Original Article

Comparison of Efficacy of Vaginal Misoprostol versus a Synthetic Osmotic Dilator (Dilapan-S) for Cervical Preparation before Operative Hysteroscopy: A Randomized Controlled Study

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Abstract

Objectives: To compare the need for mechanical cervical dilatation following vaginal misoprostol or synthetic osmotic dilator (Dilapan-S) usage for cervical preparation before operative hysteroscopy.
Materials and Methods: Fifty-five premenopausal women scheduled for operative hysteroscopic procedures with a 26 Fr resectoscope were included in this randomized, controlled clinical trial. After randomization, either 400 µg of vaginal misoprostol or intracervical synthetic osmotic dilator (Dilapan-S) was inserted 12 h before operative hysteroscopy. The need for additional mechanical cervical dilatation before insertion of the resectoscope was compared between the two groups. Initial cervical diameter before mechanical dilatation, intraoperative complications (cervical tears, creation of a false passage), and ease of dilatation were also compared between the two groups.
Results: In the misoprostol group, 92% of women required additional mechanical cervical dilatation, whereas only 36% of women in the Dilapan-S group required additional dilatation ($P < 0.05$). The median initial cervical diameter achieved with Dilapan was 9 mm (Q1: 7 mm; Q3: 10 mm), and with misoprostol, it was 6 mm (Q1: 4.5 mm; Q3: 8 mm) ($P < 0.05$). There was no significant difference in other outcome parameters between the two groups.
Conclusion: Synthetic osmotic dilator (Dilapan-S) is more efficacious than vaginal misoprostol at ripening the cervix before operative hysteroscopy.

Keywords: Cervical ripening, Dilapan-S, misoprostol, operative hysteroscopy, resectoscope

Introduction

Operative hysteroscopy using resectoscope is a standard procedure for treating uterine lesions like submucous myomas, endometrial polyps, uterine septa, and intrauterine adhesions.[1] It is also used for endometrial resection or ablation in women with heavy menstrual bleeding.[2] Conventional resectoscopes have a diameter of 8–9 mm, which makes cervical dilatation necessary before resectoscope insertion in most women. Difficult cervical dilatation or difficult entry of the resectoscope through the cervix may result in complications like cervical laceration, creation of a false track, and uterine perforation.[3] Cervical preparation before operative hysteroscopy may reduce these complications.

Cervical ripening agents like prostaglandins (misoprostol, dinoprostone) and osmotic dilators (laminaria) have been evaluated in several studies for cervical preparation before operative hysteroscopy.[4-8] A Cochrane systematic review on preoperative cervical preparation before operative hysteroscopy concluded that misoprostol was more effective than placebo and had lesser complications like false tracks

Article History:
Submitted: 28-Sep-2022
Revised: 13-May-2023
Accepted: 18-May-2023
Published: 07-Sep-2023

Access this article online

Quick Response Code:

Website: https://journals.lww.com/gmit

DOI: 10.4103/gmit.gmit_111_22

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How to cite this article: Nair AK, Subbaiah M, Maurya DK. Comparison of efficacy of vaginal misoprostol versus a synthetic osmotic dilator (Dilapan-S) for cervical preparation before operative hysteroscopy: A randomized controlled study. Gynecol Minim Invasive Ther 2023;12:225-9.

and cervical lacerations.[9] They also found that laminaria could be more effective than misoprostol but emphasized the need for more studies.

Laminaria is a naturally occurring osmotic dilator with several disadvantages like allergic reaction, sepsis, and less predictable effects due to inconsistent shape and dimensions.[10-12] Synthetic osmotic cervical dilators do not have these disadvantages. Only one study has evaluated a synthetic osmotic dilator for cervical preparation before operative hysteroscopy.[13] Dilapan-S is a 2nd-generation synthetic osmotic dilator made from hygroscopic polyacrylonitrile called AQUACRYL. There are no studies comparing the efficacy of Dilapan-S versus misoprostol in cervical preparation before operative hysteroscopy. This study was done to compare the efficacy of vaginal misoprostol versus Dilapan-S for cervical preparation before operative hysteroscopy.

Materials and Methods

This was a randomized controlled trial done in the Department of Obstetrics and Gynaecology, Jawaharlal Institute of Postgraduate Medical Education and Research (JIPMER), Pondicherry, India, and included premenopausal women (age >18 years) scheduled for operative hysteroscopic procedures. The study enrolment was from May 2020 to January 2022. The study was approved by the Institute Ethics Committee and was registered under Clinical Trials registry India (CTRI/2020/04/024844).

