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## RESEARCH ARTICLE

### SUBLINGUAL VERSUS VAGINAL MISOPROSTOL FOR CERVICAL RIPENING BEFORE HYSTEROSCOPY

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Misoprostol,  
Hysteroscopy,  
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#### ABSTRACT

**Study design:** Comparative clinical trial.

**Objective:** To evaluate the efficacy of misoprostol (sublingual versus vaginal) for cervical ripening before hysteroscopy.

**Patient and Methods:** Sixty women who were admitted to Banha University hospital department of obstetrics and gynecology for surgical hysteroscopy. The sixty women were divided into two groups. Group one 30 cases received 400 µg misoprostol (two tablets each tablet 200 µg) under the tongue 6h before hysteroscopy. Group two 30 cases took 400 µg misoprostol (two tablets each tablet 200 µg) administered into the posterior fornix of vagina by investigator 6h before hysteroscopy. The degree of cervical dilatation. The duration of dilation, hysteroscopic and drug complications were recorded for all cases.

**Results:** There were statistically Significant difference between sublingual group and vaginal group as regard cervical dilatation and operative time. cervical width in the sublingual group ( $6.4 \pm 0.9$ ). in vaginal group ( $5.4 \pm 1.3$ ) Operative time in minutes ( $1.095 \pm 0.22$ ) in sublingual group, ( $2.05 \pm 0.150$ ) in vaginal group. No significant difference between sublingual and vaginal group as regard post hysteroscopic complication.

**Conclusion:** Sublingual administration of misoprostol is more effective than the vaginal route for preoperative cervical ripening.

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## INTRODUCTION

Hysteroscopy is the main diagnostic and therapeutic procedure applied for patients with infertility, suspected intrauterine pathologies and abnormal bleeding. It is also a therapeutic method for several uterine pathologies all over the world. Its low cost and quick and simple procedure have made it widely popular (Campo *et al.*, 1999). Although hysteroscopy has been considered as a safe and less invasive procedure, some complications such as cervical tear, bleeding, uterine perforation, pain and discomfort may occur during the process. Many women need dilatation prior to hysteroscopy to make the procedure simpler (Jansen *et al.*, 2000). Misoprostol (prostaglandin E1 analog) is a drug of choice for cervical ripening, labor induction, post-partum hemorrhage and pregnancy termination (Goldberg *et al.*, 2001). Cervical ripening before hystero-scopy with misoprostol could make passage of hysteroscope easier with fewer complications (Fig. 1) (Ngai *et al.*, 1997).

Sublingual and vaginal routes are common routes of misoprostol applied for cervical ripening before hystero-scopy. Rapid absorption leading to reach peak concentration and higher bioavailability are advantages of sublingual route administration, while vaginal route administration leads to longer sustained and regular uterine contractions (Khan *et al.*, 2004).

#### Aim of the work

The objective of this study was to compare the effectiveness of sublingual versus vaginal misoprostol used to facilitate cervical dilatation before surgical hysteroscopy.

#### Patients and methods

This study was a comparative clinical trial, it was performed on 60 women admitted to Banha University hospital department of obstetric and gynecology for surgical hysteroscopy during the period from beginning of January 2014 till end of august 2014.

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Written consent was taken after full explanation of the procedure to the patients, the sixty women were divided into two groups.

Group one 30 cases received 400 µg misoprostol (two tablets each tablet 200 µg) under the tongue 6h before hysteroscopy. Group two 30 cases took 400 µg misoprostol (two tablets each tablet 200 µg) administered into the posterior fornix of vagina by investigator 6h before hysteroscopy.

### Inclusion criteria

Women in child-bearing period requiring diagnostic hysteroscopy due to infertility with no previous vaginal deliveries.

