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Different routes of Misoprostol for same-day cervical priming prior to hysteroscopy a randomized controlled single blind trial

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Abstract: Introduction: Hysteroscopic surgery, with prior cervical ripening by misoprostol (a synthetic prostaglandin E1 analogue, PGE1), has been widely used to treat gynecological diseases including submucosal myoma, endometrial polyps and uterine synechia in non-pregnant women**.** The route of administration of misoprostol for cervical dilatation can be oral, vaginal or sublingual. **Aims:** The aim of the present study was to evaluate the efficacy 400 µg misoprostol administered orally, vaginally or sublingually on cervical ripening before hysteroscopy. **Methodology:** Study setting: Sayed Galal Hospital. Study duration: April 2017 to April 2018. Number of patients: Included 300 patients. **Study Design:** A prospective randomized controlled single blind trial. Non-pregnant women scheduled for hysteroscopy were divided randomly into four groups using sealed opaque envelopes to receive 400 mg of misoprostol, administered either orally (n =75) or vaginally (n =75) 6–8 h prior to surgery or 400 mg sublingually (n =75) 2–4 h prior to surgery or control group (n =75) received nothing. The primary outcome in this study was the preoperative cervical width as measured by the largest number of Hegar dilators. The duration of cervical dilatation was also recorded along with side effects related to misoprostol and complications during surgery for each group. **Results:** The mean ±SD cervical widths for the oral, sublingual, vaginal, and control groups were 7.60 ± 1.76 mm, 7.56 ±1.64 mm, 7.57 ± 2.06 mm, and 5.65 ±2.17 mm, respectively, which was statistically significant. Time to cervical dilatation was also significantly longer in the control group than in the other three groups. Misoprostol-related adverse effects and hysteroscopy-related complications were comparable among the four study groups. **Conclusion:** All routes (oral, sublingual, vaginal) of administrations of misoprostol are equally effective in inducing proper cervical priming before hysteroscopy compared to the control group.

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Keywords: Misoprostol, Hysteroscopy, cervical priming, cervical ripening

1. Introduction

Hysteroscopic surgery, with prior cervical ripening by misoprostol (analog prostaglandins E1, PGE1), has been widely used to treat gynecological diseases including submucosal myoma, endometrial polyps and uterine synechia in non-pregnant women **(Crane et al., 2006) (Fiala et al., 2007)**. Misoprostol has been shown to be equally effective when compared with laminaria in inducing cervical priming prior to hysteroscopic surgery with minimal time required for cervical dilatation, easy administration, reduced costs and increased patient convenience **(Darwish et al., 2004)**.

Hysteroscopy is a minimally invasive intervention that can be used to diagnose and treat many intrauterine and endocervical problems. Hysteroscopic polypectomy, myomectomy, and endometrial ablation are just a few of the commonly performed procedures. Given their safety and efficacy, diagnostic and operative hysteroscopy have become standards in gynecologic practice **(Corfman,1988)**.

Complications encountered during the procedure are partly related to difficulties in cervical dilatation. These include cervical tears, creation of a false track, haemorrhage, uterine perforation requiring laparoscopy, or simply difficulty in entering the internal cervical os with the resectoscope **(Loffer, 1989)**.

The incidence of these complications can be reduced if the cervix is ripened before the procedure by inserting laminaria into the cervical canal the night before surgery **(Ostrzenski,1994)**.

Misoprostol, a synthetic prostaglandin (PG) E1 analogue widely prescribed for prevention and

treatment of gastric ulcers, has been shown to have cervical ripening effects in both pregnant and non-pregnant patients when administered either orally or vaginally **(Ngai et al., 1997) (Preutthipan and Herabutya, 2000).**

The systemic bioavailability of misoprostol is three times greater when it is administered vaginally than orally **(Zieman et al., 1997)**.

A pharmacokinetic study compared the absorption kinetics of oral, vaginal and sublingual routes of administration of misoprostol. **(Tang et al., 2002),** It found that sublingual misoprostol has the shortest time to peak concentration, the highest peak concentration and the greatest bioavailability when compared to other routes. The peak concentration is achieved about 30 minutes after sublingual and oral administration, whereas following vaginal administration; it takes 75 minutes. **(Tang et al.,2002)**

Therefore, it appears that the sublingual and oral routes have the quickest onset of action. After 400µ g of misoprostol, a sublingual dose achieves a higher peak concentration than that of oral and vaginal administration. This is due to rapid absorption through the sublingual mucosa as well as the avoidance of the first-pass metabolism via the liver.