Women with acute pelvic inflammatory disease, allergy to the study drugs, uterine prolapse, or a history suggestive of cervical incompetence were excluded from the study. Women who agreed to be part of the study and gave informed consent were randomized into the misoprostol group and Dilapan-S group. In the misoprostol group, 400 µg of misoprostol was inserted into the posterior fornix of the vagina 12 h before the surgery.

In the Dilapan-S group, a single Dilapan-S (4 mm × 55 mm; MEDICEM Technology, Czech Republic) was inserted into the cervical canal 12 h before the surgical procedure. This insertion of Dilapan-S was done on an outpatient basis using Cusco's self-retaining speculum. After disinfecting the cervix with povidone-iodine, Dilapan-S was grasped at its end, where the string is attached, using a Ring forceps, and was inserted into the cervical canal till the internal os. If there was any difficulty during the insertion of Dilapan, cervix was held with a tenaculum to facilitate its insertion. Local anesthetic was injected into the anterior lip of the cervix before holding it with a tenaculum. Pain at the time of Dilapan insertion was assessed using a visual analog scale (VAS score; 0–10).

Block randomization with varying block sizes; generated using a computer was used to randomize the patients in the study arms in the ratio of 1:1. Sequentially numbered, opaque, sealed envelope allocation was used for concealment. In both groups, any adverse effects like bleeding, fever, nausea, allergies, overnight abdominal cramps, or systemic side effects due to insertion of the agent was noted down before shifting the patient to the operation theatre. Dilapan-S and misoprostol remnants were removed by one of the investigators in the operation theatre after the administration of anesthesia. All the hysteroscopic surgeries were performed in the early proliferative phase of the menstrual cycle with a 26 Fr bipolar resectoscope (Karl storz; Germany) by a single experienced surgeon under regional anesthesia using normal saline as distension media.

The primary outcome was the need for additional mechanical cervical dilatation before insertion of the resectoscope. Other outcome variables included initial cervical diameter before mechanical dilatation, intraoperative complications (cervical tears, creation of a false passage, uterine perforation), ease of dilatation, and incidence of backflow of fluid during the procedure. The need for additional mechanical dilatation was assessed by directly passing the 26F resectoscope. If the surgeon could not pass the resectoscope directly, then cervical dilatation was carried out using Hegar's dilators. The initial cervical diameter was assessed by the size of the Hegar's dilator entering the cervix without resistance. Subjective assessment of the ease of dilatation was recorded by the surgeon when inserting a 9-mm Hegar dilator into the cervix using a 5-point Likert scale (1 - very difficult; 5 - very easy). Patients in each group were followed up after 3 weeks and were clinically examined to rule out any pelvic infections.

Statistical analysis

In a study by Karakus *et al*. comparing laminaria and misoprostol for cervical priming before operative hysteroscopy, 100% of women in the misoprostol group and 15% in the laminaria group required additional mechanical dilatation resulting in a difference of 85%.[8] Assuming a difference of 40% between the misoprostol and Dilapan groups in our study, with an alpha value of 5% and power of 90%, the total sample size was calculated to be 50 (25 in each group). The sample size was calculated using OpenEpi Version 3 (Atlanta, Georgia,USA).

The distribution of data on categorical variables was expressed as frequency and percentage, and their comparison between the groups was carried out using Chi-square or Fisher's exact test. The distribution of data on continuous variables was expressed as mean with standard deviation or median with range depending upon the normality of distribution. Kolmogorov–Smirnov test was used to

determine normality of data. The continuous variables were compared with independent Student's *t*-test or Mann–Whitney *U*-test. A $P < 0.05$ was considered statistically significant. Statistical analysis was performed using IBM SPSS software version 21.0. (IBM Corp, Armonk, NY).

Results

Fifty-five women were assessed for eligibility, and 50 were included in the study [Figure 1]. Baseline demographic features of patients are shown in Table 1. There was no significant difference in age, parity, body mass index, and other demographic data between the two groups. Dilapan-S could be inserted easily in 23 (92%) women without any difficulty using only Cusco's self-retaining speculum. In 2 (8%) women, Dilapan could be inserted into the cervix only after holding the cervix with a tenaculum. Both were nulliparous and reported mild pain (VAS: 1–3).

