Original Research Paper

Volume-9 | Issue-4 | April-2019 | PRINT ISSN No 2249-555X

Gynecology

# COMPARATIVE STUDY OF SUBLINGUAL VERSUS VAGINAL MISOPROSTOL FOR THE MANAGEMENT OF MISSED MISCARRIAGEAT TERTIARY CARE HOSPITAL IN WESTERN RAJASTHAN

| | |
|---|---|
| **Dr. Swati Kochar** | Professor, Department of Obstetrics & Gynaecology, S.P. Medical College & A.G.H., Bikaner (Rajasthan) |
| **Dr. Kamlesh Kumar Meena*** | Resident, Department of Obstetrics & Gynaecology, S.P. Medical College & A.G.H., Bikaner (Rajasthan) *Corresponding Author |
| **Dr. Santosh Khajotia** | Professor, Department of Obstetrics & Gynaecology, S.P. Medical College & A.G.H., Bikaner (Rajasthan). |
| **Dr. Sushma** | Senior resident, Department of Obstetrics & Gynaecology, S.P. Medical College & A.G.H., Bikaner (Rajasthan) |

**ABSTRACT**

**Objective:** To compare the efficacy of sublingual and vaginal misoprostol in the medical management of missed miscarriage up to 20 weeks of gestation.

**Methodology:** A hospital based randomized comparative study comprised of 200 females up to 20 weeks pregnancy with missed abortion was conducted in the Department of Obstetrics and Gynecology, Sardar Patel Medical College associate groups of hospitals, Bikaner, Rajasthan. Women in group A received 400 µg of misoprostol sublingually every three hours for a maximum of 5 dose and those in group B received 400 µg of misoprostol vaginally every three hours for a maximum of 5 doses. Women who aborted were sent for ultrasound pelvis to exclude any RPOCs.

**Results:** Mean decrease in hemoglobin in sublingual group before and after abortion there was significant difference with p-value 0.021 and similarly, in per-vaginal group there was significant difference with p-value 0.037. Mean decrease in Hb in both groups was also comparable implying similar blood loss in these two methods. Majority of abortions (45%) were performed in 5-8 weeks of gestation. Majority of abortion occurred at number of dose 3 (44% in sublingual; 39% in per-vaginal) followed by number of dose 2 (25% in sublingual; 27% in per-vaginal). The mean duration for abortion in sublingual group was 6.1±3.6 hours and in per-vaginal group is 6.6±3.9hours. Complete abortion was seen in 83 % women in sublingual and 85 % in per-vaginal and this difference was not found statistically significant (P=0.793).

**Conclusion:** Misoprostol as a single agent can be used safely and effectively as 1st line treatment for abortion both by sublingual and vaginal route.

**KEYWORDS :** Misoprostol, Miscarriage, Incomplete Abortion

## INTRODUCTION

One of the most preventable tragedies for womankind is the problem of unwanted pregnancy and unsafe abortion. Each year 42 million induced abortions are estimated to be performed worldwide of these an estimated 20 million abortions are unsafe with developing nations burdened with 97%.[1] In India the annual estimates of abortion vary from 3.9 to 6 million with some projections claiming upward of 12 million.[2]

Miscarriage occurs in 10-20% of clinical pregnancies.[3] Women experiencing a missed abortion generally have little or no bleeding and no other overt signs or symptoms.[4] Causes of such miscarriages include anembryonic gestation, foetal chromosomal abnormalities, maternal diseases, placental abnormalities, and uterine anomalies. Treatment options of missed miscarriage include expectant management (waiting for spontaneous expulsion), medical management (administration of misoprostol), surgical management (evacuation of the uterus under anaesthesia).[5]

In the management of missed miscarriages, use of misoprostol alone without anti-progesterone is valid as level of progesterone declines due to fetal demise.[6] It is often used alone or in combination with the progesterone receptor antagonist Mifepristone to induce abortion.[7] Medical management with misoprostol with its high expulsion rate has reduced the need of surgical evacuation. Misoprostol can be administered by various routes and in different doses.[8]

The efficacy and safety of misoprostol alone for missed abortion was established in many studies. However, route of administration of misoprostol and success rates varied among the studies. It could be given by oral, sublingual or vaginal, while the doses ranged from 100 µg to 800 µg. The most suitable route and dose of misoprostol for missed abortion is not yet clear. A single dose of 800 µg of misoprostol by vaginal or oral for missed abortion was recommended by National Institute for Health and Care Excellence (NICE). However some studies reported converse opinion, by pointing out that a lower dose or different routes of misoprostol may be equally effective.[9] So we evaluated the existing evidence for the medical management of missed abortion using two different routes of administration of misoprostol, with the hope of finding alternate suitable management strategies for surgical termination, which must be highly effective and with fewer side effects.

