Comparison of vaginal misoprostol and dinoprostone for cervical ripening before diagnostic hysteroscopy in nulliparous women

Hasan Ali Inal, M.D.,[a] Zeynep Hafiza Ozturk Inal, M.D.,[a] Esra Tonguc, M.D.[b] and Turgut Var, M.D.[b]

[a] Konya Education and Research Hospital, Konya; and [b] Dr. Zekai Tahir Burak Women's Health Research and Education Hospital, Ankara, Turkey

Objective: To compare the effectiveness of vaginal misoprostol and dinoprostone for cervical ripening before diagnostic hysteroscopy in nulliparous women.
Design: Placebo-controlled, double blind, randomized trial.
Setting: Teaching and research hospital.
Patient(s): Ninety women of reproductive age eligible for diagnostic hysteroscopy.
Intervention(s): Randomly assignment to receive 400 μg of misoprostol (n = 30) or 10 mg of dinoprostone (n = 30) vaginally before diagnostic hysteroscopy, with a control group (n = 30) not receiving any cervical priming agent.
Main Outcome Measure(s): Primary outcome: the number of women requiring cervical dilatation; secondary outcomes: cervical width before surgery, duration of dilatation time, ease of dilatation, complications during surgical procedure, and side effects of the drugs.
Result(s): In the placebo group, 23 patients required cervical dilatation compared with 17 in the misoprostol group and 9 in the dinoprostone group. The mean (± standard deviation) cervical widths for the placebo, misoprostol, and dinoprostone groups were 4.23 ± 0.43 mm, 5.43 ± 0.5 mm, and 5.83 ± 0.64 mm, respectively. These widths were statistically significantly different. The duration of dilatation was also statistically significantly longer in the control group.
Conclusion(s): Vaginally administered dinoprostone before diagnostic hysteroscopy is more effective than misoprostol for inducing cervical priming. Further studies are required to elucidate the most efficient option with the least side effects for cervical ripening.
Clinical Trial Registration Number: NCT01620814. (Fertil Steril® 2015;103:1326–31. ©2015 by American Society for Reproductive Medicine.)
Key Words: Cervical ripening, dinoprostone, hysteroscopy, misoprostol

Discuss: You can discuss this article with its authors and with other ASRM members at http://fertstertforum.com/inalh-misoprostol-dinoprostone-cervical-ripening-hysteroscopy/

Use your smartphone to scan this QR code and connect to the discussion forum for this article now.*

* Download a free QR code scanner by searching for "QR scanner" in your smartphone's app store or app marketplace.

Hysteroscopy is commonly used in the diagnosis and treatment of intrauterine lesions such as polyps, fibroids, septa, and adhesions, and in the presence of abnormal bleeding and during the removal of an intrauterine device or foreign body. While diagnostic hysteroscopy provides panoramic visualization of the uterine cavity, operative hysteroscopy is a noninvasive approach for the treatment of uterine lesions (1–3). One of the most significant problems during this surgical procedure is the difficulty of passing the instrument through the cervical canal and the internal os; complications related to this include cervical injuries and tears, bleeding, a false track, or uterine perforation (4). For the passage of the hysteroscope, cervical ripening and widening of the cervical canal to a specific diameter are necessary.

Cervical ripening is made possible by the use of medication through different routes (5–7). The most commonly used agent is misoprostol, a synthetic prostaglandin E1 (PGE1) analog that is frequently administered in off-label use in obstetrics and gynecology for medical abortion, labor induction, endometrial biopsy, dilatation and curettage, intrauterine device insertion, myomectomy, postpartum hemorrhage, and cervical ripening.

Received September 30, 2014; revised and accepted January 23, 2015; published online February 21, 2015.
H.A.I. has nothing to disclose. Z.H.O.I. has nothing to disclose. E.T. has nothing to disclose. T.V. has nothing to disclose.
Reprint requests: Hasan Ali Inal, M.D., Konya Education and Research Hospital, 42090 Meram Yeni Yol, Konya, Turkey (E-mail: dr.hasanaliinal@yahoo.com).

Fertility and Sterility® Vol. 103, No. 5, May 2015 0015-0282/$36.00

http://dx.doi.org/10.1016/j.fertnstert.2015.01.037

Misoprostol was first used to prevent peptic ulcus from forming in patients taking nonsteroidal anti-inflammatory drugs (8, 9). It has been argued that misoprostol administration before hysteroscopy makes cervical passage easier and decreases the risk of cervicouterine complications (5, 10). In contrast, dinoprostone, a natural PGE2, is mostly used in obstetrics for cervical ripening and the stimulation of uterine contractions to induce labor. Studies have reported that dinoprostone is comparable to or better than misoprostol for cervical ripening in labor induction (11). Our study compared the effectiveness of vaginally administered misoprostol and dinoprostone for cervical ripening before diagnostic hysteroscopy.

