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Vaginal Misoprostol for Cervical Priming before Hysteroscopy: A Randomized Study

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Abstract

Introduction: The objective of the present study was to compare the effectiveness of vaginal misoprostol on cervical ripening in patients undergoing hysteroscopy.

Method: The patients in the study group (Group A) received 400 microgram of misoprostol in the posterior fornix of vagina 6 hours prior to the operative procedure . The baseline cervical dilatation was evaluated immediately prior to the beginning of hysteroscopy. The outcome measures in the study were baseline cervical dilation, the number and percentage of patients who required cervical dilatation to allow passage of hysteroscopy, ease of dilatation, complications during the procedure and treatment emergent side effects.

Result and Conclusion

We conclude that vaginal misoprostol applied before hysteroscopy decreases the cervical resistance, reduces the need for further cervical dilatation, facilitates the cervical dilatation (if it is required).

Keywords: Cervical Priming, Hysteroscopy, Vaginal Misoprostol

Introduction

Hysteroscopy is a term derived from the greek word "hystera" , which means uterus and skopeo, which means "to view"[1]. Hysteroscopy is a minimally invasive technique for observing the uterine cavity for a variety of gynecological problems, and has become a valuable diagnostic and therapeutic procedure. The advantages of hysteroscopy as an accurate diagnostic procedure are that, it not only allows direct visualization and accurate localization of pathology but also provides a method to locate the site most likely to yield positive results.

The potential risks of introducing a hysteroscope in the endometrial cavity are largely limited to cervical trauma and uterine perforation. These include cervical tears, creation of a false track, and rarely uterine perforation**.** The prevalence of complications can be reduced if the cervix is ripened before hysteroscopy [2,3]. Misoprostol has now emerged as the drug of choice as it is cheaper, highly efficacious and stable at room temperature and is available as tablet form[4].

Misoprostol gets extensively absorbed and undergoes rapid de-esterification to its free acid which is responsible for its action[4].

Misoprostol is available in many formulations: tablets or gelcaps, at doses of 200, 400, 800, and 1,000 mcg, and can be administered by oral, sublingual, buccal, vaginal or rectal route. Misoprostol is meant for oral administration but pharmacokinetic studies have shown that the plasma concentration of the active metabolite is sustained for a longer period after vaginal administration as compared to oral administration[4,5].The bioavailability of vaginally administered misoprostol is three times higher than orally.

The utility of diagnostic hysteroscopy can be improved by facilitating its use in an office setting. But one limiting factor is cervical dilatation. Process of cervical dilatation is the most unpleasant part of these procedures. Cervical priming prior to operative procedures facilitates the operation Agents commonly used for this purpose include various prostaglandin preparations. The off-label use of misoprostol for gynecological procedures has received less attention, despite reports of its effectiveness in inducing cervical dilatation. If misoprostol could decrease or eliminate the need for cervical dilatation , hysteroscopy could be accomplished more easily. We thus undertook this study to determine if the use of misoprostol would improve baseline cervical dilatation before diagnostic hysteroscopy and obviate the need for dilatation .

Material and Methods

A hospital based randomized comparative study was done on 90 patients who underwent hysteroscopy admitted to day care or gynae ward in Department of Obstetric and Gynecology Santokba Durlabhji Memorial Hospital, Jaipur (Raj.) from Jan 2018-Dec 2018.

Inclusion criteria

1. All patients undergoing hysteroscopy.

Exclusion criteria

1. Presence of any contraindications for use of misoprostol like history of bronchial asthma, allergy to prostaglandins, irritable bowel syndrome and cardiovascular diseases.

2. Pregnant females

3. Local vaginal or cervical infection or inflammation etc.

3. H/o drug allergy to prostaglandins.

Study Type	Randomized comparative study
Study Design	Prospective study.
Study Area	The study was carried out in the department of Obstetrics and Gynaecology at Santokba Durlabhji Memorial Hospital, Jaipur
Study Duration	Jan 2018-Dec 2018
Study Population	All patients undergoing hysteroscopy.

Sample Size : Sample size was calculated at 80% study power and α power of 0.05 assuming SD of 0.8mm in baseline cervical width as found in the study of **Saha SP et al**[6] (International Journal of Health Sciences Vol-1 Issue-2 July 2007 page no 185-193).

