

Efficacy and Safety of Sublingual Misoprostol for Cervical Priming Prior To First Trimester Suction Evacuation

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Abstract

Objective To evaluate the role of sublingual misoprostol as a cervical priming agent in first trimester pregnancy termination by suction evacuation

Material and Methods A prospective randomized study carried was conducted in Dr Baba Saheb Ambedkar Hospital, Delhi over a period of two years. 80 women between 6-12 weeks of gestational age, seeking termination of pregnancy were randomized into two groups. Women in group I received sublingual misoprostol two hours prior to suction evacuation. Women in group II did not receive any treatment. The Outcome measures of the study : cervical dilatation, blood loss, duration of procedure and side effects were comparatively evaluated.

Result The mean cervical dilation was 8.1 mm in sublingual misoprostol group compared to 2.5 mm in control (p value < 0.001). Blood loss and operative time was also significantly less. Minor side effects like nausea, vomiting and pain observed with misoprostol were well tolerated.

Date of Submission: 02-04-2018

Date of acceptance: 17-04-2018

I. Introduction

Of the 56 million induced abortions that took place each year during 2010– 2014, an estimated 25 million (45%) were unsafe.¹ According to recent estimates, at least 8% of maternal deaths worldwide are from unsafe abortion; at least 22,800 women die each year from complications of unsafe abortion. Almost all abortion-related deaths occur in developing countries.²

Most induced abortions should be done in the first trimester because the risk of complications increase 10-fold in the second trimester. Medical abortion has come up in a big way in the last decade. However, the rate of incomplete abortion, treatment failure and continuation of pregnancy with increasing gestational age, besides, the cost of treatment, non availability of 24 hour emergency services in outreach areas, the desire of the patient to opt for sterilization in the same sitting precludes their use in a large number of cases.³ Surgical methods mainly suction evacuation still play a major role for terminating first trimester pregnancies. Cervical dilatation prior to suction evacuation is probably the most critical step in the first trimester termination of pregnancy. The need for mechanical dilatation of the cervical canal during suction evacuation carries an increased risk of cervical laceration and uterine perforation and may have an adverse long term effect on future fertility.⁴ In addition; complication like hemorrhage, infection and incomplete evacuation of the products of conception may arise as a result of insufficient or difficult dilatation.⁵ Effective pre operative cervical priming can significantly reduce this kind of morbidity.⁶ Prostaglandin analogues have a well established role as cervical priming agents before first trimester suction evacuation.

Misoprostol- a synthetic prostaglandin E-1 analogue has been shown to be better alternative to the other prostaglandin preparation. It has several advantages of easy availability; ease of administration, low cost, stability at room temperature, long shelf life and fewer side effects as compared to older analogues. The sublingual route uses the most vascular area of the oral cavity and avoids the first pass effect through the liver, which is associated with oral administration. Pharmacokinetic studies have been shown that sublingual misoprostol may be more potent than the other routes, as shown by shortest time (20 min) to peak concentration, its highest peak concentration and greatest bioavailability.⁷ Thus, the current study was undertaken to study the role of 400 microgram sublingual misoprostol as a cervical priming agent when administered two hours prior to suction evacuation under general anesthesia and to evaluate its efficacy and side effects.

II. Material and methods

The present prospective randomized study was carried out on 80 women between 6-12 weeks of gestational age, seeking termination of pregnancy in the department of obstetrics and gynecology Dr Baba Saheb Ambedkar Hospital, Delhi.