In the misoprostol group, 23 (92%) women required additional mechanical cervical dilatation, whereas only 9 (36%) women in the Dilapan group required additional dilatation ($P < 0.05$), as shown in Table 2. The median initial cervical diameter achieved with Dilapan was 9 mm (Q1: 7 mm; Q3: 10 mm) and with Misoprostol, it was 6 mm (Q1: 4.5 mm; Q3: 8 mm) ($P < 0.05$). There was cervical tear in one woman in the misoprostol group. None of the women in either group had other complications like uterine perforation or fluid overload. None of the women in both groups had backflow of fluid due to excessive cervical dilatation.

After 12 h of Dilapan insertion, none of the women complained of overnight abdominal pain or vaginal bleeding. However, in the Misoprostol group, 3 women (12%) complained of mild abdominal pain, and 1 woman (5%) complained of vaginal bleeding after 12 h of misoprostol placement. None of the women in the misoprostol group had fever, nausea, diarrhea, or other side effects. None of the women reported any expulsion of misoprostol or Dilapan.

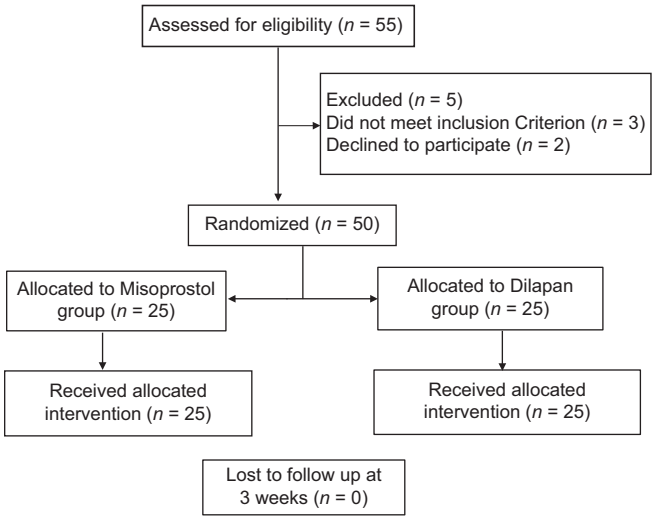

Figure 1: Consort flow diagram

The difficulty of cervical dilatation was evaluated based on the subjective assessment by the surgeon using a 5-point Likert scale. In the Dilapan group, only nine women needed additional mechanical dilatation, out of which one was assessed as very difficult. Out of the 23 women who underwent additional mechanical dilatation in the Misoprostol group, 4 of them were assessed as very difficult by the surgeon. However, these results were not statistically significant ($P = 0.66$). All the women were followed up at 3 weeks postsurgery and clinically examined. There was no evidence of pelvic infection in both groups.

Discussion

Fifty-five patients were included in this study and underwent cervical ripening with either misoprostol or Dilapan-S before

Table 1: Baseline patient characteristics

Patient characteristics	Misoprostol group (*n*=25), *n* (%)	Dilapan group (*n*=25), *n* (%)	*P*
Age (years), mean (SD)	40.2 (6.37)	40 (6.68)	0.914
BMI, kg/m^2, mean (SD)	23.82 (3.18)	25.69 (5.2)	0.131
Nulliparous	9 (36)	6 (24)	0.354
Prior cesarean delivery	5 (20)	7 (28)	0.508
Surgery			
Hysteroscopic myomectomy	10 (40)	7 (28)	0.37
Hysteroscopic septal resection	7 (28)	4 (16)	0.305
Transcervical resection of endometrium	7 (28)	10 (40)	0.37
Hysteroscopic polypectomy	1 (4)	3 (12)	0.277
Hysteroscopic adhesiolysis	0	1 (4)	0.312

SD: Standard deviation, BMI: Body mass index

Table 2: Intraoperative outcome parameters

	Misoprostol group (*n*=25)	Dilapan group (*n*=25)	*P*
Need for mechanical dilatation, *n* (%)	23 (92)	9 (36)	<0.001
Initial cervical diameter (mm)*, median (Q1–Q3)	6 (4.5–8)	9 (7–10)	<0.001
Total operative time (min)*, median (Q1–Q3)	23 (16–36)	26 (19–42)	0.704
Fluid deficit (mL)*, median (Q1–Q3)	460 (280–1000)	560 (430–1425)	0.174
Cervical tear, *n* (%)	1 (4)	0	1

*Mann–Whitney *U*-test used

operative hysteroscopy using a 26 Fr bipolar resectoscope. In the misoprostol group, 92% of women required additional mechanical cervical dilatation, whereas only 36% of women in the Dilapan-S group required additional dilatation ($P < 0.05$). The mean initial cervical diameter was also significantly more in the Dilapan-S group than in the misoprostol group.

