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ORIGINAL ARTICLE

A comparative study between isosorbide mononitrate (IMN) versus misoprostol prior to hysteroscopy

Waleed El-Khayat *, Ahmed Maged, Hassan Omar

Department of Obstetrics and Gynecology, Faculty of Medicine, Cairo University, Egypt

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KEYWORDS

Hysteroscopy;
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Abstract *Objective:* To compare the efficacy of a nitric oxide donor (isosorbide mononitrate) and a prostaglandin E1 analogue (misoprostol) for cervical priming before hysteroscopy.
Design: Comparative clinical trial.
Methods: A total of 162 patients with diagnosed intrauterine lesions scheduled for hysteroscopy were allocated to two groups: in group A patients (n = 81) IMN 40 mg was inserted into the posterior fornix of the vagina while misoprostol 200 μg was inserted into the posterior fornix of the vagina in group B patients (n = 81).
Results: There was no significant difference between IMN and misoprostol with regard to the duration of application or difficult dilatation. In contrast, there was a significant difference between IMN and misoprostol with regard to baseline cervical dilatation (5 mm for IMN and 8 mm for misoprostol) and duration of dilatation (73 s for IMN and 49 s for misoprostol). There was no significant difference between IMN and misoprostol with regard to nausea, vomiting and hot flushes. In contrast, there was a significant difference between IMN and misoprostol with regard to abdominal pain (17 cases for IMN and 55 cases for misoprostol) and headache (65 cases for IMN and 9 cases for misoprostol).

* Corresponding author. Address: Lecturer of Obstetrics and Gynecology, Faculty of Medicine, Cairo University, 5 Qura Ibn Shourik Street of Mourad Street, Giza 12211, Egypt. Tel.: +20 202 35733565, mobile: +2 0105135542.
E-mail address: waleed_elkhyat@yahoo.com (W. El-Khayat).

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Conclusion: Misoprostol is superior to isosorbide mononitrate regarding better baseline cervical dilatation, less duration of dilatation, less incidence cervical injury and finally better feasibility of the procedure.

1. Introduction

Prostaglandin-E1 agonist misoprostol is well established in labor induction at term and cervical ripening (1). However, the most common side effect after misoprostol is abdominal pain. Recent studies using nitric oxide donors for cervical ripening have been conducted. It has been shown that nitric oxide donors are effective in priming the cervix before suction evacuation of the uterus in terminating first-trimester pregnancies. There were no serious side effects reported, and the most common side effect was headache (2–4). One of the major problems of hysteroscopic surgery is difficulty in entering the internal cervical os with the outer sheath of the operative hysteroscope. Traditional cervical dilatation using Hagar's dilators may not be feasible in some patients with very tight cervix or cervical abnormalities (5). Cervical priming would have a central role in facilitating the procedure. The aim of the present study was to evaluate whether isosorbide mononitrate is more effective than misoprostol by a 1-mm change in cervical dilatation.

2. Materials and methods

The present study was carried out at the Gynecologic Endoscopy Unit, Kasr El Aini Hospital, from February 2007 to May 2009. The study was approved by the local ethical committee. Inclusion criteria included healthy women with primary or secondary cervical stenosis (defined as difficult or failed cervical sounding in the office) who were scheduled for operative hysteroscopy. Excluded from the study were women with previous cervical surgery and known allergy to either IMN or misoprostol. The ethical committee in the department of Obstetrics and Gynecology approved the study and consent was obtained from all the participants.

Patients were randomly divided into two groups. Group A (81 cases) received 200 μg misoprostol (Misotac; Sigma Co., Egypt) into the posterior fornix 8 h prior to surgery. Patients in group B (81 cases) received 40 μg IMN (Effox; Roche, Basel, Switzerland) into the posterior fornix 8 h prior to surgery. The patient was put in the dorsal lithotomy position, where a sterile Cusco's speculum was applied. Randomization was done 8 h before hysteroscopy using alternating numbers. It was an open label study where the surgeon was aware of the drug used.

In the operating room, the degree of initial cervical dilatation was assessed by introducing Hagar's dilators under general anaesthesia. It was defined as the maximal caliber dilator that passed without resistance in a descending order, starting with the largest size dilator. The duration of subsequent cervical dilatation until reaching 10 mm, and feasibility of the procedure, was recorded in seconds.

Cervical canal dilatation complications (false passage or perforation) were reported. At the end of the procedure, we recorded doctor assessment in the form of feasibility of the hysteroscopic operation and patient impression in the form of insertion difficulties, convenience and fear of either method. The incidence of abdominal pain and hot flushes was also recorded.

