

The Effect of Various Dosages of Misoprostol for Cervical Preparation Before the Hysteroscopy

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ABSTRACT

Background & Objective: Hysteroscopy is an impressive diagnostic and therapeutic procedure for uterine cavity abnormalities. There are several methods for cervical preparation prior to hysteroscopy, among which misoprostol (a prostaglandin E1 analog) is the most common. However, misoprostol has some side effects, including uterine cramps, vaginal hemorrhage, nausea, vomiting, and fever-like feelings, the severity of which escalates by increasing the dosage. Therefore, in this study, we aimed to compare vaginal misoprostol in two different dosages of 200 and 400 µg with a control group to prescribe the lower dosage of misoprostol in case they were equally effective.

Materials & Methods: In this randomized clinical trial study, 87 patients, who had hysteroscopy indications at Yas Hospital, were randomly assigned into three groups (i.e., 200 µg vaginal misoprostol, 400 µg vaginal misoprostol, and placebo). Afterward, the dilatation time of the cervical response and side effects associated with medication and surgery were assessed.

Results: The mean dilatation time in the 200 µg misoprostol, 400 µg misoprostol, and placebo groups were 46.7±35.8, 36.8±31.1, and 67.6±49.5 seconds, respectively. These differences were significant ($P=0.038$).

Conclusion: It seems that administering vaginal misoprostol is an easy, effective, and safe procedure for cervical preparation before the hysteroscopy. Considering that increasing the dosage of misoprostol did not significantly change the dilatation time, it is recommended that 200 µg misoprostol be used to reduce the side effects.

Keywords: Misoprostol, Hysteroscopy, Cervical dilatation



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Introduction

Hysteroscopy is an effective diagnostic and therapeutic procedure for uterine cavity abnormalities, such as endometrial polyps, submucosal myomas, uterine septum, and synechiae (1-5). Cervical dilatation is one of the surgeon concerns when performing a hysteroscopy. This problem is more noticeable in cervical stenosis, as well as in nulliparous and menopausal patients. In addition, more than half of the side effects related to hysteroscopy (including cervical rupture, false tract creation, and uterine perforation) occur during the entry into the cervix. The prevalence of these side effects can be reduced by proportion cervical preparation prior to hysteroscopy (6).

There are several methods for preparing the cervix before hysteroscopy. They reduce the risk of hysteroscopy-associated side effects (7-10). Among them, administering misoprostol, a prostaglandin E1 analog, is the most common (11).

Misoprostol is a prostaglandin E1 analog widely consumed to prevent and treat gastric ulcers caused by

long-time consumption of nonsteroidal anti-inflammatory drugs. Furthermore, it is applied to prepare the cervix for labor induction, the first trimester pregnancy termination, and for missed abortion treatment.

Misoprostol for cervical preparation before the hysteroscopy can be administered orally, sublingually, and vaginally; however, there are still some controversies over the most effective method of administering misoprostol for cervical dilatation. No studies have mentioned the definite dosage or method for administering misoprostol in patients undergoing hysteroscopy.

In addition, misoprostol has side effects, including uterine cramps, vaginal hemorrhage, nausea, vomiting, and fever-like feelings, the severity of which escalates by increasing the dosage. Hence, in this study, we aimed to compare vaginal misoprostol in two different dosages of 200 and 400 µg with a control group to prescribe the lower dosage of misoprostol in case they were equally effective.

Materials and Methods

This double-blind clinical trial study was done on 87 patients who had hysteroscopy indications at Yas Hospital from October 2017 to February 2018. Inclusion criteria included patients who were candidates for diagnostic and surgical hysteroscopy due to irregular uterine hemorrhage or intrauterine lesions seen in hysterosalpingography or ultrasound.

Exclusion criteria were being pregnant, suffering from genital infections, having a history of cervical surgery, cervical insufficiency, or GnRH agonist treatment, dealing with prominent uterovaginal prolapse that affected vaginal use of misoprostol, observing a space-occupying lesion in the endocervical canal, having contraindication for prostaglandin use (asthma, glaucoma, hypertension, severe heart disease, and renal failure), and withdrawing to take part in the study.

This study was conducted in compliance with the Helsinki Declaration and approved by the Tehran University of Medical Sciences ethics committee (IR.TUMS.MEDICINE.REC.1396.2628). All the patients signed informed agreement.