## MATERIAL AND METHODS

This hospital based randomized comparative study was conducted from 1st October 2017 to 30th September 2018, in the Department of Obstetrics and Gynecology, Sardar Patel Medical College associate groups of hospitals, Bikaner, Rajasthan. The study group comprised of 200 females up to 20 weeks pregnancy with missed abortion. **Inclusion criteria:** Pregnant women who were candidate for termination of pregnancy with legal medical permission having missed abortion. **Exclusion criteria:** Women with severe liver disease, chronic lung disease, previous LSCS, mitral valve stenosis, inflammatory bowel disease and a history of allergy to prostaglandins, asthma, glaucoma, hypertension and severe bleeding.

First, women were discussed about vaginal and sublingual misoprostol for termination of pregnancy and also potential complications, and then written informed consent was obtained from all of them. Pregnant women were divided randomly into two groups: 1) Group A- 100 women who received misoprostol by sublingual route. 2) Group B- 100 women who received misoprostol by vaginal route.

Women in group A received 400 µg of misoprostol sublingually every three hours for a maximum of 5 dose and those in group B received 400 µg of misoprostol vaginally every three hours for a maximum of 5 doses. Oral paracetamol was given if the women complained of severe lower abdominal pain. Women who aborted were sent for ultrasound pelvis to exclude any RPOCs. Those who failed to abort after receiving 5 doses of misoprostol were treated accordingly.

## RESULTS

Mean age of group A study participants was 24.5 ± 4.2 years whereas in group B it was 25.8 ± 4.2 years. The p-value is 0.471 which is statistically not significant. The Mean±SD of parity in group A is 0.83±0.97 and group B is 0.97±0.99. The p-value is 0.0121 which is

statistically significant.

72% of study participants in group A and 67% of study participants in group B were belong to urban area as depicted in above table. There are 28% and 33% women of the rural area in the two groups. Here, 11 % study participants of group A were graduates or post graduates while these were 13 % in group B. In group A 48% cases had 5-8 weeks of pregnancy, 37% cases had 8.1-12 weeks of pregnancy and 15% cases had 12.1-20 weeks of pregnancy. Similarly, in group B 42% cases had 5-8 weeks of pregnancy, 39% cases had 8.1-12 weeks of pregnancy and 19% cases had 12.1-20 weeks of period of gestation. There is no significant difference in gestation week in both groups. (p=0.0872) (Table:1).

Table-2 shows that the difference in mean haemoglobin (Hb) in group A (10.52 ± 1.28gm%) and in group B (10.3 ± 1.24gm%) before giving the treatment was not statistically significant (p=0.251). Similarly after abortion mean haemoglobin in group A (9.99 ± 1.31gm%) and in group B (9.76 ± 1.27gm%) was also not statistically significant (p=0.307). But in groupA before and after abortion there was significant difference with p-value 0.021 and similarly, in groupB there was also significant difference with p-value 0.037. Mean decrease in Hb in both groups was also comparable implying similar blood loss in those two methods.

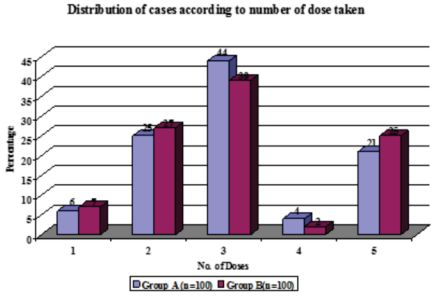
**Table 1: Comparison of baseline characteristics of two groups.**

| | Group-A | Group-B | p-Value |
|---|---|---|---|
| Age (in Years) (Mean±SD) | 24.5±4.2 | 25.8±4.2 | 0.471 (NS) |
| Parity (Mean±SD) | 0.83±0.97 | 0.97±0.99 | 0.0121(S) |
| Period of gestation | | | |
| 5-8 weeks | 48 | 42 | 0.0872 (NS) |
| 8.1-12 weeks | 37 | 39 | |
| 12.1 - 20 weeks | 15 | 19 | |