The abundant blood supply under the tongue and the relatively neutral pH in the buccal cavity may be contributing factors.

The rapid onset and high peak concentration means that of all the possible routes the systemic bioavailability, as measured by the AUC in the first 6 hours, is greatest for sublingual administration.

In contrast to the previous study by Zieman et al., the AUC 360 after oral and vaginal administration are similar but only 54% and 58% respectively of that after sublingual administration. **(Tang et al.,2002)**

The difference in the findings on the bioavailability of these two studies may be due to the wide variation in the absorption of misoprostol through the vaginal mucosa among different women.

On the other hand, although vaginal absorption has been shown to be slower and the peak concentration lowers than that for the other routes, the serum level of misoprostol is sustained at that low level for a longer period of time.

In fact, at the end of 6 hours the serum level of misoprostol acid after vaginal administration is higher than those of the sublingual and oral routes.

Common side effects include diarrhea and abdominal pain. It is pregnancy category X meaning that it is known to result in negative outcomes for the baby if taken during pregnancy like Möbius Syndrome (a child with oromandibular-limb hypogenesis and expressionless face due to bilateral facial nerve palsies and missing fingers). Uterine rupture may occur **(The American Society of Health-System Pharmacists, 2015)**.

The route of administration of misoprostol for cervical dilatation can be oral, vaginal or sublingual. However, it is still unclear which route is more effective for cervical dilation before trans-cervical procedures in non-pregnant women. Cervical ripening is required to prevent complications during the trans-cervical procedure **(Schulz et al., 1983)**.

Previous studies have shown that misoprostol was effective when compared with placebo for cervical ripening whether the route of administration was oral or vaginal **(Ngai et al., 1997) (Preutthipan and Herabutya, 2000). (Crane et al., 2006) (Fiala et al., 2007) (Thomas et al., 2002) (Oppegaard et al., 2008) (Uckuyu et al., 2008) (Waddell et al., 2008).**

Two prior reports compared the effects of preoperative oral and vaginal misoprostol on cervical ripening before hysteroscopic surgery, one study found that vaginal administration was more effective than the oral route for preoperative cervical ripening in non-pregnant premenopausal women **(Batukan et al., 2008)** while the other found no difference between the two routes **(Choksuchat et al., 2006)**.

The aim of the present study was to evaluate the efficacy of 400 µg misoprostol administered orally, vaginally or sublingually on cervical ripening before hysteroscopy.

2. Materials and Methods

This study was conducted between April 2017 to April 2018 at the department of Obstetrics and Gynecology at Sayed Galal Hospital. All patients were scheduled for elective hysteroscopy either diagnostic or surgical. Informed consent was taken prior to participation in the study, all participants were undergo a physical examination detailed medical, obstetric and gynecologic history was obtained and Trans vaginal ultrasound was done.

Patients's inclusion criteria:

This study was conducted on patients who were scheduled for elective hysteroscopy either diagnostic or surgical.

Patients's exclusion criteria:

1. Patients with any evidence of a contraindication or allergy to prostaglandins (asthma, glaucoma, hypertension).
2. Patients with any sign of genital infection, history of cervical surgery, endometrial lesions with suspected endo- or exo-cervical lesions that could affect the cervical resistance.

A total of 300 patients were included in the study and the patients were divided randomly into four groups using sealed opaque envelopes:

Group I:

Patients who received 400 µg misoprostol administered orally (n=75) for cervical priming 6-8 hours before hysteroscopy.

Group II:

Patients who received 400 µg misoprostol administered vaginally (n=75) for cervical priming 6-8 hours before hysteroscopy.

Group III:

Patients who received 400 µg misoprostol administered sub-lingual (n=75) for cervical priming 2-4hours before hysteroscopy.

Group IV:

the control group (n=75) took nothing before hysteroscopy.

Patients were randomly allocated at the outpatient department to the following treatment regimens. A study doctor generated the four groups randomly using sealed opaque envelopes. The study was conducted in a single-blinded fashion; the drug administered was unknown (blinded) to the surgeon. After the operation, the patients were monitored at the post-anesthesia care unit for a minimum of 2 h and returned for follow-up visits 1 day and 1 week after the operation.

All included women were subjected to the following:

- History taking: Important elements of the history include menstrual history, sexual history; illnesses and infections; surgeries; medications used; exposure to certain environmental agents (alcohol, radiation, steroids, chemotherapy, and toxic chemicals).
- Trans vaginal ultrasound (TVS): Ultrasound evaluation was used to identify intrauterine pathology, such as submucosal myoma, endometrial polyps, and congenital cavitary anomalies such as a septate uterus.
- Routine laboratory investigations including complete blood picture, hematocrit, coagulation profile, virology, liver and kidney function tests.
- Preoperative senior anesthetist assessment.

