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Vaginal misoprostol prior to intrauterine device insertion in women delivered only by elective cesarean section: a randomized double-blind clinical trial☆

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Abstract

Objective: The current study aims to evaluate if vaginal misoprostol (400 mcg) administered prior to intrauterine device (IUD) insertion increases the ease and success of insertion among women who had delivered only by elective cesarean delivery (CD).

Study design: The current study was a randomized, double-blind, placebo-controlled trial conducted in Assiut Women's Health Hospital, Egypt, between the 1st of April 2015 and the 31st of March 2016 and included women who delivered only by elective CD. One hundred forty women were randomized into two groups; misoprostol group received two misoprostol 400-mcg tablets vaginally, and placebo group received two placebo tablets 3 h before a copper T380A IUD insertion. The primary outcome measure was the difference in the ease of insertion score using a 10-cm visual analog scale between both groups with 0 = *very easy insertion*, and 10 = *terribly difficult insertion*.

Results: The ease of insertion score was lower in the misoprostol group (2.2±0.5 vs. 4.2±0.5, p=.0001) with higher number of successful IUD insertions than the placebo group (69 [98.6%] vs. 61 [87.1%], p=.009). The mean pain score reported by the women was lower in misoprostol group (2.7±0.6 vs. 4.3±0.8) with higher level of satisfaction from the whole procedure (8.9±0.4 vs. 7.9±0.2) with p=.001 for both.

Conclusions: Misoprostol 400 mcg vaginally prior to IUD insertion eases and increase the success of insertion with reduction of pain among women who had delivered only by elective CD.

Implications: The use of vaginal misoprostol before IUD insertion in women who had never delivered vaginally before may increase the ease and success of insertion. Moreover, it may reduce the pain felt by women during the procedure.

Keywords: Intrauterine device; Misoprostol; Cesarean delivery; Contraception

1. Introduction

Unintended pregnancy is a worldwide problem with increasing rates. The extensive use of long-acting reversible contraception (LARC) methods is one of the recommended solutions to reduce the rates of unintended pregnancy [1]. The intrauterine device (IUD) is proved to be a reliable, safe and extremely effective LARC method [2]. In spite of that, it is used only in 7.6% of women in developed countries and 14.5% in developing countries [3]. This can be attributed to fears of pain and difficulty of insertion from both women and health care providers [4].

IUD can elicit pain in several ways: use of the speculum to inspect the cervix; use of the tenaculum to grasp the cervix and straighten the uterus; transcervical procedures as measuring the uterine length by the sound, introducing the IUD insertion tube; and placement of the IUD inside the uterus [5]. Extensive researches have been published aiming to decrease the perception of pain during IUD insertion with no consensus on an effective method [6].

Nulliparous women and those who delivered only by cesarean delivery (CD) are suspected to experience more pain during IUD insertion [7]. The rate of CDs is continued to rise all over the world [8], and women who had delivered only by elective CD are considered as nulliparous as regard IUD insertion. Many health care providers do not advise IUD

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insertion for women with previous CD because of concerns about pain and difficulty of insertion [4].

Misoprostol is an inexpensive, widely present prostaglandin E1 analog used successfully for cervical ripening and thus dilatation prior to minimally invasive gynecological procedures as evacuation and hysteroscopy [9,10]. Trials of its use before IUD insertion reported conflicting results. Some of them found an easier insertion after its use but no difference in pain [11,12], while others report neither easier insertion nor pain relief [13,14]. All studies reported that women treated with misoprostol experienced more unwanted adverse effects as abdominal cramps, nausea, vomiting, shivering and diarrhea [11–14]. A previous single study focused on the effect of misoprostol on women who had never delivered except by elective CD reported no improvement in the ease of insertion or pain relief with sublingual misoprostol prior to IUD insertion [15].

As there is no consensus that has yet been reached in the literature as regard the administration of misoprostol prior to IUD placement in women with previous CD, the current study aims to determine if misoprostol 400 mcg vaginally administered prior to IUD placement increases the ease and success of insertion procedure among women who had delivered only by elective CD.

