

## THE STUDY OF EFFICACY OF SUBLINGUAL MISOPROSTOL IN TERMINATION OF EARLY PREGNANCY

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### Abstract

**Introduction:** Nearly 20% of all confirmed pregnancies end in spontaneous abortion. Misoprostol's use in early pregnancy failure is varied and dose and route are not well established. AIM: To study the efficacy of sublingual misoprostol in causing expulsion of products of conception in early pregnancy failure.

**Methods:** Women with an ultrasound diagnosis of early pregnancy failure, less than 12 weeks gestation were included in the study. Tablet Misoprostol 600 mcg was given six hourly sublingually for 3 doses. All observations were noted and analyzed.

**Results:** Mean gestational age was  $7.946 \pm 1.2$  weeks. Mean induction abortion interval was  $18.241 \pm 1.2$  hours. Women with gestational age six to eight weeks had least mean induction-abortion interval time of  $17.38 \pm 2.86$ . Mean dose required was 1560mcg. Efficacy of protocol was 92.85% in achieving complete abortion.

**Conclusion:** The regime had 92.85% efficacy, acceptability (90%) and few side effects. Thus by using a lower dose and appropriate interval between two doses (six hours), the side effects were lessened with high efficacy.

**Keywords:** Efficacy, Missed Abortion, Misoprostol.

### Introduction

Vacuum aspiration for uterine evacuation in cases of early pregnancy failure is associated with morbidity and mortality. However, the high expense of the PGE2 OR PGF2a vaginally and its instability in room temperature were barriers to their use in developing countries. Misoprostol-a synthetic prostaglandin E1 analogue, is cheap, stable at room temperature and effective in inducing uterine contractions<sup>[1]</sup> However, the regimes for its use in early pregnancy failure are varied. Clinical trials had shown vaginal misoprostol to be superior to oral misoprostol<sup>[2]</sup>. Misoprostol given vaginally took longer to start working, had a lower peak (peak concentration after 60 mins), but a more sustained effect. Thus, smaller doses were needed when misoprostol was used vaginally. Pharmacokinetics now show that sublingual misoprostol has the shortest onset of action, the highest peak concentration and greatest bioavailability among the routes of administration<sup>[3]</sup>.

### Aim:

The aim of this study was to study the efficacy and the side effects of 600 mcg of sublingual misoprostol six hourly for three doses in causing complete expulsion of products of conception in early pregnancy failure.

### Methods:

This was an observational hospital based prospective study conducted from June 2016 to august 2017. Women with an

ultrasound diagnosis of early pregnancy failure, singleton pregnancy, less than 12 weeks gestation, who had not experienced uterine cramping, no active bleeding ; closed on per vaginal examination) and were in a normal frame of mind to give consent and willing for a surgical evacuation in case of failure with medication or active bleeding, were included in the study. Pregnant women with more than 12 weeks amenorrhea ,not compliant to treatment were excluded from study. The USG criteria used for diagnosis of early pregnancy failure (missed abortion) were-embryo greater than 7 mm with no embryonic cardiac activity or irregular gestational sac with mean sac diameter greater than 16 mm or a gestational sac more than 15 mm with no visible fetal pole. Sample size was calculated at 80% study power and alpha error of 0.05 assuming standard deviation for duration of induction to abortion interval of 5 hours and minimum difference to be detected of 2 hours. Thus sample size came to be 50 patients which were enhanced 55 assuming 10% dropout rates. After counselling and informed written consent, the women were given sublingual tablet Misoprostol 600 mcg every 6 hourly for 3 doses. The dose was decreased to lessen the side effects. Evaluation was done 6 hours after 3rd dose of misoprostol, i.e.at 24 hours. If the uterus was not felt empty on per vaginal examination or ultrasonography shows products of conception, then dilatation and evacuation was done and was considered a true drug failure.

**Results:**

The mean age of women in the study was  $23.79 \pm 5.1$  years. 70% women came with complaints of bleeding per vagina. 30 % women had come for routine checkup and USG had shown missed abortion. 79.78% of the women had fetal pole absent or irregular gestational sac in the ultrasonographic findings. The other finding was a blighted ovum seen in 20.22%.

Mean gestational age was  $7.946 \pm 1.2$  weeks. 48% women had an induction abortion interval of 12 to 18 hours. 39.28% aborted in 18 to 24 hrs. Only 5.36% aborted in 6 to 12 hours. Mean Induction abortion interval was  $18.241 \pm 1.2$  hours. Duration of induction to abortion interval of more than 24 hours was seen in 7.15% and was considered true drug failure and these women were surgically evacuated. Efficacy of protocol was 92.85% in achieving complete abortion (Table 1).