For minimum detectable difference of 0.5 mm in baseline cervical width,40 patients in each group were required in sample size which was further enhanced and rounded off to 45 patients in each group as final sample size for present study expecting 10% attrition.

$$n = \frac{2(Z_{1-\alpha\div2} + Z_{1-\beta})^2 \times \sigma^2}{(M_1 - M_2)^2}$$

n = sample size

$Z_{1-\alpha\div2}$ = 1.96 (corresponding 'Z' value for α error of 0.05)

Z_{1-b} = 0.84 (corresponding 'Z' value for 80% study power)

σ = assumed standard deviation

$(M_1 - M_2)$ = difference of means to be detected

$$n = \frac{2(1.96 + 0.84)^2 \times (0.8x0.8)}{(0.5x0.5)}$$

Sample size = 40.14+10% =45 Study was carried out in the Department of Obstetrics and Gynaecology at Santokba Durlabhji Memorial Hospital, Jaipur. This study was a prospective randomized clinical study . After going through inclusion and exclusion criteria, the first 90 women who were scheduled to have hysteroscopy for various indications were included in this study. The patients were randomly allocated into two parallel groups (A and B) having 45 patients each. The patients in the study group (Group A) received 400 microgram of misoprostol in the posterior fornix of vagina 6 hours prior to the operative procedure. Patient was asked about the possible side effects of misoprostol before induction of general anaesthesia such as abdominal pain, nausea, vomiting, headache, dyspepsia and loose motion.

The baseline cervical dilatation was evaluated immediately prior to the beginning of hysteroscopy. It was assessed by placing a Hegar dilator(starting from the lowest number) that could be inserted without resistance at the beginning of the procedure. Both sides were used with the lower number first. The number represented the cervical diameter in mm. The largest Hegar dilator that could be inserted without resistance was considered as the baseline cervical dilatation then diagnostic hysteroscope was introduced. At the time of entry, if the cervical canal was too tight precluding passage of hysteroscope, then further dilatation was done using Hegar dilator of larger size. Surgeon was asked about the ease of dilatation. This assessment was done on the basis of the experience of the surgeon by noting their hands movement (screwing movement) and amount of pressure required for dilatation. If hegar dilator was easily introduced without any resistance it was considered as easy. If introduction of hegar dilator required pressure on dilatation and hand movements like screwing of dilator was seen and resistance was felt during dilatation then it was considered as difficult. During the procedure complications like creation of false passage, cervical injury and uterine perforation were noted. After the operation, the woman remained in the hospital for a minimum of 6 hours and was discharged

Results and Discussion

We used misoprostol as a cervical priming agent before diagnostic hysteroscopy with the main objective to see the effectiveness of the drug in this regard. Though the diagnostic hysteroscopy could be performed by using 4 mm scope without any prior cervical dilatation and without using any anaesthesia in many cases, it was our observation from clinical experience that in number of cases we had to face difficulties during introduction of hysteroscope without prior dilatation of cervix particularly in nulliparous and elderly women.

Table 1: Results of misoprostol administration

Parameters	Group	N	Mean	SD	Median	Min.	Max.	'p' value*
Baseline Cervical Dilation	Case	45	4.24	1.06	4	3	7	<0.001
	Control	45	3.63	0.40	3.5	3	5	

