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Randomized assignment to copper IUD or depot-medroxyprogesterone acetate: feasibility of enrollment, continuation and disease ascertainment

Paul J. Feldblum[a,*], Jennifer Caraway[a], Luis Bahamondes[b], Mohamed El-Shafei[c], Do Quan Ha[d], Edwin Morales[e], Silver Wevill[a], Sean Condon[a]

[a]*Family Health International, P.O. Box 13950, Research Triangle Park, NC 27709, USA*
[b]*Department of Obstetrics and Gynecology, School of Medicine, Universidade Estadual de Campinas, Campinas, Brazil*
[c]*Fertility Care Unit, Mansoura University Hospital, Mansoura, Egypt*
[d]*National Hospital of Obstetrics and Gynecology of Vietnam (formerly, the Institute for the Protection of Mother and Newborn), Hanoi, Vietnam*
[e]*APROFAM, Guatemala City, Guatemala*

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Abstract

Objectives: We conducted a feasibility study to enroll and follow family planning acceptors who were randomly assigned to use an intrauterine device (IUD) or injectable depot-medroxyprogesterone acetate (DMPA).

Methods: Centers in Brazil, Guatemala, Egypt and Vietnam aimed to enroll 100 participants per site. Enrolled women were randomly assigned to have inserted a TCu 380A IUD, or to receive injections of 150 mg of DMPA every 3 months, and scheduled for up to 12 months of follow-up. We tested for cervical infection at first and final visits, and examined for signs of pelvic inflammatory disease (PID) at each visit.

Results: The sites screened 555 women and enrolled 368. Two women (0.5%) had three discomfort signs of PID during follow-up. The prevalence of gonorrhea at each woman's final follow-up visit was 0.5%, and the prevalence of chlamydia at final visit was 5.4%. Sixty-eight percent of women either completed 12 months of observation with their assigned method or were still using their method at the end of the study.

Conclusion: A larger, definitive clinical trial appears feasible. The majority of women we approached agreed to participate; nearly 400 women were enrolled; two thirds continued to use their assigned method until study closeout; and the STI risk was moderate.

Keywords: Pilot study; Randomized controlled trial; Copper IUD; Depot-medroxyprogesterone acetate; Pelvic inflammatory disease

1. Introduction

Although the intrauterine device (IUD) has long been associated by users and clinicians with pelvic inflammatory disease (PID), whether IUDs continue to increase PID risk once the insertion-related risks have passed is unclear. Studies reported through the 1970s found strong associations between IUD use and PID [1]; large studies from the 1980s reported less extreme but still elevated PID risk among IUD users, with relative risk estimates ranging from 1.6 to 2.3 [2,3]. Some of the increased PID risks were attributable to the Dalkon shield [4]. Uterine contamination explained another portion of the elevated risk, as shown by high PID rates during the initial 20 days postinsertion and low and constant rates thereafter [5].

How could we improve on earlier comparative studies with known diagnostic and confounding biases? To determine the relative disease risks among users of family planning methods, a study should incorporate a standardized diagnostic protocol to minimize diagnostic bias. It must be large enough to measure relatively rare events like PID. Finally, it should be randomized to eliminate confounding bias. However, the feasibility of randomizing women to dissimilar contraceptive groups is uncertain.

We conducted a study to test the feasibility of a randomized controlled trial (RCT) to compare the incidence of PID in IUD users to the incidence in users of injectable depot-medroxyprogesterone acetate (DMPA). Study objectives were to determine the feasibility of enrolling and

* Corresponding author. Tel.: +1 919 544 7040; fax: +1 919 544 7261.
E-mail address: pfeldblum@fhi.org (P.J. Feldblum).

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following family planning acceptors who have been randomly assigned to use the IUD or DMPA, and to collect information on the suitability of our four participating sites for a possible larger clinical trial in terms of STI risk and study implementation.

2. Materials and methods

We aimed to randomize and enroll 400 family planning clinic attenders to the IUD or DMPA study group for up to 12 months of observation.

