Original Article

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

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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.

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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 prostaglandin E1 analogue was administered for prevention 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 effectiveness 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 incompetency, and current pregnancy were not included. The patients who had any contraindications for use of misoprostol, such as history of asthma, hypertension, and glaucoma, were not included.

Age, menopausal status, parity, and cervical patency 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 dilatation 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 parallel groups (A and B) having 28 patients in each of the two arms using computer generated randomization protocol.

All the patients were admitted on the day before operation and undergone detailed history taking and clinical examination. Routine baseline investigations were also performed.

The patients in the study group (Group A) received 200 μg 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 control 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 systemic effects by vaginal administrations. Also there was no report of its effects on cervical tissue or uterine (4, 6). We had used both the misoprostol and vitamin B6 tablets in round compressed 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 investigators 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. Upon passage of Hegar dilator, curettage was successfully completed. If not passed, progressively smaller sizes of Hegar dilator were applied. Cervical response was assessed by the largest size Hegars dilator that could be inserted without resistance at the beginning of the surgical procedures. 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, vaginal bleeding, pyrexia of significance, loose motions, *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

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 participates 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 1. Cervical status at the beginning of surgical procedures in the study group in comparison to the placebo group

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

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

Table 2. Cervical status at the beginning of surgical procedures in the misoprostol group in comparison to the placebo group

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

* Mean±SD, ** Mann-Whitney U test, *** Chi-square test

Table 3. Operative procedures undertaken in both groups based on menopausal status

Menopausal status	Postmenopausal			Premenopausal		
	Misoprostol	Placebo	p-value	Misoprostol	Placebo	p-value
Cervical width pre-procedure * (*mm*)	4.3±1.3	4.1±1.1	0.863 **	5.0±0.9	3.9±1.1	0.003 **
No. 5 Hegar passed	1(11.1%)	3(42.9%)	0.146 ***	14(73.7%)	5(23.8%)	0.002 ***
No. 5 Hegar did not pass	8(88.9%)	4(57.1%)	0.001 ***	5(23.6%)	16(76.2%)	0.004 ***

* Mean±SD, ** Mann-Whitney U test, *** Chi-square test

Table 4. Operative procedures undertaken in both groups based on nulliparity

Parity	Nulliparous		
Groups	Misoprostol	Placebo	p-value
Cervical width before dilatation * (*mm*)	4.8±1.2	3.6±1.5	0.066 **
No. 5 Hegar dilator passed	6(54.5%)	2(28.6%)	0.367 ***
No. 5 Hegar dilator did not Pass	5(45.4%)	5(71.4%)	0.557 ***

* 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 hypoestrogenic state in postmenopausal women. Oppegaard et al. reported that after 2 weeks of using vaginal estrogen in postmenopausal women, 1 *mg* misoprostol 12 *hr* before curettage reduces the cervical resistance (15). Bisharah et al. also reported that misoprostol did not produce cervical priming effect when used in hypoestrogenic state cases through leuprolide acetate injection (16). In the present study, by increasing age, the efficacy of misoprostol declined probably due to estrogen deficiency.

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.

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