Ideal Time of Vaginal Misoprostol Administration in Nulliparous Women Undergoing Office Hysteroscopy

Ahmed Abdelmaguid Mohammed, Ismail Talaat Elgarhy, Ahmed Samy Amer & Ashraf Hamdy Mohammed

Abstract:

Background: hysteroscopy is the process of viewing and operating in the endometrial cavity from a transcervical approach. It is the gold standard procedure for uterine cavity exploration. Objective: to detect ideal time of vaginal misoprostol administration for cervical priming in nulliparous women prior to office hysteroscopy by comparing between giving 400 microgram 3 hours, 6 hours and 12 hours before office hysteroscopy. Patients and Methods: randomized double-blind placebo-controlled study. This study was done on 198 patients to whom office hysteroscopy was done as a part of investigation of (infertility, recurrent miscarriage or abnormal uterine bleeding). those patients divided into three groups each group 66 patients, Group A, received 400μgm vaginal misoprostol 12 hours before office hysteroscopy and placebo 6 hours and 3 hours before office hysteroscopy. Group B received 400μgm vaginal misoprostol 6 hours before office hysteroscopy and placebo 12 hours and 3 hours before office hysteroscopy. Group C received 400 μgm vaginal misoprostol 3 hours before office hysteroscopy and placebo 12 hours and 6 hours before office hysteroscopy. Our main outcome measures were pain score (visual analogue scale), ease of entry (Likert scale), procedural time in minutes, patient acceptability (Likert scale), vaginal bleeding and also to detect side effects of misoprostol and complication of its use. Result: in group A which received 400μgm vaginal misoprostol 12 hours before office hysteroscopy, pain score was lower (2.6 ± 1.3) compared to group B (5.3 ± 1.3) compared to group C (7.3 ± 1.2). Procedural time was shorter in group A (2.7 ± 0.9) compared to group B (5.2 ± 1.2) compared to group C (7.4 ± 1.3), cervical entry was easier in group A (4.2 ± 0.7) compared to group B (3.5 ± 0.5) compared to group C (2.5 ± 0.6), baseline cervical dilatation was greater in group A (5.9 ± 0.8) compared to group B (4.7 ± 1.1) compared to group C (3.9 ± 0.8) vaginal bleeding was least in group A compared to group B compared to group C patient acceptability was higher in group A (4.2 ± 0.7) compared to group B (3.5 ± 0.5) compared to group C (2.5 ± 0.6). No complication detected in both groups. Side effects were minimal and transient. Conclusion: use of 400μgm vaginal misoprostol 12 hours before hysteroscopy is better than using it 6 hours and 3 hours in facilitating cervical ripening with minimal side effects without use of anaesthesia, as it decrease pain score, decrease procedure duration, increase ease of cervical entry, higher patient acceptability and with minimal side effects.

Keywords: Office Hysteroscopy, Misoprostol, Cervical Priming.
1. INTRODUCTION

Hysteroscopy is the process of viewing and operating in the endometrial cavity from a transcervical approach. It is the gold standard procedure for uterine cavity exploration (1).

In many practices, diagnostic hysteroscopy is the preferred procedure for the diagnosis and treatment of intrauterine pathology and intrauterine anomalies (2).

Hysteroscopy allows direct visualization of the uterine cavity, the endometrium and the cervical canal. The examination may be practiced on an out-patient basis, without anesthesia, using appropriate small-caliber instruments and irrigation with physiological saline (3).

Hysteroscopic examination includes detailed evaluation of the cervical canal, isthmus and uterine cavity. Focused evaluation of the region of the utero-tubal junction and the first few millimeters of the tube with particular reference to the tubal ostia was attempted (4).

Since it allows direct visualization of the endometrium, hysteroscopy has essential role in the evaluation of the uterine causes of infertility as it can detect small lesions that might not otherwise be readily diagnosed by other methods (5).

Hysteroscopy is associated with minimal patient discomfort, excellent visualization and very low complication and failure rates (6).