Collected data were revised and coded for computerized data entry. A data entry file was created on EPI Info version 6. After complete data entry, the file was converted to an SPSS file. Analysis was undertaken using SPSS version 11 and data were expressed as mean ± SD. Statistical methods were applied including descriptive statistics (frequency, percentage, mean and SD) and tests of significance [two-tailed Student's *t*-test, analysis of variance (ANOVA) and χ^2]. $P < 0.05$ was considered statistically significant.

3. Results

There was no significant difference between IMN and misoprostol with regard to the duration of application or difficult dilatation. In contrast, there was a significant difference between IMN and misoprostol with regard to baseline cervical dilatation (5 mm for IMN and 8 mm for misoprostol) and duration of dilatation (73 s for IMN and 49 s for misoprostol).

There was no significant difference between IMN and misoprostol with regard to nausea, vomiting and hot flushes. In contrast, there was a significant difference between IMN and misoprostol with regard to abdominal pain (17 cases for IMN and 55 cases for misoprostol) and headache (65 cases for IMN and 9 cases for misoprostol). There was a single case of injury in the group of misoprostol while the cervix was injured in four cases in IMN group.

4. Discussion

When hysteroscopy is done by an experienced surgeon, the risk of perforation and other complications is less than 1% especially in operative hysteroscopy (5). To facilitate the procedure and thereby reduce the risk of complication, preoperative cervical ripening is undertaken. As this treatment may have adverse effects, it was needed to know which is better in efficacy and less in side effects. In the present study, misoprostol was found to enhance cervical dilatation in a way that is better than IMN (Table 1). We chose the difference of 1 mm cervical dilatation as a marker of efficacy based on previous randomized controlled trial (1).

In addition to evaluation of efficacy, safety profile of either method was assessed, the present study was concerned with safety as side effects were strictly observed and recorded to allow for an appropriate comparison. Abdominal pain was reported more with misoprostol but headache was reported much more with IMN (Table 2). Side effects were experienced more than 4 h after administration of the tablets and that the intensity of the side effects gradually increased. It should be noted that the frequency of side effects in IMN group was higher than what has previously been described. It was previously reported that 15 out of 22 women (68%) were symptom free following treatment with 40 mg of IMN for 3 h (6).

Table 1 Technical characteristics and difficulties of the two studied groups.

	Group B IMN (No. = 81)	Group A misoprostol (No. = 81)	*P* value
Duration of application (h)	8.4 ± 0.6	8.2 ± 0.5	NS
Cx dilatation (mm)	5 ± 1	8 ± 1	< 0.001
Duration of dilatation (s)	73 ± 34.2	49 ± 20.1	< 0.001
Difficult dilatation (No.)	8	7	NS
Feasibility of procedure			
Easy	50(62.2%)	68(83.9%)	< 0.001
Difficult	31(37.8%)	13(16.1%)	< 0.001

Table 2 Comparison of side effects of isosorbide mononitrate and misoprostol.

	Group B IMN (No. = 81)	Group A misoprostol (No. = 81)	*P* value
Nausea	42(50%)	37(45.6%)	NS
Vomiting	16(19.7%)	14(17.2%)	NS
Abdominal pain	17(20.9%)	55(67.9%)	< 0.001
Hot flushes	20(24.7%)	17(21%)	NS
Headache	65(80.2%)	9(11.1%)	< 0.001

In the present study, we chose the dose of 200 μg to reduce the side effects reported with misoprostol as it has previously been demonstrated that the cervical ripening effect and the frequency of side effects caused by misoprostol are dependent on dosage as well as time interval (7). Previous studies have concluded that 400 mg of vaginally administered misoprostol 3–4 h before surgical abortion provides optimal cervical dilatation (8). However, in our study we just wanted cervical ripening rather than optimal cervical dilatation as the aim is to facilitate entry of the hysteroscope rather than expulsion of intrauterine contents.

The nitric oxide-generating system has been shown to exist in human female genital tract and has been tested in various clinical applications including cervical ripening during first-trimester pregnancy and third-trimester pregnancy and treatment of preeclampsia (9). However, very limited information is available concerning the application of nitric oxide donor in hysteroscopy. Thus, our study adds to the medical literature as it did not only evaluate the use of nitric oxide donors but compared it with the traditionally used misoprostol.

The results of the present study match well with those of other investigators who did not find additional value for IMN over misoprostol (10). In this context, one should consider the advantages of misoprostol as it is cheap and effective and does not require special storage conditions and can be taken vaginally or orally or even sublingually (11).

From this study, it is concluded that both IMN and misoprostol were shown to be effective in inducing adequate cervical priming prior to operative hysteroscopy. However, misoprostol is superior as it has the following advantages: better baseline cervical dilatation, less duration of dilatation, less incidence of cervical injury and finally better feasibility of the procedure.

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