



COMPARISON BETWEEN DIFFERENT ROUTES OF MISOPROSTOL IN THE MANAGEMENT OF FIRST TRIMESTER MISSED ABORTION

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ABSTRACT **Aim:** The aim of the present study is to compare between sublingual administration of misoprostol and vaginal administration in the management of missed abortion. **Materials and Methods:** It was a randomised controlled study conducted in Department of Obstetrics & Gynaecology, SMS Medical College, Jaipur on 240 patients diagnosed as missed abortion by ultrasonographic examination. Cases were divided into two groups : Group-A - tab misoprostol 400 g sublingually every 3 hrs for maximum of 4 doses, Group-B - tab misoprostol 400 g vaginally every 3 hrs for maximum of 4 doses. Patients of the two groups were observed for the induction-abortion interval, amount of vaginal bleeding, number of doses required, presence of RPOC, need for evacuation and side-effects. **Result:** During the follow-up of our cases we found that sublingual route is more effective than vaginal route in the management of missed abortion. The difference between the two groups in percentage of conceptus expulsion was statistically significant, 78.33% in the sublingual group and 60% in the vaginal group. Compared with vaginal group, those women in sublingual group experienced more complications including nausea and vomiting (20% v/s 5%) and diarrhoea (16.67% v/s 5%). IAI between two group was also significant, 13.78±2.20 in vaginal group versus 11.01±2.10 in sublingual group. Mean dose required in Group-A was 1084 g and 1288 g in Group-B **Conclusion:** Sublingual administration of misoprostol is more effective than its vaginal administration in missed abortion management. Side effect of misoprostol as nausea, vomiting, diarrhoea is more common with sublingual administration in comparison with its vaginal administration.

KEYWORDS : Misoprostol, sublingual

INTRODUCTION

Missed abortion is defined as death of conceptus without expulsion of its contents with closed cervix before fetal viability. Abortion occurs in approximately 10–20 % of all pregnancies. The risk of spontaneous abortion increases with old maternal age, high gravidity, and increased paternal age.¹ Successful pregnancy is dependent on the integration of complex genetic, hormonal, immunologic and cellular events, and must involve complete cooperation during the conception, implantation and evolution of the embryo.²

Management of missed abortion includes the following: Surgical evacuation and Medical evacuation³. Surgical procedures to terminate pregnancy include dilatation and curettage, aspiration and evacuation. Medical management of first trimester abortions have significant economic advantages over traditional surgical management^{4,5}.

Missed abortion is usually associated with bulky pregnancy products and its adherence to the uterine wall and closed cervix; that is why, surgical management may be complicated by incomplete evacuation, uterine perforation, and cervical trauma.⁶

However, the costs of surgery and hospitalization, as well as the complications associated with surgery and anaesthesia are a major unresolved concern. Besides infection and bleeding, decreased fertility caused by intrauterine adhesions may be unacceptable for women with missed abortion, who have not yet fulfilled their motherhood desires.⁷

Misoprostol is a synthetic prostaglandin E1 (PGE1) analog that is used for gastritis and gastric ulcers' treatment, to induce labor, and as an abortifacient. Absorption of misoprostolic acid is rapid in reaching peak plasma concentration within 15–30 min and has a plasma half-life of 13–40 min. It can be used as oral, sublingual, buccal (between the cheeks and the gums), vaginal, and rectal routes.⁶

However several problems have been identified with vaginal misoprostol like inconsistent absorption and incomplete absorption in addition to women finding vaginal administration uncomfortable.⁸⁻¹⁰ Misoprostol given vaginally though took longer for onset and had a lower peak (peak concentration after 60 minutes it had a more sustained effect as compared to oral misoprostol). Subsequently a new route of giving misoprostol by sublingual administration has been developed.¹¹ The sublingual mucosa, being very vascular, serves the

purpose of better absorption. Sublingual application also avoids the first pass effect through the liver.

This study was undertaken to compare the efficacy of 400 µg sublingual misoprostol with 400 µg of vaginal misoprostol, in repeated doses, for medical management of missed miscarriage.

MATERIAL AND METHODS

STUDY TYPE - Randomised control study.

STUDY DESIGN - Prospective study

PLACE OF STUDY- Department of Obstetrics & Gynaecology, SMS Medical College, Jaipur.

DURATION OF STUDY– From May 2019 to July 2020 and two months for data analysis and data compilation.

