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ORIGINAL ARTICLE

Prospective Comparative Study of Oral Versus Vaginal Misoprostol for Second-Trimester Termination of Pregnancy

Suyash S. Bhandekar[1] · Anahita R. Chauhan[1] · Arun Ambadkar[2,3]

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About the Author

Dr. Suyash S. Bhandekar completed his MS in Obstetrics and Gynecology from Seth G.S. Medical College and K.E.M. Hospital in Mumbai, India. During his residency, he presented papers at local and national conferences and won prizes for the same. He is interested in high-risk pregnancy and endoscopy and is currently busy setting up his practice in Mumbai.

Suyash S. Bhandekar is an Ex-Registrar in the Department of Obstetrics and Gynecology, Seth G.S. Medical College and K.E.M. Hospital, Mumbai, Maharashtra, India; Anahita R. Chauhan is former Professor & Head of Unit in the Department of Obstetrics and Gynecology, Seth G.S. Medical College and K.E.M. Hospital, Mumbai, Maharashtra, India; Arun Ambadkar is an Assistant Professor in the Department of Obstetrics and Gynecology, B.J. Medical College, Pune, and Ex-Registrar, Seth G.S. Medical College and K.E.M. Hospital, Mumbai, Maharashtra, India.

✉ Anahita R. Chauhan
anahitachauhan@gmail.com

[1] Department of Obstetrics and Gynecology, Seth G.S. Medical College and K.E.M. Hospital, Mumbai, Maharashtra, India

[2] Department of Obstetrics and Gynecology, B.J. Medical College, Pune, India

[3] Seth G.S. Medical College and K.E.M. Hospital, Mumbai, Maharashtra, India

Abstract

Background Various medical methods for second-trimester medical termination of pregnancy (MTP) exist. Misoprostol alone has been used with myriad variations in route and dosage. Comparison between oral and vaginal routes of misoprostol forms the basis of this study.

Methods This was a prospective comparative study of misoprostol for second-trimester (14–20 weeks) MTP, comparing oral versus vaginal routes. Sixty patients were randomly allotted to two groups; 30 received oral misoprostol 400 μg 4 h up to a maximum of five doses (2000 μg), and 30 received vaginal misoprostol in the same dose and duration. In both groups, oxytocin infusion was started if abortion did not occur. Efficacy of oral versus vaginal misoprostol, induction–abortion interval (AI) and need for surgical intervention were analyzed.

Results Both groups were well matched in terms of age, parity, previous LSCS, mean gestational age and indication for MTP. Overall mean induction–abortion interval was 19.59 h (21.66 vs. 18.57 h, oral vs. vaginal, respectively), with vaginal group taking lesser time (p 0.09). Sixty percentage in oral group required five doses, while 70% in vaginal group required 3–4 doses of misoprostol (p 0.010). 23.7 versus 6.7% in oral versus vaginal group required check curettage (p 0.038). There were no major complications, and there was only one failure in oral group.
Conclusions Though both oral and vaginal misoprostol are safe, vaginal route appears to be more efficacious for second-trimester MTP.

Keywords Misoprostol · Abortion interval · Second-trimester MTP · Curettage

Introduction

Worldwide, about a million abortions are estimated to take place annually and approximately half may be unsafe. Though the Medical Termination of Pregnancy (MTP) Act has liberalized indications for which abortion is legal in India and incidence of abortion has declined due to improved access to contraception, the availability of ultrasonographic diagnosis of fetal abnormalities tends to increase the incidence of abortion in the second trimester. Though second-trimester MTPs account for 20% of all MTPs, they are responsible for two-thirds of abortion-related complications and a threefold higher morbidity. Because of the potential for bleeding and complications, it is advisable that second-trimester terminations take place in a health-care facility where blood transfusion and emergency surgery are available [1].

