Cervical Priming by Misoprostol before Diagnostic Dilatation and Curettage: A Randomized Clinical Trial

Shima Mohammadian 1, Anahita Tavana 2, Shahruz Tavana 2, Aida Mohammadian 3, Masoumeh Fallahian 4*

1- Department of Obstetrics and Gynecology, Taleghani Hospital, Shahid Beheshti University of Medical Sciences, Tehran, Iran
2- Department of Natural Sciences, University of Texas at Austin, Texas, USA
3- Qazvin University of Medical Sciences, Qazvin, Iran
4- Department of Obstetrics and Gynecology, Infertility and Reproductive Health Research Center, Taleghani Hospital, Shahid Beheshti University of Medical Sciences, Tehran, Iran

Abstract

Background: Difficulty in cervical dilatation is a hard situation during the procedure of diagnostic dilatation and curettage in some cases. This study was performed to evaluate the effect of vaginal misoprostol for cervical priming before diagnostic dilatation and curettage.

Methods: In this study 56 women were selected as the candidates for dilatation and curettage. The study was double blind and was performed for two parallel groups. One misoprostol tablet (200 μg) was administered in posterior fornix of vagina 2-4 hr before operation in 28 patients whereas in other 28 patients, placebo (VitB6) was used. Then, the two groups were compared according to the patency of the cervix measured by No. 5 Hegar dilators and the duration of dilatation and curettage procedure as well. Chi-square test, t-test, and Mann-Whitney U test were used for comparing two groups, and a p-value less than 0.05 was considered as statistically significant.

Results: Before the procedure of dilatation and curettage, the patency of the cervix was measured by passing Hegar dilator number 5 through the cervical canal in fifteen (53.6%) patients in the misoprostol group and 8 patients (28.6%) in the placebo group (p=0.05) which their difference was statistically significant. The effect of misoprostol was not significant in nulliparous women and postmenopausal period either.

Conclusion: Vaginal misoprostol is a useful drug for ripening and dilating the cervix. It also facilitates the procedure of dilatation and curettage in premenopausal and multiparous women. Misoprostol was less effective in nulliparous women and in postmenopausal period.

Keywords: Cervical ripening, Curettage, Dilatation, Misoprostol.

Introduction

Abnormal uterine bleeding is a common problem that gynecologists encounter and most of the patients have benign disease, but need more evaluation especially after the age of 35 (1). Difficulty in dilating the internal cervical os is a common problem in performing curettage. The complications related to this problem include cervical trauma, creation of false tract and uterine perforation (2). Ripening the cervix before curettage reduces commonness of these complications. A few studies are available on the use of misoprostol for ripening the cervix prior to gynecological procedures on women. Nowadays misoprostol has become a desirable agent due to its beneficial effects on cervical ripening on nonpregnant women (3-5).
Originally, misoprostol as a synthetic prosta-
glandin E1 analogue was administered for preven-
tion and treatment of gastric ulcer diseases. One
of the effects of this agent has been dilatation of
cervix which is used in gynecology because of its
effectiveness and ease of administration (6, 7).
After oral administration, misoprostol is rapidly
absorbed. The half life of this agent is about 20 to
40 minutes (7). Adverse effects of misoprostol
after oral administration are nausea, vomiting,
diarrhea, abdominal cramps, and fever which are
dose dependent. Gastrointestinal side effects are
decreased if the tablets are administered vaginally.
Vaginal application of misoprostol, results in a
slower increase in plasma but overall exposure to
the drug is increased (8).
This study was conducted in order to evaluate ef-
fectiveness of misoprostol on ripening the cervix
before dilatation and curettage.