*Unpaired 't' test

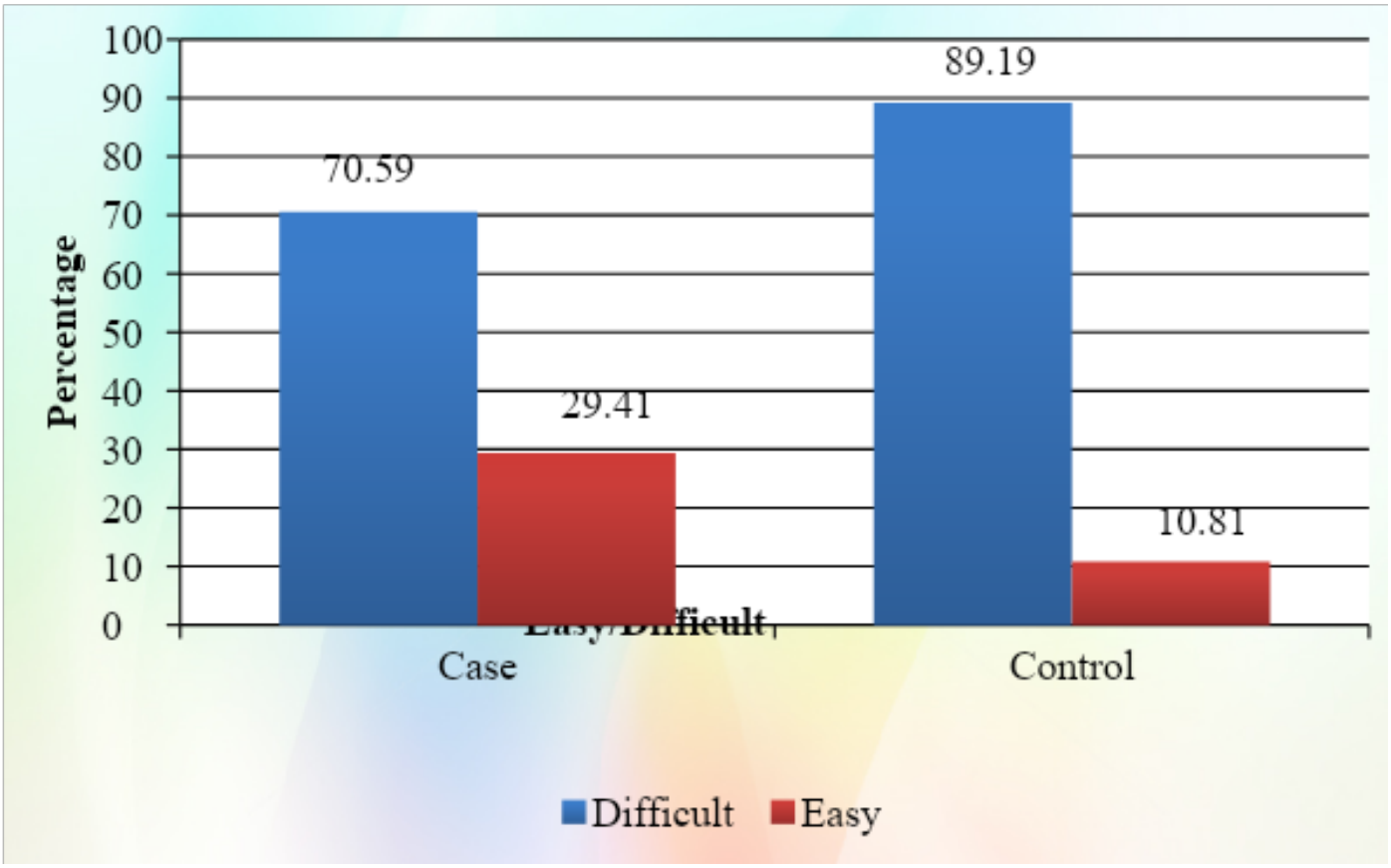
Baseline cervical dilatation was defined as the maximum number of hegar dilators that could be introduced into the cervix without resistance before hysteroscopy. The number of hegar dilators represented the cervical diameter in mm. From the results it was evident that baseline cervical dilatation at the beginning of hysteroscopy was superior in the case group which was statistically highly significant (p<0.001).

Table 2: Results of misoprostol administration

Dilator Required	**Case**		**Control**		**Total**	
	No.	**%**	**No.**	**%**	**No.**	**%**
Yes	17	37.78	37	82.22	54	60.00
No	28	62.22	8	17.78	36	40.00
Total	45	100.00	45	100.00	90	100.00

Fisher Exact Test P <0.001

After assessing baseline cervical dilatation, a hysteroscope was introduced. At the time of entry, if the cervical canal was too tight precluding passing of hysteroscope, then further dilatation was done using Hegar dilator of larger size. The above table shows a comparison of further dilatation requirements in both the groups. The difference between the groups was statistically significant.(p >0.001).



Ease of dilatation was also noted in both groups. This assessment was done on the basis of the experience of the surgeon by noting their hands movement (screwing movement) and amount of pressure required for dilatation. In the case group, amongst patients who required dilator, in 29.41 % patient's dilator was easily introduced without any resistance whereas in 70.59 % patients hegar dilator was introduced with difficulty. In the control group, 10.81 % patient's dilator was introduced easily whereas in 89.19 % patients hegar dilator was introduced with difficulty. The difference in ease of dilatation was found to be statistically insignificant between the 2 groups which can be attributed to subjective variation due to involvement of different surgeons

Table 3: Comparison of both groups according to hegar dilator requirement in nulliparous females

Dilator Required	Case		Control		Total	
	No.	%	No.	%	No.	%
Yes	9	60.00	18	100.00	27	81.82
No	6	40.00	0	0.00	6	18.18
Total	15	100.00	18	100.00	33	100.00

Fisher Exact Test P = 0.005

This indicates nulliparous patients receiving misoprostol had a significantly greater cervical dilatation compared with patients receiving no treatment. Nulliparous women receiving misoprostol prior to undergoing diagnostic hysteroscopy are more

likely to avoid the need of further cervical dilatation. The difference between the two groups was found to be statistically significant (p= 0.005).