MATERIALS AND METHODS

Patients

This randomized, double-blind, placebo-controlled clinical trial was conducted between July 2012 and December 2013 at Dr. Zekai Tahir Burak Women's Health Research and Education Hospital and Konya Education and Research Hospital. A total of 99 women with suspected intrauterine lesions (such as uterine polyps and filling defects in the uterine cavity) on the basis of abnormal findings from hysterosalpingography, ultrasonography, or saline-infusion-graphy were enrolled in the study during this time period. This study was approved by the institutional ethics review board (reference number: 2012/31), was registered with ClinicalTrials.gov (identifier: NCT01620814), and was prepared in accordance with the trial's protocol. All patients signed informed consent forms before being enrolled in the study.

Patients included were infertile (failure to conceive despite 1 year of regular sexual activity) nulliparous women with no contraindication for hysteroscopy. The exclusion criteria were as follows: an allergy or contraindication to prostaglandins such as hypertension, severe asthma, cardiac disease, glaucoma, renal failure, or uncontrolled diabetes mellitus; genital tract infection; history of cervical surgery such as dilatation curettage, loop electrosurgical excision procedure, or cryotherapy; previous treatment with a gonadotropin-releasing hormone agonist; or cervical incompetence. Additionally, nine women refused to participate. Consequently, the remaining 90 patients were included in the study: 30 in the placebo group, 30 in the vaginal misoprostol group, and 30 in the vaginal dinoprostone group. A flowchart of the study is presented in Figure 1.

Study Protocol

The participants were randomly assigned to the placebo, vaginal misoprostol, or dinoprostone groups by means of a computer-generated random number table. The study nurse prepared sequentially numbered, sealed, opaque envelopes for the research groups (placebo, misoprostol, or dinoprostone). After the women had been hospitalized, a randomized envelope was opened by the nurse, and the treatment indicated inside the envelope was administered to the patient.

The women in the placebo group were administered one vaginal tablet of *Lactobacillus acidophilus* (Gynoflor; Abdi Ibrahim Ilac Sanayi). The women in the misoprostol group were administered 400 μg of misoprostol (Cytotec; Ali Raif), and those in the dinoprostone group were administered 10 mg of dinoprostone (Probess; Ferring). All drugs were administered to the posterior fornix of the vagina 6 to 8 hours before the hysteroscopy. To prevent bias, the next morning, the vagina was cleaned, and any drug tablets were removed by the physician assistant in charge of the operation in all cases. Additionally, the patients were asked whether they experienced any of the possible side effects of the drugs, including nausea, vomiting, headache, lower abdominal pain, vaginal bleeding, diarrhea, or flushing.

The hysteroscopy was performed in the proliferative phase of the menstrual cycle. The patients were given general intravenous anesthesia (propofol/fentanyl) after the vulvar and vaginal area had been disinfected with a 7.5% Betadine solution by the surgical nurse. A rigid standard hysteroscope (Karl Storz) with an outer sheath measuring 5.5 mm in diameter and a scope with a 30° viewing angle was used. A speculum was introduced into the vagina, and the uterine cervix was visualized. Initially, the surgeon attempted to pass through the cervical canal with the tool directly. When that was not possible or when the cervical canal was too rigid or too tight, the cervix was grasped with a tenaculum.

The cervical width was assessed by cervical dilatation with Hegar's dilatator. A number 1 Hegar's bougie was introduced through the cervical canal; subsequently, larger bougies, up to a number 6, were inserted through the internal os without resistance. The largest bougie that could be passed without resistance was recorded as the initial cervical width. The time period from the onset to the end of dilatation was recorded. The ease of dilatation was recorded by the surgeon on a 5-point Likert scale (1 = very difficult, 2 = difficult, 3 = fair, 4 = easy, 5 = very easy).

The hysteroscope was advanced into the uterine cavity, and the cavity was distended with a saline solution while carefully monitoring the insufflation pressure to maintain it at 100–125 mm Hg to avoid fluid leakage. The cavity and tubal ostia were visualized. If any lesions were present, biopsy samples were obtained. The time from entering the uterine cavity until the completion of the procedure was recorded as the operative time. After the operation, the patients were monitored for 2 hours in the postanesthesia care unit; after discharge, they were observed for 4 weeks.

Outcome Measures

The primary outcome measure was the number of women who required cervical dilatation. The secondary outcome measures included the cervical width before surgery, duration of dilatation, ease of dilatation, possible side effects of drugs before operation, and any procedure-related complications.

Statistical Analysis

A total sample size of 84 (28 per group) was determined to be capable of detecting at least a 40% difference in the prevalence of the need for cervical dilatation between any two groups with a power of 80% at a statistical significance level