Inclusion criteria

- Healthy pregnant women of 20-40 year.
- Gestational age 6-12 weeks

Exclusion criteria

- Women with known allergy to misoprostol
- A h/o previous uterine surgery (eg. myomectomy) or LSCS
- History of minor or major cervical operations (electrocautery, conization, cervical cerclage)
- Hemoglobin less than 9 gm%
- IUCD in situ
- Uterine anomaly
- Bleeding or spotting during the current pregnancy or threatened or missed abortion.
- Chronic medical disorder like hepatic, renal, or cardiac disease.
- H/o Bronchial asthma
- Sign of genital infection
- H/o Heavy smoking

After taking a thorough history, complete physical (vital signs e.g. Blood pressure, temperature, pulse rate), systemic examination, per abdomen, per speculum and bimanual pelvic examination was done. Routine investigations including blood group, Rh group, hemoglobin, urine analysis, Blood sugar, ECG were carried out. Period of gestation was estimated clinically. Gestational age was determined by a reliable menstrual history and confirmed by pelvic examination. Ultrasonography was performed when any discrepancy between the two was found, or if size of the uterus was difficult to assess. A written and informed consent for study was taken and form I and form C, as per MTP act was filled.

Patients were admitted to the ward and were divided by simple randomization, into two groups.

1. **GROUP I:** Women received sublingual misoprostol two hours prior to suction evacuation.
2. **GROUP II:** Women in the control group did not receive misoprostol.

Women, in whom suction evacuation got delayed beyond two hours due to unavoidable circumstances, were excluded from the study. The route of administration of misoprostol was known to the patient and the investigator, but surgeon was blinded. No premedication was given but the woman was told that should they experience pain, analgesics were available. All the suction evacuations were performed by the same surgeons to reduce bias.

Preoperatively, side effects associated with misoprostol including pain, nausea, vomiting, diarrhea, giddiness, fever, shivering and vaginal bleeding and were recorded. Pre-operative vaginal bleeding were graded on a scale of 0-3 (0-no bleeding, 1-minimal spotting, 2- bleeding like menstrual flow, 3- heavy bleeding with clots) pain were graded on a scale of 0-3 (0-no pain, 1-mild pain, 2-moderate pain, 3-severe pain requiring injectable analgesics)

All patients underwent suction evacuation under general anaesthesia. Cervical dilatation was measured with Hegar's dilator using sequentially smaller dilators until dilator entered the internal os easily without resistance. The size of largest dilator that could be passed into the cervical os without resistance was recorded as the cervical dilatation achieved. If the cervix was having a dilatation appropriate or more for that period of gestation, no further dilatation will be performed. In patient with insufficient dilatation serial dilatation was done using Hegar's dilator.

Suction evacuation was performed using a Karman's cannula of the same size as the period of gestation which was followed by check curettage. Duration of surgery was measured from the start of dilatation until the end of curettage. Intra-operative fluid loss was measured with a graduated cylinder as the volume of total uterine aspirate, after sieving away the product of conception. The appropriate amount of liquor for that period of gestation was subtracted to achieve the amount of actual blood loss. Any cervical or uterine injuries ranging from superficial cervical laceration to an ascending cervical tear, uterine perforation or injury to any other intra-abdominal organs were noted. The patients underwent IUCD insertion or sterilization as desired during the same sitting.

Postoperative side effects like nausea, vomiting, vaginal bleeding, fever, dizziness, diarrhea, bad taste and shivering were noted. All women received analgesics for 2 days and antibiotics for five days after the

procedure and were instructed to return if vaginal bleeding persists for more than 3 days or if they develop fever or pain in lower abdomen. Follow up was done twice, first after seven to ten days and subsequently after one month or after the first menstrual period.

Outcome measures of the study were:

1. Cervical dilatation prior to suction evacuation
2. Operative blood loss.
3. Time duration of surgery.
4. Adverse effects related to misoprostol.

Statistical analysis was done by applying One Way ANOVAs test for cervical dilatation & operative blood loss quantitative outcome variables, for duration of procedure outcome variables Kaplan & Meier / One Way ANOVAs study was applied. Chi square/ Fisher Exact (where applicable) was applied for qualitative outcome variables. P value < 0.05 was considered as significant.

