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ORIGINAL ARTICLE

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A prospective, randomized, controlled trial comparing vaginal misoprostol and osmotic dilator in achieving cervical ripening before operative hysteroscopy

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Abstract The purpose of this study was to compare the effectiveness of vaginal misoprostol and an osmotic dilator in achieving cervical ripening before operative hysteroscopy in pre-menopausal women. One hundred patients undergoing operative hysteroscopies with a 9-mm hysteroscope were prospectively and randomly assigned to two groups. In group 1 (the misoprostol group), 53 patients received 400 μg of vaginal misoprostol 12 h before the operation. In group 2 (the osmotic dilator group), 47 patients had an osmotic dilator inserted into the cervical canal 12 h before the operation. The primary outcome measure in this study was cervical width, assessed by the largest number of Hegar dilators that could be inserted into the cervix without resistance. The secondary outcome measure was the subjective assessments of the ease of dilatation to 9 mm by the surgeon. Adverse effects experienced including preoperative pain and vaginal bleeding were recorded for each group. There was no difference between the two groups with regard to demographic variables. The spontaneous cervical dilatation (mean ± SD) in the osmotic dilator group (9.6±2.2 cm) was significantly (P<0.01) greater than that in the misoprostol group (8.0±1.8 cm). In addition, the proportion of difficult dilatation in the osmotic dilator group (8 out of 47, 17.0%) was significantly less than that in the misoprostol group (22 out of 53, 41.5%). The occurrence of vaginal bleeding in the misoprostol group (77.4%) was significantly (P<0.01) higher than that in the osmotic dilator group (31.9%). The osmotic dilator is more effective than misoprostol at achieving cervix ripening prior to operative hysteroscopy.

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Introduction

Operative hysteroscopy is a commonly performed gynaecologic procedure nowadays and the operative hysteroscope commonly used is 9 mm in diameter. Complications encountered during the procedure are in part related to difficulties in cervical dilatation including cervical laceration, creation of a false passage, uterine perforation and haemorrhage [1]. However, the incidence of these complications can be greatly reduced if the cervix is ripened before the procedure [2].

Osmotic dilators have been used to ripen the cervix in gynaecologic and obstetric procedures for many years. The combined effect of softening and dilatation of the cervix reduces the chance of stretch injury or perforation [3]. Misoprostol, a synthetic prostaglandin E1 analogue, had also been shown to have cervical ripening effects in both pregnant and non-pregnant patients when administered either orally or vaginally [4]. The purpose of this study was to compare the effectiveness of two cervical ripening agents, namely vaginal misoprostol and a synthetic osmotic dilator, at facilitating cervical dilatation in pre-menopausal women before operative hysteroscopy.

Patients and methods

From August 2001 to Jan 2002, 100 patients scheduled for hysteroscopic operations (with a 9-mm hysteroscope) were recruited into the study. Ethical approval was obtained from the research department of Fuxing Hospital, Beijing, China. Informed consent was obtained from each patient participating in the study. All patients were assigned to one of two groups by a computer-generated series of random numbers. In group 1 (the misoprostol group), 400 μg misoprostol was inserted into the posterior fornix of the vagina 12 h prior to the operation. In group 2 (the osmotic

dilator group), a cervical osmotic dilator (disposable, synthetic hygroscopic polyacrylonitrile rod-shaped dilators, with a diameter of 6 mm and a sectional expanding rate of 100%; Fengxing Medical Devices, Jinan, China; Fig. 1) was inserted into the cervical canal until it passed the internal os, 12 h before the surgical procedure. The osmotic dilator was removed immediately before the patient was transferred to theatre. The surgeons therefore had no knowledge of what the patient received (misoprostol or osmotic dilator) prior to the surgery. All the hysteroscopic surgeries were performed in the early proliferative phase of the menstrual cycle with an Olympus 9-mm hysteroscope under epidural anaesthesia.

The primary outcome measure in this study was cervical dilatation, which was assessed by the size of the Hegar dilator entering the cervix without resistance, up to a maximum of 11 mm. The largest number of Hegar dilators that could be inserted into the cervix without resistance, called spontaneous dilatation, was recorded. The secondary outcome measure was subjective assessments of the ease of dilatation recorded by the surgeon when inserting a 9-mm Hegar dilator into the cervix. Adverse effects experienced, including preoperative pain, preoperative vaginal bleeding and any other complications, were recorded for each group.

The results are presented as the mean ± SD for quantitative variables and frequency (percentage) for qualitative variables. Spontaneous cervical dilatation in the misoprostol group and the osmotic dilator group were compared with two independent sample *t* tests. The ease of dilatation and adverse effects were compared between groups using 2×2 contingency table analysis. The significance level was set at $P<0.05$. All analyses were performed using SPSS software.

