Sublingual misoprostol is better for cervical ripening prior to hysteroscopy in post-menopausal women

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Summary

Background: The aim of the present study was to evaluate the efficacy of misoprostol administered sublingually, vaginally or rectally on cervical ripening before hysterescopic surgery in post-menopausal women. *Materials and Methods:* Post-menopausal women were randomised to receive either 400 ug of misoprostol, administered sublingually, vaginally or rectally six hours and 12 hours prior to operative hysterescopy. *Results:* Patients were randomized to receive receive sublingual (n = 30), rectal (n = 30) or vaginal (n = 30) misoprostol. The control group did not receive misoprostol (n = 30). The four groups were comparable in terms of preoperative cervical width after misoprostol administration. The mean cervical widths for control group was 9.0 ± 1.1 mm and the mean post-treatment cervical widths for the sublingual, vaginal, and rectal groups were 7.1 ± 1.1 mm, 8.9 ± 1.3mm, and 8.6 ± 1.5 mm, respectively. The cervical widths of sublingual group were significantly different from control, vaginal, and rectal groups ($p < 0.001$). *Conclusion:* Four hundred micrograms of sublingual misoprostol, 12 and six hours prior to operative hysteroscopy has a significant cervical ripening effect compared with vaginal, rectal, and control groups in post-menopausal women.

Key words: Cervical ripening; Hysteroscopy; Misoprostol.

Introduction

Hysteroscopy is a valuable procedure to the direct study of the uterine cavity. It permits a panoramic view of the uterine cavity and direct biopsy of lesions, but has some limitations, including the occasional need for cervical dilatation. Cervical ripening and dilatation is a critical step in operative hysteroscopy. Complications such as bleeding, cervical tear, and uterine rupture might be related to the difficulties with cervical dilatation. Nulliparous and post-menopausal women are particularly at risk of these complications [1, 2].

Different methods are effective for ripening the cervix: mechanically with osmotic dilators, or balloon catheters, and biochemically with misoprostol or antiprogestins, although prostaglandins are the most commonly used agent for cervical ripening [3].

Cervical ripening with misoprotol before hysteroscopy may facilitate passage of the hysteroscope through the cervix and complications may be avoided or reduced. However the route of administration, optimal dosage is still unclear for misoprostol usage in post-menopausal women [1-3].

To date there have been a few reports that have evaluated the effects of preoperative misoprostol on cervical ripening before hysteroscopic surgery in post-menopausal women [4, 5].

One study found that vaginal misoprostol and estradiol were more effective than placebo for preoperative cervical ripening in post-menopausal women [4]. While the other found no difference between oral misoprostol and placebo [5]. However, there have been no studies comparing different route of administration of misoprostol in post-menopausal women before hysteroscopic surgery.

The aim of our prospective study was to evaluate the effect of different route of administration of misoprostol for cervical ripening before hysteroscopy in post-menopausal women.

Materials and Methods

This prospective study was conducted between October 2011 and September 2012 at the department of Obstetrics and Gynecology at the Derince Education and Research Hospital. The primary outcome measure in this study was the preoperative cervical width after misoprostol administration. Patients who had post-menopausal bleeding were suspected as having intrauterine pathology, such as atrophic endometrium, endometrial polyps, endometrial cancer, endometrial hyperplasia or other endometrial pathologies based on the transvaginal ultrasound were enrolled. All patients who had post-menopausal bleeding were scheduled for hysteroscopic surgery and were admitted to the hospital at the day of surgery. The institutional ethics review committee approved the study, and informed consent was obtained prior to participation of study.

All participants underwent a physical examination, and detailed medical, obstetric, and gynecological histories were obtained. The study included post-menopausal women whose bleeding began at least one year after cessation of their menses. Exclusion criteria included any evidence of a contraindication or allergy to prostaglandins, any sign of genital infection, women taking hormonal replacement therapy, bleeding dyscrasias, anticoagulant therapy, transvaginal ultrasound showing adnexal pathology or patients that were not candidates for surgery.