III. Results

Table I Patient characteristics

Gravidity	Group I	Group II	P value
	Mean±S.D.	Mean±S.D.	
Age	28.4 ±3.8	28.3±3.3	0.97
Gravidity	4.1± 1.1	3.9±1.3	0.62
Parity	2.8±0.8	2.7±0.9	0.63
Living children	2.78±0.8	2.67±0.8	0.88
Previous abortions	0.3±0.7	0.2±0.5	0.86

The two treatment groups were similar with respect to age, gravidity, parity, no of living children and no of previous abortions

Table 2: Intraoperative Parameters

	Group I	Group II	P value
Cervical dilation >8mm No. (%)	28 (70%)	-	
Cervical Dilation (mm) Mean ± S.D.	8.137 ± 1.63	2.5 ± 0.53	<.001
Blood loss (ml) Mean ± S.D.	14.75 ± 4.57	17.45±5.08	0.015
Duration of Procedure (min) Mean ±S.D.	4.12 ± 1.74	5.45 ±1.86	0.002

Successful dilation achieved in 70% women in sublingual misoprostol group. The mean cervical dilation achieved was 8.1 mm in group I and 2.5 mm in Group II. The p value calculated was <0.001 which was statistically significant. The mean blood loss during procedure was significantly lower in Group I (14.75 ml and 17.45 respectively; p value 0.015) The mean duration of procedure was 4.12 min. in Group I and 5.45 min in Group II. The p value calculated was 0.002 which was statistically significant

Table 3: Pre- operative side effect

	Group I		Group II		P value
	No.	%	No.	%	
Nausea	6	15	0	0	0.011
Vomiting	2	5	0	0	0.152
Diarrhea	4	10	0	0	0.040
Giddiness	1	2.5	0	0	0.314
Fever	1	2.5	0	0	0.314
Shivering	2	5	0	0	0.152
Bleeding/1	6	15	0	0	<0.009
Pain/1	11	27.5	0	0	<0.001

The pre operative side effects of nausea, diarrhea, spotting and pain in abdomen were significantly increased in the sublingual misoprostol group.(Table III). However, the symptoms were mild and women were not much inconvenienced by them.

Table 4: Post operative side effects

	Group I		Group II		P value
	No.	%	No.	%	
Nausea	23	57.5	5	12.5	<.001
Vomiting	10	25.0	2	5	0.012
Giddiness	4	10	2	5	0.369
Heavy Bleeding	12	30	8	20	0.300
Pain	7	18	18	45	0.001

The post operative side effects reported were nausea, vomiting, giddiness, fever; shivering, heavy bleeding (bleeding per vagina) and pain in abdomen (require oral or iv analgesic). The p value was statistically significant for nausea, vomiting, and pain in abdomen for the difference in two groups.No major side effects or complications such as excessive hemorrhage(>500ml), uterine perforation or incomplete abortion were seen in either group.

IV. Discussion

The need for mechanical dilatation of cervix prior to suction evacuation for termination of first trimester pregnancy carries the risk of cervical laceration,uterine perforation and risk of hemorrhage or incomplete evacuation. Adequate dilatation decreases pain and the duration of surgery and increases operative ease. Early onset of action, high bioavailability,hepatic bypass and avoidance of uncomfortable vaginal examination makes sublingual misoprostol a good alternative to study as a cervical priming agent prior to suction evacuation in first trimester termination of pregnancy.

Study group of Saxena at el (2003) received 400 microgram misoprostol 3 h prior to vacuum suction as compared to two hours in our study. ⁸The success rate of sublingual group reported by Saxena et al was higher than (100% vs. 70%) in present study. The mean blood loss 14.75 ml in present study is less than 16 ml in their study. The duration of procedure in present study is also less (4.12 min vs. 4.3 min) in their study. The

incidence of pre operative side effects like spotting (15% vs. 40%) was higher in their study and mild pain in abdomen (27.5% vs. 20%), nausea, vomiting, giddiness and fever were high in present study compared to their study. In present study, the incidence of post operative side effects like nausea (57.5% vs. 2%), vomiting (25% vs. 4%), are higher compared to their study.

