

## MEDICAL MANAGEMENT OF MISSED MISCARRIAGES USING VAGINAL MISOPROSTOL- A PROSPECTIVE OBSERVATIONAL STUDY

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### ABSTRACT

#### BACKGROUND

Missed miscarriage is one of the common cases encountered by the practicing obstetricians all over the world. Diagnosis is made early due to increased use of ultrasound. Medical management is as effective as surgical management, but many still resort to surgical management due to concerns about adherence of products to uterine wall. This may result in complications like perforation, infection, cervical injury and may affect future fertility. Mifepristone followed by misoprostol is well accepted in medical abortion. Misoprostol alone is as efficient as the combination in missed miscarriage. In India, studies with misoprostol alone are limited. Hence, this study was conducted to evaluate the outcome of medical management in patients with first trimester miscarriage with misoprostol alone.

#### MATERIALS AND METHODS

After approval of Institutional Review Board, a total of 100 women with first trimester miscarriage were recruited for the study after satisfying inclusion and exclusion criteria. After necessary investigations and consent, they were treated with 800 micrograms of vaginal misoprostol followed by 600 micrograms after 3 hours. Main outcome measured was successful resolution without surgical intervention. Secondary outcomes measured were the induction delivery interval, incidence of pain, excess vaginal bleeding, infection, pyrexia and other gastrointestinal side effects.

#### RESULTS

Complete expulsion occurred in 89% patients and surgical evacuation needed in 11%. Mean induction delivery interval was 6-12 hours. Incidence of complete expulsion was more among primigravida than multigravida. In multi, complete expulsion was observed in patients with previous normal delivery than caesarean. Majority of patients had bleeding for less than 7 days. None of them had major side effects like sepsis or heavy bleeding. Minor side effects were fever, nausea, diarrhoea and abdominal pain.

#### CONCLUSION

Medical management with misoprostol is efficient, acceptable and cost-effective method for first trimester miscarriage.

#### KEYWORDS

Medical Management, Missed Abortions, Misoprostol, Surgical Management, Expectant.

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#### BACKGROUND

Missed miscarriage is defined as confirmed nonviable pregnancy on Ultrasonogram (USG) with no bleeding. Signs of this will be the loss of pregnancy symptoms and absence of foetal heart in USG. Early diagnosis is possible due to increased use of USG in the first trimester.

There are three methods of management for missed miscarriages- expectant, surgical and medical. Expectant consists of no intervention and awaiting natural passage of products. Medical management consists of medications like mifepristone and misoprostol to expel uterine contents. Surgical management is defined as mechanical removal of tissues by dilatation and curettage. Success of each of these approaches depends on several factors like type of loss and gestational age.

Expectant management has high failure rate and is associated with emotional distress of carrying a nonviable foetus.<sup>1</sup> Surgical method increases the incidence of incomplete evacuation, haemorrhage, sepsis, perforation and cervical tear, which necessitates further intervention and hospital stay.<sup>2</sup> Also, it increases the chance of Asherman syndrome.<sup>2</sup> Advantages of medical abortion over

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surgical abortion include- (1) Less invasiveness and less morbidity, (2) Lack of risk of general anaesthesia and (3) Lack of risk of secondary infertility due to scarring and Asherman syndrome. Moreover, it is less expensive. Hence, medical management should be advocated to all patients.

Medical management has an important public health impact also. There are a lot of benefits to women and healthcare system from this modality. In a low resource country like India, infection, haemorrhage and uterine damage are more reported due to poorly-performed surgical cases. Hence, promoting medical management is a tremendous step towards achieving low maternal morbidity and mortality rates.

Misoprostol is a prostaglandin, which binds to myometrial cells to cause strong myometrial contractions and expulsion of products. It causes uterine contractions and cervical ripening. Medical management of abortion using misoprostol with or without mifepristone is well established in clinical practice.<sup>3,4</sup> Addition of mifepristone, antiprogesterone maybe superfluous in missed miscarriage as progesterone levels are lower than in viable pregnancy.<sup>5</sup> Still many obstetricians use mifepristone followed by misoprostol, which adds to the cost of therapy as well as side effects. There are only limited studies with misoprostol alone in India. Hence, we used vaginal misoprostol alone for the management of missed abortions in our study.