**Table 1: Induction Abortion Interval**

Induction-Abortion Interval (in hrs)	No.	%	Efficacy
6-12	3	5.36	92.85% (complete abortion)
12-18	27	48.21	
18-24	22	39.28	
>24	4	7.15	7.15% (complete abortion)
Total	56	100	

Mean induction abortion interval was studied in different gestational ages. Women with less than six weeks gestational age had highest mean induction-abortion interval  $22 \pm 2$  hrs, while those with gestational age six to eight weeks had least mean induction-abortion interval time of  $17.38 \pm 2.86$  hrs. (Table 2)

**Table 2: Gestational age and Mean induction-abortion interval time**

Gestational Age (in wks)	No.	Mean Induction-Abortion Interval $\pm$ SD (in hours)
<6	3	$22 \pm 2.06$
6-8	34	$17.38 \pm 2.86$
8-10	14	$18.42 \pm 3.45$
10-12	5	$20 \pm 2.55$
Total	56	$18.123 \pm 1.4$

Majority of women with missed abortion required three doses. Women who required one dose were 5.35%. Mean dose required was 1560mcg (Table 3).

**Table 3: Number of Doses Required**

Doses	No.	%
1	3	5.35
2	18	32.14
3	35	62.51
Total	56	100

Abdominal pain was reported by almost all cases but analgesia was required only by 28.57 %. Other adverse effects requiring treatment were fever/chills (7.14%) and vomiting in 5.36%, diarrhea (more than 4 episodes) in 10.71%, headache, dizziness and mild allergy in

1.79%. Most of women did not find these adverse effects difficult to tolerate (Table 4).

**Table 4: Various Side Effects**

Side Effects	No.	%
Vomiting	3	5.36
Fever / Chills	4	7.14
Diarrhoea	6	10.71
Headache	1	1.79
Dizziness	1	1.79
Allergic Reaction	1	1.79
Abdominal Pain	16	28.57

50% women were found to be highly satisfied, 15.45% women were not satisfied because of either failure of treatment or side effect of Misoprostol. The overall acceptability of medical management was good. Most women said they would choose the medical method if they were allowed to choose again and would recommend the method to others. Three women were dropped from the study due to excessive bleeding per vaginum and were taken for surgical evacuation. One woman got severe urticaria and Misoprostol was stopped and was taken for surgical evacuation. Two women did not take second dose of sublingual Misoprostol timely so was dropped from the study.

On follow-up visit, most of cases had no complaints. Few women came with bleeding per vaginum, 3.43% which was mild in amount and no treatment was required. No women required evacuation on follow-up visit.

**Discussion:**

Mean induction abortion interval was  $18.241 \pm 1.2$  hours. Efficacy of protocol was 92.85% in achieving complete abortion. Ayres-de-Campos D et al<sup>[4]</sup> used Misoprostol 600 mcg vaginally and repeated 4 hourly. Complete medical evacuation occurred in 56.8% with higher side effects due to short interval between doses. 13.5% nausea, 5.4% vomiting, 6.8% diarrhea and 5.4% transient hyperthermia. Ngoc NT et al<sup>[5]</sup> (2004) used 800mcg vaginal Misoprostol only single dose and mean induction abortion interval was high-21hrs. Barcelo F et al<sup>[6]</sup> had a success of 87.8% with 600 mcg sublingual misoprostol every 24 h for two days but had a very long induction evacuation interval. Kushwah D. S. et al<sup>[7]</sup> in their study also reported complete abortion rate to be 92% in 600mcg misoprostol sublingual group and the side effect were hot flashes 24%, diarrhea and nausea 2% in 10% with sublingual misoprostol and 92% women were satisfied with their study. Tang OS, Lau WN et al<sup>[8]</sup> used 600 mcg of misoprostol three hourly up to three doses sublingually with success rates of 87.5%. Their interval was shorter and they noticed a higher incidence of diarrhea (70%) and fatigue was experienced.

**Conclusion:**

The advantage of evacuation by Misoprostol is that it includes no surgery and hence no anaesthesia. Misoprostol tablet has advantage of low cost, long shelf life, lack of need for refrigeration and its easy availability. Thus, it may be advocated to be used in outpatient setting in the

treatment of early pregnancy failure even at the primary care level. However, the dose schedule should be adhered to. According to the route, these should be altered.

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