Over recent years hysteroscopy is being increasingly used in out-patient facilities which alongside the standard advantages of hysteroscopy also provide greater comfort for the patients, since it excludes the need to stay in hospital and decreases the time of treatment, but also the time needed to prepare the patient for further procedures, e.g. medically assisted conception (7).

In post-menopausal women with abnormal uterine bleeding, hysteroscopy with endometrial biopsy shows a high diagnostic accuracy in diagnosing endometrial cancer or hyperplasia (8), whereas premenopausal infertile patients with recurrent IVF failures may experience substantial benefits in terms of increased pregnancy rates (9).

The role of hysteroscopy in infertility investigation is to detect possible intrauterine changes that could interfere with implantation or growth or both of the conceptus (10).

With the invention of miniature hystroscope, it is possible to perform hysteroscopy in an office setting (Outpatient hysteroscopy; OH), for diagnostic and certain therapeutic intervention (11).

There is a growing consensus towards its use in the primary investigation of infertile women prior to In-Vitro Fertilization (12), as well as in the management of hydrosalpinges in such patients, in place of laparoscopy (13).

Hysteroscopy is currently acknowledged as the ‘gold standard’ investigation of the intrauterine abnormalities (14).

However, despite the high efficacy of the procedure in the above mentioned settings, both as a diagnostic or therapeutic tool, hysteroscopy may be associated with certain complications (15).

Although the incidence of these complications is low, 1–1.5% (16), almost 50% of them are related to insertion of the hysteroscope or to the dilatation of the cervical canal (16).

Taking into account that an efficient method to facilitate an easier uncomplicated entry during the hysteroscopic procedure could substantially minimize the risk of complications, several modalities for cervical ripening prior to hysteroscopy have been adopted (17).

Cervical priming prior to diagnostic hysteroscopy softens the cervix and lessens the force needed for dilation (18), thereby potentially reducing the probability of procedural complication such as uterine perforation, cervical laceration, failure to dilate, and creation of a false track that can occur during cervical entry (19).

Cervical ripening is clinically diagnosed by softening, effacement, and dilatation of the uterine cervix (20).

The synthetic analogue of prostaglandin E1, misoprostol, is the agent used most often for cervical preparation prior to hysteroscopy (21).

Consequently, given its high efficacy in dilating the cervix in pregnant women one could hypothesize that misoprostol would also facilitate dilatation in women undergoing hysteroscopy (22).

It can be given orally, vaginally, sublingually, buccally, or rectally (23). There is evidence supporting the use of misoprostol as a cervical priming agent before some gynecologic procedures, such as intrauterine device insertion (24) and hysteroscopy (25).
The vaginal route appears to be superior to the oral route (26).

Based on the available evidence on the use of misoprostol prior to hysteroscopy, no solid guideline can be provided with regards to the optimal time of misoprostol administration prior to the office hysteroscopy.

So we tried in our study to test for appropriate time by comparing between 3 hours, 6 hours and 12 hours vaginal misoprostol administration prior to office hysteroscopy.

2. AIM OF THE WORK
A- Research hypothesis:
   Vaginal misoprostol (400 micrograms) is the agent used most often for cervical preparation prior to office hysteroscopy, no solid guideline can be provided with regards to the ideal time of misoprostol administration prior to the office hysteroscopy.

B- Research question:
   What is the ideal time of vaginal misoprostol administration in nulliparous women prior to office hysteroscopy?

C- Aim of the work:
   This work aims to determine the ideal time of vaginal misoprostol administration in nulliparous women undergoing office hysteroscopy by comparing between giving the dose 3 hours, 6 hours and 12 hours before office hysteroscopy.

3. PATIENTS AND METHODS
3.1 Type of the study:
   Randomized double-blind placebo-controlled study.
   - Double blinded means that: neither participants nor operator know which intervention will be received.
   - Placebo is: an “inert” substitute for a treatment or intervention. “Inert” means the compound has no known activity that would be expected to affect the outcome. Factually, a placebo effect is a psychosomatic effect.