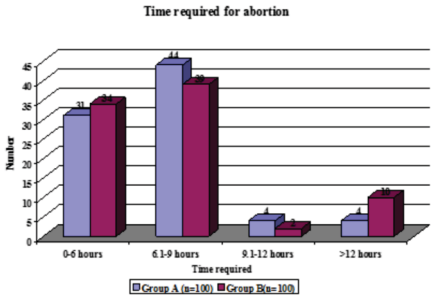
**Table: 2 Comparison of outcome and side effect of two groups.**

| No. of Doses | Group-A | Group-B | P-value |
|---|---|---|---|
| 1 | 6 | 7 | 0.4580 (NS) |
| 2 | 25 | 27 | |
| 3 | 44 | 39 | |
| 4 | 4 | 2 | |
| 5 | 21 | 25 | |
| Pre abortion Hb (gm%) | 10.52±1.28 | 10.3±1.24 | 0.251 (NS) |
| Post abortion Hb (gm%) | 9.99±1.31 | 9.76±1.27 | 0.307 (NS) |
| Mean time for abortion (in hours) | 6.1±3.6 | 6.6±3.9 | 0.3473 (NS) |
| Success | 83 | 85 | 0.793 (NS) |
| Failure | 17 | 15 | |
| Side Effects | | | |
| Nausea | 7 | 6 | 0.7748 (NS) |
| Vomiting | 4 | 1 | 0.1753 (NS) |
| Diarrhoea | 15 | 7 | 0.0713(NS) |
| Fever | 8 | 11 | 0.4705 (NS) |
| Shivering | 8 | 5 | 0.3907 (NS) |
| Unpleasant taste | 19 | 8 | 0.0232 (S) |

Here, in group-A 6% cases aborted with 1 dose of misoprostol, 25% cases aborted with 2 doses of misoprostol , 44% cases aborted with 3 doses of misoprostol, 4% cases aborted with 4 doses of misoprostol and 21% cases aborted with 5 doses of misoprostol. Similarly in group-B 7% cases aborted with 1 dose of misoprostol, 27% cases aborted with 2 doses of misoprostol, 39% cases aborted with 3 doses of misoprostol, 6% cases aborted with 4 doses of misoprostol and 25% cases aborted with 5 doses of misoprostol. The p-value is 0.4580 i.e. is non-significant difference between doses required for abortion in two groups (Fig: 1).




The mean hour for abortion in groupB is 6.6±3.9hours. The difference is not statistically significant with p-value 0.3473 (Fig: 2).




Success (complete abortion) was seen in 83 % women in group A and 85% in group B and this difference was not found statistically significant (p=0.793). There is significant difference in unpleasant taste in sublingual as compared to per vaginal group (p= 0.0232).

## DISCUSSION

In the present study we found that mean decrease in hemoglobin in sublingual group before and after abortion there was significant difference with p-value 0.021 and similarly, in per-vaginal group there was significant difference with p-value 0.037. Mean decrease in Hb in both groups was also comparable implying similar blood loss in these two methods. Parveen et al[10] found that intra-operative blood loss was more in the sublingual group as compared to the vaginal. Saxena P.[11] found that blood loss was more in the sublingual group (17.9±6.3 ml) as compared to the vaginal (16.9±7.0 ml). In our study we did not find any significant difference in blood loss in both groups. This may be probably due to smaller numbers of patients and early decision for evacuation after the failure of five doses in our study.

In our study majority of abortions (45%) were performed in 5-8 weeks of gestation. In coherence with this study by Pattanaik et al[12] found that majority of abortions around 79.8% were performed in the first trimester and 20.2% in the second trimester.

Majority of abortion occurred at number of dose 3 (44% in sublingual; 39% in per-vaginal) followed by number of dose 2 (25% in sublingual; 27% in per-vaginal). Ayati et al[13] found that majority of abortion occured at number of dose 1 (44.6% in sublingual; 50% in per-vaginal) followed by number of dose 2 (27.2% in sublingual; 34% in per-vaginal).

The mean duration for abortion in sublingual group was 6.1±3.6 hours and in per-vaginal group is 6.6±3.9hours. The difference was not statistically significant with p-value 0.3473. In consistent with this study by Ayati et al[13] found similar results. In their study mean hour for abortion in sublingual group is 11.62±6.76 hours and in per-vaginal group is 11.08±3.41 hours. The difference is not statistically significant with p-value 0.61. Pandey et al[14] found the induction - abortion interval was 14.4 ± 5.3 hours in vaginal route and 15.4 ± 8.08 hours with the sublingual route. (P = 0.5662, NS). So they found that both success rate and induction-abortion interval were comparable for the two routes of administration. Thus both sublingual and vaginal routes are effective for medical abortion in Second trimester. This is consistent with pharmacokinetics of misoprostol by sublingual and per-vaginal route. The induction to abortion interval was shorter in the sublingual group than the vaginal group but the difference was statistically insignificant. This may be due to the shortest time to peak concentration, highest peak concentration and greatest bioavailability of the sublingual administration of the drug. Misoprostol is rapidly absorbed through the sublingual mucosa because of its rich blood supply and neutral pH of the buccal cavity. The induction to abortion interval is longer in the vaginal administration but has a similar successful abortion rate. This can be explained by the fact that although the peak concentration of misoprostol attained is lower by vaginal route but it is sustained at that level for a longer period of time.