All Patients were randomly allocated at the outpatient department to the oral, sublingual, vaginal, or control group at a 1:1:1:1 ratio using sealed opaque envelopes were prepared by the study doctor and each contained a folded slip of paper with the treatment route (orally, sublingually, vaginally, or no medication) written on it. When the patients agreed to participate in this study at the outpatient clinic, the envelopes were opened by the study doctor, and the randomization took place. All misoprostol tablets were identical.

The study was conducted in a single-blinded fashion; the drug administered was unknown (blinded) to the surgeon. The vaginal and oral groups received 400 µg of misoprostol, and the patients self-administered the medication vaginally or orally 6–8 h before surgery. The sublingual group received the same dose of misoprostol and took the tablets sublingually 2–4 h before surgery. In the control group, hysteroscopy was performed without a misoprostol administration. To prevent bias, in all cases the vagina was cleaned, and any remnant of the misoprostol tablets was removed by the resident or physician assistant in charge before the operating surgeon began the procedure. Additionally, the patients were asked about pain, other misoprostol associated side effects and the acceptability of the self-administration of medications through a self-reported question before entrance into the operating room. The operator performing the procedure was blinded to the group allocation.

The patients were given general intravenous anesthesia after the resident or physician assistant in charge prepared the patients for surgery by disinfecting the vulva and vaginal area with a betadine solution. After performing cervical dilatation with Hegar dilators, hysteroscopy was done and the uterine cavity was distended with normal saline at an insufflation pressure of 100 –150 mm Hg, with careful monitoring of the fluid balance. After hysteroscopy the patients were monitored in the post anesthesia care unit for a minimum of 2 hours and returned for follow-up visits 1day and 1 week after surgery.

The primary outcome measure in this study was the preoperative cervical width at the time of surgery after misoprostol administration. The cervical width was assessed by performing cervical dilation, beginning with a number 10 Hegar dilator and subsequently inserting smaller Hegar dilators until the dilator could pass through the internal os without resistance. The largest one that could be passed was recorded as the initial cervical width. The Secondary outcomes measurements included [1] the duration of cervical dilatation. [2] Self-reported misoprostol-associated adverse effects before the procedure, such as uterine cramping, uterine bleeding, diarrhea, nausea, vomiting [3] Complications during cervical dilatation and hysteroscopy. The patients were asked about possible side effects of misoprostol before induction of general anesthesia.

We assumed that equivalence was of clinical significance if the difference in the initial cervical width was < 1.5 mm among groups with an SD of the initial cervical width of 2.3 mm. Setting the type 1 error and power to 5% and 80%, respectively, and allowing a 7% dropout rate, the estimated sample size required was 75 patients in each group.

SPSS 20 (SPSS) was used for the statistical analysis. Data are presented as the mean ±SD or median (range) for quantitative variables and frequency (percentage) for qualitative variables. Comparisons of quantitative variables were performed

using a one-way ANOVA as a para metric test or a Kruskal-Wallis test as a nonparametric test and adjusted by Bonferroni's correction for multiple comparisons. Frequency distributions between categoric variables among the four groups were compared using the x2 test or Fisher's exact test. A P value of <.05 was statistically significant.

3. Results

This study included 300 women who were scheduled for elective hysteroscopy. None of the study subjects changed groups or stopped participating in the study after randomization or before surgery.

Table-1: Outcome of cervical priming of all groups.

Misoprostol, 400 µg doses

Characteristic	Oral (n=75)	Sublingual (n=75)	Vaginl (n=75)	Control (n=75)	P value
Preoperative cervical width, mm	7.60± 1.76 Range (4.5-15)	7.56± 1.64 Range (2.5-15)	7.57± 2.06 Range (2-16)	5.65± 2.17 Range (2-15)	<.001
Duration of cervical dilatation, seconds	47.48± 20.12 Range (20-130)	48.03± 18.71 Range (20-130)	46.33± 20.98 Range (20-145)	84.18± 39.49 Range (24-225)	<.002

The mean preoperative cervical widths for the oral, sublingual, vaginal, and control groups were 7.60±1.76 mm, 7.56±1.64 mm, 7.57±2.06 mm, and 5.65±2.17 mm, respectively. These cervical widths were similar among the oral, sublingual, and vaginal groups, but the cervical width in the control group was significantly narrower than those in the three misoprostol groups (P <.001), indicating that the use of misoprostol (regardless of administration route) before hysteroscopy reduced the difficulty in the cervical dilation. The time to cervical dilatation was 47.78± 20.12 seconds in the oral group, 48.03± 18.71 seconds in the sublingual group, 46.33± 20.98 seconds in the vaginal group, and 84.18± 39.49 seconds in the control group. It took a significantly longer time to dilate the cervix in the control group than in the other three groups (P <.002).