3.2 Setting of the study:
   This study was conducted at El Sahel Teaching Hospital from March 2017 till October 2018.

3.3 Protocol approval by ethical committee:
   Before the beginning of the study and in accordance with the local regulation followed, the protocol and all corresponding documents were declared for Ethical and Research approval by the Council of Obstetrics and Gynecology Department, Al-Azhar-University.

3.4 Patient selection:
   One hundred ninety eight nulliparous patients were subjected to office hysteroscopy with the following selection criteria:
   a- Inclusion criteria:
      - Age: childbearing period or postmenopause. (from 20 to 50 years)
      - Nulliparous women.
      - Indication for hysteroscopy could be one of the following:
         o Infertile patients either primary or secondary infertility.
         o Patients with history of recurrent miscarriage.
         o Patients with history of abnormal uterine bleeding.

   b- Exclusion criteria:
      - Contraindications to office hysteroscopy: Any uterine abnormality such as pinhole cervix that would obviate passage of a catheter through the cervix, marked cervical stenosis, recent or current
pelvic inflammatory disease, known cervical malignancy, pregnancy, profuse uterine bleeding, or recent uterine perforation.

- Contraindications to prostaglandins: Known sensitivity to prostaglandins, cardiovascular disease, hypertension, severe bronchial asthma, renal failure, or glaucoma
- Multiparous women.
- Concomitant neurologic disease that could affect the correct evaluation of pain.

3.5 After obtaining informed consent, all included women were subjected to:

a) Thorough history taking: including:
   - Age.
   - Duration of marriage.
   - Gravidity.
   - Detailed menstrual history.
   - History of abnormal uterine bleeding: onset, course, duration, amount, colour, relation to the cycle and associated pain.
   - History of vaginal or pelvic infection.
   - History of infertility and infertility duration.
   - History of any medical disorders.
   - History of any previous operations.

b) Full examination: including:
   - General examination: vital signs, pallor. general causes of bleeding and diseases causing infertility.
   - Abdominal examination.
   - Pelvic examination: inspection, bimanual examination and speculum examination.

c) Pelvic ultrasound:
   - Either transabdominal or transvaginal.

d) Laboratory investigations:
   - Serum pregnancy test: to exclude pregnancy.

3.6 Interventions:
   - The patients were divided into 3 groups randomly, each group contained 66 patients.
   - Method of randomization.

A- First group (long interval misoprostol group):
   - Two misoprostol tablets (400 micrograms) were given vaginally 12 hours prior to office hysteroscopy.
   - Two placebo tablets were given vaginally 6 hours and 3 hours prior to office hysteroscopy.

B- Second group (intermediate interval misoprostol group):
   - Two placebo tablets were given vaginally 12 hours prior to office hysteroscopy.
   - Two misoprostol tablets were given vaginally 6 hours prior to office hysteroscopy.
   - Two placebo tablets were given vaginally 3 hours prior to office hysteroscopy.

C- Third group (short interval misoprostol group)
   - Two placebo tablets were given vaginally 12 hours and 6 hours prior to office hysteroscopy.
   - Two misoprostol tablets were given vaginally 3 hours prior to office hysteroscopy.
   - The hysteroscopy was scheduled in the proliferative menstrual phase from the 5th day to the 14th day of the cycle. Informed written consent was signed by all the patients.
3.7 Technique:

Patient preparation is one of the most important aspects for successful office hysteroscopy, thus the procedure was described to every patient prior to the examination and each step was explained during the procedure so the patients were active participants and this helped them to understand the experience and relieved anxiety. The hysteroscope used in this study was that of Karl Storz, (Germany 1996). It is a rigid continuous flow panoramic hysteroscopy 25 cm in length, 4 mm in diameter with an outer sheath of 5.5 mm and a 30 degree fibro optic lens.

The light source used in this study was a metal halide automatic light source from Circon Acmi G 71A/Germany with 150 watt lamp. A fibro optic cable was connected to the light source and to the hysteroscope. A hysteroscopic camera of Karl Storz, Germany which was fitted to the eye piece of the optic sheath where it was transmitted to LCD monitor.