Sample Size

Sample size of 106 patients in each group were required as sample size at 80% study power and -error of 0.05 assuming 70% & 51.25% successful outcome in sublingual and vaginal misoprostol group as per results of seed article {Comparison between sublingual and vaginal administration of misoprostol in management of missed abortion. Sokkary HHAH El. The Journal of Obstetrics and Gynaecology of India. Sept-Oct 2016; 66(S1) : S24-S29.}. It was further enhanced and rounded off to 120 patients in age group as final sample size expecting 10% drop out/attrition.

Inclusion Criteria

- Gestational sac with mean sac diameter of >25 mm, without fetal pole (blighted ovum).
- The presence of fetal pole >7 mm, with no cardiac pulsations.
- Gestational sac mean diameter <18 mm, with no interval growth being observed on rescanning 10 days later.
- The absence of embryo with heartbeat at least 2 weeks after an ultrasound scan that showed a gestational sac without a yolk sac.
- The absence of embryo with heartbeat at least 11 days after an ultrasound scan that showed a gestational sac with a yolk sac
- Women giving informed consent

Exclusion Criteria

- Incomplete abortion

- RPOC
- Hb <8 g/dl
- Coagulopathy or anticoagulant therapy
- Glaucoma
- Inherited porphyria
- Hypersensitivity to these drugs
- Bronchial asthma

Methodology

- All the cases were subjected to full history taking, including age, gravity, parity, last menstrual period (LMP), and present complaint (e.g., amenorrhea, regression of symptoms of pregnancy, pain, bleeding), complete general examination, obstetric examination, and transvaginal ultrasound examination to confirm the diagnosis. Cases were divided into 2 groups-
 - **Group-A:** 400 µg of misoprostol sublingually every three hours for a maximum of 4 doses
 - **Group-B :** 400 µg of misoprostol vaginally every three hours for a maximum of 4 doses.
- From intake of the first dose till 24 hrs after the last dose, follow-up was done and closely observed for induction-abortion interval, amount of vaginal bleeding (excessive if >2 pad/hr for >2 hours) gastrointestinal side effects such as nausea, diarrhea, stomach cramps.
- USG was repeated after 24 h after the last dose and after expulsion of parts of conception to assure complete evacuation of the uterine cavity.
- The absence of remnant of conception or endometrial interface thickness less than 15 mm was mandatory to diagnose complete abortion.
- Surgical evacuation was done in all other cases that showed no uterine colic, internal os dilatation, and complete evacuation with endometrial interface more than 15 mm within 24 h from the last dose.
- Rh anti D was given to Rh –ve mother.

RESULTS

Table – 1 Demographic Characteristics

Variables	Group-A	Group-B
Maternal Age (in yrs)	25.86 4.19	26.09 4.19
Primigravida	56 (46.67%)	61 (50.83%)
1 Previous Vaginal Delivery	39 (32.50%)	37 (30.83%)
2 or More Previous Vaginal Delivery	25 (20.83%)	22 (18.34%)
Presenting Complaint		
Bleeding P/V	106 (88.33%)	105 (87.50%)
Gestational Age (in wks)	7.90 1.37	8.13 2.29
Anembryonic Sac	11.67%	8.33%

Table – 2 Distribution of Cases According to Need for Surgical Evacuation

Need for Surgical Evacuation	Group-A		Group-B	
	No.	%	No.	%
Required	26	21.67	48	40.00
Not Required	94	78.33	72	60.00
Total	120	100.00	120	100.00

p = 0.0021

Table – 3 Distribution of Cases According to Side-effects

Side-effects	Group-A		Group-B		p-value
	No.	%	No.	%	
Nausea / Vomiting	24	20.00	6	5.00	0.0004
Diarrhoea	20	16.67	6	5.00	0.0036
Fever / Chills	18	15.00	9	7.50	0.0660
Excessive Bleeding	8	6.67	5	4.17	0.3923

Table – 4 Distribution of Cases According to Misoprostol Dose Required

Misoprostol Dose Required	Group-A		Group-B	
	No.	%	No.	%
1	6	5.00	2	1.67
2	53	44.17	20	16.66
3	31	25.83	45	37.50
4	30	25.00	53	44.17
Total	120	100.00	120	100.00
Mean ± SD	2.71 ± 0.90		3.24 ± 0.79	

