

RESEARCH ARTICLE

Effectiveness of vaginal misoprostol after oral mifepristone in second trimester abortion

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ABSTRACT

Background: Of all abortions done globally, 10-15% happen in second trimester, with few procedures causing complications leading to maternal morbidity. This prospective study examined the efficiency and safety of vaginal misoprostol after oral mifepristone in second trimester abortion. **Methodology:** This study was conducted at tertiary care hospital from Oct 2020 to Sept 2021. Sixty patients were enrolled, 200 mg oral mifepristone was followed after 36 hrs by 800 mcg vaginal misoprostol; association between induction abortion interval, side effect of drugs, blood loss and completeness of the process was evaluated. **Results:** Total 60 patients with mean age 29.88 ± 4.17 years, and eligible for termination under MTP act 1971 with LMP and ultrasound confirmed gestation between 12-20 weeks and singleton pregnancy were enrolled. 37 women were multiparous. Total 83.3% had complete evacuation. Mean induction to abortion interval was 7.34 ± 4.59 hours, range 1 hour 15 minutes to 21 hours. The mean induction abortion interval in woman < 16 weeks of gestation was 6.35 hours compared to 8.09 hours in woman ≥ 16 weeks of gestation, and 8.37 hours in primigravida compared to 6.7 hours in multiparous. There was no association between parity, period of gestation and induction abortion interval ($p > 0.05$). The mean drop in hemoglobin after the procedure was 0.81 grams. **Conclusion:** The combination of oral mifepristone followed by vaginal misoprostol is safe, effective regimen for MTP in second trimester with few side effects, less blood loss and short duration of hospital stay.

Keywords: Placenta, misoprostol, mifepristone, termination of pregnancy.

Of the total 42 million abortions globally, 10–15% of termination of pregnancies take place in the second trimester¹. As compared to first trimester, second trimester abortions disproportionately contribute to major abortion-related complications, maternal morbidity and mortality especially in low resource countries where access to safe second trimester abortion is limited^{1, 2}. Intra or extra amniotic administration of ethacridine lactate is still used in several developing countries to terminate late second trimester pregnancies, even though it is listed as outdated by WHO³. The drawbacks include longer duration of labor, hospitalization for several days and then need for curettage.

As a safe alternative to surgical termination of pregnancy, prostaglandins or their analogues have been used frequently for medical abortion with good success rates and

few complications⁴. Patil SB et al compared combination of mifepristone and misoprostol regime for second trimester termination with a single drug misoprostol on 60 women and concluded that mifepristone followed by misoprostol regimen was more effective, had shorter IAI, lesser failure rate and fewer side effects compared to misoprostol alone⁵. The use of mifepristone (anti antiprogesterone), and misoprostol (a synthetic analogue of naturally occurring prostaglandin E1) together has increased the safety and efficiency of second trimester medical abortion procedure significantly, by softening the cervix, increasing the sensitivity to prostaglandins thus converting a quiet pregnant uterus into an organ of spontaneous activity, and reduction in the induction-to-abortion interval by almost 50%⁶. The combination reduces the total dose of misoprostol required,

Received: 20th December 2022, Peer review completed: 24th July 2023, Accepted: 15th August 2023.

Sood S, Kaur N, Sood I. Effectiveness of vaginal misoprostol after oral mifepristone in second trimester abortion. The New Indian Journal of OBGYN. 2025; 11(2): 217 - 21.

thereby lessening associated side effects and morbidity. The combination of oral mifepristone 200 mg followed by vaginally or orally administered misoprostol provides a noninvasive and effective regimen for first and mid-trimester termination of pregnancy⁶.

In this context, the present prospective study was conducted to assess effectiveness and safety of vaginal misoprostol after oral mifepristone in second trimester termination of pregnancy on induction abortion interval, side effects of drugs, complications of the procedure, blood loss and completeness of the process with this regimen.

Materials and methods

This was a prospective observational study, conducted at tertiary care teaching hospital, in the department of Obstetrics and Gynecology from October 2020 to September 2021, over a period of one year. Sixty indoor obstetric patients eligible for termination under MTP act 1971 with LMP and ultrasound confirmed gestation between 12-20 weeks and singleton pregnancy in the age group of 18-45 years were enrolled after appropriate obstetrician consultation and after obtaining informed consent. Pregnant women below 12 weeks and above 20 weeks gestation, history of allergy or intolerance to the mifepristone, misoprostol or other prostaglandins, Hb below 9, on anticoagulant treatment, and co-existing medical disorders (cardiac disease, adrenal failure, renal failure, on long term steroid treatment, pregestational diabetes, hypertension) were excluded. Prior approval was obtained from the ethical review committee of institute.

