

**Research Article**

**A randomized controlled trial comparing sublingual routes of misoprostol  
with vaginal routes of misoprostol in the management  
of first trimester missed abortion**

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**ABSTRACT**

**Objective:** To compare the sublingual and vaginal routes of misoprostol in termination of first trimester missed abortion.

**Methodology:** The study was carried out in the Department of Obstetrics&Gynecology THQ Hospital, Jahanian from January 2017 to June 2017. Total 60 patients who presented with first trimester fetal loss, confirmed on ultrasonography were included.

**Results:** The mean age (years) of the study subject was  $30.12 \pm 4.94$ . In vaginal group mean age (years) was  $30.03 \pm 4.13$ . In sublingual group mean age (years) was 30.20. Mean gestational age was 8.87 weeks with minimum 7 and maximum 13 weeks. Mean induction to abortion interval was 13.55 hours with minimum time is 5 hours and maximum 24 hours. Complete abortion was seen 20(66.7%), incomplete in 7(23.3%) and failure of abortion 3(10%) cases.

**Conclusion:** Both vaginal and sublingual misoprostol regimens with success rate of 70% is an effective, cheaper and safe method for the termination of first trimester missed abortion and most effective upto 9 week of gestation. The side effects were comparatively more with sublingual route but most of the side effects were well tolerable or easily managed by medication.

**Key Words:** Misoprostol, vaginal, sublingual, first-trimester missed abortion

**INTRODUCTION**

Missed abortion is a relatively common event, occurring in up to 15% of recognized pregnancies<sup>1</sup>. Missed abortion is in utero death of the embryo or fetus before the 20th week of gestation with retained products of conception. Missed abortions also may be referred to as blighted ovum, anembryonic pregnancy, or fetal demise<sup>2</sup>. For the past 50 years, surgical evacuation by dilatation and curettage (D&C) has been the primary treatment of missed abortion. This procedure is generally considered safe, but

complications such as infection, bleeding, uterine perforation and decreased fertility occur in up to 10 percent of women<sup>3</sup>. Recent studies have questioned the need for routine D&C, suggesting that expectant or medical management might be more appropriate<sup>4</sup>.

A medical abortion is one that is brought about by taking medications that will end a pregnancy<sup>5</sup>. Many drugs are used for medical abortion these are misoprostol, mifepristone and methotrexate. Misoprostol and mifepristone are commonly used

drugs for medical abortion<sup>6</sup>. Misoprostol is the prostaglandin of choice in developing countries as it is cheap, easily available and stable at room temperature<sup>7</sup>. Mifepristone, however, is expensive and only available in a limited number of countries<sup>8</sup>.

Misoprostol is a synthetic prostaglandin E1 analogue that was initially used for the treatment of gastric ulcer<sup>9</sup>. Vaginal misoprostol is a safe, effective and acceptable method of inducing abortion with a reported effectiveness of 88–94%<sup>10,11</sup>. Sublingual misoprostol is convenient to take, avoids the painful vaginal administration and gives more privacy during the abortion process<sup>12</sup>. The side effects of misoprostol are diarrhoea, fatigue, lower abdominal pain, headache, chills and fever, but these effects are transient and can be managed by medication<sup>13,14</sup>.

## MATERIAL AND METHODS

The study was carried out in the Department of Obstetrics & Gynecology THQ Hospital, Jahanian from January 2017 to June 2017. Total 60 patients who presented with first trimester fetal loss, confirmed on ultrasonography were included after taking informed written consent from them. Patients with known hypersensitivity to misoprostol, Therapeutic, threatened and incomplete abortion, Chronic and metabolic disorders, Glaucoma, Sickle cell anemia and Breast-feeding were excluded.

Diagnosis was made by history of regression of pregnancy symptom, smaller size of uterus in relation to duration of pregnancy on bimanual pelvic examination, pregnancy test and absent cardiac activity. Patients who presented at 5<sup>th</sup> week or smaller gestational sac transvaginal ultrasound were performed to look for cardiac activity. All the patients with absent cardiac activity were called back after a week for the confirmation of cardiac activity.

Data was collected on a pre-designed performa containing patient information and study variables.

Two groups were made randomly. First group was vaginal group and other was sublingual.

Each case among vaginal group received misoprostol 800µg per vagina with 2.5ml hydroxyethyl gel. Which was squirted into posterior vaginal fornix and carefully watched. In case of failure to abort 400µg misoprostol was repeated at six hourly intervals for maximum two doses.