Methods
This study was performed over a period of six
months between October 2011 and April 2012 at
Taleghani teaching Hospital in Tehran Iran.
This is a clinical trial (IRCT2013022712632N1)
with random allocation followed by a double
blind design for two parallel groups.
56 nonpregnant women admitted for diagnostic
dilatation and curettage due to abnormal uterine
bleeding were the participants of this study. After
counseling with the patients in clinic, the patency
of the cervix was as closed as to prevent passage
of hystrometer were included. Patients who had
history of cervical surgery, cervical incompeten-
cy, and current pregnancy were not included. The
patients who had any contraindications for use of
misoprostol, such as history of asthma, hyperten-
sion, and glaucoma, were not included.
Age, menopausal status, parity, and cervical pa-
tency were recorded.
Initially, 102 patients were enrolled for this
study. 46 patients were excluded from the study
either due to not meeting the inclusion criteria
(n=38) or due to refusal (n=8).
Fifty six women scheduled to have diagnostic di-
latation and curettage due to abnormal uterine
bleeding were included in this study after going
through inclusion and exclusion criteria.
The patient were randomly allocated to two paral-
lel groups (A and B) having 28 patients in each of
the two arms using computer generated randomi-
ization protocol.
All the patients were admitted on the day before
operation and undergone detailed history taking
and clinical examination. Routine baseline inves-
tigations were also performed.
The patients in the study group (Group A) re-
ceived 200 $\mu g$ misoprostol (Searle & Company
(now Pfizer) under the trade name Cytotec, USA)
in posterior fornix of vagina, 2-4 hr prior to the
operative 1 procedures and the patients in the con-
trol group (Group B) received vitamin B6 (Kimia
Daroo, Iran) in posterior fornix of vagina 2-4 hr
prior to the operative procedures.
Selection of vitamin B6 tablet as a placebo is due
to the fact that it doesn’t have any significant sys-
temic effects by vaginal administrations. Also
there was no report of its effects on cervical tissue
or uterine (4, 6). We had used both the miso-
prostol and vitamin B6 tablets in round com-
pressed shape (white in color), and the smaller
size of vitamin B6 tablet was the only difference.
For having double blinded study, both of the
drugs were in identical sealed envelope. The duty
Resident doctor, just before application of the
drugs, opened the sealed envelope and applied
them in posterior fornix of the patients. The inves-
tigators did not have any information about the
agents that were administered.
To determine the cervical width, a No. 5 Hegar
dilator was first applied to the cervical canal. Up-
on passage of Hegar dilator, curettage was suc-
cessfully completed. If not passed, progressively
smaller sizes of Hegar dilator were applied. Cer-
vical response was assessed by the largest size
Hegars dilator that could be inserted without re-
sistance at the beginning of the surgical proce-
dures. Other outcome measures were needed for
further cervical dilatation (larger than No. 5 Hegar
dilator).
Development of any pre-operative side effects,
such as nausea, vomiting, abdominal cramp, vagi-
nal bleeding, pyrexia of significance, loose mo-
tions, etc. were also noted.
Per-operative complications, if any were also
taken into consideration.
The data was analyzed using SPSS 14 statistical
software. To compare the outcomes between the
study group and the placebo group for statistical
analysis, Chi-square test, t-test and Mann-
Whitney U test were used. A p-value less than
0.05 was considered as statistically significant.

Ethical consideration: The study was approved by
"The Ethics Committee" at Shahid Beheshti

Mohammadian Sh, et al.
University of Medical Sciences, No. 400/1731; 31-2-91. Before enrolments for the study, all women provided a written informed consent after full counseling about advantages and disadvantages of misoprostol.

**Results**

The average of age of participants was 50.7±9 years in misoprostol group and 50.4±9 years in the control group. Eleven patients in misoprostol group and 7 in placebo group were nulliparous. There were 9 menopausal patients in misoprostol group and 7 in the control group. There was no significant difference in the clinical characteristics (age, weight, parity, and menopause status) between misoprostol and control groups either (Table 1). With an increase in age, misoprostol was less effective (p=0.008) but body weight of the patients did not have any correlation with misoprostol dose (p=0.5).

In fifteen patients (53.6%) of misoprostol group and 8 patients (28.6%) in the placebo group, the Hager dilatators number 5 could pass the cervix. This result was statistically different between two groups (p=0.05). The use of vaginal misoprostol facilitated dilatation and curettage. Cervical os was wider in misoprostol group (4.8±1 mm) than in control group (4.0±1 mm), p=0.01. Operative procedures undertaken in both groups were also comparable. Procedural time (minutes) from the beginning of procedures through the external cervical was significantly shorter in misoprostol group (13.5±1.4 min) than in placebo group (19.4±0.9 min) (p<0.001). Requirement of further cervical dilatation and the time required for that was also significantly less in the study group (Table 2).

In premenopausal women, the cervical width (based on number of Hegar dilator) before dilatation and curettage was 5.0±0.9 mm in misoprostol group versus 3.9±1 mm in placebo group (p=0.003). In postmenopausal women, the cervical width before dilatation and curettage was 4.3±1.3 mm in misoprostol group versus 4.1±1 mm in control group (p=0.86). The difference between the two groups in postmenopausal patients was not significant. Requirement of further cervical dilatation for that in premenopausal patients was also significantly less in the study group. The number of post menopause cases was too low to evaluate distinctively (Table 3).

In nulliparous patients, the cervical width before dilatation and curettage was 4.8±1.2 mm in misoprostol group versus 3.6±1.5 mm in control group (p=0.066). Therefore, there was no significant difference in cervical width between groups. Moreover, there was no difference in requirement for further cervical dilatation (Table 3).