In this context, finding the optimum method for termination of second-trimester pregnancy is critical. Ethacridine lactate which was used previously is not available; numerous studies have elucidated the safety and efficacy of mifepristone–misoprostol, or misoprostol alone, in various dose combinations. Misoprostol, a synthetic prostaglandin analogue with good uterotonic potential, is used for cervical ripening and induction of abortion in different doses and by different routes; a comparison between oral and vaginal routes forms the basis of this study.

Methods

This was a prospective comparative study carried out at a tertiary care hospital, initiated after Institutional Ethics Committee approval. Sixty cases requiring second-trimester MTP for any indication and fulfilling inclusion criteria were selected. Aims of the study were to determine:

1. Efficacy of oral versus vaginal misoprostol for second-trimester abortion.
2. Completeness of the procedure by both routes.
3. Induction–abortion interval (AI) by both routes.
4. Need of augmentation with oxytocin and need for surgical intervention.

All patients irrespective of age and marital status, with 14–20 weeks of gestation with single live intrauterine pregnancy seeking abortion services for valid indication under the MTP Act, were included. Patients with multiple pregnancies, intrauterine device in situ, intrauterine fetal death, hemoglobin < 8.5 gm/dl, history of major medical illnesses or allergic issues, and those not willing to give consent were excluded. Detailed history, physical examination and confirmation of pregnancy by clinical examination and ultrasonography, and hemoglobin and blood group were estimated in all cases. Indication for MTP as per MTP Act was confirmed, and consent for MTP was taken in standard MTP form; if patient was < 18 years consent was taken from parent or guardian, and standard medicolegal procedures were followed. Study consent was taken separately from all patients; minors gave assent, and their guardians gave consent.

Thirty patients each were assigned to either oral or vaginal group as per random number table. Both groups received 400 μg misoprostol 4 h for a maximum of five doses. Oral group swallowed the tablets with water; in the vaginal group, misoprostol 400 μg pre-moistened with normal saline was inserted vaginally by the obstetrician under aseptic precautions. Patients in both groups were monitored 4 h prior to each subsequent dose to determine the need for further doses. Maximum of five doses (2000 μg) were used in both groups.

Study endpoints were complete abortion and induction–abortion interval (AI). "Complete abortion" was defined as complete expulsion of abortus en sac/abortion along with placenta with no products of conception retained in the uterus on bimanual examination. Surgical intervention (check curettage) was indicated in case of incomplete abortion. If patient did not abort after five doses, 4 h after the last dose, 20 units of oxytocin were started in 500 ml of Ringer's lactate till abortion occurred. In case patient failed to abort despite oxytocin after 36 h of induction, patient was labeled as "failure" and alternative methods were used for abortion. During the abortion process, suitable analgesics were administered as per need to both groups, to relieve pain. "Efficacy" was analyzed on the basis of complete abortion, total number of doses of misoprostol required, need for augmentation with oxytocin, need for check curettage in case of incomplete abortion and evidence of other complications between the two routes of administration studied. Patients were monitored for 24 h

Table 1 Maternal characteristics

Maternal characteristics	Oral group $n = 30$	Vaginal group $n = 30$
Age distribution		
16–18	02 (6.66)	0
18–20	03 (10.00)	0
21–25	06 (20.00)	10 (33.33)
26–30	15 (50.00)	16 (53.33)
31–35	03 (10.00)	04 (13.33)
> 36	1 (3.33)	0
Mean age	26.6	26.9
Parity		
Primi	12 (40)	05 (16.66)
Para 1	08 (26.66)	12 (40.00)
Para 2	07 (23.33)	10 (33.33)
Para 3	03 (10.00)	03 (10.00)
Previous abortions		
1	8 (26.66)	6 (20.00)
2	2 (6.66)	2 (6.66)
3	00	3 (10)
4	0	2 (6.66)
Previous LSCS		
Previous 1 LSCS	2 (6%)	4 (11.33%)
Previous 2 LSCS	1 (3%)	0
Gestation age (by USG)		
14 weeks 1 day–16 weeks	14 (46.66)	07 (23.33)
16 weeks 1 day–18 weeks	11 (36.66)	15 (50.00)
18 weeks 1 day–20 weeks	05 (16.66)	08 (26.66)

post-abortion for complications after which they were discharged. Comparison between two groups was done with multiple qualitative and quantitative tests—Chi-square test, Pearson's Chi-square test and Fisher's exact test.