Each case among sublingual group received 600µg (3 tablets of cytotec) sublingually, the patient was advised to keep the saliva in mouth until the tablet absorbs. In case of failure to abort or incomplete abortion 400µg misoprostol was repeated at six hourly intervals for maximum two doses.

Outcome of medical abortion was noted in both groups along with number of doses of misoprostol required and the frequency /severity of side effects in each case.

Clinical characteristics were summarized in terms of frequencies and percentages for categorical variables. For numerical variables, mean±1SD were used. Statistical analysis was done by using statistical software SPSS version 16.

## RESULTS

Thirty cases were given vaginal and other thirty sublingual misoprostol. The mean age (years) of the study subject was  $30.12 \pm 4.94$ . In vaginal group mean age (years) was  $30.03 \pm 4.13$ . In sublingual group mean age (years) was 30.20. Vaginal misoprostol group consisted of six primigravidae and twenty-four multigravidae among which four women had blighted ovum. Mean gestational age was 8.87 weeks with minimum 7 and maximum 13 weeks. Complete abortion was seen 20(66.7%), incomplete in 7(23.3%) and failure of abortion 3(10%) cases (Table-1). Mean induction to abortion interval was 13.55 hours with minimum time is 5 hours and maximum 24 hours.

Sublingual misoprostol group consisted of six primigravidae and twenty-four multigravidae among which three women had blighted ovum.

Mean gestational age was 9.3 weeks with minimum 7 weeks and maximum 12 weeks. Complete abortion was seen in 22(73.3%), incomplete in 6(20%) and failure of abortion in 2(6.7%) cases (Table-1). Mean induction to abortion interval was 13.1 hours with minimum time is 4 hours and maximum 26 hours.

Five (16.7%) cases completely aborted with the single dose of vaginal misoprostol, while 14(46.7%) required two doses and only 11(36.6%) required three doses. Eight (26.7%) cases completely aborted with the single dose of sublingual misoprostol, while 11(36.7%) required two doses and only 11(36.7%) required three doses (Table-2).

In sublingual group, side effects were severe abdominal pain observed in 4(13.3%), headache in 6(20%) while nausea vomiting and diarrhea was seen in 7(23.3%) cases. Average blood loss remained 150-200ml and no one blood transfused. However in vaginal group the side effect were severe abdominal pain (which did not

respond to oral NSAIDS) occurred in 2(6.6%) only, headache in 3(10%) while nausea vomiting and diarrhea in 2(6.6%) cases. Average blood loss remained 150-200ml, only one patient has lost more than 500ml blood with fever (38.5 C) chills and nausea on single dose of misoprostol. Immediate resuscitation done successfully and evacuation done sublingually in emergency. (Table-3).

No statistical difference between the outcome of abortion (P=. 830), induction abortion interval and doses of misoprostol (p=0.591) between vaginal and sublingual group observed. However side effects of misoprostol between the two groups there is a significant difference. More GIT adverse effects found in sublingual group as shown in table No.3 Patient age had no effect on the outcome of abortion in both groups but gestational age of missed abortion mattered. Outcome of abortion was seen maximally 95% in 9 weeks missed abortion generally.

**Table –1:** Outcome of medical termination

Route	Outcome of abortion			Total n(%)	P. Value
	Complete abortion n(%)	Incomplete abortion n(%)	Failure to abort n(%)		
Vaginal	20 (66.7)	7 (23.3)	3 (10)	30 (100)	<b>0.830</b>
Sublingual	22 (73.3)	6 (20)	2 (6.7)	30 (100)	
<b>Total</b>	<b>42 (70)</b>	<b>13 (21.7)</b>	<b>5 (8.3)</b>	<b>60 (100)</b>	

**Table-No. 2:** No. of doses of misoprostol required

Route	No. of doses of misoprostol required			Total n(%)	P. value
	One n(%)	Two n(%)	Three n(%)		
Vaginal	5 (16.7)	14 (46.7)	11 (36.6)	30 (100)	<b>0.591</b>
Sublingual	8 (26.7)	11 (36.7)	11 (36.7)	(100)	
<b>Total</b>	<b>13 (21.7)</b>	<b>25 (41.7)</b>	<b>22 (36.7)</b>	<b>60 (100)</b>	