Table-2: Adverse effects of cervical priming of all groups.

Misoprostol, 400 µg doses

Characteristic	Oral (n=75)	Sublingual (n=75)	Vaginl (n=75)	Control (n=75)	P value
Adverse effects related to Misoprostol:	16(21.3%)	14(18.7%)	18(24%)	4(5.3%)	.052
• Cramping	7(9.3%)	5(6.7%)	7(9.3%)	2(2.7%)	.406
• Bleeding	4(5.3%)	5(6.7%)	7(9.3%)	2(2.7%)	.599
• Diarrhea	1(1.3%)	2(2.7%)	2(2.7%)	0(0%)	.999
• Nausea	2(2.7%)	1(1.3%)	1(1.3%)	0(0%)	.999
• Vomiting	2(2.7%)	1(1.3%)	1(1.3%)	0(0%)	.999

The rate of adverse effects in the control group was lower than that in the other three groups (oral, sublingual and vaginal) (5.3% vs. 21.3% –18.7%–24.0%), but this difference did not reach statistical significance (P<.052). The rates of adverse effects were similar among the three misoprostol groups (oral, sublingual, and vaginal), and there was no case in which the surgery had to be delayed because of misoprostol adverse effects, all of which were tolerable.

Table-3: Complications during cervical dilatation & hysteroscopy of all groups.

Misoprostol, 400 µg doses

Characteristic	Oral (n=75)	Sublingual (n=75)	Vaginl (n=75)	Control (n=75)	P value
Complications during cervical dilatation & hysteroscopy	2(2.7%) A cervical tear occurred in one subject and Creation of a false tract during cervical dilation occurred also in one subject	1(1.3%) Creation of a false tract during cervical dilation occurred in one subject	2(2.7%) A cervical tear occurred in one subject and Creation of a false tract during cervical dilation occurred also in one subject	3(4%) A cervical tear occurred in two subject and Creation of a false tract during cervical dilation occurred also in one subject	<.999

Complications are more in the control group than the other three groups but this difference did not reach statistical significance (P<.999). Complications during cervical dilation occurred in two subjects. A cervical

tear occurred in one subject in the oral group, one subject in the vaginal group and two subjects in the control group; however, the length of the cervical tear was< 10 mm in all cases, which did not require suturing. Creation of a false tract during cervical dilation occurred in one subject in the oral group, one subject in the sublingual group, one subject in the vaginal group and one subject in the control group but the subjects were managed conservatively without any intervention. One subject in the oral group was admitted for close observation of profuse uterine bleeding after hysteroscopic myomectomy. The remaining subjects were discharged after 2 hours of observation, and no complications occurred during this period.

Table-4: Baseline Characteristics of all groups.

Misoprostol, 400 µg doses

Characteristic	Oral (n=75)	sublingual (n=75)	Vaginal (n=75)	Control (n=75)	P value
Age, years	34.03± 5.09 Range (19-47)	28.92± 5.96 Range (20-45)	29.91± 5.39 Range (22-43)	27.57± 5.66 Range (20-48)	.546
BMI, Kg/m2	23.89± 2.46 Range (20-33)	20.35± 2.57 Range (15-26)	20.01± 2.42 Range (17-26)	20.60± 2.06 Range (17-26)	.573
Parity Nulliparous Parous • History of vaginal delivery. • History of C/S	49(65.3%) 26(34.7%) 15)20%) 11(14.7%)	53(70.7%) 22(29.3%) 19(25.3%) 3(4%)	43(57.3%) 32(42.7%) 20(26.7%) 12(16%)	52(69.3%) 23(30.7%) 15(20%) 8(10.7%)	.627 .709 .716

Note: All data are not statistically significance. Data are expressed as mean± SD, median (range), or number (percentage) if appropriate. C/S = cesarean section; BMI, Body Mass Index.

4. Discussion

The route of administration of misoprostol for cervical dilatation can be Oral, sublingual, or vaginal. However, no solid conclusions have been reached as to which route is most effective for cervical dilation before hysteroscopy.

