

Original Research Article

Randomized comparison of vaginal and sublingual misoprostol with mifepristone priming in termination of second trimester pregnancy

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ABSTRACT

Background: Sublingual Misoprostol 200 ug 4 hrly is as effective or less effective than vaginal Misoprostol 200ug 4hrly with 200mg oral Mifepristone in termination of second trimester pregnancy.

To compare effectiveness, side-effects, and patient satisfaction of sublingual vs vaginal misoprostol administration.

Methods: It was prospective randomized open label study. 60 women 13-20 weeks of gestation with a valid legal indication for termination of pregnancy as per MTP act in INDIA were enrolled for study, randomly divided into Group A- Sublingual (n=30) group B-Vaginal (n=30). For group A, 200 mg of Mifepristone was given, 48h later Misoprostol 200 µg was given sublingually 4hrly up to a maximum of 5 doses. If abortion does not occur, the pregnancy was terminated with vaginal misoprostol, in group A. Same procedure repeated in group B. If abortion fails to occur after 5 doses, then second course of vaginal misoprostol was given in group B. Failure of procedure was defined as failed expulsion of foetus at 48 hrs.

Results: Mean induction-abortion interval in vaginal group was 12.8±4.38h and 11.47±4.42h in sublingual group was comparable with insignificant p value (p=0.136). All the side effects were comparable in both groups. The overall success rate was 93.3% in the sublingual group while it was 100% in the vaginal group.

Conclusion: Vaginal misoprostol with oral mifepristone priming in second -trimester medical abortion has a shorter time to pregnancy termination compared with a sublingual regimen. However, both the routes are equally effective for induction of abortion.

Keywords: Mifepristone, Misoprostol, Second Trimester, Sublingual, Vaginal

INTRODUCTION

Safe and legal abortion is considered to be a key intervention for improving women's health and quality of life.¹

Worldwide 42 million legal abortion and 10 to 12 million clandestine abortion takes place every year of which 10 to 15% are performed in second trimester.²⁻⁴ In India alone, 6.7 million induced abortions occur annually, of which late abortions constitute 10.7 to 15%.⁵ According to the

MTP Act, medical termination of pregnancy (MTP) in India is allowed up to 20 weeks. Two-thirds of major abortion related complications and half of abortion related mortality occur in pregnancies terminated after 13 weeks of gestation.^{6,7} For second trimester medical termination of pregnancy, the optimal regimen is still under development but is likely to be characterized by a short induction abortion- interval, devoid of any serious side effect, high acceptability, easy to perform and cost effective. Published evidence provides reassurance on the safety and efficacy of medical abortion using

mifepristone in combination with a prostaglandin analogue.⁸⁻¹³ Mifepristone, a progesterone receptor antagonist has been shown to be effective in shortening the induction abortion interval.^{14,15}

Misoprostol is used by four routes in India (Oral, Vaginal, Sublingual, and Rectal). Two common routes of administration of misoprostol are sublingual and vaginal; they have different pharmacokinetics and effectiveness.¹⁶ We used mifepristone 200mg for priming followed by misoprostol every 4h which is according to WHO guidelines (2012).^{17,18} Failure rate of this combination is very low ranging from 0.3% to 3%.¹⁹

METHODS

It was a Randomised Open Label Study of 60 cases conducted in patients at Obstetrics and Gynaecology department of T. N. Medical college and BYL Nair hospital, Mumbai from June 2016 to October 2017.

All of 60 women 13- 20 weeks of gestation with a valid legal indication for termination of pregnancy as per MTP act in INDIA were enrolled for study.

Inclusion criteria

Healthy women (aged between 18 and 35 years) requesting legal second trimester (13-20 weeks) termination of pregnancy were recruited in this study.

Exclusion criteria

Women with anaemia, suspected ectopic and molar pregnancy, pelvic infection and congenital malformation of uterus, haemorrhagic disorders and treatment with anticoagulants, history of cardiac disease, an intrauterine device in utero, nursing mothers, multiple pregnancies, contraindications to prostaglandins use (bronchial asthma, glaucoma), previous uterine surgery and caesarean section, placenta praevia were excluded.

A structured form was used to record age, previous obstetric history, the time interval between misoprostol application and foetus expulsion, the number of tablets required, side effects and patient's preferences on the route of administration. In all cases written informed consent was taken and duration of pregnancy was confirmed by history, clinical and sonological examination. Routine blood investigations were done at the initial consultation.

Selected cases were randomly divided into Group A- Sublingual (n=30) group B- Vaginal (n=30). For group A, 200 mg of Mifepristone was given, 48h later Misoprostol 200 µg was given sublingually 4hrly up to a maximum of 5 doses. Following administration of misoprostol, the vitals were monitored hourly. Analgesia was administered as required

If abortion does not occur after 5 doses, the pregnancy was terminated with vaginal misoprostol, in group A. Same procedure repeated in group B. If abortion fails to occur after 5 doses, then second course of vaginal misoprostol was given in group B. Failure of procedure was defined as failed expulsion of foetus at 48 hrs

After expulsion of the fetus, 10 units of oxytocin was administered intramuscularly into the upper thigh to facilitate placental delivery. 20 Spontaneous expulsion of the placenta within 60 minutes of abortion was awaited, if not digital exploration of the uterine cavity and blunt curettage done.

Statistical analysis

Statistical Analysis was done from the outcome. All variable were calculated by $\pm 2SD$. Collected data were analysed and statistical test was done with the help of Microsoft excel and Med Calc software. Test for the statistical significance was applied by using Chi square test and Mann-Whitney U test for analyzing the differences between the two groups ($p < 0.05$ was considered significant).