<table>
<thead>
<tr>
<th>Characteristics</th>
<th>Misoprostol (n=28)</th>
<th>Placebo (n=28)</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age * (year)</td>
<td>50.7±9.3</td>
<td>50.4±9.1</td>
<td>0.908 **</td>
</tr>
<tr>
<td>Weight * (kg)</td>
<td>69.8±9.5</td>
<td>69.9±9.2</td>
<td>0.977 **</td>
</tr>
<tr>
<td>Nulliparity</td>
<td>11(39.3%)</td>
<td>7(25%)</td>
<td>0.252 ***</td>
</tr>
<tr>
<td>Multiparity</td>
<td>17(60.7%)</td>
<td>21(75%)</td>
<td>0.39 ***</td>
</tr>
<tr>
<td>Postmenopausal</td>
<td>9(32.1%)</td>
<td>7(25%)</td>
<td>0.554 ***</td>
</tr>
<tr>
<td>Premenopausal</td>
<td>19(67.9%)</td>
<td>21(75%)</td>
<td>0.76 ***</td>
</tr>
</tbody>
</table>

* Mean±SD, ** t-test, *** Chi-square test

<table>
<thead>
<tr>
<th>Cervical Status before dilatation</th>
<th>Misoprostol (n=28)</th>
<th>Placebo (n=28)</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cervical width * (mm)</td>
<td>4.8±1.1</td>
<td>4.0±1.1</td>
<td>0.01 **</td>
</tr>
<tr>
<td>Duration of operation * (min)</td>
<td>13.5±1.4</td>
<td>19.4±0.9</td>
<td>&lt;0.001 **</td>
</tr>
<tr>
<td>No. 5 Hegar passed</td>
<td>15(53.6%)</td>
<td>8(28.6%)</td>
<td>0.05 ***</td>
</tr>
<tr>
<td>No. 5 Hegar did not pass</td>
<td>13(46.4%)</td>
<td>20(71.4%)</td>
<td>0.057 ***</td>
</tr>
</tbody>
</table>

* Mean±SD, ** Mann-Whitney U test, *** Chi-square test
Misoprostol had minor and transient side effects; nausea was reported in three patients, abdominal pain in two patients (25%), diarrhea in two patients (25%), and no cases of fever or vomiting were reported. These side effects were also not significantly higher than the placebo group. There was a case of vaginal bleeding related to misoprostol use.

Discussion

Our findings showed that misoprostol is effective in cervical priming for dilatation and curettage in premenopausal women. Procedures such as dilatation and curettage are frequently performed for different gynecological problems in both pre and postmenopausal women either for diagnostic or for therapeutic purposes. Cervical dilatation is difficult part of the procedure. Cervical ripening prior to operative procedures makes the operation easier and decreases the risk of cervical injury and uterine perforation which are often associated with mechanical cervical dilatation. Laminaria and prostaglandin agents are usually used for this purpose (9).

Discomfort and complications due to cervical dilatation despite local anesthesia and precise techniques are serious problems in those women. Cervical narrowing or stenosis, the frequently encountered condition during these procedures is a major cause of these undesirable effects. Misoprostol, a prostaglandin E1 analogue was used in obstetrics because of its uterotonic and cervical ripening effects in different studies (7, 10). Ngai et al. had reported that oral misoprostol was effective for cervical ripening in nulliparous woman (8) but it was not proved in the present report.

Cervical incompetency usually accompanies uterine anomalies except arcuate uterus (11); therefore, misoprostol is likely to be applicable to dilate the cervix in arcuate uterus cases as well. Mathlouthi et al. reported that there is no significant difference between two groups (placebo and misoprostol) in cervical width prior to curettage. Their result is different from our findings (12). It might be due to route of misoprostol administration; in our study administration was vaginal, while in their study was sublingual. Sublingual administration has lower effect on cervix and uterine (7).

However, some studies reported that preoperative use of vaginal misoprostol did not reduce the cervical resistance particularly when used in postmenopausal women (13, 14). It might be due to route of misoprostol administration; in our study administration was vaginal, while in their study was sublingual. Sublingual administration has lower effect on cervix and uterine (7).

Preoperative use of vaginal misoprostol reduced the need of higher cervical dilatation in many pa-
tients. Dilatation of the cervix was also easier in the cases. Ripening of the cervix by vaginal misoprostol reduces the pain during cervical dilatation. Saving the operation time and using lower dose of anesthesia drugs are other advantages. There are other studies which reported the same results in premenopausal patients. Cervicouterine injury during operation was very rare (only a single case of cervical injury out of 28 women) in the misoprostol group. Although vaginal use of misoprostol produced mild abdominal discomfort and slight vaginal bleeding in some women, there were no serious side effects seen in patients.

The only limitation of vaginal use of misoprostol tablets is the requirement for prior hospitalization of patients. Sublingual route of misoprostol may be the solution in this case.

The limitations of our study were performing the procedure by several resident doctors and variation in anesthesia for the patients. History of vaginal delivery is also likely to have an effect on cervical patency as well. Future studies are needed to be carried out for limiting the effects of these variables.

Conclusion

It was found that vaginal misoprostol applied in nonpregnant premenopausal women before dilatation and curettage facilitates the cervical dilatation and minimizes cervical or uterine injuries. The effect is not significant in nulliparous or postmenopausal women.

Conflict of Interest

The authors declare no conflict of interest.

References