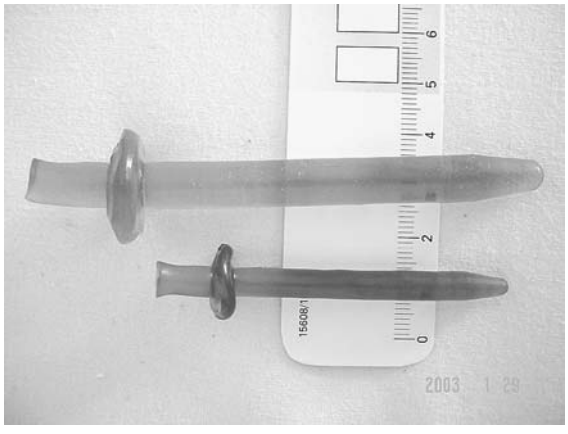

Fig. 1 The synthetic osmotic dilators used in our study. The smaller dilator represents the original size prior to insertion, whereas the bigger one represents the size of the dilator immediately after removal from the cervix, having been in place for 12 h. The enlargement was due to the absorption of water whilst the dilator was in the cervical canal

Results

One hundred patients were recruited to the study, with 53 patients in group 1 (the misoprostol group) and 47 patients in group 2 (the osmotic dilator group). There were no differences between the two groups with regard to age, number of previous miscarriages, parity and types of hysteroscopic procedures performed (Table 1).

The outcomes including spontaneous dilatation of the cervix, difficult dilatation of the cervix and preoperative bleeding in the two groups are shown in Table 2. The spontaneous cervical dilatation in the osmotic dilator group (9.6±2.2 cm) was significantly ($P<0.01$) greater than that in the misoprostol group (8.0±1.8 cm). In addition, the proportion of difficult dilatation in the osmotic dilator group (8 out of 47, 17.0%) was significantly ($P<0.01$) less than that in the misoprostol group (22 out of 53, 41.5%). The occurrence of preoperative vaginal bleeding in the misoprostol group (77.4%) was significantly ($P<0.01$) more frequent than that in the osmotic dilator group (31.9%). However, the amount of the vaginal bleeding was small in all cases and intervention was not required.

Four patients in the osmotic dilator group experienced mild lower abdominal pain after the dilator was inserted into the cervix. There had been no cervical damage, false passage, uterine perforation or infection in any of the patients studied.

Discussion

Misoprostol, a synthetic prostaglandin E_1 analogue, is commonly used in priming the cervix prior to abortion, induction of labour and treating postpartum haemorrhage. It has also been used to ripen and soften the cervix prior to operative hysteroscopy. Although some investigations did not find it particularly useful [5, 6], many others found it effective and made dilatation easier prior to operative hysteroscopy. Ngai et al. [7] demonstrated that the cumulative forces required to dilate the cervix were 61% lower in women who received 400 μg of misoprostol orally 12 h before hysteroscopic surgery compared with a control group. Thomas et al. [8] found that oral misoprostol made cervical dilatation easier, not only in pre-menopausal but also in postmenopausal women.

However, there are several practical aspects of the use of misoprostol that need to be considered. How should misoprostol be given: orally or vaginally? When and how much should be given? In 1997, a study by Zieman et al. [9] concluded that when misoprostol was administered vaginally, the effectiveness at ripening the cervix was three times greater than when administered orally. Since then, three randomized controlled trials (Table 3) [10–12] have shown that vaginal misoprostol at a dose of 200–400 μg administered 9–12 h prior to the operation was effective and permitted dilatation of the cervix up to 7+ cm, compared with 3–5 cm in the control group.

Osmotic dilators have also been found to be effective in ripening the cervix prior to operative hysteroscopy [13,

Table 1 The characteristics of patients in the two groups of patients receiving misoprostol and osmotic dilatation prior to operational hysteroscopy

	Misoprostol group (n=53)	Osmotic dilator group (n=47)	P
Age (years)*	39.5±10.8	40.3±11.8	>0.05
Previous miscarriage*	1.8±1.3	2.0±1.5	>0.05
Parity*	1.0±0.9	0.9±1.0	>0.05
Types of hysteroscopic surgery			
Endometrial resection**	34.0% (18/53)	31.9% (15/47)	>0.05
Resection of polyp**	18.9% (10/53)	21.3% (10/47)	>0.05
Myomectomy**	39.6% (21/53)	38.3% (18/47)	>0.05
Intrauterine device extraction**	7.5% (4/53)	8.5% (4/47)	>0.05

*Mean ± SD, comparison using Student's t test
**Comparison using 2×2 contingency table analysis

14]. There has only been one randomized study comparing misoprostol and laminaria, a natural dilator, and no significant difference between them was found (Table 3) [15]. Our study is the first one conducted to compare the efficacy of misoprostol and a synthetic osmotic dilator, and showed the latter agent produced significantly better results.