Complete abortion was seen in 83 % women in sublingual and 85 % in per-vaginal and this difference was not found statistically significant (P=0.793). Complete abortion rates achieved in both the groups are comparable to those observed in a study done by Sonsanoh et al[15] in Thailand. Zhang J et al[16] observed a much higher complete abortion rate (87.5% and 88% respectively) than our study which may be

attributed to the higher dose of misoprostol used in their study. Also, we subjected our cases to surgical evacuation if expulsion was not achieved with five doses.

Assessment of patients satisfaction was limited in our study as being an open label study, patients already knew the route of administration they were assigned to and the treatment outcome may have affected their preference. Another major limitation of our study was its small sample size. However, this study can serve as a pilot study for a future large randomized double blind clinical trial to compare the efficacy of sublingual versus vaginal misoprostol in the management of missed miscarriage.

## SUMMARY AND CONCLUSION

In conclusion, misoprostol as a single agent can be used safely and effectively as 1st line treatment for abortion both by sublingual and vaginal route. This non-invasive procedure offers the advantage of avoiding surgery and anesthesia related risk in a significant portion of patients. Also, the side effects are generally mild and may be managed with simple medication. Nevertheless, further studies are required to determine the optimal dose and route of administration of misoprostol alone resulting in highest complete abortion and minimum side effects.

## REFERENCES


1. Haddad LB, Nour NM.Unsafe abortion: unnecessary maternal mortality.Rev Obstet Gynecol 2009;2(2):122-6.
2. FOGSI ICOG Good Clinical Practice Recommendation Medical Termination of Pregnancy. The Journal of Obstetrics and Gynecology of India January / February 2011:90-92.
3. Alberman E, Stabile S, Grudzinkas G, Chard T. Spontaneous abortion: diagnosis and treatment. London: Springer- Verlag 1992;9-20.
4. Gemzell-Danielsson K, Ho PC, Gómez Ponce de León R, Weeks A, Winikoff B. Misoprostol to treat missed abortion in the first trimester. Intern J Gynecol Obstet 2007;99(2):182-5.
5. Bagratee JS, Khullar V, Regan L, Moodley J, Kagoro H. A randomized controlled trial comparing medical and expectant management of first trimester miscarriage. Hum Reprod 2004;19:266-71.
6. Koopersmith TB, Mishell DR. The use of misoprostol for termination of early pregnancy. Contraception 1996;57:237-42.
7. Nahar KN, Chowdhury SB, Shamim S, Nasrin B, Hossain F, Begum N. Role of Misoprostol in Missed Abortion.Bangladesh J Obstet Gynaecol 2011; 26(2) : 92-99.
8. Lamba A, Kaur R, Sardana P. A study to compare the clinical outcome of Sublingual and vaginal misoprostol in the medical management of missed miscarriage in first trimester. Int J Reprod Contracept Obstet Gynecol 2016;5:491-94.
9. Wu HL, Marwah S, Wang P, Wang QM, Chen XW.Misoprostol for medical treatment of missed abortion: a systematic review and network meta-analysis.Sci Rep 2017 7(1):1664-66.
10. Parveen S, Khateeb ZA, Mufti SM, Shah MA, Tandon VR, Hakak S, Singh Z, Yasmeen S, Mir SA, Tabasum R, Jan N. Comparison of sublingual, vaginal and oral misoprostol in cervical ripening for first trimester abortion. Indian J Pharmacol 2011;43:172-75.
11. Saxena P. Comparison between the sublingual and oral route of misoprostol for pre-abortion cervical priming in first trimester abortions. Human Reproduction 2004;19(1):77–80.
12. Pattanaik S, Patnaik L, Subhadarshini A, Sahu T.Socio-clinical profile of married women with history of induced abortion: A community-based cross-sectional study in a rural area. J Family Med Prim Care 2017;6(1):93-96.
13. Ayati S, Vahidroodsari F, Farshidi F, Shahabian M, Afzal Aghaee M.Vaginal versus sublingual misoprostol for labor induction at term and post term: a randomized prospective study.Iran J Pharm Res 2014;13(1):299-304.
14. Pandey A, Kundu S, Deshmukh PY. A comparison of intravaginal misoprostol with sublingual misoprostol for second trimester medical termination of pregnancy. Int J Reprod Contracept Obstet Gynecol 2015;4:402-7.
15. Sonsanoh A, Chullapram T. Comparison of sublingual and vaginal misoprostol for termination of early pregnancy failure. Thai J Obstet Gynaecol 2014;22:128-36.
16. Zhang J, Gilles JM, Barnhart K, Creinin MD, Westhoff C, Frederick MM et al for the National Institute of Child Health Human Development (NICHD) management of early pregnancy failure trial. A comparison of medical management with misoprostol and surgical management for early pregnancy failure. New England J Med 2005;353(8):761-9.