Hysteroscopy was mainly performed in the proliferative phase of the menstrual cycle. The type of anesthesia was spinal. The patients were allocated to three groups using the block randomization method. In the first group, 200 µg vaginal misoprostol (Samisaz Pharmaceutical Company) was administered; 400 µg vaginal misoprostol (Samisaz Pharmaceutical Company) was administered in the second group, and a placebo (Caspian Tamin Pharmaceutical Company vitamin B6) was administered in the third group 4-6 hours before the surgery.

before the hysteroscopy in the lithotomy position, for cervical dilatation, Hegar dilators (numbers 1 to 7) were used according to the width of the cervix. Hysteroscopy was then performed.

For double blinding, vaginal and hysteroscopic medications were inserted by different people; the surgeon and patients were not aware of the medication administered. Simultaneous laparoscopy was performed in case of rupture or suspected uterine anomaly. The primary outcome included the duration time of dilatation up to the number 7 Hegar dilator and surgery-related side effects.

All the statistical analyses were performed using SPSS version 24.0 (SPSS Inc., Chicago, Ill., USA). A P-value of less than 0.05 was considered as the level of statistical significance. For normally distributed data, the analysis of variance (ANOVA) was utilized, and the Kruskal-Wallis test was employed for data, which did not have a normal distribution according to the Kolmogorov-Smirnov test. The univariate analysis of

variance was used to show the interaction effect of variables. For determining the intensity of the effectiveness of the three intervention methods, two-by-two comparisons were performed among the groups using the post hoc test.

Results

In this study, 87 patients were studied. The mean of the patients' age was 41.1 ± 8.3 years. Among these patients, 86 people (98.9%) were married, and only one person (1.1%) was single.

There was no significant difference ($P > 0.05$) between the three groups in terms of baseline variables, including age, body mass index (BMI), gravidity, history of normal vaginal delivery number or C-section number, marital status, and menopause. All three groups were identical in terms of these baseline variables ([Table 1](#)).

In the present study, the most prevalent hysteroscopy indication was abnormal uterine bleeding (AUB) with polyps, which included 24 patients (27.6%). This indication was the most common cause in all three study subgroups.

The mean dilatation time in the 200 µg misoprostol group was 46.7 ± 35.8 seconds; it was 36.8 ± 31.1 in the 400 µg misoprostol group and 67.6 ± 49.5 in the placebo group, indicating a significant difference among these groups in the dilatation time for the preparation prior to hysteroscopy ($P = 0.038$). Since the dilatation time was significantly different in these three groups, the post hoc test was done to find the significant component, the results of which were presented in [Table 2](#) in detail.

Overall, 13 participants were menopausal (14.9%). The general linear model (GLM) test showed that the occurrence of menopause did not make a difference in the results, and there was no significant difference between menopause and non-menopause patients in the three groups ([Table 3](#)).

Moreover, intraoperative side effects were examined among the participants. The results demonstrated that, among the studied patients, we only had one case of intraoperative side effects, which was a false tract, and 86 patients (98.9%) did not experience any intraoperative side effects. The difference between this variable was not statistically significant in the three study groups.

Table 1. The baseline characteristics in the study groups

Variables	Group name			P-value
	200 µg Misoprostol	400 µg Misoprostol	Vitamin B6 (control)	
Age	41.45±7.10	41.52±8.82	40.38±9.1	0.846
BMI	27.38±3.31	27.97±3.35	27.48±3.73	0.791
Gravidity	3.31±2.02	2.55±2.13	3.55±1.37	0.061
NVD number	2.07±1.90	1.34±1.85	2.34±1.49	0.059
C/S number	0.41±0.78	0.62±0.90	0.41±0.73	0.560
Menopause	2 (6.9)	6 (20.7)	5 (17.2)	0.309

BMI: body mass index, NVD: normal vaginal delivery, C/S: cesarean section

Table 2. The comparison of dilatation time amongst the study groups

Comparison Groups	Dilatation time (Mean/Mean Difference ± SE)			P-value
	200 µg Misoprostol	400 µg Misoprostol	Vitamin B6	
Between 3 G	46.7±35.8	36.8±31.30	67.6±49.5	0.038
G1-G2		9.89±10.47		0.360
G1- G3		- 20.91±10.64		0.049
G2-G3		-30.80±10.64		0.005

G: group, G1: Misoprostol 200, G2: Misoprostol 400, G3: Vitamin B6

Table 3. Using the GLM analysis to assess menopause and misoprostol dosage effects on the dilatation time

