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Contraception xx (2016) xxx-xxx

Contraception

Review article

Tara C. Jatlaoui*, Katharine B. Simmons, Kathryn M. Curtis

Division of Reproductive Health, US Centers for Disease Control and Prevention, Atlanta, Georgia
Received 3 April 2016; revised 24 May 2016; accepted 27 May 2016

Abstract

Objective: The objective was to assess risk of pelvic inflammatory disease (PID) among women with current asymptomatic undiagnosed cervical infection or who are at high risk of sexually transmitted infections (STIs), comparing those who have a copper-bearing (Cu-) or levonorgestrel (LNG-) intrauterine device (IUD) placed with women who do not.

Study design: We searched PubMed and Cochrane Library for articles from January 1984 through January 2016 addressing our objective. We assessed study quality using the United States Preventive Services Task Force evidence grading system.

Results: Our search strategy yielded 2220 articles, of which 10 met inclusion criteria. Two studies provided direct evidence of PID rates in women with undiagnosed gonococcal or chlamydial (GC/CT) infection or at high risk for STIs initiating IUDs versus other contraceptive methods (level II-2, fair to poor), and neither study found a difference. Eight studies provided indirect evidence (II-2 to II-3, fair to poor). One study found no difference in PID rates between initiators of Cu- versus LNG-IUDs. Five studies compared algorithms based on patient factors with laboratory GC/CT screening to predict cervical infection. Based on likelihood ratios, none of these algorithms adequately identified women at high risk of asymptomatic cervical infection who should not undergo IUD placement. Two studies compared IUD placement on the same day as STI screening with delayed placement after screening and found no difference in PID rates.

Conclusion: Limited evidence suggests that IUD placement does not increase the risk of PID compared with no IUD placement among women with asymptomatic undiagnosed cervical infection or at high risk of STIs. Algorithms based on patient characteristics to identify women with asymptomatic GC/CT may be overly restrictive, leading to missed opportunities for IUD initiation. Historical concerns about higher PID risk among women at risk for STIs who use IUDs may not be relevant with modern devices and STI screening and treatment practices.

Published by Elsevier Inc.

Keywords: Intrauterine device; Cervical infection; Pelvic inflammatory disease; Gonorrhea; Chlamydia

1. Introduction

Intrauterine devices (IUDs) offer highly effective contraception and are considered safe or generally safe for most women [1,2]. The use of IUDs has increased, and currently 10.3% of contraceptive users in the United States (US) use IUDs [containing either copper (Cu) or levonorgestrel

(LNG)] [3]. However, IUD use remains low for younger women; only 2.8% of those aged 15–19 years who received services at Title X sites in 2013 used IUDs [4]. Women perceived as being at higher risk of sexually transmitted infections (STIs) or pelvic inflammatory disease (PID), such as young women or women with multiple partners, often face barriers to obtaining IUDs, including provider bias, which may partially explain this lower rate of use [5,6].

The risk of PID among IUD initiators is elevated in the first weeks following placement; however, the absolute risk of PID is very low [7]. US guidelines presently recommend that women should not have an IUD placed if they currently have purulent cervicitis, gonococcal or chlamydial (GC/CT) infection, or PID [2]. The Centers for Disease Control and

[☆] Financial disclosures: none.

^{**} Disclaimer: The findings and conclusions in this report are those of the authors and do not necessarily represent the official position of the US Centers for Disease Control and Prevention.

^{*} Corresponding author. Tel.: +1 770 488 6537; fax: +1 770 488 6391. E-mail address: tjatlaoui@cdc.gov (T.C. Jatlaoui).

Prevention (CDC) Sexually Transmitted Diseases (STD) Treatment Guidelines, 2015, recommend annual gonorrhea and chlamydia screening by nucleic acid amplification test (NAAT) for sexually active women aged less than 25 years, for women aged 35 years and under in correctional facilities and for other women at high risk based on history, sexual practices and the prevalence of disease in the community [10]. Most women who have been screened according to current CDC STD Treatment Guidelines do not need additional screening prior to IUD placement, and those who screen positive may be treated without IUD removal [8]. However, the risk of PID from an ascending asymptomatic cervical infection, which most commonly is caused by GC/CT infection, following IUD placement compared with no IUD placement is unknown [9]. This systematic review aimed to assess risk of PID among women with current asymptomatic undiagnosed cervical infection or who are high risk of STIs, comparing those who had a Cu- or LNG-IUD placed with those who did not have an IUD placed.

