	666	20.7	797	18.3	

^a*p*-value is from comparison between IUD users and non-IUD users.

^bHistory of STI includes self-reported history of chlamydia infection, gonorrhea, syphilis, trichomoniasis, genital herpes, genital warts, human papillomavirus infection, human immunodeficiency virus infection, or pelvic inflammatory disease.

^cSTI at baseline includes positive test for chlamydia, gonorrhea, trichomonas, syphilis or human immunodeficiency virus.

^dNumber (*n*) for this variable is equal to 3,488 and represents only participants who reported having sex within the past 30 days at enrollment.

^eDrug use includes “yes” responses to any of the five questions asking participants if they use weed, use ecstasy, smoke/snort/swallow/inhale any other drug, shoot up any drugs, or exchange sex for drugs.

IUD, intrauterine device; SD, standard deviation; STI, sexually transmitted infection.

TABLE 2. PELVIC INFLAMMATORY DISEASE RATE (%) AND 95% CONFIDENCE INTERVALS BY IUD USE BY 6-MONTH INTERVIEW

	N	PID rate	95% CI	p
All	7611	0.30	0.18–0.43	
IUD	4371	0.46	0.26–0.66	0.005
non-IUD	3240	0.09	0.00–0.20	
<i>Stratified by CT/GC</i>				
CT/GC positive	215	0.47	0.00–1.38	
IUD	91	1.10	0.00–3.28	0.42
non-IUD	124	0.00	0.00–0.00	
CT/GC negative	7396	0.30	0.17–0.42	
IUD	4280	0.44	0.24–0.64	0.008
non-IUD	3116	0.10	0.00–0.21	

CI, confidence interval; CT, *Chlamydia trachomatis*; GC, *Neisseria gonorrhoeae*; PID, pelvic inflammatory disease.

Our study is not without limitations. First, chart review is severely limited as a diagnostic tool for PID; prospective clinical evaluations with objective PID criteria would have been ideal. However, clinical assessment for PID also has significant limitations.^{19,20} Clinicians are more likely to diagnose abdominal/pelvic pain as PID in IUD users compared with non-IUD users.²¹ Current guidelines for initiating treatment of PID are sensitive but not specific, allowing for a high rate of false positives. Women using IUDs are counseled to be aware of pelvic pain and may therefore be more likely to seek healthcare and subsequently receive a diagnosis of PID. We selected our comparison group to be women using the implant, DMPA, OCPs, patch, or ring as our comparison group because they represent the largest group of contraceptive women in the U.S.; 34.7% of reproductive-age American women using contraception use one of these methods according to the latest National Survey of Family Growth.²² We considered classifying condom users as the comparison group, but their risk of STIs and PID is lower if they are using a barrier method consistently and correctly. We also considered comparing IUD users with women using no contraception; however, women using no method are at higher risk for STI and PID than most women, and very few women in CHOICE chose no method at the time of enrollment. We were unable to stratify our analysis by important subgroups and potential confounding variables (e.g., smoking, prior history of STI, higher total number of lifetime sexual partners, condom use, etc.) because of the small number of PID cases identified. Finally, women with PID often do not have symptoms or have mild symptoms such that relying on self-report likely underestimates PID.²³

Conclusion

In a cohort of over 5,000 IUD users, we found that PID is a rare complication of IUD use, even among women testing positive for GC and/or CT. Clinicians should dispel the myths and misconceptions regarding young age, IUD use, and infection risk. IUDs should be offered as first-line contraceptive options for most women, including high-risk women. In addition, same-day IUD insertion should be considered, as the rate of infectious morbidity is low even in the highest risk groups.

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