### Exclusion criteria

- Women with previous vaginal deliveries were excluded from the study.
- Any contraindication to hysteroscopy:
  - a. Pregnancy.
  - b. Recent or current vaginitis, cervicitis or PID.
  - c. Profuse uterine bleeding.
  - d. Known cervical malignancy.
  - e. Recent uterine perforation.
- Any contraindication to prostaglandin:
  - a. Cardiovascular disease.
  - b. Hypertension.
  - c. Severe asthma.
  - d. Glaucoma.
  - e. Renal failure.
- History of allergy to prostaglandins.
- Uncontrolled diabetes mellitus.
- Fever.

### Patient's evaluation

#### History

- Personal history including age.
- Patients menstrual history, date of last menstrual period.
- Parity, number and mode of deliveries, as well as contraceptive method currently used.
- History of drug intake, especially hormonal treatment or anti-coagulant therapy.
- Patient's compliant and presence of vaginal bleeding.
- Past and family history.

#### Examination

- Complete general, abdominal pelvic and local examination with cervical score before intervention.
- To exclude a contraindication to hysteroscopy.

#### Investigations

Routine preoperative investigation & results of any previous investigation; namely ultrasound, hysteroscopy, hysterosalpingography or endometrial biopsy were received and data registered in the patients record.

#### Intervention

The patient was asked to empty her bladder. After thorough explanation of the procedure, the patient was placed in the dorsal lithotomy position. The thighs should be at a 90 degree angle to the pelvis in order to create enough space for the surgeon to manipulate the hysteroscope. The patient perineum should be just past the edge of the table. Operative hysteroscope was done under general anesthesia. Normal saline was used for uterine distension connected to the inflow channel on the sheath with intravenous tubing.

A vaginal disinfection with a non irritating watery disinfection solution was performed without placing speculum. Before the hysteroscope and sheath were inserted into the external os, the sheath was flushed to remove the air. The tip of the hysteroscope was positioned in the vaginal introitus, the labia being slightly separated with fingers. The vagina was distended with saline. The scope was driven to the posterior fornix to readily visualize the portion and slowly backwards to identify the external cervical os. When this is become visible, the scope was carefully moved forward to the internal os and then the uterine cavity with least possible trauma. The uterine cavity was systematically explored to identify any anomaly in the uterine walls and/or the right and left tubal ostia. Finally the evaluation and finding data were written in details by the surgeon and Any complication were registered in the patient sheet.

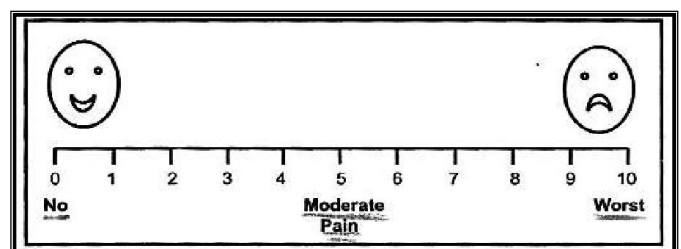
### Postoperative outcome measurements in the study

1. Cervical dilation measured by Hegar dilator is the primary outcome measure.
2. Pain score of the patients were determined using (0-10) visual analogue scale as shown below:

(0) (1) (2) (3)..... (10) no pain worst pain

The day before surgery, all patients were informed about the procedure and would be trained to use the visual analogue scale (VAS). In horizontal imaginable line. It was a 10 cm. Where 0= no pain and 10 = worst pain.

Patient would be asked to indicate on the line where the pain is in relation to the two extremes.



Moderate: 4-6 Severe:7-10 Mild: 0-3

Visual analogue scale

### Complications

This includes both complication of misoprostol and complications of hysteroscopy.

#### Complication of misoprostol

- a. Vaginal spotting.

- b. Uterine contractions (lower abdo-minal cramp).
- c. Fever.
- d. Shivering.
- e. Diarrhea.
- f. Nausea and vomiting.

#### Complication of hysteroscopy

- a. Uterine perforation.
- b. Vaso-vagal reaction.
- c. Laceration.
- d. Failure of hysteroscopy.