The technique used to provide constant uterine distention was by 3 L volume saline bags to dual infusion tubing which is suspended one meter above the patient level. Each bag was then wrapped in a pressure infusion cuff similar to that used in blood pressure to reach a pressure of 150-200 mmHg. The tubing was connected to the hysteroscope.

It was helpful and more comfortable for the operator to sit on a low chair and to elevate the foot of the examination table to perform the procedure. After the patient was installed in the lithotomy position then the gynecologist used sterile gloves and after putting together the instruments, checking the flow of the distention medium, the hysteroscope was introduced under direct vision into the cervix without the use of anesthesia or analgesia, using a specific technique. No cervical dilatation was done and the cervical width was assessed by the largest number of Hegar dilator that could be inserted without resistance.

3.8 Statistical Analysis

Data were entered on the computer using "Microsoft Office Excel Software" program (2010) for windows. Data was then transferred to the Statistical Package of Social Science Software program, version 23 (IBM SPSS Statistics for Windows, Version 23.0. Armonk, NY: IBM Corp.) to be statistically analyzed. P values less than 0.05 were considered statistically significant.

4. RESULTS

Table (1): Comparison between groups as regard demographic data.

<table>
<thead>
<tr>
<th>Demographic DATA</th>
<th>Group A (n=66)</th>
<th>Group B (n=66)</th>
<th>Group C (n=66)</th>
<th>P Value</th>
<th>A*B</th>
<th>A*C</th>
<th>B*C</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age: Mean ± SD</td>
<td>33.6 ± 8.1</td>
<td>33.6 ± 7.3</td>
<td>32.7 ± 6.8</td>
<td>0.753</td>
<td>0.999</td>
<td>0.801</td>
<td>0.781</td>
</tr>
<tr>
<td>Range</td>
<td>20 - 49</td>
<td>22 – 50</td>
<td>22 - 50</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Duration of marriage: Mean ± SD</td>
<td>10.4 ± 5.7</td>
<td>10.5 ± 5.6</td>
<td>9.9 ± 5.2</td>
<td>0.817</td>
<td>0.991</td>
<td>0.883</td>
<td>0.819</td>
</tr>
<tr>
<td>Range</td>
<td>2 – 25</td>
<td>3 – 25</td>
<td>4 - 25</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Gravidity:</td>
<td></td>
<td></td>
<td></td>
<td>0.125</td>
<td>0.726</td>
<td>0.117</td>
<td>0.055</td>
</tr>
<tr>
<td>MG</td>
<td>30 (45.5%)</td>
<td>28 (42.4%)</td>
<td>39 (59.1%)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>NG</td>
<td>36 (54.5%)</td>
<td>38 (57.6%)</td>
<td>27 (40.9%)</td>
<td></td>
<td></td>
<td></td>
<td></td>
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<tr>
<td>Prev. cervical procedure:</td>
<td></td>
<td></td>
<td></td>
<td>0.533</td>
<td>0.559</td>
<td>0.273</td>
<td>0.571</td>
</tr>
<tr>
<td>Cerclage</td>
<td>15 (22.7%)</td>
<td>18 (27.3%)</td>
<td>19 (28.8%)</td>
<td></td>
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<td></td>
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</tr>
<tr>
<td>Cautery</td>
<td>14 (21.2%)</td>
<td>10 (15.2%)</td>
<td>6 (9.1%)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Biopsy</td>
<td>3 (4.5%)</td>
<td>1 (1.4%)</td>
<td>3 (4.5%)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>No previous surgery</td>
<td>34 (51.6%)</td>
<td>37 (56.1%)</td>
<td>38 (57.6%)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Indications:</td>
<td></td>
<td></td>
<td></td>
<td>0.455</td>
<td>0.975</td>
<td>0.207</td>
<td>0.281</td>
</tr>
<tr>
<td>Infertility</td>
<td>26 (39.4%)</td>
<td>26 (39.4%)</td>
<td>31 (47%)</td>
<td></td>
<td></td>
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</tr>
<tr>
<td>Abortion</td>
<td>18 (27.3%)</td>
<td>19 (28.8%)</td>
<td>22 (33.3%)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Bleeding</td>
<td>22 (33.3%)</td>
<td>21 (31.8%)</td>
<td>13 (19.7%)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Data were expressed as number ± standard deviation, percent (%).
F- ANOVA test; # Chi-square test
P-value > 0.05 NS

