

# VAGINAL MISOPROSTOL IN THE MANAGEMENT OF FIRST TRIMESTER MISSED ABORTION

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## ABSTRACT

**Objective:** To assess the efficacy and side effects of vaginal misoprostol in termination of first trimester missed abortions.

**Materials and Methods:** This study was conducted from April 2015 to March 2016 at Gynae Unit, Naseer Teaching Hospital Peshawar.

A total of 52 patients, with first trimester missed abortion were included. Misoprostol (400mcg) was inserted vaginally and the second dose of 800mcg of misoprostol in case passage of tissues did not occur with the first dose. Without successful abortion in 48hrs, misoprostol administration was abandoned in favor of surgical induction. Main outcome measures of the study were induction –expulsion interval, complete expulsion of products of conception and side effects of misoprostol.

**Results:** Successful abortion was seen in 45(86.5%) patients. Seven patients ended up in surgical evacuation. Of these 4 patients had incomplete abortion and 3 had failed induction.

Side effects included abdominal cramps (3.8%), nausea, vomiting (5.7%) and diarrhea (1.9%).

**Conclusion:** Misoprostol is highly effective in inducing successful abortion without any major increase in side effects.

**Key words:** Misoprostol, Missed Abortion, Anembryonic Pregnancy, Medical Abortion.

## INTRODUCTION

Missed abortion is defined as unrecognized intra-uterine death of the embryo or fetus without expulsion of the products of conception. It constitutes approximately 12-15% of clinically diagnosed pregnancies.<sup>1</sup>

With a very high success rate, surgical evacuation is regarded as the standard treatment for missed abortion, which had been widely performed all over the world in the past 50 yrs.<sup>2</sup> However the costs of surgery and hospitalization, as well as the complications associated with surgery and anesthesia are a major concern. Expectant and medical management of the first trimester miscarriage has significant economic advantages over surgical management.<sup>3</sup>

Expectant management has a variable success rate ranging from 25-76%.<sup>4,5</sup> However, the uncertainty of timing associated with expectant management and the anxiety of carrying a nonviable pregnancy may be unacceptable for some women.<sup>6</sup>

Medical management of the missed abortion is very effective, safe and economic alternative to surgical evacuation.<sup>7</sup> Misoprostol is a synthetic prostaglandin

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E1 analogue which was originally developed to prevent non-steroidal anti-inflammatory drugs related gastric ulcers. It is widely used for the medical management of missed abortion. However, route of administration of misoprostol and success rates varied among the studies. It can be given by oral, sublingual or vaginal routes, while the doses ranged from 100 micrograms to 800 micrograms.<sup>8,9,10</sup>

Misoprostol has the advantage of being cost effective, stable at room temperature and a strong uterotonic.<sup>11</sup> It has little side effects such as nausea, vomiting, diarrhea, chills, fever and pelvic pain. Several studies have been conducted to compare oral and vaginal misoprostol success rate and complications to end pregnancies in first and second trimester of pregnancy. In some of these studies, the success of vaginal and in some studies oral success rate was high.<sup>12,13</sup> There are some studies that show the same effects of oral and vaginal methods.<sup>14</sup> Nowadays, misoprostol is considered to be the gold standard for early pregnancy termination.<sup>15,18</sup>

Efforts to optimize the route and dose of misoprostol, to maximize the effectiveness and minimize side effects are important. This study is therefore designed to test whether vaginal administration of 800 micrograms misoprostol is optimal for termination of first trimester abortion or not.

## MATERIAL AND METHODS

This descriptive, cross sectional study was conducted at Naseer Teaching Hospital Peshawar, from

April 2015 to March 2016. A total of 52 patients were recruited in this study. Eligibility criteria was women with a pregnancy of <13wks gestation, who had been diagnosed as having early fetal /embryonic demise.

The exclusion criteria was severe hemorrhage, severe asthma, hemolytic disease or blood dyscrasias, pyrexia above 37.5C and patients with scar on uterus and uterine malformations like bicornuate uterus or uterus didelphys.

Patients fulfilling the above mentioned criteria were admitted in the Gynae ward. Their written informed consent was obtained. Complete history and physical examination was done. Routine investigations like blood complete, random blood sugar, urine routine examination, blood group and blood coagulation profile were done. Misoprostol 800mcg (4 tablets) were inserted vaginally. If no passage of tissues occurred after 24 hours, then the second vaginal dose of 800mcg misoprostol was used. However with no passage of tissues after 48 hours, the patients were referred for uterine aspiration. Patients were monitored by the duty doctor for side effects like abdominal pain, fever etc. Successful abortion rate was defined as complete abortion within 48 hours of initiation of induction of abortion. All those who aborted had ultrasonographic examination after 24 hours to exclude any retained products of conception.

Data collection was done by a questionnaire, which included demographic information, information on previous and current pregnancies and misoprostol treatment process. Side effects were also recorded. Sampling technique is consecutive non probability sampling .Primary outcome measures were complete evacuation of products of conception, mean induction to delivery time and occurrence of side effects.

Data was analyzed using SPSS version 16. The study was approved by the Hospital ethical committee.

## RESULTS

A total of 52 patients were included in the study. Out of these 5 (9.6%) were primigravida, 22 (42.3%) were grand multigravida. Table-1 shows the demographic characteristics of women. Successful abortion rate was 86.5% (45) patients. In 7 (13.4%) patients surgical evacuation was performed, of these 3 (42.8%) had failed induction and 4 (57.2%) had incomplete abortion. Pregnancy was terminated in 29 (55%) with the first dose of misoprostol and 16 (30.7%) required second dose. No important side effects were noted due to vaginal misoprostol treatment. Table-3 shows the side effects encountered during the study. Mean induction expulsion interval in our study is 14.5 hrs. The induction abortion interval is shown in Table 2.