2. Materials and methods

We conducted this systematic review according to Preferred Reporting Items for Systematic Reviews and Meta-Analyses guidelines [11]. We searched PubMed for studies conducted from 1984 (date of Cu-T380A IUD approval in the US) to January 2016 using the following search strategy: (("Pelvic Inflammatory Disease" [MESH] OR pelvic inflammatory disease OR PID OR Salpingitis) OR ("Sexually Transmitted Diseases" [Mesh] OR "sexually transmitted diseases" OR "sexually transmitted disease" OR "sexually transmitted infections" OR "sexually transmitted infection") OR (gonorrhea OR gonorrhea OR chlamydia) OR ("Uterine Cervicitis" [Mesh] OR cervicitis)) AND (((levonorgestrel AND intrauterine devices[mesh] OR iud OR iucd OR ius OR iuc OR intrauterine system OR intra-uterine system OR intrauterine device OR intra-uterine device OR intrauterine contraceptive OR intrauterine contraception) OR mirena) OR (("Intrauterine Devices" [Mesh] OR "Intrauterine Devices, Medicated" [Mesh] OR "Intrauterine Devices, Copper" [Mesh]) OR iud OR iucd OR ius OR iuc OR intrauterine system OR intra-uterine system OR intrauterine device OR intra-uterine device OR intrauterine contraceptive OR intrauterine contraception)). We also searched the Cochrane Library for any reviews examining IUDs and PID.

We included primary research articles in all languages that directly answered the question, "Among women with asymptomatic GC/CT or at high risk of STIs, is the risk of PID increased for women who undergo CuT380A or LNG-IUD placement compared with women who do not undergo IUD placement?" We included indirect evidence that examined algorithms for identifying women at increased risk of STIs prior to Cu- or LNG-IUD placement. We also

considered indirect evidence studies that compared PID rates among LNG- and Cu-IUD initiators to examine whether PID risk differs between IUD types, and studies that reported PID rates in women screened versus not screened for GC/CT infection before Cu- or LNG-IUD placement.

Two coauthors (T.C.J. and K.B.S.) independently graded the articles according to the United States Preventive Services Task Force evidence grading system [12]. Quality factors assessed for randomized controlled trials (RCTs) included adequate randomization, allocation, concealment and blinding. Quality factors for cohort studies included exposure or intervention definitions/assessment (diagnosis of GC/CT infection by culture or NAATs or other defined screening, IUD type specified), outcome assessment (whether presence of PID was assessed by a provider using criteria consistent with CDC STD Treatment Guidelines [10] or by medical record validation), assessment of potential confounders (e.g., age, condom use, sexual behavior, history of STIs or PID, contraceptive method) at baseline and in modeling, loss to follow-up, and sample size and power. We did not include case-control studies that examined PID and IUD use if they could not assess the timing of PID diagnosis after IUD placement or assess whether a cervical infection was present at the time of IUD initiation. Due to the heterogeneity of study designs, we did not compute summary measures.

3. Results

This search identified 2220 articles of which 2 met our inclusion criteria for direct evidence and 8 for indirect evidence.

3.1. Direct evidence

A secondary data analysis (level II-2, fair) of a US prospective cohort study examined the rate of PID over 6 months among 4371 Cu-IUD or LNG-IUD initiators compared with 3240 non-IUD contraception initiators (Table 1) [13]. All women were screened for GC/CT at baseline with NAAT, and asymptomatic women initiated the IUD on the same day as screening. PID was assessed by self-report and confirmed through chart review. Among the 215 asymptomatic women testing positive for GC/CT at baseline, 1 of 91 women initiating an IUD developed PID compared to none of 124 women who did not initiate an IUD (rates of 1.1 vs. 0.0, respectively; p=.42). Most of these women began antibiotics according to national guidelines within 2-3 weeks of enrollment. Across all women regardless of baseline GC/CT status, rates of PID were low but were significantly higher among IUD users at 6 months [0.46%; 95% confidence interval (CI), CI 0.26–0.66] compared with non-IUD users (0.09%; 95% CI, 0-0.20; p = .005).

One US retrospective cohort study (level II-2, poor) at a tertiary care inner city clinic reported PID rates among

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