### Table (2): Comparison between groups as regard outcome measures:

<table>
<thead>
<tr>
<th>Outcome Measures</th>
<th>Group A</th>
<th>Group B</th>
<th>Group C</th>
<th>VALUE</th>
<th>A and B</th>
<th>A and C</th>
<th>B and C</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Level of pain according to VAS:</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mean ±SD</td>
<td>2.6 ± 1.3</td>
<td>5.3 ± 1.3</td>
<td>7.3 ± 1.2</td>
<td>&lt;0.001</td>
<td>&lt;0.001</td>
<td>&lt;0.001</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Range</td>
<td>1 – 5</td>
<td>3 – 9</td>
<td>5 – 10</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Ease of entry according to LIKERT scale:</strong></td>
<td></td>
<td></td>
<td></td>
<td>&lt;0.001</td>
<td>&lt;0.001</td>
<td>&lt;0.001</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Mean ±SD</td>
<td>4.2 ± 0.7</td>
<td>3.5 ± 0.5</td>
<td>2.5 ± 0.6</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Range</td>
<td>1 – 5</td>
<td>3 – 4</td>
<td>1 – 4</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Baseline cervical dilatation by Hegar dilator:</strong></td>
<td></td>
<td></td>
<td></td>
<td>&lt;0.001</td>
<td>&lt;0.001</td>
<td>&lt;0.001</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Mean ±SD</td>
<td>5.9 ± 0.8</td>
<td>4.7 ± 1.1</td>
<td>3.9 ± 0.8</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Range</td>
<td>5 – 7</td>
<td>3 – 6</td>
<td>3 – 5</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Duration of procedure in minutes:</strong></td>
<td></td>
<td></td>
<td></td>
<td>&lt;0.001</td>
<td>&lt;0.001</td>
<td>&lt;0.001</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Mean ±SD</td>
<td>2.7 ± 0.9</td>
<td>5.2 ± 1.2</td>
<td>7.4 ± 1.3</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Range</td>
<td>1 – 4</td>
<td>3 – 8</td>
<td>5 – 10</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Vaginal bleeding:</strong></td>
<td></td>
<td></td>
<td></td>
<td>&lt;0.001</td>
<td>0.008</td>
<td>&lt;0.001</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Mild</td>
<td>3 (4.6%)</td>
<td>12 (18.2%)</td>
<td>30 (45.5%)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Moderate</td>
<td>1 (1.5%)</td>
<td>5 (7.6%)</td>
<td>10 (15.2%)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>No</td>
<td>62 (93.9%)</td>
<td>49 (74.2%)</td>
<td>26 (39.3%)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Patient acceptability:</strong></td>
<td></td>
<td></td>
<td></td>
<td>&lt;0.001</td>
<td>&lt;0.001</td>
<td>&lt;0.001</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Mean ±SD</td>
<td>4.2 ± 0.7</td>
<td>3.5 ± 0.5</td>
<td>2.5 ± 0.6</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Range</td>
<td>1 – 5</td>
<td>3 – 4</td>
<td>1 – 4</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Data were expressed as number ± standard deviation, percent (%)

### Table (3): Comparison between groups as regard side effect of misoprostol.

<table>
<thead>
<tr>
<th>Misoprostol side effects</th>
<th>Group A (n=66)</th>
<th>Group B (n=66)</th>
<th>Group C (n=66)</th>
<th>Value</th>
<th>A*B</th>
<th>A*C</th>
<th>B*C</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Pain</strong></td>
<td>5 (7.6%)</td>
<td>10 (15.2%)</td>
<td>12 (18.2%)</td>
<td>0.125</td>
<td>0.217</td>
<td>0.054</td>
<td>0.717</td>
</tr>
<tr>
<td><strong>Nausea</strong></td>
<td>3 (4.5%)</td>
<td>7 (10.6%)</td>
<td>9 (13.6%)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Diarrhea</strong></td>
<td>2 (3%)</td>
<td>3 (4.5%)</td>
<td>5 (7.6%)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>No Side effects</strong></td>
<td>56 (84.8%)</td>
<td>46 (69.7%)</td>
<td>40 (60.6%)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Data were expressed as number, percent (%)