Results

A total of 60 patients (30 in each group) were studied. Maternal characteristics are shown in Table 1. Majority of cases were seen between 26 and 30 years in both groups; mean age was 26.67 and 26.9 years in oral and vaginal group, respectively. Forty percentage of patients in oral group were primigravidae; only 16% in vaginal group were primigravidae. Majority of patients did not have a prior abortion. There were six cases of previous 1 LSCS, two in oral and four in vaginal group, as well as one case of previous 2 LSCS in oral group. The mean gestational age in both groups was 16 weeks 5 days. 46.66% of cases in oral group were between 14 and 16 weeks of gestation, while 50% of cases in vaginal group were between 16 and 18 weeks. There was no statistical difference noted in any of these parameters (age, parity, previous abortion or LSCS, mean gestational age) between the two groups.

Failure of contraception was the major indication for MTP in both groups (50% each), followed by congenital malformations (23.3 and 26.7% in oral and vaginal group, respectively) and social reasons mainly unmarried status (20 and 3.3% cases in oral and vaginal group, respectively). The mean hemoglobin was 10.51 g%, and no patients required blood transfusion.

In both groups, approximately a third of patients aborted within 12–16 h. However, the main difference was that additionally 40% cases in the vaginal group aborted at 17–20 h of induction, as compared to only 10% in oral group; cumulatively, 93.3 and 76.6% in vaginal and oral group, respectively, aborted within 24 h. The overall mean AI was 19.59 h, with 21.66 and 18.57 h in the oral and vaginal groups, respectively; this difference was statistically significant (p value 0.09), with vaginal group taking lesser time. Majority of the cases in oral group (60%) required five doses of misoprostol, while vaginal group cases (70%) required only 3–4 doses of misoprostol. The overall mean number of doses was 4.12, with 4.3 and 3.93 doses each in the oral and vaginal groups, respectively; this

Table 2 Induction–abortion interval and misoprostol requirement

Induction–abortion interval (hours)	Oral group ($n = 30$)	Vaginal group ($n = 30$)
12–16	09 (30%)	10 (33.3%)
17–20	03 (10%)	12 (40%)
21–24	11 (36%)	06 (20%)
25–28	06 (20%)	02 (6.66%)
>28	01 (3%)	00
Number of doses of misoprostol	Oral group ($n = 30$)	Vaginal group ($n = 30$)
3	9 (30.0%)	10 (33.3%)
4	3 (10%)	12 (40.0%)
5	18 (60%)	8 (26.7%)

Unpaired t test; p value 0.09 (significant)

Pearson's Chi-square test; p value 0.010 (significant)

difference was also statistically significant (p value 0.010). Mean dose of misoprostol required overall for our study was 1648 ± 696 µg; requirement of oral dose was higher (1720 ± 736 µg) as compared to vaginal dose (1572 ± 696 µg). Oxytocin was required in 34.5% cases in oral group, but only 10% in vaginal group; this difference was statistically significant (p value 0.023). Induction time and doses required are outlined in Table 2.

As shown in Fig. 1, overall efficacy of misoprostol in achieving complete abortion was 83.3% (73.3 and 93.3% in oral and vaginal group, respectively), with 15% incomplete abortion and 1.7% failure. All cases of incomplete abortion needed oxytocin, and 23.7% of cases in oral group compared to only 6.7% of vaginal group required check curettage; this difference was statistically significant (p value 0.038). Only one case (1.7%) in oral group, second gravida with no high risk factor, failed to abort despite maximal doses of misoprostol and oxytocin for total of 36 h and was labeled as failure; she subsequently required hysterotomy. Minor side effects like nausea, fever, shivering, vomiting and diarrhea were seen in three and 4% of oral and vaginal group, respectively.

