Designing Clinical Research – Summer 2009 – Final Protocol
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Title and Investigators:

Acceptability and success of long-term progestin-only contraception following surgical abortion- Tushani Illangasekare, MS4, Justin Dietrich, MD, Jody Steinauer, MD, Eleanor Drey, MD

Study Aim:

To determine differences in the one-year continuation rates of the etonorgestrel implant (Implanon), levonorgestrel IUS (IUS), and depot medroxyprogesterone acetate (DMPA) in women who have recently undergone a surgical abortion and initiated the method at the time of the abortion at San Francisco General Hospital.

Background:

The U.S has one of the highest rates of unintended pregnancy among industrialized nations around the world, with 48% of women aged 15-44 reporting that they have had an unintended pregnancy.[1] Women undergoing elective abortions are at especially high risk of having another unintended pregnancy. Nearly half (46%) of women getting an abortion have already undergone one or more abortions previously.[2,3] Women who have abortions have often experienced method failure with hormonal methods such as oral contraceptive pills, the patch and the ring, as well as with barrier methods and condom use. Non-compliance, the predominant reason for method failure, is eliminated with long acting methods.[1] Further, initiation of contraceptive methods on the day women choose them increases continuation. Therefore, offering women long-acting methods at the time of abortion has great potential to decrease the rates of repeat, unintended pregnancy.

Two new, long-acting methods have the potential to meet this need. The first, the levonorgestrel containing intrauterine device (LNG-IUS, IUS, or Mirena), is a highly effective, safe, user-independent form of birth control that can be used for up to five years. Placement in the post-abortion setting has been demonstrated to be safe with no increased risk of perforation or infection. [4] Estimates of post-abortion expulsion rates have varied from being equivalent to insertion in non-pregnant uteri (8%) to being nearly twice as high (8% v. 15%) after second-trimester abortion.[5,6]

The second method, the etonorgestrel, subdermal contraceptive implant, Implanon, is also a highly effective, safe, user-independent contraceptive method that can be used for up to three years. [7] Compared to the IUS, there is no increased risk of significant adverse events associated with insertion such as expulsion, perforation or uterine infection. [8,9] Placement of the implant at the time of abortion has the potential to have high acceptability when placed under conscious sedation, but has not been described in the literature.

Both methods require office visits for insertion and removal. However, once in place, they do not require any further administration like other methods such as episodic condom use, daily pills, weekly patches, monthly rings, or every three-month shots. The extremely high efficacy (99.9%) of both, in combination with the reversibility and ease of use, make them

excellent methods for women at high risk of unintended pregnancy, such as those who have recently undergone an abortion. Furthermore, the acceptability and side effect profiles of the implant and levonorgestrel IUS are already well described in the non-post-abortion setting [5,6,13]

In contrast, DMPA (Depo Provera) is a popular, long-acting, progestin-only method that consists of an intramuscular injection of 150mg medroxyprogesterone acetate. Because injections are necessary every three months, this method requires more user adherence than the implant and LNG-IUS. In typical use, DMPA has an efficacy of 97%, though most users do not use it for an entire year. Studies of this contraception method show one-year continuation rates as low as 20% and as high as 40%.[15] Despite lower efficacy and continuation rates than the longer acting progestin methods it is frequently prescribed, both outside of pregnancy and in the post-abortion setting. Eighty-one percent of U.S. clinicians prescribe DMPA in adolescent patients. When asked why, 67% cite patient noncompliance with other methods and 21% say the method was requested by their patients.[15]

The main aim of this study is to determine the twelve month continuation rates and satisfaction with LNG-IUS and Implanon compared to DMPA in order to evaluate which is most effective in preventing repeat unintended pregnancy and abortion rate. This will be accomplished through assessing the contraceptive practices and outcomes of women who have chosen one of these three progestin methods in the post-abortion setting. We hypothesize that women who choose the IUS or the implant will be more likely to successfully continue their contraceptive methods for one year after their abortions compared to women who choose DMPA.

Abortion is one of the most common health services provided in the US. [17] Reducing unintended pregnancy is the most effective way to reduce abortion rates. [17] By investigating these aims, we will gain a better understanding about women's contraceptive practices and the decisions they make surrounding their post-abortion reproductive practices. The results of our study will help to inform abortion providers about the feasibility and acceptance of offering the implant, as well as comparing it to other highly effective forms of contraception in the post-abortion setting. This will help increase the effectiveness of contraceptive options after abortion and help decrease the need for repeat abortions for noncompliance and less effective means of contraception.

Design:

This will be a prospective cohort study to identify continuation rates, factors associated with acceptability, and post-abortion bleeding side effects of the Implant and IUS compared with Depo in women who initiate the method on the same day of their abortions. Subjects will be enrolled and consented when they appear for their abortions. In addition to completing a baseline survey, subjects will keep a prospective menstrual diary for three months and will be followed up with telephone surveys at one, three, six and twelve months after their abortions.

Study Subjects

Study subjects will be women who present for an abortion at the San Francisco General Hospital's (SFGH) Women's Option Center (WOC). These women are mostly uninsured or have MediCal. This population is financially challenged, frequently young, and often not well-educated. These characteristics define a group of women who are at very high risk for having

difficulties with contraception and, therefore, repeat unplanned or unwanted pregnancies. Eligible subjects will have selected to receive the progestin-only method of their choice to be started after their abortion.
Additional eligibility criteria will include women who:

- are between 15 and 44 years of age;
- have a gestational duration up to 23 weeks and one day at the time of their abortion;
- are able and willing to keep an accurate prospective menstrual record card;
- are determined to be eligible for progestin-only contraception by her clinician;
- have regular monthly menstrual cycles; and
- if Depo-Provera has been used in the last year, whose normal menstrual cycles have resumed with at least two normal, consecutive menses.