2. Materials and methods

The current study was a single-center, randomized, double-blind, placebo-controlled trial conducted in Assiut Women's Health Hospital, Egypt, between the 1st of April 2015 and the 31st of March 2016. The Assiut University Medical Ethical Review Board approved the study. This trial was designed and reported according to the revised recommendations of Clinical Trials. Gov for improving the quality of reporting RCTs (registered trial; NCT02412033).

We clinically evaluated all women who attended the Family Planning Clinic during the study period and who requested for an IUD insertion and invited them to participate in the study if they have no contraindications for IUD insertion in accordance with World Health Organization eligibility criteria [16].

We included nonpregnant women, aged 18–45 years, delivered before only by elective CD and did not receive any analgesics in the 24 h prior to IUD insertion. We excluded women with any uterine abnormalities as congenital anomalies, endometrial lesions, adenomyosis, fibroids, intrauterine adhesions, chronic pelvic pain, spasmodic dysmenorrhea, abnormal uterine bleeding and history of cervical surgery. Moreover, we excluded women with allergy to misoprostol or any medical disease that contraindicates its use and those who refused to participate in the study.

All eligible participants included in the study signed a written informed consent before participation after explaining the nature of the study. One of the study researchers (A.M.A.) approached all included women and collected the following data: age, parity, body mass index (BMI), the number of previous miscarriages, the number of previous CD, educational level, duration from the last pregnancy, previous contraceptives use and history of previous IUD insertion.

Then, the researcher explained the standard 10-cm visual analog scale (VAS) to the participants for pain scoring [17]. The severity of pain was assessed with VAS (with 0 = *no pain* and 10 = *worst imaginable pain*). Each woman received a copper T380A IUD (Paragard®T380A; Teva Pharmaceuticals USA, Inc. North Wales) for insertion. IUD insertion was performed while women were menstruating. The day of the menstrual cycle ranged from the first to the fifth.

We randomly allocated all participants into one of two groups: misoprostol group: women received two tablets of misoprostol 400 mcg vaginally (Misotac®; Sigma Pharma, SAE, Egypt) and placebo group: women received two placebo tablets created by a pharmacist in the Department of Pharmaceuticals, Faculty of Pharmacy, to be identical in size, shape, weight and color to the misoprostol tablets. A single pharmacist was responsible for the packaging of both preparations, so neither the physician nor the patient knew the type of the preparation (double-blind study). A trained clinic nurse introduced the tablets, digitally without using speculum, 3 h before IUD insertion into the posterior vaginal fornix of the woman while lying in the lithotomy position.

One of the study researchers (A.M.H.) who was experienced in IUD insertion using the standard technique of application prescribed by the manufacturer inserted the IUD in all women. Firstly, she placed the speculum into the vagina, and the cervix was cleansed with Povidone-iodine. Then, she grasped the anterior lip of the cervix with a single toothed vulsellum for fixation of the uterus and inserted the uterine sound for measurement of the uterine length followed by IUD insertion. Immediate complications such as uterine perforation, failure of insertion and vasovagal reaction besides the duration of insertion were recorded.

A research assistant present beside the woman asked her to rate the intensity of pain at the time of IUD insertion using a sheet of paper showing the 10-point VAS. After the end of insertion, the inserting physician reported the ease of IUD insertion using the ease of insertion score (ES). The ES was calculated at a graduated VAS-like scale from 0 to 10; in which 10 means *terribly difficult insertion* and 0 means *very easy insertion*. In addition, all women expressed their level of satisfaction with IUD insertion by completing a 10-cm VAS (with 0 = *no satisfaction* and 10 = *maximum satisfaction*). Finally, the researcher asked all women about the need for any additional analgesics at 15 min after completing the procedure. Women were offered ibuprofen 400 mg as an additional analgesic since it was readily available in our clinic.

We reported side effects of the medications encountered by the participants before IUD insertion in order to ensure