## DISCUSSION

Traditionally, surgical curettage was the gold standard for the management of miscarriage. The

**Table 1: Demographic characteristics of patients**

Age in Years	No. of Patients	Percentage
18 – 20	15	28.8%
21 – 30	27	51.9%
31 – 40	6	11.5%
> 40	4	7.7%
Parity		
Primigravida	5	9.6%
1 – 4	18	34.6%
5 – 7	22	42.3%
> 7	7	13.4%

**Table 2: Induction – abortion interval n = 45 (86.5%)**

Intervals in Hrs.	No of Patients and percentage
< 8 hrs.	2 (3.8%)
8 – 12 hrs.	33 (63.4%)
12 – 24 hrs.	8 (15.3%)
24 – 48 hrs.	2 (3.8%)

**Table 3: Side effects with misoprostol**

Side Effects	No. of Patients and Percentage
Nausea and vomiting	3 (5.7%)
Diarrhea	1 (1.9%)
Fever	3 (5.7%)
Abdominal cramping and pain	2 (3.8%)

introduction of medical management of miscarriage increased options for women as well as clinicians. Misoprostol is a known safe and efficacious agent for pregnancy termination, produces the least number of complications, the least amount of stress for patient and is most effective.<sup>16</sup>

Our study shows successful abortion rate of 86.5% compared to 68% and 98% as reported by Naz<sup>17</sup> and Mazhar<sup>18</sup> in their studies. Ganguly et al have shown that complete abortion in sublingual misoprostol group was more than the oral 9( $p=0.0338$ ) and vaginal group ( $p=0.562$ ).<sup>19</sup> However, in another study conducted by Madhuri, there was no statistical difference in the complete abortion rate between oral and vaginal groups.<sup>12</sup> According to NICE guidance on the management of miscarriage, there is a wide variation in efficacy rates ranging from 13% to 96%.<sup>20</sup> The efficacy of medical management may be influenced by multiple factors such as the type of miscarriage, total dose, and duration of use and route of administration of prostaglandins. Higher success rates (70-96%) are associated with

incomplete miscarriage, high dose misoprostol (1200-1400 micrograms) with a repeat dose if required and prostaglandins administered vaginally.<sup>21</sup> In an Iranian study conducted Farhadifer, the complete abortion rate by vaginal administration of misoprostol in first trimester is 80%.<sup>22</sup> A study compared 800mcg oral with the same dose of vaginal misoprostol with no difference in efficacy, but the mean time to expulsion was significantly longer in the oral group.<sup>23</sup>

The induction to abortion interval in this study is 14.5 hours, which is comparable to  $13.9 \pm 9$  hours as reported earlier by Mazhar.<sup>18</sup> However they used 800 micrograms misoprostol vaginally followed by 400 micrograms 6 hourly in three doses. Vaginal route appears to be the most effective followed by sublingual with oral being the least effective. Sublingual misoprostol needs more frequent administration, to achieve a similar effectiveness to the vaginal route.<sup>23,24,25</sup> In a study by Dehbashi mean time of follow up for women prescribed with sublingual and vaginal inducers were  $570 \pm 217$  min and  $514 \pm 28$  min respectively with no difference between the groups ( $p=0.6$ ).<sup>11</sup> Another study comparing sublingual misoprostol with vaginal misoprostol for termination of missed abortion showed that the induction to abortion interval was slightly shorter in the sublingual group than the vaginal group, but the difference was not statistically significant. The number of women who aborted within 12 hours was 57% in the sublingual group compared to 41.6% in the vaginal group. This can be explained by the quicker and higher peak serum concentration of sublingual misoprostol compared to the vaginal route.<sup>26,27</sup> Similar findings were seen by Parveen et al, the mean time taken for cervical ripening was less in sublingual administration (3.7+1.2) as compared to the vaginal (4.9+2.6). The differences in misoprostol administration time to abortion may be due to various doses prescribed in various studies.<sup>28</sup>

The incidence of side effects is more common with sublingual or oral intake of misoprostol as compared with vaginal administration.<sup>7</sup> Distaste in mouth, gastrointestinal symptoms, fever and chills are the commonly encountered side effects of oral or sublingual misoprostol.<sup>29</sup> The side effects associated with vaginal administration of misoprostol were rare in our study. There was 5.7% incidence of nausea, vomiting, fever and abdominal cramps were in (5.7%) and (3.8%) respectively. Similar results were seen in a study conducted by Dehbashi et al, which showed that compared with vaginal group, the women in sublingual group experienced more side effects like diarrhea(22.2% verses 20.2%) nausea and vomiting (22.2% verses 0.0%).<sup>11</sup> Two other studies comparing sublingual and vaginal misoprostol have reported a significantly increased frequency of unpleasant taste in mouth in women taking sublingual misoprostol.<sup>7,30</sup> The increased frequency of side effects may be explained by higher bioavailability of sublingual misoprostol.<sup>27</sup> Other researchers, have explored that sublingual misoprostol has equivalent

efficacy compared with vaginal misoprostol in inducing complete miscarriage, but is associated with more frequent diarrhea.<sup>30,31</sup>

This study has certain limitations like small sample size and exclusion of patients with scarred uterus from the study. In addition to this patient preference and comfort of route used wasn't taken into consideration. Misoprostol is inexpensive, stable at room temperature and worldwide available, it is also very useful in undeveloped countries.

## CONCLUSION

Vaginal use of 800 micrograms of misoprostol results in an effective termination of pregnancy in first trimester and has a lower complication rate.

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