Exclusion criteria include:

- inability read or write Spanish or English;
- having current or previous genital tract or breast malignancy;
- having had evaluation or treatment for abnormal uterine bleeding in the last three months.

Sampling, Recruitment and Consent

All women who present for an abortion at the WOC are counseled regarding their contraceptive plans. During this counseling, patients are presented with the available contraceptive options and are encouraged to initiate it immediately after the procedure. All patients who indicate an interest in starting the implant, Mirena or DMPA immediately after their abortions are asked if they are willing to participate in the study, and are assessed for their eligibility. All potential subjects will receive a thorough overview of the study protocol and will review the consent form with study staff. Each potential subject will be advised that a decision not to participate in the study will not affect the quality of care she can receive at the clinic. Each subject will also be advised that she can stop participating in the study at any time for any reason, and that this will not impact the services she receives. A consecutive sample of women who present at the WOC and who agree to immediately begin the highly-effective contraception after their abortion and who meet the inclusion criteria will be enrolled into the study.

Participating women are asked to complete menstrual diaries prospectively for three months to quantify bleeding patterns. In addition to bleeding patterns, women are instructed how to record side effects, concurrent medications and adverse events. Patients will use the diaries as an aid to answer questions during follow-up phone surveys. Patients will receive a $20 gift card to Target or Safeway after completing their baseline survey and after each follow-up phone survey. They will receive a $50 gift card after completing their 1-year follow-up survey.

Measurements:

Predictor Variables

The main predictor variable is type of contraceptive method (implant, IUS or DMPA). Other variables that might be associated with continuation of contraceptive method (and may also be possible confounders) include age, bleeding irregularities, side effects, partner satisfaction, and sexual activity post-abortion. These variables will be collected from the patient medical record,

or from the baseline and follow-up surveys. Additional variables that may be associated with the outcomes include procedural factors such as gestational duration at the time of abortion and complications, and historical factors such as bleeding history, past pregnancy numbers and outcomes, and past contraception practice. These variables will be abstracted from the medical record and baseline survey.

Outcome Variable

The primary outcome variable for women receiving their method on the day of their abortion will be continuation of the contraceptive method at twelve months, with the duration of continuation assessed by telephone interviews. Other secondary outcome measures include patient pain, acceptability and satisfaction at the time of implant placement, and bleeding patterns in the first three months after the abortion as measured by the WHO criteria for bleeding.[16]

Statistical Issues

Sample Size

The population presenting at the WOC for an abortion is known to be difficult to follow, and we anticipate loss to follow-up rate of 40 percent based on prior studies with this population. We will use the following estimated continuation rates based on the literature in the non-post-abortion setting: IUS 70% (79% in non-post-abortion setting less 9% additional expulsions), implant 62%, and DMPA 30%.

Sample Size Assumptions

1. Estimating continuation of 70% IUS and 30% DMPA: effect size 40%
2. Estimating continuation of 60% Implant and 30% DMPA: effect size 30%
3. 2-sided alpha 0.025
4. Beta 0.2

Sample Size and Recruitment estimates

1. DMPA sample size: 60
2. IUS sample size: 23
3. Implant sample size: 55
4. Recruiting goals adjusting for 40% loss to follow-up rate:
    a. IUS – 92 women
    b. Implanon – 92 women
    c. DMPA – 100 women

The null hypothesis to our study aim is that there is no difference in one-year continuation rates between the three different long-term progestin-only contraception methods (IUS vs. DMPA and Implant vs. DMPA).

Data Analysis

In general, to describe the characteristics of the study population, chi-square will be used to compare proportions and multivariable analysis will be used to identify independent predictors if possible.

Study Logistics and Timeline:

Pretest plans:

As the majority of our surveys will be computer based, we will be testing the baseline and follow-up questionnaires prior to patient recruitment. We will create Sample study ID numbers and have the study staff test the data editing system to ensure that our database management system is functional and secure.

Quality Control and Data Management:

Once a patient has been consented for the study, she will be assigned a study ID number. This number will be arbitrary and will never be associated with the patient's last name, birth date or medical record number. We will enter this Study ID into a master database with calculated follow-up dates based on their initial recruitment date. A thorough chart abstraction will be included with the patient's initial entry packet, which will be carefully labeled with the patient's study ID number and recruitment date. After this data is collected, we will enter this data into a database using the Survey Crafter application. The data will be organized by Study ID number and will not contain any other identifying information.

Ethical considerations:

All women who present for an abortion at the WOC are counseled regarding their contraceptive plans as a standard aspect of clinic procedure. We will not approach women about the study until after they have been independently counseled and have made the final decision to terminate the pregnancy. During this counseling, patients are presented with the available contraceptive options. We do not want to influence a patients' method choice, as our study will have some monetary reimbursement. All patients who indicate an interest in starting the implant, Mirena or DMPA immediately after their abortions are asked if they are willing to participate in the study, and are assessed for their eligibility. We will go through a thorough consenting process with each patient and will carefully list the risks and benefits in participating in the study. Every participant is informed that they are able to disenroll from the study at any time. They will be counseled that participation is voluntary and that their care at the WOC will not me affected by any decision they make regarding the study.

Timeline

We are anticipating that it will take 10 months to recruit subjects; we are planning to recruit 12-15 subjects per week. We will then follow subjects for up to one year. We will enter data throughout the study and will spend the final two months analyzing and preparing the manuscript.

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