Variables	Unstandardized Coefficients		T	P-value
	B	Std. Error		
(Constant)	35.61	17.488	2.036	0.045
Menopause	-6.257	12.887	-0.486	0.629
Misoprostol Dosage	10.994	5.48	2.006	0.048

GLM: general linear model

Discussion

This study indicated that administering misoprostol led to a suitable dilatation (required for hysteroscopy) much better and faster than the placebo. Because about half of the hysteroscopy-related side effects happen when entering the cervical canal (including cervical rupture, false tract creation, and uterine perforation), the occurrence of these side effects can be greatly decreased by creating proper cervical dilatation (12-13).

Although, in this study, we did not compare dilatation time based on different routes of misoprostol (oral vs vaginal), previous evidence suggested that there was no remarkable diversity in cervical dilatation according to misoprostol routes; however, cervical dilatation occurs more rapidly in the vaginal type, and diarrhea is less common in the vaginal misoprostol (14).

In the current study, 200 and 400 µg misoprostol significantly shortened the dilatation time (20.19 and 30.80 seconds, respectively) compared to the placebo. This finding is consistent with the results of Song *et al.*, Saha *et al.*, and Hua *et al.*, reporting an important

variation in the cervical preparation with misoprostol compared to the placebo (15-17).

In the present study, it was shown that the misoprostol effect was similar in both premenopausal and postmenopausal women. This finding is similar to the results of a study performed by Gkrozou *et al.*, which mentioned that vaginal misoprostol decreased the requirement for cervical dilatation in both premenopausal and postmenopausal patients (18). However, our finding is contrary to the results of a study conducted by Oppegaard *et al.*, which reported that misoprostol did not affect the cervical preparation in postmenopausal women (19), as well as the results of a study carried out by Mohammadian *et al.*, which concluded that misoprostol facilitated dilatation and curettage in multiparous and premenopausal patients but was lower efficient in nulliparous and postmenopausal women (20).

The strength of this study was the observance of the principles of randomization and blinding, as well as the

use of the control group. However, there were some limitations in the current study, such as the small sample size. Besides, in the present study, only vaginal misoprostol was examined; therefore, it is recommended that future studies be performed with a larger sample size and consider possible confounding variables.

Conclusion

It seems that administering vaginal misoprostol is an easy, effective, and safe procedure for cervical preparation before the hysteroscopy. Considering that increasing the dosage of misoprostol did not significantly change the dilatation time, it is recommended that 200 µg misoprostol be used to reduce the side effects.

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Conflict of Interest

Authors declared no conflict of interests.

