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Vaginal Misoprostol Prior to Curettage for Cervical Dilatation in Perimenopausal Women: A Randomized Controlled Trial

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ABSTRACT

Objective To compare the effectiveness of vaginal misoprostol and placebo inserted 6 hours prior to curettage for pre-operative cervical dilatation.

Design Randomized comparative study.

Setting Department of Obstetrics and Gynaecology, King Chulalongkorn Memorial Hospital.

Subjects Twenty-six perimenopausal women who underwent outpatient curettage during January 2003 to June 2003.

Intervention Subjects were randomly assigned into two groups. In the first group, one tablet of 200 µg misoprostol was inserted in posterior fornix 6 hours prior to curettage. One tablet of placebo (vitamin B6) was inserted in the second group. Cervical dilatation was assessed by Hegar dilator before and at 6 hours after misoprostol or vitamin B6 insertion.

Measurement and main results Baseline cervical dilatation were no statistically significant difference between two groups. The mean differences of post-pre treatment cervical dilatation were 1.85 ± 0.99 mm and 0.38 ± 0.51 mm in misoprostol and placebo group, respectively. The cervical dilatation was significantly increased in misoprostol group compared to placebo group ($p < 0.001$). None of the patients had clinically significant side effects.

Conclusion Vaginal misoprostol of 200 µg was effective for pre-curettage cervical dilatation in perimenopausal women. No clinically significant side effects were found in this setting.

Keywords: Perimenopausal women, vaginal misoprostol, curettage, cervical dilataion

Perimenopausal women who presenting with abnormal uterine bleeding or other symptoms, usually need to undergo curettage for detection of the endometrial pathology. Difficulty in entering the internal os is a common problem in performing curettage for perimenopausal women. The complications that related to this problem include cervical damage, creation of false tract and uterine perforation.[1]

Numerous studies have demonstrated that vaginal administration of prostaglandin given, preceding vacuum aspiration during the first trimester in pregnant women, softens and dilates the cervix. Thus reducing complications from procedure. Also, the vaginal use of prostaglandin E_2 3 hours prior to hysteroscopy in sterile patient had reported to be effective for cervical dilatation and softening.[2]

However, PGE_2 is too expensive and requires refrigeration.

Recently, misoprostol, a synthetic prostaglandin E_1 analogue that is inexpensive, easy to storage, transport and administer, has been demonstrated to be effective for cervical priming by both oral[3] and vaginal administration 10-12 hours before hysteroscopy.[4]

From the study of Zeiman et al (1997)[5], it showed that in pregnant women receiving vaginal misoprostol, the plasma concentration of misoprostol acid rose gradually reached maximum value between 60 and 120 minutes, and declined slowly to an average of 61% of the peak value at 240 minutes after administration. Therefore, we have carried out a randomized, double-blinded comparative study in 26 perimenopausal women who had an indication for curettage and assigned a 6 hours before curettage would be adequate in perimenopausal women. We have decided to compare the effectiveness between 200 µg misoprostol and placebo.

The purpose of our study was to determine that 200 µg vaginal misoprostol is effective for cervical dilatation when it is given 6 hours before curettage.

Materials and methods

Patients

Perimenopausal women, age of 45 years old and above, who had an indication for out-patient curettage at Department of Obstetrics and Gynaecology, King Chulalongkorn Memorial Hospital were eligible in this study. Criteria for inclusion were perimenopausal women who currently have menstruation or whose menstruation has ceased not more than 5 years. Criteria for exclusion were unstable vital signs, profused vaginal bleeding, contraindication for misoprostol administration and patients who recieved steroids and anticoagulant.

Study Design

We conducted a randomized, controlled trial designed to evaluate efficacy of 200 µg vaginal misoprostol for cervical dilatation when it was given 6 hours before curettage. After informed consent, randomization was performed without stratification by computer using numbered, sealed envelopes. Subsequently, patients were assigned to receive either vaginal suppository 200 µg misoprostol or placebo (vitamin B6).

The study was approved and granted by Ethical Committee, Faculty of Medicine, Chulalongkorn University.

Pre-treatment evaluation

Measurements of blood pressure, temperature, and pulse rate were carried out. Any discomforts such as abdominal pain, nausea, diarrhea and headache were recorded. The pelvic examination was performed before misoprostol or placebo administration. Cervical canal was measured using the largest Hegar dilator that could be passed through the cervical canal without resistance.

Each patient was assigned to receive a vaginal suppository tablet into the posterior fornix 6 hours prior to curettage. Every tablets were moistened with water before insertion and patients were instructed to remain recumbent for at least 3 hours post administration.

Post-treatment evaluation

Any side effects such as nausea, vomiting, abdominal pain, diarrhea and vertigo as well as vaginal bleeding were asked and recorded. Blood pressure, temperature and pulse rate were also recorded.

A pelvic examination was again carried out 6 hours after insertion, when particular attention was paid to the cervical softness, bleeding and lesion. In addition, calibration of the cervical canal was performed, and the largest possible Hegar dilator which could be inserted without resistance was noted.

Curettage was performed under a paracervical blockade. Following the operation, the patients were observed in the recovery room for 1-2 hours before discharged. All were followed up 1 week after the operation, a pelvic examination was performed and the side effects were assessed again.