#### Statistical Analysis

Results are expressed as mean  $\pm$  standard deviation (SD) or number (%). P value  $<0.05$  was considered statistically significant.

## RESULTS AND DISCUSSION

The uterine cervix is essentially a connective tissue organ. Smooth muscle cells account for less than 8% of the distal part of the cervix.

**Table 1. Demographic characteristics of the sublingual and vaginal misoprostol groups**

	Sublingual (n=30)	Vaginal (n=30)	p. value
Age	28.2 $\pm$ 4.7	28.5 $\pm$ 5.0	0.253
History of abortion	7(23.3%)	7(23.3%)	0.362
Previous history of cesarean section	4(20%)	2(10%)	0.144

No significant difference between the sublingual group and vaginal groups as regards age, number of abortion and Previous history of cesarean section.

**Table 2. Comparison between sublingual and vaginal groups regarding the indication of hysteroscopy**

	Sublingual (n=30)	Vaginal (n=30)	p. value
Normal diagnosis	16(53.3%)	17(56.7%)	0.795
Submucous myoma	4(13.3%)	5(16.7%)	0.718
Endometrial polyp	5(16.7%)	4(13.3%)	0.718
Intrauterine synechia	2(6.7%)	3(10.0%)	0.640
Uterine Septum	3(10.0%)	1(3.3%)	0.301

No significant difference between two group regarding the indication of hysteroscopy.

**Table 3. Intraoperative finding in sublingual and vaginal groups as regard outcome measurements**

	Sublingual (n=30)	Vaginal (n=30)	p. value
Cervical width in mm (after misoprostol administration)	6.4 $\pm$ 0.9	5.4 $\pm$ 1.3	0.014
Need of cervical dilatation	0(0%)	3(10%)	0.022
Intraoperative time of cervical dilatation in minutes	1.1 $\pm$ 0.2	2.1 $\pm$ 0.5	0.019
Cervical laceration	1(3.3%)	1(3.3%)	0.999

Significant difference between vaginal and sublingual group in cervical dilatation and operative time.  
No significance in cervical laceration.

**Table 3. Comparison between sublingual and vaginal groups as regard post hysteroscopic complication**

Hysteroscopic	Sublingual (n=30)	Vaginal (n=30)	p. value
Cervical bleeding after hysteroscopy	1(3.3%)	2(6.7%)	0.635
Hypotension	2(6.7%)	2(6.7%)	0.241
Syncope	0(0%)	0(0%)	1.00
Vasovagal	0(0%)	0(0%)	1.00
Uterine perforation	0(0%)	0(0%)	1.00
Creation of false track	0(0%)	0(0%)	1.00

No significant difference in sublingual and vaginal group in post hysteroscopic complication

**Table 4. Comparison between sublingual and vaginal groups as regard side effects of misoprostol**

	Sublingual (n=30)	Vaginal (n=30)	p. value
Abd pain	1(3.3%)	2(6.7%)	0.574
Diarrhea	0(0%)	1(3.3%)	0.626
Headache	1(3.3%)	0(0%)	0.626
Fever	0(0%)	0(0%)	1.00
Nausea	1(3.3%)	0(0%)	0.626
Vaginal bleeding	0(0%)	0(0%)	1.00

No significant difference in sublingual and vaginal groups in side effects of misoprostol

**Table 5. Comparison between sublingual and vaginal group as regarding visual analogue scale (VAS)**

VAS	Sublingual (n=30)	Vaginal (n=30)	p. value
No pain	25(83.3%)	22(73.3%)	0.467
Mild	5(16.7%)	7(23.3%)	
Moderate	0(0.0%)	1(3.3%)	
Severe	0(0.0%)	0(0.0%)	

No significant difference in sublingual and vaginal groups as regarding visual analogue scale (VAS)