**Table-3:** Side effects of misoprostol in vaginal and sublingual group

Characteristics	Vaginal (n=30)	Misoprostol TG	Sublingual misoprostol TG (n=30)
Abdominal Pain	2(6.6%)		4 (13.3%)
Headache	3 (10%)		6 (20%)
Vomiting	2 (6.6%)		7 (23.3%)
Diarrhea	2 (6.6%)		7 (23.3%)
Fever	1(3.3%)		0(0.00%)
Chills	1(3.3%)		0(0.00%)
Hemorrhage(more than 500ml)	1(3.3%)		0(0.00%)

## DISCUSSION

The inclusion of prostaglandins in the management of termination of first trimester fetal demise has changed the conventional way of surgical evacuation of the uterus. This alternative approach for such problems is based on the uterotonic properties of the misoprostol. It is the cheap, safe and acceptable method of inducing abortion with an effectiveness of 70% in my study. Misoprostol tablet meant for oral use but can be used frequently by vaginal, rectal or sublingual routes as well<sup>15</sup>.

Present study shown misoprostol was effective in 66.6% cases vaginally and 73.3% sublingually but no statistical difference between the two routes ( $p < 0.5$ ). Similar is true about insertion to abortion interval ( $p < 0.5$ ), however the GIT side effects are more with the sublingual route and misoprostol is highly effective for abortion upto 9 weeks. In cases where abortion was unsuccessful (incomplete or failure) surgical evacuation was easy due to prior softening and dilatation of the cervix by misoprostol administration in both groups.

In a study carried out by Gronlund et al<sup>16</sup> in Denmark, outcome of medical termination was 71% in first trimester missed abortion with 96% complete abortion upto 9 week of gestation, the findings are consistent with my study.

Tang OS et al<sup>17</sup> in march 2002 found in case study of 50 women of first trimester missed abortion that overall complete abortion rate was 86% with mean number of doses required  $4.1 \pm 1.1$ . The results are higher than my study but they used 600mcg of misoprostol and repeated 600mcg at 3 hourly interval and maximum 5 doses of misoprostol.

In an eighty patient trial by Ngai SW<sup>18</sup> the overall efficacy of vaginal misoprostol was 85% in pregnancies upto 9 week that is less as compare to my study (95% upto 9 weeks). The more better out come might be due to the fact that in my study multiple doses of misoprostol was used at 6 hourly interval as compare to Nagi in which multiple doses were repeated at day 1, 3 and 5. In my study multiple doses at days interval was not possible due to fact that most of the patients were not willing to stay for days to get rid of dead fetus with medical intervention. Even if we allow them to go home, patients may be unable to get medical care at the time of excessive bleeding that may occur, because most of them were uneducated and live far away from tertiary care hospital.

In a study by Wood SL, Brain PH<sup>1</sup> the complete abortion occurred in 80% cases with single dose of misoprostol. Such high result might be due to the fact that the cases were given adequate time

and assessed after day 2 and waited upto day 7 for completion of abortion.

In a study by John et al<sup>19</sup>, the efficacy of vaginal misoprostol alone was 88%, the promising good result were due to the fact that researchers repeated the dose after 24 hours for maximum 3 doses.

In a study by Wakabayashi<sup>20</sup> et al, the side effect of misoprostol like headache, fever, chills, nausea, vomiting and diarrhea were minimal with vaginal administration for missed abortion which is comparable with my study.

In a comparative study between vaginal and sublingual route of misoprostol by Tang OS, Lau WN, et al<sup>21</sup> eighty women of first trimester missed abortion were given a trial of 600µg misoprostol. The success rates of medical management were 87.5% and 95% respectively. The numbers of side effects were more frequent with sublingual route.

In a study by Blanchard K<sup>22</sup> et al side effects of misoprostol were observed in 234 patients. In sublingual study group headache was seen in 8% fever and chills in 3% and nausea vomiting and diarrhea in 15% of the patient in comparison to vaginal misoprostol where there were minimal gastrointestinal side effects. The above two studies closely match with my study in which sublingual misoprostol was associated increased frequency of side effect in comparison to vaginal route.

Results seem to confirm that with, medical abortion is safe and effective and option for first trimester pregnancy termination and both the vaginal and sublingual routes are effective but sublingual route has slightly more side effects.

From all this discussion it is clear that multiple randomized trials of sufficient size should undergo to find out the optimal schedule and dosage of misoprostol to be used among different routes.

## CONCLUSION

Both vaginal and sublingual misoprostol regimens with success rate of 70% is an effective, cheaper and safe method for the termination of first

trimester missed abortion and most effective upto 9 week of gestation. The side effects were comparatively more with sublingual route but most of the side effects were well tolerable or easily managed by medication.

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