References

- Clark TJ, Voit D, Gupta JK, Hyde C, Song F, Khan KS. Accuracy of Hysteroscopy in the Diagnosis of Endometrial Cancer and Hyperplasia: A Systematic Quantitative Review. *JAMA*. 2002;288(13):1610-21. [DOI:10.1001/jama.288.13.1610] [PMID]
- Polyzos NP, Zavos A, Valachis A, Dragamestianos C, Blockeel C, Stoop D, et al. Misoprostol prior to hysteroscopy in premenopausal and post-menopausal women. A systematic review and meta-analysis. *Hum Reprod Update*. 2012;18(4):393-404. [DOI:10.1093/humupd/dms014] [PMID]
- Hamou JE. *Hysteroscopy and microcolpohysteroscopy: text and atlas*. Appleton & Lange; 1991.
- Bakour SH, Jones SE, O'Donovan P. Ambulatory hysteroscopy: evidence-based guide to diagnosis and therapy. *Best Pract Res Clin Obstet Gynaecol*. 2006 Dec 1;20(6):953-75. [DOI:10.1016/j.bpobgyn.2006.06.004] [PMID]
- Carneiro MM. What is the role of hysteroscopic surgery in the management of female infertility? A review of the literature. *Surg Res Pract*. 2014;2014:105412. [DOI:10.1155/2014/105412] [PMID] [PMCID]
- Schulz K, Grimes D, Cates Jr W. Measures to prevent cervical injury during suction curettage abortion. *The Lancet*. 1983;321(8335):1182-5. [DOI:10.1016/S0140-6736(83)92464-9]
- Darwish AM, Ahmad AM, Mohammad AM. Cervical priming prior to operative hysteroscopy: a randomized comparison of laminaria versus misoprostol. *Hum Reprod*. 2004;19(10):2391-4. [DOI:10.1093/humrep/deh397] [PMID]
- Gupta N, Gupta B, Dadhwal V, Mittal S. Efficacy of intrauterine lignocaine plus vaginal misoprostol for pain relief in premenopausal women undergoing endometrial aspiration and ambulatory hysteroscopy. *Acta Obstet Gynecol Scand*. 2010;89(8):1066-70. [DOI:10.3109/00016349.2010.499444] [PMID]
- Lin YH, Hwang JL, Seow KM, Huang LW, Chen HJ, Hsieh BC. Laminaria tent vs misoprostol for cervical priming before hysteroscopy: Randomized study. *J Minim Invasive Gynecol*. 2009;16(6):708-12. [DOI:10.1016/j.jmig.2009.07.003] [PMID]
- Preuthipan S, Herabutya Y. A randomized comparison of vaginal misoprostol and dinoprostone for cervical priming in nulliparous women before operative hysteroscopy. *Fertil Steril*. 2006;86(4):990-4. [DOI:10.1016/j.fertnstert.2006.03.039] [PMID]
- Selk A, Kroft J. Misoprostol in operative hysteroscopy: a systematic review and meta-analysis. *Obstet Gynecol*. 2011;118(4):941-9. [DOI:10.1097/AOG.0b013e31822f3c7b] [PMID]
- Jansen FW, Vredevoogd CB, van Ulzen K, Hermans J, Trimbos JB, Trimbos-Kemper TC. Complications of hysteroscopy: a prospective, multicenter study. *Obstet Gynecol*. 2000;96(2):266-70. [DOI:10.1097/00006250-200008000-00021] [PMID]
- Grimes DA, Schulz KF, Cates WJ, Jr. Prevention of Uterine Perforation During Curettage Abortion. *JAMA*. 1984;251(16):2108-11. [DOI:10.1001/jama.1984.03340400036021] [PMID]
- Abdelhakim AM, Gadallah AH, Abbas AM. Efficacy and safety of oral vs vaginal misoprostol for cervical priming before hysteroscopy: A systematic review and meta-analysis. *Eur J Obstet Gynecol Reprod Biol*. 2019;243:1111-9. [DOI:10.1016/j.ejogrb.2019.10.023] [PMID]
- Song T, Kim MK, Kim ML, Jung YW, Yoon BS, Seong SJ. Effectiveness of different routes of misoprostol administration before operative hysteroscopy: a randomized, controlled trial. *Fertil Steril*. 2014;102(2):519-524. [DOI:10.1016/j.fertnstert.2014.04.040] [PMID]
- Saha M, Chakraborty A, Chattopadhyay S, Saha S, Paul J, Das A. Effect of misoprostol for cervical priming before gynecological procedures on nonpregnant premenopausal women. *J Nat Sci Biol Med*. 2015;6(Suppl 1):S123. [DOI:10.4103/0976-9668.166116] [PMID] [PMCID]
- Hua Y, Zhang W, Hu X, Yang A, Zhu X. The use of misoprostol for cervical priming prior to hysteroscopy: a systematic review and analysis. *Drug design, Drug Des Devel Ther*. 2016;10:2789. [DOI:10.2147/DDDT.S111625] [PMID] [PMCID]
- Gkrozou F, Koliopoulos G, Vrekoussis T, et al. A systematic review and meta-analysis of randomized studies comparing misoprostol versus placebo for cervical ripening prior to hysteroscopy. *Eur J Obstet Gynecol Reprod Biol*. 2011;158(1):17-23. [DOI:10.1016/j.ejogrb.2011.04.022] [PMID]

19. Oppegaard KS, Lieng M, Berg A, Istre O, Qvigstad E, Nesheim BI. Does self-administered vaginal misoprostol result in cervical ripening in postmenopausal women after 14 days of pre-treatment with estradiol? Trial protocol for a randomised, placebo-controlled sequential trial. BJOG. 2008;115(7):917-e10. [[DOI:10.1111/j.1471-0528.2008.01727.x](https://doi.org/10.1111/j.1471-0528.2008.01727.x)] [[PMID](#)] [[PMCID](#)]
20. Mohammadian S, Tavana A, Tavana S, Mohammadian A, Fallahian M. Cervical Priming by Misoprostol before Diagnostic Dilatation and Curettage: A Randomized Clinical Trial. J Reprod Infertil. 2015;16(3):162-166.

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