A detailed menstrual, marital, obstetric, past, family and drug allergy history was taken along with physical examination. Lab investigations including hemoglobin, blood grouping and typing were done. All patients were given 200mg of oral mifepristone, followed by vaginal insertion of 800 mcg of misoprostol 36 hours later. Misoprostol 400 mcg was repeated vaginally every 3 hourly to a maximum of 4 doses in 24 hours. Induction abortion interval was calculated from the time between first dose of misoprostol to the complete expulsion of the fetus along with products of conception (POC). Patients were observed for complications like heavy bleeding, retained products of conception (RPOC), uterine rupture and failure of the procedure described as unable to abort within 24 hours of the first dose of misoprostol. Blood loss was estimated by difference in the hemoglobin before and after the procedure. Anti-D injection was given to women with Rh-ve negative blood group after expulsion of the fetus. Follow up was done

after 2 weeks of discharge, when vaginal bleeding pattern was asked, and sonography was done to check for RPOC. If significant RPOC were found and patient had significant bleeding, dilatation and curettage (D&C) was done.

The findings were recorded on a predefined performa, and data were compiled in a Microsoft Excel sheet and subsequently statistically analyzed on GraphPad Prism 4.0 for Windows. Continuous variables were analyzed using the Mann–Whitney U test, and Chi-square tests were used for the analysis of noncontinuous variables. A p value of < 0.05 was considered significant.

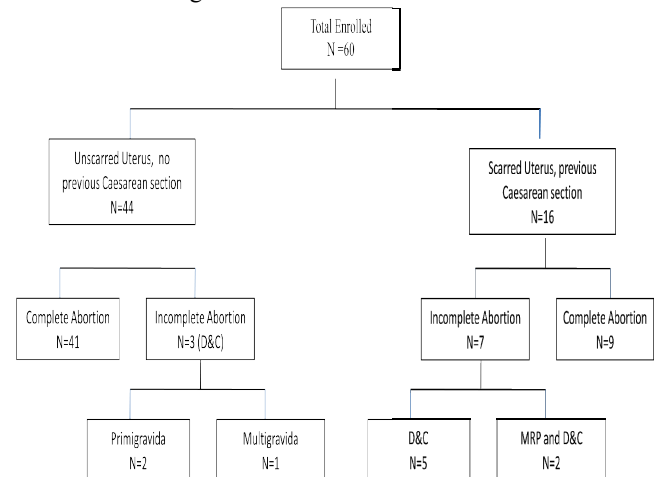


Figure 1: Flow chart depicting enrollment and outcome details

Results

Demographic details are mentioned as in table 1, enrollment details depicted in figure 1. Total 60 patients, with mean age 29.88 ± 4.17 years (range of 18-40) were enrolled. Majority of patients were married for 1-5 years (43.3%). 2 patients had history of second-degree consanguineous marriage. 37 women were multiparous. 16 patients had history of previous caesarean. Total of 50 patients (83.3%) had complete evacuation, among them 41 patients were with unscarred uterus; while 9 patients had scarred uterus due to previous caesarean section (CS). Out of 10 (16.7%) patients with incomplete evacuation, 7 patients had CS with scarred uterus. Of these 5 patients had significant retained products of conception (RPOC) for which D&C was done under anesthesia and 2 patients had retained placenta for which manual removal of placenta was done under anesthesia. Out of 44 patients without scarred uterus, only 3 patients had incomplete abortion with significant RPOC requiring D&C. Blood loss was calculated by the difference between the hemoglobin before and after the procedure. The mean hemoglobin before the procedure was 12.12 gram%,

which fell to 11.32 gram% after the procedure, with the mean drop in hemoglobin being 0.81gram%.

Table 1: Demographic details

Age group in years	No (%)
18-25	8(13.3)
26-30	21(35)
31-35	26(43.3)
36-40	5(8.3)
Years of marriage	
<1	4(6.7)
1-5	26(43.3)
6-10	25(41.7)
>10	5(8.3)
Parity	
Multigravida	37(61.7)
Primigravida	23(38.3)
Previous LSCS	
No	44(73.3)
Yes	16(26.7)
Previous abortion	
Nil	38(63.3)
1-2 Abortions	18(30)
≥ 3 Abortions	4(6.7)
Indication for abortion	
Foetal anomaly	48(80)
Failure of contraception	11(18.3)
Maternal indications	1(1.7)
Induction to abortion interval (IAI)	No. (%)
<5 hours	21(35)
5-10 hours	27(45)
>10 hours	12(20)
Adverse effects of medicine	
Abdomen Pain	23(38.3)
Vomiting	4(6.7)
Chills	3(5)
Fever	3(5)
Breathlessness	1(1.7)
Loose stools	1(1.7)
Nausea	1(1.7)
NIL	24(40)
Hemoglobin fall	
≤ 0.5 gm	13(21.7)
0.5-1 gm	30(50)
≥ 1 gm	17(28.3)
Incomplete abortion requiring evacuation	
Dilation & Curettage for retained products of conception under anesthesia	8(13.33)
Manual removal of placenta under anesthesia	2(3.3)

Mean induction to abortion interval was 7.34 ± 4.59 hrs ranging from 1 hour 15 minutes to 21 hours. (table 1). The mean induction abortion interval for primigravida was 8.38 hours in comparison to 6.7 hours in multigravida. The mean