The aim of the present study was to evaluate the efficacy and the side effects of 400 µg misoprostol administered orally, vaginally or sublingually on cervical ripening before hysteroscopy and the complications during cervical dilatation & hysteroscopy of all groups compared to a control group.

The current study was conducted at Sayed Galal Hospital during the period between April 2017 to April 2018. The study was conducted on patients who were scheduled for elective hysteroscopy.

The main finding of this study was that outcomes with regard to cervical priming with misoprostol by oral, sublingual, and vaginal administration were comparable, and all adverse effects were similar among all groups and were tolerable.

Our results indicate that misoprostol, regardless of the route of administration; play a role as a cervical priming agent before hysteroscopy.

This finding is consistent with a recent meta-analysis **(Polyzos et al.,2012)** that analyzed 21 randomized, controlled trials involving 1,786 subjects and evaluated the effects of misoprostol before hysteroscopy for cervical dilatation. The mean cervical width before hysteroscopy was significantly wider in premenopausal women treated with misoprostol compared with placebo (mean difference [95% confidence interval (CI)]: 2.47 mm [1.81 –3.13 mm]). Furthermore, cervical laceration was significantly lower in subjects treated with misoprostol than in subjects treated with placebo (relative risk [95% CI]: 0.22 [0.09 –0.54]). These authors concluded that misoprostol before hysteroscopy facilitates an easier and uncomplicated procedure in premenopausal women.

The frequencies and types of adverse effects were similar among the three misoprostol groups, consistent with findings from previous studies **(Choksuchat et al.,2006)** However, the frequency of adverse effects was lower than in previous studies.

This discrepancy might be due to a relatively short time between medication and hysteroscopy, because the symptoms related to adverse effects could be masked during surgery under general anesthesia and after the procedure. Furthermore, similar to previous studies, there was no delay in the planned procedure based on misoprostol use, and all adverse effects were tolerable without the need for additional treatment. Although the difference did not reach statistical significance (P<.052), the rates of adverse effects in the three misoprostol groups were higher than that in the control group (21.3% –18.7%–24.0%vs. 5.3%).

This result is in line with a recent meta-analysis that analyzed seven randomized, controlled trials involving 568 subjects and evaluated the use of misoprostol in operative hysteroscopy **(Selk et al.,2011).** Compared with the Placebo group, there

was an increase in side effects (cramps, vaginal bleeding, nausea, vomiting and diarrhea) in the misoprostol group (relative risk [95% CI]: 4.28 [1.43 – 12.85]). The researchers concluded that current evidence does not support the routine use of preoperative misoprostol in operative hysteroscopy **(Selk et al.,2011).**

A potential weakness of this study is that the same surgeon did not perform all the procedures and that the resistance during cervical dilatation was assessed subjectively. This may introduce the potential for bias because each clinician may have a different perception of cervical resistance. It has been suggested that the force applied during cervical dilatation can be measured by a tensinometer to overcome this drawback **(Ngai et al.,1997).**

Our study had several limitations. First, the measurement of cervical width was not objective. It has been suggested that the forced applied during cervical dilation can be measured by atensinometer to overcome this drawback **(Ngai et al.,1997).** However, measurements by a Hegar dilator have been acceptable and used in many previous studies **(Polyzos et al.,2012) (Darwish et al.,2004) (Preutthipan et al.,2006) (Batukan et al.,2008).**

Second, the control group was not given a ‘‘placebo’’ intervention, which might have led to a reduction of adverse effects related to misoprostol medication. Meanwhile, the strength of this study is that a single blinded fashion with a control group.

Previous study showed that the routes of misoprostol at the same dose given sublingually, orally and vaginally, before hysteroscopic surgery in premenopausal non pregnant women, were statistically equal with regard to the post-medication cervical width without any difference in cervical dilatation time to Hegar number 10, complications during cervical dilatation or drug side effects **(Lee et al.,2010).** Cervical ripening is required to prevent complications during the transcervical procedure **(Grimes et al.,1984) (Schulz et al.,1983).**

Previous studies have shown that misoprostol was effective when compared with placebo for cervical ripening **(Ngai et al.,1997) (Crane et al., 2006) (Fiala et al.,2007)**. whether the route of administration was oral **(Ngai et al.,1997) (Thomas et al., 2002)** or vaginal **(Preutthipan and Herabutya, 2000) (Oppegaard et al.,2008) (Uckuyu et al.,2008) (Waddell et al.,2008).**

However, there are only two studies that have compared the oral and the vaginal routes of administration, with different results **(Choksuchat et al.,2006) (Batukan et al.,2008).** The different outcomes between the two studies can be attributed to two possible factors. The first aspect is the difference in dosage (200 μg versus 400 μg) for the vaginal route and the second factor is that both of the studies assessed cervical force based on the ease of passage of the Hegar dilator, which is dependent on the individual surgeon.