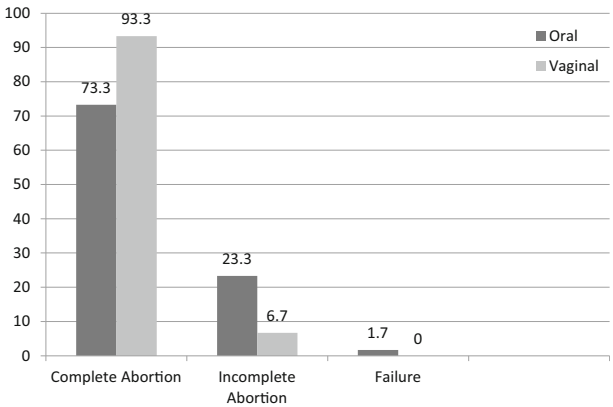

Fig. 1 Efficacy of misoprostol by oral and vaginal routes

Discussion

Unsupervised and unsafe abortions continue to be a major cause of maternal morbidity worldwide [2]. In our country, the liberal MTP Act has unfortunately been misused for second-trimester termination of pregnancy following sex determination and has been intricately (and wrongly) related to the PC-PNDT Act. Due to legal implications and close monitoring by authorities, many practitioners may even refuse to perform second-trimester MTP, even when indicated [3]. Elsewhere in the world, second-trimester abortion has become a topic of feminist activism, enhancing the medical importance of this topic [4].

The introduction and availability of drugs which can cause "mini-labor" have revolutionized the performance of termination of pregnancy, and the emphasis is less on surgical techniques and more on administration of drugs like mifepristone and misoprostol. The rationale of not priming with mifepristone prior to misoprostol is based on evidence from studies that have evaluated the use of misoprostol alone with good success rate for second-trimester MTP in various routes, dosages and schedules. Added advantages of reduced hospital stay, low cost and higher bed turnover rate make misoprostol alone an attractive option especially in low resource settings. In this context, the present study was designed to compare oral and vaginal routes for second-trimester MTP.

The average age of patients in our study was 26 years. Lower maternal age has been specifically described as a factor which reduces the likelihood of a patient seeking abortion services early. We had five patients (12%) who

were < 20 years of age, with two being below 18 years [5]. Majority of our patients were primigravidae. Though increased parity may reduce time for expulsion of fetus in MTP, we did not find this in our study [6].

A similar study by Bangal et al. analyzed 148 women seeking MTP over a 3-year period. They used an initial dose of 400 μg of misoprostol by vaginal route, followed by 200 μg every 4 h till maximum of six doses. Overall success rate was 92%; average induction–abortion interval was 14 h, and average dose required for complete abortion was 1200 μg. The overall success rate for vaginal group in the present study was comparable at 93%, though the average dose (1572 μg) and induction–abortion interval were slightly higher at 18.57 h [7]. Tanha et al. compared the efficacy of two routes of administration of misoprostol (sublingual and vaginal) in 134 women desiring medical termination of second-trimester pregnancies for various indications. They found no differences between the vaginal and sublingual groups in terms of efficacy. The mean dose of misoprostol in both groups was around 1340 μg [8].

Ting compared two dose variations, 200 or 400 μg of priming vaginal misoprostol, followed by 200 μg of misoprostol orally at 6 h intervals in 101 patients and found no significant difference in the abortion time (median 16.3 h) in groups that received different doses of priming vaginal misoprostol [9]. Ting reported just one failed case in their study, similar to the present study. With the existing methods and dosage patterns of misoprostol, failure is extremely uncommon.