A Cochrane systematic review on preoperative cervical ripening before operative hysteroscopy compared misoprostol with placebo.[9] It concluded that misoprostol was more effective than placebo in cervical ripening; fewer women who used misoprostol required mechanical cervical dilatation compared to the placebo group. The misoprostol group had fewer complications like false tracks and cervical tears.[9] However, side effects like mild abdominal pain, fever, and vaginal bleeding were more common in the misoprostol group. In our study, also we found that 12% of women in the misoprostol group complained of mild abdominal pain, and 5% had vaginal bleeding before operative hysteroscopy. However, none of the women had other side effects like fever or diarrhea.

The optimal timing and dosage of vaginal misoprostol administration before hysteroscopy has not been established.[7] Some studies have found vaginal misoprostol administration 12 h before hysteroscopy to be more effective than 3 h before hysteroscopy.[14] In our hospital, we use 400 µg of vaginal Misoprostol administered 12 h before operative hysteroscopy.

Vaginal osmotic dilators can be naturally occurring (e.g., laminaria) or synthetic (e.g., Dilapan-S). Only four studies have compared osmotic dilators with Misoprostol for cervical preparation before operative hysteroscopy.[8,13,15,16] A Cochrane systematic review on cervical ripening before operative hysteroscopy compared Misoprostol with osmotic dilators and concluded that osmotic dilators provided better cervical dilatation than misoprostol.[9]

Only one study has compared Misoprostol with a synthetic osmotic dilator for cervical priming before operative hysteroscopy. This study was done by Yu *et al*., and they used a 6 mm synthetic osmotic dilator available in China.[13] This study included 100 premenopausal women undergoing operative hysteroscopy with 26F resectoscope; one group received 400 µg vaginal Misoprostol and the other group received the synthetic osmotic dilator 12 h before the surgery. They found that the osmotic dilator group had a higher mean initial cervical diameter and less need for additional mechanical dilatation.

An *in vitro* study compared the natural and synthetic osmotic dilators and concluded that synthetic dilators were superior to laminaria. They reached higher maximum diameters, acted faster, and were more consistent.[12] The other disadvantages of laminaria are allergic reactions and infection.[10] Dilator entrapment or fracture is a rare complication reported with both natural and synthetic osmotic dilators. None of the women in our study had any of these complications.

Misoprostol is an inexpensive, widely available, and easy-to-store drug. However, we found Dilapan-S was better than Misoprostol in cervical preparation before operative hysteroscopy. Misoprostol was also associated with side effects like abdominal pain and vaginal bleeding. The disadvantages of Dilapan are the cost and availability. Moreover, it has to be inserted into the cervix a few hours before the surgery, which may require additional hospital visits. This insertion may be difficult for some women and may cause pain and discomfort. Administration of analgesics may reduce this pain.[17] Using a gentle technique and avoiding holding the cervix with a tenaculum may also reduce this pain.[14]

The strength of the present study is that all the surgeries were done by a single surgeon. This eliminated interobserver variability. The limitation of the study is the relatively small sample size. Another limitation of this study is using a subjective 5-point Likert scale for measuring ease of dilatation instead of a cervical tonometer as done by Ngai *et al*.[18] In women with cervical stenosis, insertion of osmotic dilator may be difficult. None of the women in our study had cervical stenosis. The efficacy of Dilapan in women with cervical stenosis needs to be assessed in further studies. Larger studies involving more homogenous populations are needed to confirm our findings.

Conclusion

Synthetic osmotic dilator (Dilapan-S) is more efficacious than vaginal Misoprostol at ripening the cervix before operative hysteroscopy.

Financial support and sponsorship

This study was funded by JIPMER Intramural fund (63:2020–2022).

Conflicts of interest

There are no conflicts of interest.

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