Patients were randomly allocated into four groups at the gynecology department to the following treatment regimens. The vaginal, rectal, and sublingual groups received a total 400 ug of

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Table 1. — *Demographic characteristics of patients in the oral, vaginal, and rectal and control groups.*

Characteristics	Misoprostol, 400-ug doses				
	Sublingual l(30)	Vaginal (30)	Rectal (30)	Control (30)	*p*
Age, years	55.7±3.9	56.1±3.1	56.4±2.9	55.5±3.4	0.532
BMI (kg/m2)	23.2±3	22.9±2.7	23.5±2.5	22.7±2.9	0.366
Pathologic findings					
Atrophic endometritis	16 (53.3%)	18 (60 %)	19 (63.3%)	17 (56.6%)	
Endometrial polyp	6 (20%)	5 (16.6%)	3 (10%)	4 (13.3%)	
Simple hyperplasia without atypia	4 (13.3%)	5 (16.6%)	5 (16.6%)	6 (20%)	
Simple hyperplasia with atypia	2 (6.6%)	1(3.3%)	3 (10%)	1(3.3%)	
Complex hyperplasia without atypia	1(3.3%)	1(3.3%)	0	1(3.3%)	
Complex hyperplasia with atypia	1(3.3%)	0	0	1(3.3%)	

Data are expressed as mean±SD

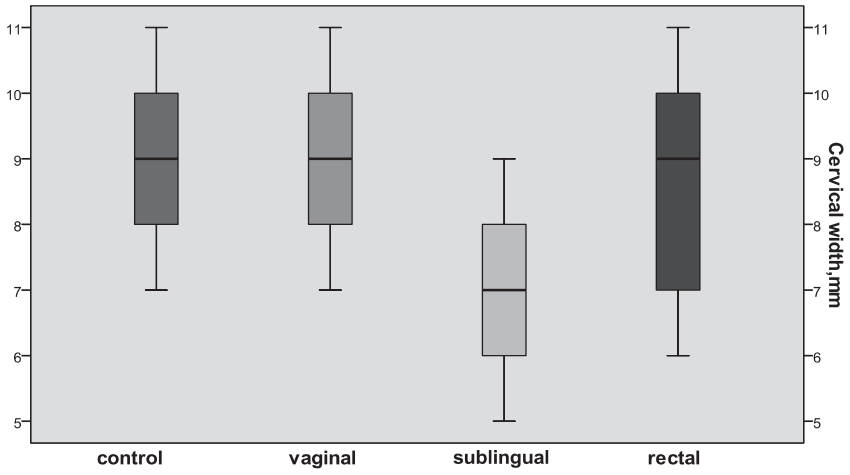

Figure 1. — Comparision of control, vaginal, sublingual, and rectal misoprostol.

misoprostol (two tablets of 200 ug), and the patients were administered the medications vaginally, rectally or sublingually 12 hours and six hours before surgery. Same doctor performed all of the hysteroscopic procedures to decrease interobserver variability. Before the operative hysteroscopy, the operator measured the preoperative degree of cervical dilatation by passing Hegar dilators through the cervix in ascending order starting with a size of two mm. The size of the largest dilator passed into the inner cervical ostium without subjective resistance felt by the operator recorded as the preoperative degree of dilatation. If there was initial resistance with Hegar dilator size of two mm, the result recorded as zero mm. After the cervical canal was dilated to a Hegar dilator of size 11 mm, operative hysteroscopy with bipolar electrode was passed into the uterine cavity with using a ten- mm, 15-degree optical system under anesthesia. A sodium chloride 0.9 % isotonic solution was used as uterine distension, with an insufflator that maintains 100–150 mmHg pressure in the uterine cavity. A bipolar resectoscope unit was routinely used for resection of endometrial polyps and targeted endometrial biopsies. For haemostasis, a current of 50 watts was applied. After the operation, the patients were monitored at the post-anesthesia care unit for a minimum of one hour and transfered gynecology unit. After hysteroscopy, the women were observed for six hours before being sent home. The primary outcome measure in this study was the preoperative cervical width after misoprostol administration. Statistical analyses were performed with SPSS software for Windows. Results are expressed as means ± SD (standard deviation). Study groups were analysed with one-way ANOVA and post hoc Tukey tests. Homogeneity of variances were evaluated with Levene test and, p values < 0.05 were considered statistically significant.