Table 4: Comparison of both groups according to hegars dilator requirement in parous females (up to parous 2)

Dilator Required	Case		Control		Total	
	No.	%	No.	%	No.	%
Yes	4	21.05	13	72.22	17	45.95
No	15	78.95	5	27.78	20	54.05
Total	19	100.00	18	100.00	37	100.00

Fisher Exact Test P = 0.003

The difference between the groups was statistically significant (p >0.001). This indicates multiparous patients (parity up to 2) receiving misoprostol had a significantly greater baseline cervical dilatation compared with patients receiving no treatment.

Table 5: Comparison of both groups according to hegars dilator requirement in multiparous females (>2 parity)

Dilator Required	Case		Control		Total	
	No.	%	No.	%	No.	%
Yes	4	36.36	6	66.67	10	50.00
No	7	63.64	3	33.33	10	50.00
Total	11	100.00	9	100.00	20	100.00

Fisher Exact Test P = 0.370

This table shows requirement of further cervical dilatation in multiparous females (parity>2). The difference between the groups was not statistically significant. This indicates multiparous patients (parity more than 2) may not experience any substantial benefit by using misoprostol prior to the hysteroscopy.

Present study was conducted to compare vaginal misoprostol versus no medication for cervical priming before diagnostic hysteroscopy in females undergoing hysteroscopy.

We used misoprostol as a cervical priming agent before diagnostic hysteroscopy with the main objective to see the effectiveness of the drug in this regard. Though the diagnostic hysteroscopy could be performed by using 4 mm scope without any prior cervical dilatation and without using any anaesthesia in many cases, it was our observation from clinical experience that in number of cases we had to face difficulties during introduction of hysteroscope without prior dilatation of cervix particularly in nulliparous and elderly women. From our study, it was evident that there was a significant difference between the study and control groups in terms of cervical dilatation as determined by increased basal cervical dilatation in the case group. Preoperative application of vaginal misoprostol decreased the need for further cervical dilatation in a large number of cases. The change in the cervical dilatation is crucial in assessing the real efficacy of misoprostol.

However few studies showed that preoperative use of vaginal misoprostol did not facilitate cervical dilatation when used in postmenopausal women[7,8,9]. It might be due to hypoestrogenic state in postmenopausal women.

We compared the use of misoprostol for cervical priming before hysteroscopy based on parity also. As parity increased it was seen that the passage of hysteroscope was easier (p value-<0.01, significant) this was because of higher baseline dilatation in those with high parity along with the combined effect of misoprostol. Since multiparous women(parity more than 2) already have parous os misoprostol even if not used in these patients, hysteroscopy will still be easy to conduct whereas in nulliparous patients and multiparous patients with parity up to 2 usually requires misoprostol before hysteroscopy. So we can avoid using vaginal misoprostol before hysteroscopy in patients who are multiparous with parity >2.

Most common side effect of vaginal misoprostol was lower abdominal cramp (8.89%). Other side effects noted were mild vaginal bleeding (6.67%) and loose motion (2.22%) which was within tolerable limit. None of the patients required medications for the further management of side effects.

There was only one patient who had cervical injury who belonged to case group. There was no uterine perforation in both the groups. Since we have experienced gynecologists in our hospital who are expert in hysteroscopy only one complication was seen during hysteroscopy.

Strength of this study is that we compared the use of misoprostol for cervical priming before hysteroscopy based on parity also. We also found that there are minimal studies based on diagnostic hysteroscope. So we tried to consider the use of misoprostol for cervical priming before diagnostic hysteroscopy. Diagnostic hysteroscopy can be done in an office setting . If misoprostol can decrease or eliminate the need for cervical dilatation, diagnostic hysteroscopy can be easily done without anesthesia in an office setting .Since all patients were anaesthetized so ease of dilatation which was calculated had eliminated biasing factor of patient apprehension. Uniformity was maintained before study began.

Conclusion

We conclude that vaginal misoprostol applied before hysteroscopy decreases the cervical resistance, reduces the need for further cervical dilatation, facilitates the cervical dilatation(if it is required).

It is safe ,effective and inexpensive drug which is easily available. It has minimal side effects. Misoprostol should be considered for cervical priming before hysteroscopy.

Further studies on misoprostol dosing and route and timing of administration of misoprostol are needed for good efficacy in cervical priming before hysteroscopy.

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