Chi-square test
P-value < 0.05 Significant; p-value > 0.05 Non significant

### 5. DISCUSSION

The data presented in this study revealed that the efficacy of vaginal misoprostol in cervical priming prior to office hysteroscopy in nulliparous patients is time dependent. To our knowledge, this
Misoprostol is used before office hysteroscopy to soften the cervix and to dilate the cervical canal. Misoprostol increases the influx of leucocytes to cervical stroma, stimulates matrix metalloproteinases activity (which degrades connective tissue matrix), increases hyaluronic acid and water content in the cervical stroma, thereby leads to cervical softening and dilation. Moreover, misoprostol stimulates uterine contractions, which increase the dilation of the softened cervix.

Misoprostol can be administered orally, vaginally, or sublingually. Misoprostol is rapidly absorbed after administration via oral or sublingual routes. The plasma level of its active metabolite (misoprostol acid) peaks within 30 minutes, and then the plasma level of misoprostol acid rapidly declines within 2 hours. After vaginal administration, the plasma level of misoprostol acid peaks within 70–80 minutes, and then the plasma level of misoprostol acid declines gradually, reaching 60% of the peak level 6 hours after misoprostol administration. The plasma levels of misoprostol acid remain elevated for a longer period after misoprostol administration via the vaginal route compared with the oral and sublingual routes. Vaginal misoprostol induces more powerful uterine contractions that persist for a longer period and therefore could be more effective in dilating the cervix. Regular uterine contractions persist for more than 6 hours after vaginal misoprostol administration; therefore, we think it is necessary to wait for more than 6 hours after vaginal misoprostol administration to obtain the maximal cervical dilation.

El-Khayat et al. compared the efficacy and safety of two different doses of vaginal misoprostol for cervical priming at doses of 200 µg vs. 400 µg 3 h before diagnostic OH with-out anesthesia in patients with infertility, AUB or recurrent abortion. The results of the study indicate that the use of 400 µg vaginal misoprostol significantly facilitated the procedure of OH: Cervical entry was easier, procedural time was shorter, patient acceptability was higher, and pain scoring was lower in the 400 µg vaginal misoprostol group compared with the 200µg vaginal misoprostol group. Misoprostol related side effects(nausea, vomiting, abdominal pain) were infrequent, minor,and transient with no statistically significant difference between both groups, and no complications were reported.

Bastu et al., they found that the use of vaginal misoprostol both in doses of 200 µg and 400 µg, significantly facilitated the procedure of OH compared to the controls as cervical entry was easier; procedural time was shorter; baseline cervical width was larger; and pain scoring was lower. On the other hand, increasing the dose of vaginal misoprostol from 200 µg to 400 µg did not improve the effect on cervical dilation.

In a randomized controlled trial, 200 µg misoprostol administered sublingually 2 hours before office hysteroscopy was more effective than lidocaine spray in minimizing pain experienced during office hysteroscopy.

Bakas et al. administered 200 µg oral misoprostol to one group (12 hours before), 200 µg vaginal misoprostol (12 hours before) to another, and 200 µg vaginal misoprostol (4 hours before) to a third group. Their results support the preoperative use of 200 µg of vaginal misoprostol 12 hours before the OH, again in line with the findings of the present study.

El-Mazny and Abou-Salem compared 200-µg vaginal misoprostol with the control group in which placebo was not used; they found that cervical entry was easier, procedure time was shorter, patient acceptability was higher, and pain scoring was lower in the misoprostol group, which is in line with our findings.
Our study we also supported with Sordia-Hernandez et al. they studied 75 patients that were enrolled and distributed in three groups of 25 patients each and they found that vaginal misoprostol at a dose of 200 µg inserted 12 hours apart, starting 24 hours before OH for investigation of infertility, reduces pain and the procedural time compared with oral misoprostol administration and placebo. They reported only one patient with nausea and two patients with referred abdominal pain in the vaginal misoprostol group (33).