Rahimi-Sharbaf compared the effectiveness of misoprostol via vaginal or sublingual administration versus a combined vaginal and sublingual route in the termination of 13–24 week pregnancies in 195 women. 400 μg misoprostol was inserted in the posterior fornix every 4 h for 48 h in the vaginal group; the same dosage schedule was given sublingually in the sublingual group. In the combination group, initially 400 μg misoprostol was inserted in the posterior fornix, followed by 400 μg sublingually every 4 h for 48 h. The overall success rate did not significantly differ among the three groups, though the mean duration of abortion (655 ± 46 min) and number of tablets required were least in the sublingual group, and overall patient satisfaction was also highest in this group [10]. While the success rate of vaginal with sublingual routes of 400 μg misoprostol was similar, Milani et al. [11] found that the abortion interval was shorter with the sublingual route and the patients preferred the sublingual route over the vaginal route. In Indian setting, Garg et al. [12] have studied the sublingual route and observed better outcomes over vaginal administration, not only in second trimester, but also in first-trimester abortions.

The mean induction abortion duration in the vaginal group in our study was 18.57 h. This is in contrast to the study by Desai et al. [13] who reported a shorter induction–abortion interval 7.9 h, though the route described by them was a less common intracervical route. In a similar study by Nautiyal et al., 400 μg misoprostol every 4 h for a maximum of four doses was used sublingually, vaginally and orally in 150 women between 12 and 20 weeks gestation. Induction–abortion interval in sublingual (9.8 ± 3.6 h) and vaginal (10.6 ± 2.9 h) groups was less than that in oral group (14.3 ± 3.3 h), but there were no significant differences in failure rate and need for surgical intervention. Oral group was best tolerated by patients [14].

In our study, the same dosage of misoprostol (400 μg) was used for patients with scarred uteri. However, Pluchon and Winer [15] recommend that caution be exercised when misoprostol is used for scarred uteri, with a reduction in dosage. Clouqueur et al. [16] has recommended a dose of 100 μg in patients with previous cesarean scar.

None of our patients had fever. Rahimi-Sharbaf et al. [10] had highlighted that use of combination (oral followed by vaginal) can result in a higher chance of fever. Nautiyal had observed that the chance of fever was higher with the vaginal group than the oral group. Hyperpyrexia is a problem even when administered in smaller doses for the management of first-trimester abortions [14]. Sajjan et al. have reported complete avulsion of cervix from the lower part of the uterus, which is a rare complication with intravaginal misoprostol. Though there were no local complications in the present study, due diligence should be exercised by clinicians [17].

When used by vaginal route, pre-moistened misoprostol using saline is most popular, as in our study also. However, Bhattacharjee compared vaginal administration of acetic acid-moistened misoprostol tablets with those of dry tablets and concluded that moistening misoprostol tablets with acetic acid did not have any benefit [18]. Huang et al. have studied a newer dosing pattern which is 800 μg initial loading dose followed by sequential vaginal and sublingual misoprostol dosages. They found that higher dosage per administration resulted in an equally efficacious dosing pattern and reduced the number of pelvic examinations in the aborting woman [19].

A recent 2017 publication by FIGO on their updated recommendations for misoprostol use alone recommends a dose of 400 μg misoprostol (sublingual, buccal or vaginal) every 3 h till expulsion (no maximum doses suggested), for termination of pregnancy between 13 and 26 weeks. They also concluded that misoprostol can be used for women with previous cesarean or other transmural uterine scars in the second trimester, as evidence from studies show that the risk of uterine rupture is < 0.3%, and there are no significant differences in outcomes for women with previous CS [20]. Our study and findings are in keeping with these guidelines. To conclude, 400 μg misoprostol 4 h by

both oral and vaginal routes are safe for second-trimester MTP. Vaginal route appears to be more efficacious with an overall induction–abortion interval of about 19 h, with less need for oxytocin and surgical intervention.

Compliance with Ethical Standards

Conflict of interest The authors declare that they have no conflict of interest.

Ethical Approval All procedures followed were in accordance with the ethical standards of the Institutional Ethics Committee and with the Helsinki Declaration of 1975, as revised in 2008 (5).

Informed Consent Informed consent was obtained from all patients for being included in the study.

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