**Objective**

To evaluate the outcome of patients with first trimester missed miscarriage who were treated with vaginal misoprostol alone and more specifically, (1) To investigate the proportion of them showing complete expulsion; (2) To study the proportion of them who needs surgical interventions for complete expulsion; (3) To study the proportion of them who develop any complications.

**MATERIALS AND METHODS**

This was a prospective observational study conducted in 100 patients with the diagnosis of missed miscarriage of gestational age less than 12 weeks. The study protocol was approved by the Institutional Ethics Committee for medical research. Patients were selected from those who attended the outpatient and casualty of Department of Obstetrics and Gynaecology, Government Medical College, Kottayam, during July 2015 to July 2016 using definite inclusion and exclusion criteria.

**Inclusion Criteria**

Women who meet the following inclusion criteria were selected for the study.

1. Patients with USG diagnosis of missed miscarriage less than 12 weeks.
2. Willing for surgical evacuation in case of incomplete evacuation.
3. Haemoglobin more than 10 g%.

**Exclusion Criteria**

Pregnant women with the following conditions were excluded from our study.

1. More than 12 weeks.
2. Severe haemorrhage and pain.
3. Twins, higher order pregnancies.
4. Allergic to misoprostol.
5. Liver disease.
6. Coagulopathy or women on anticoagulants.

**Analytical Frame**

All patients satisfying the inclusion criteria were given the option of medical, surgical and expectant management. Their risks, complications and follow up plans were explained to them. All of them opted for medical management. They were informed about the research and written consent obtained from them. All essential investigations done and Rh negative women were given injection anti-D intramuscularly. Then, four tablets of 200 micrograms of misoprostol were placed in posterior vaginal fornix (800 micrograms) followed by 600 micrograms after 3 hours. After the treatment, patients are sent home and asked to return on 15<sup>th</sup> day for follow up. They were advised to attend hospital in case of emergency like heavy bleeding (soaking of more than 2 pads per hour for more than 2 hours). They were also asked to record the onset of bleeding, duration of bleeding and other side effects. On follow up visit on 15<sup>th</sup> day, clinical vaginal examination and USG were done. Based on the findings of USG, patients with endometrial thickness of less than 15 mm and more than 15mm are considered as complete expulsion and incomplete expulsion, respectively. Using USG and clinical criteria, patients are classified as follows-

1. Complete expulsion without complications.
2. Complete expulsion with complications.
3. Incomplete evacuation, which needs surgical intervention.
4. Need for surgical evacuation with associated complications.

So, study tools were misoprostol, USG, questionnaire and case files. Analysis was carried out using SPSS software.

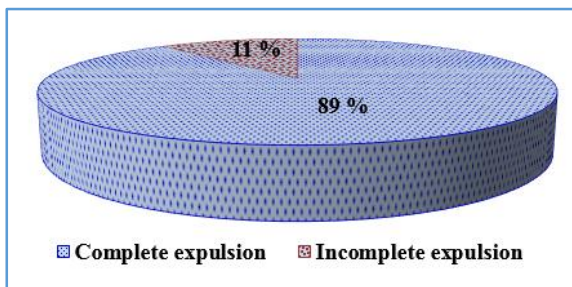
**RESULTS**

The results of our study are depicted in the following tables and pictures. Majority of women were in the age group of 25-30 years, which accounts for 34% of total. Minority (14%) comes under the age group of 37-42 years. 25% were under the age group of 18-24 years. The rest 27% comes under 31-36 age group (Table 1).

Age in Years	Number of Patients	Percentage
18-24	25	25
25-30	34	34
31-36	27	27
37-42	14	14
<b>Total</b>	<b>100</b>	<b>100</b>

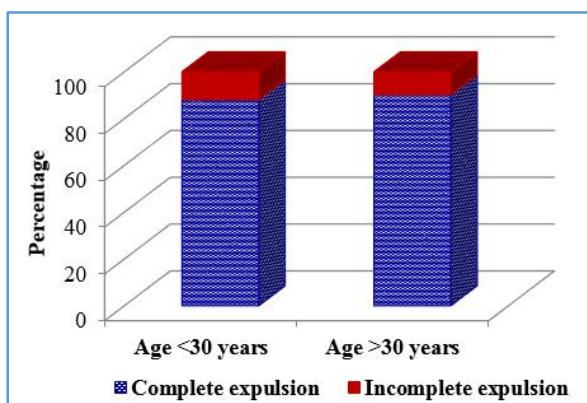
**Table 1. Distribution of Study Populations According to Age of Patients**

Complete expulsion had occurred in 89 women; 11 women showed incomplete expulsion (Figure 1).