p = 0.0000

DISCUSSION

Maximum women came with chief complaint of bleeding per vaginum i.e. 88.33% in Group-A and 87.50% in Group-B respectively. Other less common complaints were pain abdomen, and brownish discharge. 14.17% in both group came as routine check-up whose USG showed missed abortion. Majority of women had absent fetal heart pulsation or absent fetal pole i.e. 106 (88.30%) in Group-A and 110 (91.67%) in Group-B. The other findings was blighted ovum seen in Group-A (11.6%) and Group-B (8.33%). Primigravida in Group-A were 56 (46.67%) and 61 (50.83%) in Group-B. Mean gestational age in Group-A was 7.90 ± 1.37 wks and 8.13 ± 2.29 in Group-B. Mean dose of misoprostol in Group-A was 2.71 ± 0.90 and 3.24 ± 0.79 in Group-B. The results were statistically significant (p-value=0.0000). 83 (69.17%) women had induction-abortion interval between 6-12 hrs in Group-A and 12 (10.00%) women in Group-B. 11 (9.17%) women aborted within 12-18 hrs in Group-A and 60 (50.00%) women in Group-B.

In Group-A 26 (21.67%) had shown retained product of conception in USG and require evacuation and in Group-B 48 (40.00%) required evacuation. In our study, we found significant difference in the rate of complete abortion of two regimes in sublingual 78.33% and in vaginal 60.00% and did not require evacuation (complete abortion). The results were found to be statistically significant (p=0.0021). Shah N et al (2010)¹² study reported that after giving 400 g misoprostol sublingually and vaginally repeated every 3 hours found that complete abortion occurred in 52% in sublingual group and 48% in vaginal group. The explanation for this difference was that it had extended the gestational age of cases upto 20 weeks. Aly HH et al (2016)⁶ study using 100 g sublingual and vaginal misoprostol every 4 hrs found that complete abortion occur in 70% in sublingual group and 51.25% in vaginal group and the difference between both groups in relation to expulsion rates was significant. Park JY et al (2018)¹³ study found that after giving 600 g misoprostol sublingually 61.5% had a successful outcome. Similar to our study, Sharma P et al (2018)¹⁴ reported in their study that complete abortion occur in 62% in Group-1 (vaginal) and 80% in sublingual group which was comparable to our study. Thakur S et al (2018)¹⁵ study reported that after giving 200 mg mifepristone and then after 48 hrs, using 600 g and 800 g misoprostol found that complete abortion occur in >90% cases. The explanation for this difference is that they had given first 200 mg mifepristone which has antiprogesterone action. Rabiei S et al (2019)² study using 600 g misoprostol sublingually and vaginally repeated 6 hourly found that complete abortion in sublingual and vaginal group was 96% and 90% respectively.

In Group-A (sublingual) nausea and vomiting reported in 24 (20.00%) cases and require treatment whereas in vaginal (Group-B) only 6 (5.00%) reported nausea and vomiting. Other frequently reported adverse effects were diarrhoea (more than 4 episodes) in 20 (16.67%) in Group-A and 6 (5.00%) in Group-B. Fever / chills treatment required in 18 (15.00%) in Group-A and 9 (7.50%) in Group-B. 8 (6.67%) women reported excessive bleeding in Group-A and 5 (4.17%) in Group-B. This may be explained by the high bioavailability of sublingual misoprostol. Most patients considered the side-effect to be tolerant and transient and found that they decreased gradually after the first dose of treatment. Similar observation was made by Tanha FD et al (2010)¹⁶ found that although the effectiveness was high in sublingual group than in vaginal group, the sublingual experienced more prevalence rate of bleeding, pain severity, diarrhoea and fever. Shah N et al (2010)¹² found that incidence of side-effects was three times more in sublingual group than in vaginal group. The most common being an unpleasant taste (60% v/s 4%), nausea (20% v/s 4%) and shivering (24% v/s 16%). Pathak BL et al (2019)¹⁷ reported that regarding the route of administration, sublingual is an effective alternative to vaginal administration, although the prevalence of side-effects was higher in sublingual group including nausea (64% v/s 32%), vomiting (26% v/s 18%), diarrhoea (52% v/s 0%) and fever (32% v/s 8%).

CONCLUSION

From our study, we conclude that sublingual misoprostol for the medical management of missed abortion in first trimester is more effective than the vaginal route. However, it showed more adverse effect.

Management of missed abortion by misoprostol avoids the need of surgical evacuation and hence no anaesthesia and thereby avoiding

complications due to these. Misoprostol tablet has of advantage low cost, long shelf life, lack of need of refrigeration and its easy availability. Thus, it may be advocated to be used in outpatient setting in treatment of early pregnancy failure even at the primary care level and thereby decreasing sepsis and morbidity due to it.

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