Cervical Priming with Vaginal Misoprostol Prior to Insertion of an Intrauterine Contraceptive Device

Thesis

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بسم الله الرحمن الرحيم

قَالُوا سُبْحَانكَ لاَ عِلمَ لَنَا إلاّ مَا

عَلّمْتَنَا إنَّكَ أنتَ العَلِيمُ الحَكِيمُ

صدق الله العظيم

سورة البقرة آية (٣٢)

I would like to dedicate this thesis to my ***Father****, to my* ***Mother*** *and to my* ***Husband****;*
to them I will never find adequate words
to express my gratitude.

Also to all my ***Family*** *for dealing tactfully*
and patiently during this work

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Salma Ashraf Mohamed Nassar

List of Contents

List of Abbreviations

D&C : Dilatation and curettage

FDA : Food and Drug Administration

GnRH : Gonado-tropin releasing hormone

hCG : Human chorionic gonadotrophin

IUCD : Intrauterine contraceptive device

NS : Not significant

NSAIDs : Non steroidal anti-inflammatory drugs

PID : Pelvic inflammatory disease

RCT : Randomised controlled trial

SD : Standard deviation

STIs : sexually transmitted infections

UCDs : Uterine-shaped copper devices

WHO : World Health Organization

List of Tables

List of Figures

Introduction

The intrauterine contraceptive device (IUCD) provides long-term, reversible contraception equal in efficacy to tubal sterilization. Depending on the country, the use of IUCDs worldwide ranges from 2% to 75%. On average, 15% of reproductive-aged women in developing countries and 8% in developed countries use IUCDs. Increasing the number of women using IUCDs is an important public health goal ***(Grimes, 2008)***.

One barrier to IUCD use is the fear of pain during insertion. Components of the insertion procedure that may cause pain include the application of the tenaculum to the cervix to stabilize the uterus and provide traction for straightening the cervical canal, passing the uterine sound, inserting the IUCD in the inserter tube through the cervix, and irritation of the endometrial cavity with the device ***(d'Arcangues, 2007)***.

Cervical pain is mediated by S2 to S4 parasympathetic nerves while the T10 to L1 sympathetic fibers innervate the uterine fundus. While some IUDs are inserted postpartum or postabortal, most are inserted remote (more than four weeks) from pregnancy as a clinic-based procedure ***(d'Arcangues, 2007)***.

The levels of pain that women experience during IUCD insertion vary in published reports. Most women experience mild to moderate discomfort during IUCD insertion. Rarely, the pain is severe and associated with nausea and weakness. Pain may persist for a few days after insertion. Predictors of pain

during IUCD insertion include nulliparity, age greater than 30 years, lengthier time since last pregnancy or last menses, and not currently breastfeeding. Psychosocial factors including expected pain also influence the pain perceived by women undergoing the procedure ***(Hubacher, 2007)***.

The use of prophylactic non steroidal anti-inflammatory drugs (NSAIDs) prior to IUCD insertion has been advocated to reduce pain during insertion and has been common practice for years ***(Saav et al., 2007)***.

However, in a larger randomised controlled trial (RCT) comparing prophylactic 400mg ibuprofen with placebo prior to IUCD insertion, no pain reduction was shown ***(Hubacher et al., 2006)***.

Misoprostol is an inexpensive prostaglandin E1-analogue, which is associated with few side-effects ***(Goldberg et al., 2001; Wing and Affaney, 2006)*** and an effective method for treatment of missed and incomplete abortion, induction of provocative abortion as well as for labor induction and prevention and treatment of postpartum haemorrhage ***(Goldberg et al., 2001)***.

Moreover, several randomized controlled trials have shown the benefit of misoprostol as a cervical ripening agent in non pregnant women ***(Oppegaard et al., 2006; Preutthipan and Herabutya, 2006)***.

Priming with misoprostol prior to hysteroscopy and dilatation and curettage (D&C) in premenopausal women

resulted in an increased cervical dilatation and a lower rate of cervical laceration ***(Preutthipan and Herabutya, 2006)***.

A single dose of 400 mg misoprostol given vaginally 3 h before the intervention has given the best effectiveness with the least side effects. Higher doses or longer intervals do not improve the effect on the cervix, whereas higher doses actually increase side effects ***(Fiala et al., 2007)***.

Given the benefits of misoprostol prior to hysteroscopy, it was hypothesized that administering a cervical ripening agent prior toIUCD insertion would reduce failure rates, complications and pain during insertion ***(Dijkhuizen et al., 2011)***.