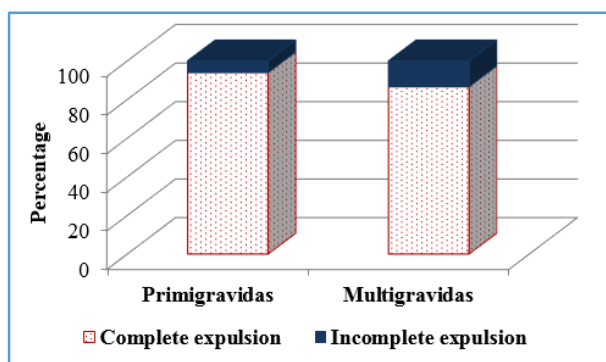
**Figure 1. Distribution of Final Outcome of Sample Population**

Incidence of complete abortion is more among women aged above 30 years (90.2%) than women aged below 30 years (88.1%) (Figure 2). But, the difference is not statistically significant (p more than 0.05).



**Figure 2. Distribution of Final Outcome in Relation with Their Age**

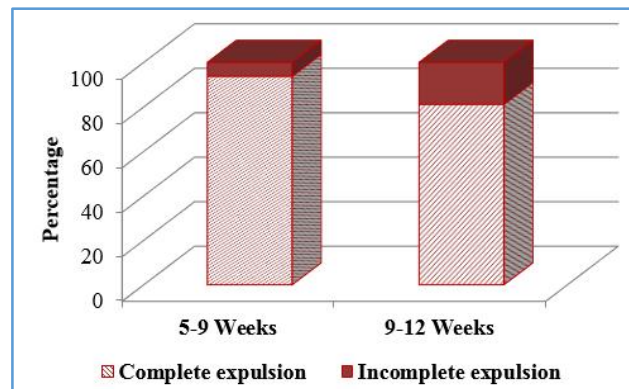
Out of the total 33 primigravidas, complete expulsion occurred in 93.9% and surgical interventions was needed in 6.1% (Figure 3). Of 67 multigravidas, 86.6% showed complete expulsion and incomplete expulsion occurred in 13.4%. Complete expulsion is more among primigravidas. But, the difference is statistically not significant.



**Figure 3. Distribution of Final Outcome as per Gravidity**

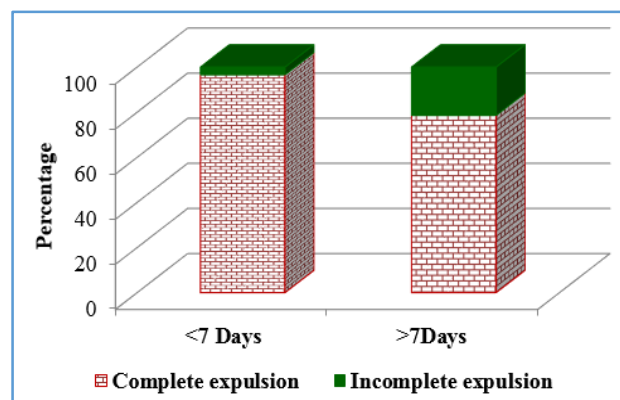
In our study, we compared the outcome between two gestational age groups (5 weeks-9 weeks and 9 weeks 12 weeks). 93.7% women in the gestational age of 5 weeks-9 weeks experienced complete abortion, whereas in the 9 weeks-12 weeks, complete abortion occurred in 81.1%

women (Figure 4). The difference is statistically significant (p=0.05). As gestational age increases, outcome is poor.



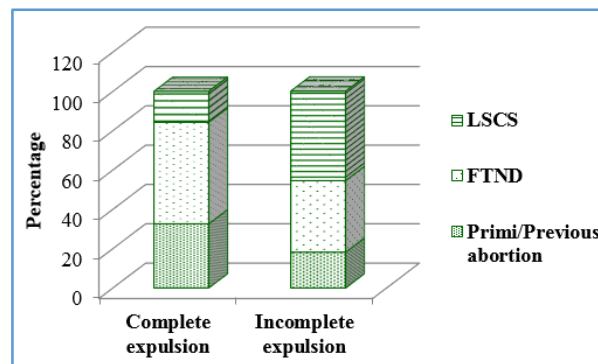
**Figure 4. Distribution of Final Outcome as per Gestational Age**

Out of total patients, 58 women had bleeding less than seven days and rest of the 42 women had bleeding more than 7 days. Women with duration of bleeding less than 7 days had a complete expulsion percent of 96.6, while only 78.6% of women with more than 7days bleeding had complete expulsion (Figure 5).