Results

From October 2011 and September 2012, 120 eligible patients were included in the study. There were 90 women in the study group and 30 women in the control group The study group were randomized to receive sublingual (n = 30), rectal (n = 30) or vaginal (n = 30) misoprostol. The control group did not receive misoprostol (n = 30). The four groups were comparable in terms of age, body mass index (BMI) and pathology (Table 1).

The mean cervical widths for control group was 9.0 ± 1.1 mm and the mean post-treatment cervical widths for the sublingual, vaginal, and rectal groups were 7.1 ± 1.1 mm, 8.9 ± 1.3 mm, and 8.6 ± 1.5 mm, respectively (Figure 1). These cervical widths were similar between the control, vaginal and rectal groups ($p > 0.05$), but the cervical widths

of sublingual group were significantly different from control, vaginal, and rectal groups ($p < 0.001$).

Complications during cervical dilatation occurred in three patients. Cervical tearing occurred at the tenaculum site in two patients in the rectal group and one patient in the vaginal group. Cervical lacerations were treated conservatively with close observation without suturing. One patient in the rectal group and one patient in the sublingual group had nausea due to misoprostol side-effects, whereas vomiting or diarrhea was not seen in any of the patients. All patients were discharged after six hours of observation without any complications.

Discussion

This trial shows that 400-ug doses of sublingual misoprostol 12 hours and six hours before outpatient hysteroscopy is effective for cervical ripening compared with vaginal and rectal groups in post-menopausal women. The need for cervical dilatation before hysteroscopy was considerably higher in the control or no treatment group. Cervical ripening is needed to prevent or reduce complications before transcervical procedures [1-4]. In the literature, there are studies that have compared vaginal and oral routes of misoproptol administration, with different results. Waddell *et al.* found the use of vaginal misoprostol hysteroscopy reduced the pain and the force needed to dilate the cervix [5]. Oppegarrd *et al.* studied self-administered vaginal misoprostol and vaginal estradiol prior to operative hysteroscopy, and found a significant cervical ripening effect compared with placebo in post-menopausal women [6]. Ngai *et al.* failed to demonstrate any beneficial effect for oral misoprostol on cervical ripening in post-menopausal women before hysteroscopy [7].

The different results of the studies can be attributed to some possible factors. The first possible factor is the difference in dosage of misoprostol and the second factor is timing of misoprostol insertion prior to hysteroscopy. The optimal dose and time interval from medication to hysteroscopy vary in literatures. Based on recent studies, 400-ug has been most widely used dose [4, 7]. The time interval before hysteroscopy varied from two to 12 hours for the oral and vaginal routes [6, 7]. The present authors compared the effectiveness of 400 micrograms of sublingual, rectal, and vaginal misoprostols given 12 hours, and six hours before hysteroscopy and found increased ease of cervical dilatation after administration of sublingual misoprostol in post-menopausal women.

The side-effects of misoprostol in this study were lower than in literature [8]. This might be a short time period between misoprotol administration and operation and side-effects were tolerable without need for further treatment.

In conclusion, no study has compared sublingual, rectal, and vaginal routes of misoprostol administration before hysteroscopy in post-menopausal women. The sublingual misoprostol is better than oral and vaginal misoprostol for cervical ripening prior to hysteroscopy in post-menopausal women. This regimen is highly acceptable and easy to use and adverse effects were few. Cervical ripening before hysteroscopy in post-menopausal women should be investigated in large series, and comparisons should be done with different routes of administration in further studies.

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