However, it is important to appreciate that there are three types of osmotic dilators available for use to ripen the cervix. The first type of device, consisting of naturally derived products, includes the Laminaria tent, which is made from the stems of *Laminaria japonica* or *Laminaria digitata* (brown sea weed), and is the type most commonly used. It swells in the presence of liquid and ripens the cervix physically and chemically, by exerting a radial force during swelling, and this outward pressure stimulates the release of F-class prostaglandins, achieving a clinical effect in between 3 and 24 h [16, 17]. The second and third types of osmotic dilators are synthetic ones with the potential advantages of assured sterility, consistency of length and shape, and, theoretically, greater predictability of effect. The second type of device, e.g. Dilapan, is a synthetic hygroscopic polyacrylonitrile (hypan plastic polymer) rod-shaped dilator, acting primarily mechanically and having a notable clinical effect within 2–4 h [18]. The third type is Lamicel, a sterile, polyvinyl sponge impregnated with magnesium sulphate, which can reversibly decouple collagen cross-linkages in cervical stroma and increase sensitivity to prostaglandin E_2 [19]. The predominant chemical action with no outward pressure on the cervical wall permits it to be placed into a narrow, stenotic cervix and swell with a minor hourglass effect [20]. These osmotic dilators have been used to ripen the cervix for induced abortion as well as to overcome stenosis in non-pregnant women requiring hysteroscopy [13–15, 17–19].

In this study, the disposal, synthetic hygroscopic polyacrylonitrile rod-shaped dilator is the second type of dilator that has been used as a cervical ripener before hysteroscopic surgery in our department for about 10 years. This synthetic dilator, with a diameter of 6 mm and a sectional expanding rate of 100%, is made in China and has the same features as Dilapan. It is inexpensive, and costs less than £1. The tip of the dilator is slender and the rod is a little bent to suit the cervical canal, which facilitates insertion into the cervix. In our study, none of the 47 patients in group 2 (the osmotic dilator group) had problems with insertion because all were premenopausal. For postmenopausal women, the cervix may be too tight and there could be some difficulties in which case either misoprostol or Laminaria, which has a smaller diameter of 2–3 mm may be used instead.

The observations in our study can be compared with the findings of three previous randomized, controlled trials, summarized in Table 3. It showed that the synthetic osmotic dilator achieved 9.6 mm of spontaneous dilatation of the cervix, in comparison to 7–8 mm in the misoprostol group in the various studies.

A possible criticism of our study, as applied to several previous studies, concerns the method used to assess cervical dilatation and whether or not it is difficult or easy. In this respect, the gold standard is the cervical tonometer, which was utilized by Ngai et al. [21]. The spontaneous dilatation of the cervix is defined as the passage of the largest dilator into the cervix at a pressure of less than 5 N.

Table 2 A comparison of spontaneous cervical dilatation, difficult dilatation and bleeding prior to operation between the two groups of patients

	Misoprostol group (n=53)	Osmotic dilator group (n=47)	P
Spontaneous cervical dilatation* (mean ± SD, cm)	8.0±1.8	9.6±2.2	<0.01
Difficult dilatation** (percentage)	22/53 (41.5%)	8/47 (17.0%)	<0.01
Bleeding preoperation** (percentage)	41/53 (77.4%)	15/47 (31.9%)	<0.01

*Student's t test
**2×2 contingency table analysis

Table 3 A summary of randomized controlled trials of the use of misoprostol ripening of the cervix before hysteroscopy

Reference	Misoprostol	Spontaneous dilator (mean±SD, mm)	Comparison group	Spontaneous dilator (mean±SD, mm)
[10]	200 μg, 9–10 h, vaginally, *n*=46	7.0±1.0	Placebo *n*=45	3.8±1.2
[11]	200 μg, 9–10 h, vaginally, *n*=73	7.3±0.7	Placebo *n*=79	3.8±1.1
[15][a]	200 μg, 8 h, vaginally, *n*=72	7.5±1.2	Laminaria 8 h, *n*=72	7.6±1.2
[12]	400 μg, 12 h, vaginally, *n*=51	7.6±1.4	No agent *n*=54	5.0±1.1
Current study	400 μg, 12 h, vaginally, *n*=53	8.0±1.8	The synthetic osmotic dilator 12 h, *n*=47	9.6±2.2

[a]A comparison of Laminaria vs. misoprostol

In the absence of such an instrument, error due to subjective bias should be reduced to a minimum by the use of a prospective, randomized, double-blinded design, as in our current study.

From our data, preoperative vaginal bleeding was more frequent in the misoprostol group than in the osmotic dilator group. The exact underlying cause of this observation is unclear, but it could be the action of misoprostol on uterine contractility in non-pregnant women [22]. However, the amount of the bleeding was small in all those cases and did not affect the operations in any way.

Conclusion

Both misoprostol and osmotic dilators can effectively ripen the cervix in pre-menopausal women prior to operative hysteroscopy. The synthetic osmotic dilator was more effective than misoprostol at ripening the cervix prior to operative hysteroscopy.

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