A study among eight women with an initially failed IUCD insertion showed that a second attempt, after pretreatment with misoprostol, was successful in all eight cases ***(Li et al., 2005)***. However, larger studies on the effect of misoprostol for IUCD insertion are lacking. Therefore RCT was conducted aiming to investigate whether pretreatmentwith misoprostol facilitates the insertion of an IUCD in nulli- and multiparous women ***(Dijkhuizen et al., 2011).***

Aim of the Work

Research hypothesis

The administration of misoprostol vaginally prior to IUCD insertion leads to easier maneuver by promoting cervical priming, which leads to more compliance of the patient and less pain and bleeding.

Research question

Does administration of misoprostol prior to IUCD insertion makes the insertion easier?

Outcome measures

The outcome measure for cervical priming is determined by introduction of serial Hegar dilators and the number of dilators introduced through the internal os of the cervix without resistance.

Intrauterine Contraceptive Devices

Intrauterine contraceptives are the most commonly used reversible method of birth control, with use by 15.5% of married women worldwide ***(United Nations 2007)***. More than 150 million women use IUDs, mainly in emerging countries, particularly in Southeast Asia and in the Middle East (30% in China), the prevalence of IUD use is much lower in European countries (range, 3-24%) ***(d'Arcanges, 2007).***

In North America, in 2002, the leading method of contraception in the United States was the oral contraceptive pills, the second leading method was female sterilization. From 1982-2002, the estimated percentage of women who used an IUD decreased from 8% to 2% (results based on the 1982, 1995, and 2002 National Surveys of Family Growth ***(Mosher et al., 2004, US Department of Health and Human Services, 2005)***.

Copper bearing IUDs consist of a plastic core surrounded by several copper wires. Copper is generally included in the vertical stem and in the horizontal arms to provide a copper surface close to the uterine fundus. The recommended duration of use for copper-bearing IUDs is generally 3-7 years, although some follow-up studies have demonstrated that these devices are highly effective for up to 12 years. In the 1970s, several studies demonstrated that the "greater the copper surface of the

IUD is, lower is the failure rate," which led to new high loaded copper IUDs ***(Tatum, 1972).***

Similarly, the addition of a silver core was found to be important to prevent fragmentation of the copper and consequently to extend the lifespan of the device ***(Sivin et al., 1992).***

The Nova-T 200 device (copper wire with a silver core and a copper surface area of 200 mm2) has been available since 1978. At the end of the 1980s, several randomized trials demonstrated lower pregnancy rates with "high-loaded" copper IUDs than with devices with a copper surface of 200-250 mm2. Studying 446 women with a Nova-T 200 device for 12 years, Baeyertz and Hartfield found a cumulative pregnancy rate of 3.5%. Consequently, a new Nova-T device was introduced with a copper surface of 380 mm2 incorporated in a new copper-silver device ***(Baeyertz et al., 1997)***.

In 2002, the Nova-T 380 copper IUD was evaluated in 400 volunteer women who were enrolled in 3 Finnish centers during a 5-year period. The cumulative pregnancy rate was 0.5% at the end of the first year and 1.9% the fifth year, with a continuation rate of 88.3% and 52.5% at 1 and 5 years, respectively ***(Batar et al., 2002).***

Finally, the TCu380A, which might be the most widely used IUD worldwide, must be considered to be the most efficient copper IUD, with an approved lifespan of 10 years. It consists of a polyethylene T-shaped body, wound with 380_23

mm2 of copper wire. The stem and arms of the device are 36 and 32 mm tall, respectively, impregnated with barium to aid with polyethylene thread is attached to the base of each device to facilitate removal ***(Thonneau et al., 2001)***.

The "frameless" intrauterine contraceptive system (GyneFix) consists of a length of non biodegradable 0-size monofilament surgical thread that is mounted with a varying number of copper tubes (6 copper tubes for the standard IUS and 4 for the mini-IUS). The upper and lower tubes are crimped on to the thread to keep them in place. The upper extremity of the thread ends with a knot that is anchored in the myometrium in the uterine fundus. Depending on the type of IUS, the total surface area of copper is 330 mm2 for the standard IUS and 200mm2 for the mini-IUS. According to the WHO, the long term efficacy of the GyneFix device ranges from 0.4-3.2 of 100 users, which is lower than that of the TCu380A ***(United Nations Development Programme, 1995).***

The efficacy of the GyneFix device could be attributed to the fact that the frameless device is anchored to the fundus of the uterus, thus preventing downward displacement, and to the optimal target delivery of the copper ions in the upper part of the uterine cavity. Nevertheless, a relatively high expulsion rate was reported with the GyneFix device with unnoticed expulsions leading to pregnancies ***(Wu et al., 2000, Dennis et al., 2001).***