Vimla et al (2004) recruited 50 women in sublingual misoprostol group in their study and cervical dilatation was more compared to the present study (8.61 mm vs. 8.13 mm).⁹ Average time required for procedure (3.08 min vs. 4.12 min) was less in their study compared to present study. The incidences of side effects in are comparable to our study.

Chitaishvili et al (2007) studied three hundred forty nine healthy women. 175 women who were randomly allocated to misoprostol group received 400 microgram misoprostol sublingually approximately one hour before the procedure.¹⁰ The preoperative cervical dilatation was 8.9 mm in misoprostol group versus 8.14 mm in present study. The amount of blood loss was 95.0 ml compared 14.75ml in the present. Need for oxytocin was less common in misoprostol group - 29 (16.6%). The duration of the procedure was 7.3 min in misoprostol group which was higher than 4.12 min in present study. There was no significant difference in terms of visual analogue scores during the procedure, patient satisfaction, and rate of side effects among the groups in their study and control groups. The result obtained in their study had shown that sublingual administration of 400 microgram misoprostol at least an hour before MVA for termination of pregnancy facilitates the abortion procedure by decreasing the need for cervical dilatation, reducing blood loss and need for oxytocin use. However there was no significant difference in operating time between the sublingual and placebo group in their study. Sublingual misoprostol has the advantage of being more convenient to administer and may be more suitable for day surgery.

Hemang et al (2010) conducted retrospective case review of six hundred eighty five patients who underwent a first trimester aspiration abortion with buccal misoprostol cervical priming.¹¹ Adequate dilatation of the cervix was achieved in 44.2% patients vs 70% in our study group. The proportion of patients with adequate dilation decreased with increasing gestational age. Patients requiring additional mechanical dilatation differed significantly between those who were parous (51.0%) and those who were nulliparous (72.4%) ($p < 0.001$).

Parveen et al (2011) carried out a prospective randomized study in one hundred fifty women who were randomized into three groups of 50 each.¹² Group A received 400 microgram of sublingual misoprostol. The median cervical dilatation achieved in their study (9.1 mm vs. 8.15 mm) was higher than present study. The mean cervical dilation achieved in vaginal group in their study was 8.1 mm. The duration of procedure (8 min vs. 4.12 min) was higher in their sublingual study group. The amount of blood loss was also higher in their sublingual misoprostol group in comparison to present study. They found the sublingual group had significant cervical dilation as compared to the vaginal and oral group.

Mathur et al (2014) randomized 150 women seeking first trimester pregnancy termination into two groups.¹³ The study group received 400mcg misoprostol three hours before suction evacuation and the control group directly underwent surgical abortion without prior cervical priming with misoprostol. The mean baseline cervical dilatation was 8.6mm vs 8.4 in the present study. They recorded an intraoperative blood loss was 27ml and operative time was 5.3min as compared to 14.75 ml and 4.12 min respectively in the present study.

Ganer H et al (2017) compared the effectiveness and patient satisfaction of different routes of misoprostol for short-term (same day) cervical priming in first trimester surgical abortions.¹⁴ They found that cervical dilatation was similar between the groups, as were cervical consistency and ease of dilation. Patients noted the greatest discomfort and side effects with sublingual administration in their study.

V. Conclusion

Optimal cervical priming in the shortest time interval, with minimum side effects is desirable before suction evacuation for first trimester pregnancy termination. Based on our study, 400 microgram sublingual misoprostol administered two hours prior to surgical evacuation seems to be an effective cervical priming agent as it achieves a significantly high cervical dilation, decreases intraoperative blood loss and decreases the duration of procedure with minor side effects.

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Dr Dolly Chawla "Neeru Malik, Dolly Chawla, Mohini Soni, Madhu Minocha, Neeraj Sharma." *IOSR Journal of Dental and Medical Sciences (IOSR-JDMS)*, vol. 17, no. 4, 2018, pp 33-38.