2.1. Ethical considerations

This study was reviewed and approved by the Family Health International (FHI) Protection of Human Subjects Committee (PHSC) and by the IRBs at three of the four study sites. The PHSC served as the reviewing IRB for the Vietnam site. All participating women read, or had read to them, the informed consent form and signed a volunteer agreement form. All women received a noncoercive compensation for travel costs at each visit.

2.2. Study populations

Sites joined the study based on their research and diagnostic capabilities, numbers of users of both study methods and expected STI and PID rates. The centers were in Campinas, Brazil; Guatemala City, Guatemala; Mansoura, Egypt; and Hanoi, Vietnam. Clinic clients who expressed an interest in using either an IUD or DMPA were approached about the study. We aimed to enroll 100 participants per study site, 50 in each arm, within 9 months. Enrolled women were randomly assigned to have inserted a TCu 380A IUD or to receive injections of 150 mg of DMPA every 3 months. Enrollment began in April 2002 and follow-up ended in September 2003.

2.3. Eligibility criteria

To enroll, each woman had to be willing to use either an IUD or DMPA for at least 1 year and have no medical contraindications to either method [6]. Other eligibility criteria included sexually active and desiring contraception; not pregnant as demonstrated by normal menses within the past 5 days, or a negative urine pregnancy test at enrollment; not known to be at high risk for STIs, and not suspected of having current STI; not currently using an IUD; and did not receive a DMPA injection within the past 6 months.

2.4. Screening and enrollment

All screening and enrollment procedures were conducted on a single day. Clinical personnel were to provide contraceptive counseling about all methods available at the clinic, explain the study and confirm eligibility; administer informed consent and have woman sign the consent form; obtain baseline demographic information, reproductive history and sexual activity data; perform speculum and bimanual pelvic examination; obtain cervical specimens for gonorrhea culture and chlamydia antigen test; randomly assign woman to IUD or DMPA; insert IUD or inject DMPA; give the participant an appointment for the first follow-up visit; instruct participant to return immediately if she has PID symptoms; and reimburse the woman for transportation.

2.5. Randomization and allocation concealment

We used sequentially numbered sealed, opaque envelopes containing the group assignment. The computer-generated randomization list was stratified by center and blocked with sizes of 10, 4 and 2. We instructed the staff never to open an envelope until the participant was fully screened, consented, confirmed eligible for the study and ready for immediate IUD insertion or DMPA injection.

2.6. Follow-up visits

Follow-up visits were scheduled at 2 weeks and 1, 3, 6, 9 and 12 months. The intense early visit schedule was chosen to optimize detection of PID early after admission, and subsequently to correspond to scheduled DMPA reinjections. Data were collected for 12 months only at each center; data from women who continued to use their method after study closeout were censored.

At all follow-up visits, we interviewed the woman, performed a pelvic examination and gave DMPA injections at the 3-, 6-, 9- and 12-month visits. We obtained endocervical specimens for gonorrhea culture and chlamydia antigen testing at each woman's final study visit.

2.7. Diagnosis of PID

We used two different criteria for PID diagnosis (Table 1). The more conservative 'sensitive' criteria, promoted by the U.S. Centers for Disease Control and Prevention (CDC) in 1998 [7], were used for initial screening at all visits. If these criteria were met, further testing determined whether the 'specific' criteria were also fulfilled; these were slightly modified from the Hager criteria [8]. Women with PID

Table 1
1998 CDC diagnostic criteria for PID [7]

Sensitive criteria: woman has all of the following	Specific criteria: woman meets sensitive criteria, and in addition, has at least one of the following
Abdominal tenderness	Positive cervical gonorrhea culture or chlamydia ELISA
Cervical motion tenderness	Oral temperature of greater than 38°C
Adnexal tenderness	Leukocytosis greater than 10,000 white blood cells per microliter
No identifiable cause other than PID	Adnexal mass on bimanual exam
	Ultrasound evidence of abscess or inflammatory complex
	Purulent material obtained on culdocentesis
	Evidence of PID by endometrial biopsy, laparoscopy or laparotomy