Preuthipan and Herabutya (34), showed that misoprostol, resulted in effective cervical priming before hysteroscopy in non pregnant woman. They reported greater cervical dilation, decreased cervical resistance, and less need for mechanical dilation before hysteroscopy or curettage with oral or vaginal misoprostol.

El Khayat et al. compared the efficacy of isosorbide mononitrate (IMN) and misoprostol for cervical priming before the hysteroscopy, there was a significant difference between IMN and misoprostol with regard to the baseline cervical dilatation (5mm for IMN and 8 mm for misoprostol)and duration of dilatation (73s for IMN and 49s for misoprostol) (35).

Mulayim et al. two groups of women who received sublingual misoprostol or placebo before hysteroscopy were compared with each other. Dilatation time was higher in placebo group. Furthermore, cervical tearing had occurred more often in placebo group than in misoprostol group (36).

Lee et al. compared various routes of misoprostol in premenopausal non pregnant women. The efficacy of sublingual misoprostol was comparable to oral and vaginal routes (19). Previous randomized studies have shown that preoperative cervical ripening with misoprostol decreased both intraoperative morbidity and duration of operative hysteroscopy, in premenopausal women (37, 21).

Batukan et al. reported that 400 µg vaginal administration of misoprostol is more effective than the oral route with the same dose for preoperative cervical ripening in premenopausal women in terms of extent of initial cervical width, percentage of patients requiring cervical dilatation, duration of cervical dilatation and procedural time as well as complications during procedure, and associated side effects (26).

Da Costa et al. also found that 200 µg of vaginal misoprostol reduced pain severity during diagnostic hysteroscopy in postmenopausal women (38). However, Oppegaard et al. concluded that 1,000 µg vaginal misoprostol 12 hours before operative hysteroscopy has a significant cervical ripening effect compared with placebo in premenopausal but not postmenopausal women (39).

Misoprostol has also been shown to induce cervical dilatation in non-pregnant women when used prior to a hysteroscopy by another older study (40).

Preuthipan & Herabutya compared the efficacy of vaginal misoprostol more effective than dinoprostone for cervical priming in nulliparous women before hysteroscopic surgery and suggested to use vaginal misoprostol for cervical priming instead of dinoprostone (21).

Choksuchat et al. suggested that 400mg oral misoprostol is as effective as 200 µg vaginal route for cervical ripening before hysteroscopy (41). Also our results agreed with Barcaite et al. (42), who demonstrated significant reduction in cervical resistance and need for cervical dilatation following priming with 400 µg of vaginal misoprostol 12 h prior to diagnostic hysteroscopy compared to placebo (42).

Preuthipan and Herabutya reported that 200 µg misoprostol 9-10 hours before the procedure lessens cervical resistance and facilitates the procedures (43).

Bahamondes et al. (44) found that pretreatment with intravaginal 100mcg of misoprostol after IUD insertion failure in 104 patients 4-10 hours before 2nd attempt was significantly better than placebo (RCT).

Scavuzzi et al. (45) randomized 179 women either 400mg vaginal misoprostol or placebo 4 hours prior to IUD insertion in nulligravidas and found less difficulty in inserting IUD in misoprostol group.

Saav et al. (24), concluded that misoprostol facilitate insertion of IUD in woman with narrow cervical canal. They investigated the use of sublingual misoprostol one hour prior to insertion of a copper-IUD among nulliparous women. Their low number of failed insertions corresponded with our figure. IUD insertion in nulliparous women who used sublingual 600 µg misoprostol and 100 mg diclofenac was significantly easier than in women who used 100 mg diclofenac alone (one hour prior to
IUD insertion). The study showed that misoprostol can be used to facilitate the insertion of an IUD in nulliparous women with a narrow cervix. However, the majority of insertions were uncomplicated and the difficulties few in both groups. Shivering was more common in the misoprostol group.