Even in the current study, all procedures were assessed subjectively; however, surgeons with similar surgical skill and the relatively even distribution of surgeons in each route of misoprostol administration make this bias less likely.

There was one study comparing sublingual misoprostol and placebo in women with GnRH (gonadotropin-releasing hormone) agonist **(Bisharah et al., 2003**) which showed negative results, similar to the findings in oral and vaginal routes **(Ngai et al., 2001) (Fung et al.,2002) (da Costa et al.,2008) (Oppegaard et al.,2008)** and in contrast with other reports **(Waddell et al.,2008) (Ngai et al.,1997)**. However the efficacy of sublingual misoprostol in women with normal estrogen status has been unknown and our results demonstrated the equal efficacy of sublingual misoprostol with oral and vaginal routes.

These findings correspond well with the sublingual use of misoprostol in pregnancy termination **(Tang et al.,2004)**. with the possible benefit of convenient administration **(Tang et al., 2004)**.

In addition to the route of administration, the optimal dose and time interval from medication to surgery remain to be determined. Based on recent studies, 400 μg has been most widely used dose for oral **(Choksuchat et al.,2006) (Thomas et al.,2002) (Healey et al.,2007)**, vaginal **(Uckuyu et al.,2008) (Waddell et al.,2008) (Barcaite et al.,2005) (Singh et al., 2009)** and sublingual **(Sääv et al.,2007)** administrations with good results. In the above-cited studies, the time interval varied from 4 to 24 h for the oral and vaginal routes.

This study used a time interval of 6–8 h, a relatively short interval, because of patient convenience. Sublingual misoprostol 400 μg with an interval of 2–4 h, in this study, was based on the studies of pregnancy termination **(Tang et al.,2004) (Hamoda et al.,2004) (Saxena et al.,2004)**.

There was one prior study with sublingual administration 1 h before intrauterine device insertion in premenopausal women **(Sääv et al., 2007)** however; the cervical widths were not assessed in that study.

The frequencies and types of side effects were comparable among the three groups, consistent with the findings of previous studies **(Choksuchat et al., 2006) (Batukan et al.,2008)**. However, the frequency of side effects was lower than in prior studies. This might be due to a relatively short time period between medication and operation because the symptoms related to side effects could be masked during surgery under general anesthesia and post-operation status.

Also, similar to prior studies, there was no delay in the planned procedure based on misoprostol use, and all side effects were tolerable without need for further treatment.

This study was performed in a single blind fashion with a control group, which could be a potential strength. Because it has been proven there are more complications during procedures without cervical ripening compared with cases with cervical ripening **(Grimes et al.,1984) (Schulz et al.,1983) (Fiala et al.,2007) (Healey et al.,2007)**

From the results of previous studies that had a control group **(Ngai et al., 1997) (Preutthipan and Herabutya, 2000) (Oppegaard et al.,2008) (Uckuyu et al.,2008)**, the average cervical widths after misoprostol administration were between 6 and 7.3 mm, which were similar to our results.

Because all women undergoing hysteroscopy might have not required cervical ripening in practice, it would be helpful to identify a population at higher risk for complication of cervical dilation.

In the current study, we could not find any significant difference in cervical width and time to cervical dilatation based on parity. However, among study population, about 65.6% (197/300) were nulliparous women. This is another limitation of this study. Further study for higher risk patients for complication of cervical dilation such as patients with nulliparity, cervical stenosis or hyperstrogen status should be warranted.

We sought to determine the efficacy of 400 µg misoprostol administered orally, vaginally or sublingually on cervical ripening before hysteroscopy using a randomized, single-blind controlled trial. Despite the need for cervical dilatation and the fact that duration of dilatation was considerably lower in the misoprostol groups than in the control group, a statistically significant difference was not found. Also, although the need for cervical dilatation and duration of dilatation were considerably lower in the misoprostol groups than in the control group, a statistically significant difference was not found in this case. However, the results are clinically important and promising as well.

Conclusion

All routes (oral, sublingual, vaginal) of administrations of misoprostol are equally effective in inducing proper cervical priming before hysteroscopy compared to the control group.

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