Table 2: Induction abortion interval in relation to parity, gestation

Categories	<5 hours	5-10 hours	> 10 hours	Total	P Value
Primigravida	7 (30.4%)	10 (43.5%)	6 (26.1%)	23 (38.3%)	0.7987
Multigravida	14 (37.8%)	17 (45.90%)	6 (16.2%)	37 (61.7%)	
< 16 weeks	10 (38.5%)	14 (53.8%)	2 (7.7%)	26 (43.3%)	0.7987
≥ 16 weeks	11(32.4%)	13 (38.2%)	10 (29.4%)	34 (56.7%)	

induction abortion interval in woman < 16 weeks of gestation was 6.35 hours compared to 8.09 hours in woman

≥ 16 weeks of gestation. There was no association between parity, period of gestation and induction abortion interval (p > 0.05) (table 2).

Discussion

Second trimester termination of pregnancy is a difficult situation owing to the prolonged time required for the abortion process and associated complications. Compared to earlier days, where surgical evacuation used to be the standard method, in the last 20 years medical methods with prostaglandins alone or in combination with antiprogesterone mifepristone are used. Misoprostol (PGE1) has proven its efficacy as an efficient abortifacient in second trimester termination of pregnancy; it is being successfully used through all routes sublingual, oral and vaginal⁷.

In the present study, effectiveness and safety of vaginal misoprostol 800mcg 36 hours after oral mifepristone 200 mg was studied in second trimester of pregnancy abortions. Maximum effect with combination of mifepristone and misoprostol is seen after 36- 48 hours interval³. According to Chai et al, the regimen using 36 hours dosing interval between the two is more effective in the second trimester termination of pregnancy⁸. The side effects of this regimen in our study were comparable to Singh et al⁹. None had major complication like rupture uterus, excessive blood loss requiring transfusion, cervical tear or infections. Success rate with our regimen was 83.3 % for complete evacuation with failure rate of 16.7% comprising 10 women requiring surgical intervention. Pereira et al study on 333 women who underwent second trimester termination vaginal misoprostol also did not observe any major complications¹⁰. We observed that the most common complication was of RPOC which required surgical intervention in form of D&C in 10 (16.7%) women and manual removal of placenta in 2 women (3.3%). The procedure was complete in 50(83.33%) of study women with this regimen.

Mean induction to abortion interval was 7.34 hours, comparable to 11.26 in Kaur et al¹¹ and 6.5 hours in Ashok et al¹². In this study induction abortion interval in relation to parity and gravida showed shorter but non-significant mean induction abortion interval in multiparous compared to

primigravidae. According to Goh et al¹³ in retrospective analysis on 386 women, the median induction to abortion

interval was 6.7 hours and multiparous women took significantly shorter time to abort (6 hours compared to 7.6 hours in nulliparous women ($p < 0.0001$))

Ashok et al¹² studied 500 pregnant women between 13-21 weeks of gestation undergoing abortion with mifepristone and misoprostol in Scottish NHS hospital and showed that the median doses of misoprostol required to induce abortion was significantly higher among gestation between 17-21 weeks compared to 13-16 weeks ($p = 0.0001$). But we did not get significant time or dose difference.

Multigravida and pregnant women with early gestation (<16 weeks of gestation) had a shorter induction abortion interval compared to nulligravidae and women with late gestation. The statistical significance was not proved due to small sample size.

In our study there was increased proportion of incomplete abortion in women with scarred uterus due to previous CS compared to unscarred uterus. But due to small sample size statistical significance could not be documented.

The mean difference in the hemoglobin fall in our study was 0.8g/dl. Agarwal et al had mean fall in hemoglobin of 0.72 g/dl in 40 women too¹⁴. We evaluated the blood loss after the expulsion by measuring hemoglobin before and after procedure. Most of other studies used quantitative measurement of blood losses¹⁵. Thus, a comparative analysis was not possible with many studies.

In our study there were 16 (26.7%) women with history of previous caesarean section; among them 9 had complete abortion, 2 required manual removal of placenta and 5 required dilatation and curettage. None of them had complications like rupture uterus. Bhattacharya et al studied the safety and efficacy of misoprostol for induced abortion during mid-trimester in women who had a prior caesarean section¹⁶ and did not find any case of scar rupture or dehiscence. This showed that medical termination of pregnancy can be used in women with scarred uterus.

Conclusion

The combination of oral mifepristone 200 mg followed by vaginally administered misoprostol is a safe, effective and noninvasive regimen termination of pregnancy between 12 and 20 weeks' gestation with short induction abortion interval, few side effects, less blood loss and short duration of hospital stay. It is an effective and safe method for second trimester abortion with high success rate. The combination of mifepristone and misoprostol can be safely used for midtrimester abortion in women with previous scarred uterus under strict monitoring. Routine surgical evacuation of

uterus after a midtrimester abortion to be performed only if excessive or continuous bleeding present and or the sonography scan showing significant retained products of conception on follows up. This regime will reduce the unnecessary anesthesia risk, cost and hospital stay of the patients.

Conflict of interest: None. **Disclaimer:** Nil.

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