But this was not in agreement with a randomized controlled study which revealed that 400 µg misoprostol administered vaginally 6 hours before office hysteroscopy was not effective in reducing pain experienced during office hysteroscopy (46).

In addition, sequential doses of 400 mg of oral misoprostol at 12 and 24 hours before surgery did not demonstrate any advantage in so far as cervical dilation (47).

Singh et al. who compared 50 patients received 400 µg vaginal misoprostol compared to 50 patients who didn’t receive anything. They found that misoprostol did not make any difference to the ease of cervical dilatation prior to diagnostic hysteroscopy, although it led to reduction in pain scores, there was no difference in patient satisfaction, need for analgesia, or sedation (48). This is may be due to they worked on smaller number of patients than our current study or may be due to the time between misoprostol administration and operation may affect its efficacy, as they applied the vaginal misoprostol 4 hours before hysteroscopy.

Fernandez et al. who gave patients three different doses of misoprostol in either 200, 400, or 800 µg 4 hours before OH, they found no significant difference in the time required for dilation and ease of dilation (49).

Bisharah et al. compared the effect of 100 µg of sublingual misoprostol administered 12 h prior to operative hysteroscopy in 20 women to placebo and found no difference in facilitation of cervical dilatation. Similarly (50), demonstrated no difference in ease of cervical dilatation following administration of 800 µg of vaginal misoprostol administered at least 5 h prior to hysteroscopy compared to placebo in postmenopausal women.

Singh et al. (51) found that increasing the dose of vaginal misoprostol to 400 µg or increasing the interval beyond 3 hours has not improved the effect on cervical dilatation, but it has increased side effects, mainly diarrhea and shivering (51).

Hald et al. reported that the major adverse effects in 15 patients who had vaginal misoprostol for cervical priming before hysteroscopy were mostly gastrointestinal symptoms. The significant adverse effects of vaginal misoprostol administration found in this study were; 15 including mild lower abdominal pain (35.6%, P. 001) and slight vaginal bleeding (19.2%, P 5. 002). All nine patients who perceived increased body temperature had no measurable fever (52).

Dijkhuizen et al. (53) conducted a RCT aiming to investigate whether pretreatment with misoprostol facilitates the insertion of an IUD in nulli- and multi-parous women and failed to show difference for use of misoprostol prior to IUD insertion. However, that study was conducted on heterogeneous group of patients both multiparous and nulliparous. This may indicate that misoprostol may be beneficial only in subset of patients like our patients.

Swenson et al. (54) estimated the effects of self-administered misoprostol compared with placebo in 108 patients before intrauterine device (IUD) insertion in women. They failed to show difference in easiness of insertion of IUD with prior use of misoprostol. However this study was not blinded for doctors or patients. More over self administration misoprostol vaginally may not be effective. These small tablets are better administrated as deep as possible by gynecologist.

Ibrahim and Sayed Ahmed (55) investigated whether sublingual 400mcg misoprostol administered one hour before Intrauterine Device (IUD) insertion reduces failed insertions, insertion-related complications and pain in multiparous women delivered only by elective Caesarean Section (CS) and found that sublingual administration of misoprostol didn’t facilitate the procedure. But the misoprostol was given in this study 1 hour only before procedure which may not be effective to soften the cervix.

6. CONCLUSION

Office hysteroscopy is an essential tool for uterine cavity environment assessment. Misoprostol is a good cervical ripening agent and was effective in changing the character of the cervix from harder and softer. This study showed that giving 400 microgram vaginal misoprostol 12 hours prior to office hysteroscopy was better than giving it 6 hours and 3 hours prior to office hysteroscopy as level of
pelvic pain was lowest in group A followed by group B followed by group C. Ease of pelvic entry was easier in group A followed by group B followed by group C. Baseline cervical dilatation was greater in group A followed by group B followed by group C. Time of the procedure was shorter in group A followed by group B followed by group C. Vaginal bleeding occurred in 3 patients of group A, 13 patients in group B and 40 patients in group C. Misoprostol related side effects as fever, abdominal pain, nausea and diarrhea were lesser in group A followed by group B followed by group C, no complications were reported.

7. REFERENCES