RESULTS

The mean age in sublingual group was 27.1 ± 5.59 yrs. and in the vaginal group was 27.9 ± 4.67 yrs. (TABLE- 1)

The mean gestational age was 16.77 ± 2.03 weeks and 17.49 ± 1.8 weeks respectively in the two groups, the difference was not statistically significant. 26.66% of the patients in sublingual group were nullipara while 73.34% were multiparous. 13.33% of the patients in prevaginal group were nullipara while 86.67% were multiparous. Both groups were comparable with regard to parity.

In the sublingual group the indications for termination were contraceptive failure (60%), fetal anomalies (6%), maternal (10%), social indications (6%). In the prevaginal group the indications were contraceptive failure (60%), fetal anomalies (10%) and maternal (23.3%), social indications (10%).

The mean induction abortion interval was 12.8 ± 4.38 hrs in the sublingual group while it was 11.47 ± 4.42 hrs in the prevaginal group. Although duration of abortion was less in vaginal group, the difference in duration between two groups was not statistically significant.

The overall success rate was 93.3% in the sublingual group while it was 100% in the per vaginal group.

The mean deficit in Hb% between Day 1 post aortal was 0.237 ± 0.09 % in the sublingual and 0.233 ± 0.08 % in the prevaginal group. Hb% deficit was same in both groups.

Table 1: Demographic characteristic. Values are expressed as n (%) or mean (SD).

Parameters	Sublingual group(n = 30)	Vaginal group(n=30)	P value	Odds ratio	95% CI for difference in the mean
Age (year)	27.1 (5.59)	27.9 (4.67)	0.550		-1.8620 to 3.4620
BMI(kg/m ²)	21.90 (2.38)	21.21(2.45)	0.273		-1.9383 to 0.5583
Gestational age (weeks)	16.77 (2.03)	17.49 (1.8)	0.153		-0.2715 to 1.7115
Haemoglobin level (g/dL)	11.073 (0.51)	11.076(0.46)	0.979		-0.2480 to 0.2540
Proabortion					
Previous deliveries	22 (73%)	26 (86.6%)	0.6668	0.8462	0.3955 to 1.8104

Table 2: Induction-abortion interval and success rate according to group.

Induction abortion Interval	Sublingual group (n=30)	Vaginal group (n=30)	p value
12 h	8(26.66%; 8/30)	14(46.66% 14/30)	0.11
12-24 h	20 (66.66%; 20/30)	16(53.33% 16/30)	0.29
24-36 h	2 (6.66%; 2/30)	0	0.00
Mean (h)	12.8±4.38h	11.47±4.42h	0.136
Success rate in 24h	28/30(93.33%)	30/30 (100%)	0.19

Table 3: Comparison of side effects in two groups.

Side effects	Sublingual group(n=30)	Vaginal group(n=30)	P value
Nausea	10 (33.33%)	14 (46.66%)	0.29
Vomiting	12 (40%)	9 (30%)	0.42
Diarrhoea	3 (10%)	2 (6%)	0.57
Fever	3 (10%)	1(3.33%)	0.30
Shivering	1 (3.33%)	4(13.33%)	0.16

The side effects seen in the sublingual group were nausea (33.33%), vomiting (33.33%), diarrhoea (10%), fever (10%), shivering (3.33%). The side effects in the prevaginal group were Nausea (46.6%), vomiting (30%), nausea (20%), diarrhoea (10%), fever (3.33) and shivering (13.33%). All the side effects were comparable in both groups.

Regarding acceptability, sublingual group was the more preferred route between the two groups, because of less discomfort caused to women by vaginal insertion.

DISCUSSION

Nearly all the women in our study aborted within 24h of receiving misoprostol, and the induction to abortion interval for both study groups was less than half of that noted by Tang et al. (2004).

Milani et al (2014) and Bartusevicus et al (2005) demonstrated that induction to abortion period is significantly shorter in the sublingual group and this group needed lower dose of drug for abortion period.^{21,22} These results were contrary to our present study as we found less induction-abortion interval in vaginal group.

El-Refaey et al (1995) and Ashok and Templeton (1999) have shown that using a combination of vaginal and oral misoprostol, upto 97% of women aborted within 15 h of administration the induction-abortion interval was also shorter when compared with the regimen from our study.^{23,24}

In Most published regimens there is an increase in abortion duration with an increase in gestation.^{25,26} Although we found association of gestational age with induction-abortion interval, but the results were not uniform for gestational age groups. Earlier gestation has not been consistently been associated with a shorter abortion interval in the present study.

The vaginal group required less misoprostol to effect abortion compared with the sublingual group (<600 micrograms compared with >600 micrograms, vaginal compared with sublingual, respectively).²³

A study on the pharmacokinetics of the sublingual, vaginal and oral route might explain the higher prevalence of side effects reported with the sublingual route of misoprostol administration.^{27,28} Our study had similar side effects in either group, contrary to study by Tang et al, 2002b.²⁹

Two patients in the sublingual group had surgical evacuation for incomplete abortion. None of the patients aborted with mifepristone alone. 96.66% (58/60) aborted within 24h, while two in the sublingual group had an induction to abortion interval of 24-36h.

Tang et al, (2004) believed that sublingual administration was acceptable to more women. We found similar results in our study.^{30,31}

Single or double blinded placebo controlled study would have been more robust study but as we could not get placebo or similar vitamin tablet, it was not possible to conduct placebo controlled study.

CONCLUSION

Vaginal misoprostol administered after oral mifepristone priming in second -trimester medical abortion is associated with a shorter time to pregnancy termination compared with a sublingual regimen. There is no significant difference in efficacy and complications between the two routes, although a larger cohort is required to get more dependable result. Sublingual regimen should be offered to those women who consider vaginal administration unacceptable.

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Conflict of interest: None declared

Ethical approval: The study was approved by the Institutional Ethics Committee

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