Assessment of response

Size of Hegar dilator indicates the width of central diameter in millimetre and the largest number of Hegar dilator that could pass through the cervical canal without resistance before and after drug insertions were calculated for the difference in baseline cervical dilatation, the main outcome indicator.

Occurrence and severity of side effects include temperature and blood pressure were compared.

Statisical analysis

From a pilot study of with type I error of 0.05 and a power of 0.90 , 11 patients were required for each group. Assuming a 15% default at follow up, the number chosen was 13 ; therefore the total sample size was 26.

Variables that were normally disturbuted were presented as mean and standard deviation. Data were analyzed using the unpaired t-test with $p<0.05$ considered statistically significant in the differences between two groups. Pre-treatment and post-treatment data were analyzed using paired t-test.

Results

From January 2003 to June 2003, 26 perimenopausal women were recruited at our hospital. Characteristics of the patients are summarized in Table 1, there was no statistically significant difference between two treatment groups regard by age, weight, height and BMI.

There was no significant difference in the baseline of cervical width prior to treatment in both groups (Table 2). The mean cervical dilatation following the insertion for 6 hours of 200 µg misoprostol and placebo were 7.54 $\pm$ 1.13 mm. and 5.92 $\pm$ 0.95 mm., respectively. One patient in misoprostol group had no cervical change. The mean difference between pre and post-cervical dilatation in misoprostol group (1.85 $\pm$ 0.99 mm) was statisically significant higher than that of placebo group (0.38 + 0.51 mm) ($p<0.001$).

There was no clinically and statistically significant change in blood pressure and body temperature in both groups. Only mild abdominal pain was complained from two patient in 200 µg misoprostol group and none in placebo groups, but it was not increased in severity after the operation completed. Other side effects such as nausea, vomiting, chilling and headache were not detected from all patients. And at one week follow up visit, none had any delayed side effects.

Table 1. Patient characteristic.

Characteristic	Misoprostol (n=13)	Placebo(n=13)	P-value
Age	49.7 + 3.2	47.9 + 2.4	NS
Weight (kg)	54.1 + 9.7	54.0 + 8.0	NS
Height (cm)	153.6 + 4.9	150.8 + 6.2	NS
BMI (kg/m^2)	23.1 + 4.1	24.2 + 4.0	NS

Table 2. Statistical comparison in two groups.

Cervical dilatation	Misoprostol 200 µg (mm)	Placebo (mm)	P-value
Pre-treatment width	5.69 $\pm$ 0.85	5.54 $\pm$ 1.05	0.686
Post-treatment width	7.54 $\pm$ 1.13	5.92 $\pm$ 0.95	0.001
Difference of cervical width between pre-post treatment	1.85 $\pm$ 0.99	0.38 $\pm$ 0.51	<0.001

Discussion

This randomized study compared the effectiveness of vaginal misoprostol and placebo for pre-curettage cervical dilatation in perimenopausal women. Our results showed that 200 µg vaginal misoprostol is more effective than placebo.

The previous investigation in 1988 shows that vaginal Meteneprost (9-deoxo-16.16, dimethyl-9-methylene PGE_2) can soften and dilate the non-pregnant cervix.[2] Later in 1997, S.W. Ngai et al. showed that oral misoprostol could prime the uterine cervix prior to hysteroscopy in non-pregnant women.

Recently, Preutthipan and Herabutya[4] demonstrated that vaginal 200 µg misoprostol for cervical priming in nulliparous women 9-10 hours before hysterectomy can lessen the cervical resistance and facilitate the procedure.

In our practice for OPD patient, the shorter operating time gives more comfortable for the patient and vaginal misoprostol has more long-lasting stimulation effect on the cervix than oral administration, so we conducted this clinical trial to use vaginal misoprostol for 6 hours before curettage. And we found that 200 µg of vaginal misoprostol could soften and dilate the cervical os more effective than placebo.

Because the misoprostol tablets are not prepared for vaginal use and local factors such as acidic media are different between the patients. Most of the patients in both groups had the particulate remnants of tablets remained in the posterior fornices, albeit in varying proportion. In tablets dissolution,[5] of the 200 µg group had minimal change in the cervical dilatation and also and significant remnants remained in the vagina. This incomplete dissolution of tablet may decreased the drug absorption. To decrease this variation, a further study needs to carries out under the specific local factors such as preparing in powder form and wetted with water or with acetic acid before insertion.

No side effects were observed in both groups. These results differ from those of Preuthipan and Herabutya(1999) who showed a relatively high frequently of side effects after vaginal misoprostol administration, particularly mild lower abdominal pain and slight vaginal bleeding.[4]

We believed that the incidence of the side effects could be lower when the treatment interval was shortened. However, as our sample size was relatively small, a more extensive study needs to be carried out to confirm these results. At the follow up visit 1 week later no signs of any side effects nor cervical lesion were observed.

In conclusion, a 200 µg vaginal misoprostol is more effective than placebo when administered 6 hours prior to curettage but the further study needs to underwent in the curettage sample size and use specific local factors to decrease the variations of drug absorption.

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