The exact mechanism leading to physiological cervical ripening is not known. The biochemical events that have been implicated in cervical ripening are (a) a decrease in total collagen content, (b) an increase in collagen solubility, and (c) an increase in collagenolytic activity. The changes in extracellular matrix components during cervical ripening were described as similar to an inflammatory response. Indeed, during cervical ripening there is an influx of inflammatory cells into the cervical stroma, which increases matrix metalloproteinases and thereby leads to the degradation of collagen and cervical softening. (Aronsson et al., 2005)

This study is a randomized clinical trial performed on 60 women admitted in Banha University Hospital Department of Gynecology for surgical hysteroscopy. Study aimed to compare the effectiveness of sublingual versus vaginal misoprostol used to facilitate cervical dilatation before hysteroscopy. The age of the patients in sublingual and vaginal group was comparable as the mean age was 28 years, approximately. According to the indication of hysteroscopy normal hysteroscopic findings were reported in sublingual group (53%) and in vaginal group (56%). Uterine septum was found in vaginal group (3%) and in sublingual group (10%). Endometrial polyp was found in sublingual group (16%) and in vaginal group (13%). There were no statistical significant differences between the two groups as regards the indication of hysteroscopy.

The main outcome measurements in this study were the degree of cervical dilatation, need to dilate the cervix during introduction of hysteroscope, operative time in minutes until the cervix was dilated cervical laceration. Cervical width was represented as (mean±SD) in mm the priming outcome measurement. It was (5.35±1.30) in vaginal groups, (6.4±0.99) in sublingual group. Sublingual group was better than vaginal group regarding cervical dilatation. So pretreatment with misoprostol is significantly reduced the resistance of the cervix. No women required cervical dilatation in sublingual group, compared with (3)10% in vaginal group. So the number of patients who needed further cervical dilatation was significantly lower in those pretreated with sublingual misoprostol. It is believed that a decrease in women requiring additional cervical dilatation has the most profound potential clinical benefit in decreasing the number of uterine perforation and cervical dilatation.

The time elapsed in minutes until cervix was dilated (1.095±0.2) minutes in sublingual group, (2.05±0.2) minutes in vaginal group. Pain prescription was lower in sublingual group compared to the vaginal group. In a study by Muloyim et al., (2010) two groups of women who received sublingual misoprostol or placebo before hysteroscopy were compared with each other. The need for cervical dilatation and duration of dilatation lower in the misoprostol group than in the placebo group among women with no previous vaginal deliveries, a statistically significant difference was not found in this case. In another study, Bisharah et al., (2003) (Bisharah et al., 2003) evaluated 40 women who were randomly assigned to treatment with 100µg sublingual misoprostol or placebo before hysteroscopy. They observed no significant difference in degree of cervical dilatation between two groups.

Our study was evaluated two different routes of misoprostol. Other studies evaluated only one route of misoprostol. Preuthipan and Herabutya, (2006) (Preuthipan and Herabutya, 2006) recognized that vaginal miso-prostol applied before operative hysteroscopy reduced the need for cervical dilatation, facilitated hystero-pscopic surgery and minimized cervical complications on the other hand. Fernandez et al., (2004) (Fernandez et al., 2004) found that vaginal misoprostol applied 4h, at three different doses before hystero-scopy not effective for cervical dilatation. The other form of misoprostol oral route, had also been previously investigated for cervical ripening. Sordia-Hernandez et al., (2011) (Sordia-Hernández et al., 2011) applied oral and vaginal forms before hysteroscopy in 75 infertile patients. They reported that surgical time of cervical dilatation and pain was significantly lower in vaginal group in comparison with oral and placebo groups.

On other hand Choksuchat et al., (2006) (Choksuchat et al., 2006) suggested that 400µg oral misoprostol is as effective as 200µg vaginal route for cervical ripening before hysteroscopy. Tanha et al., (2013) (Tanha et al., 2013) they found that significant difference between vaginal and sublingual misoprostol groups in cervical dilatation and duration of dilatation of cervix and they concluded that sublingual route of misoprostol could be considered as an effective medication before surgical hysteroscopy in perimeno-pausal women.

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