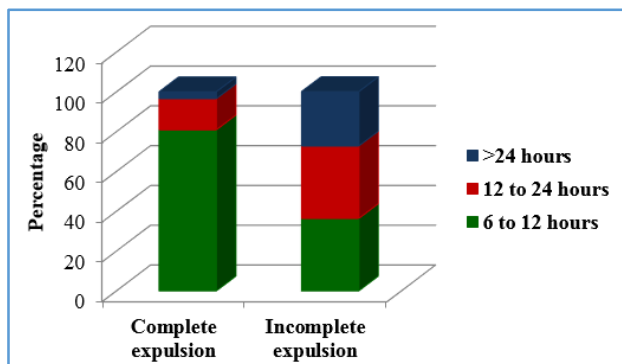
**Figure 5. Distribution of Final Outcome of Medical Management in Relation to Duration of Bleeding**

In our study, we compared the rate of complete expulsion based on the type of previous delivery. Complete expulsion more in those with previous normal deliveries than those with LSCS and primi/previous pregnancy loss (Figure 6).



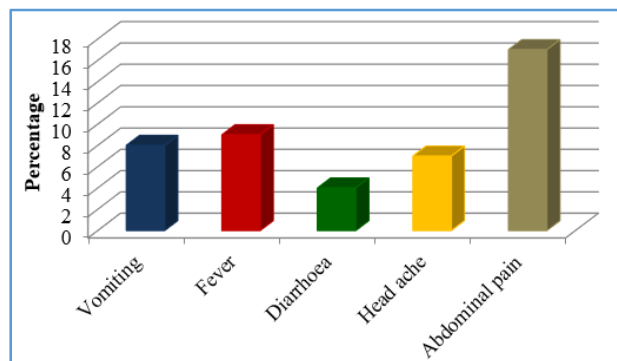
**Figure 6. Distribution of Final Outcome of Medical Management in Relation to Type of Previous Delivery**

Figure 7 compares the induction expulsion interval between patients showing complete and incomplete expulsion. Maximum induction expulsion interval was 6-12 hours, which accounts for 76% of total. 18% showed an expulsion time of 12-24 hours and the rest 6% experienced more than 24 hours. It is evident that as induction expulsion interval gets prolonged, chance of incomplete expulsion is high.



**Figure 7. Distribution of Final Outcome and Expulsion Time in Hours**

Figure 8 depicts the side effects of the drug in the whole study sample. Among the whole study group, 8% of women developed vomiting, fever in 9% of cases, 4% had diarrhoea, headache for 7% and analgesics were required for 17% for abdominal pain. Abdominal pain was the commonest side effect.



**Figure 8. Distribution Showing Side Effects and Complications**

**DISCUSSION**

Induction of abortion needs meticulous and effective care. Surgical methods are associated with more maternal morbidity and mortality. Medical abortion has become a safe alternative to vacuum aspiration and dilatation and curettage.<sup>6</sup> Misoprostol is the prostaglandin of choice in medical abortion. Different doses of oral and vaginal misoprostol have been used, but ideal dose and route yet to be established.<sup>7</sup> Regimens using repeated doses as in our study have the advantage of requiring less hospital visits and USG and more success rate.<sup>8</sup>

In this study, there was complete expulsion in 89% of cases. In the 11 cases of incomplete abortion, 5 reported after one week with abdominal pain and vaginal bleeding.

The USG showed products in the cervical canal, which could have been expelled with an additional dose vaginally in them. Since the patients were anxious, surgical evacuation was done. For the remaining 5, only 3 needed surgical evacuation for incomplete abortion in USG and for 2 it was done on 5<sup>th</sup> or 6<sup>th</sup> day due to bleeding.

In total, more favourable outcome was observed in our study with medical management giving a complete expulsion rate, which is in accordance with or greater than similar studies. Table 2 shows the comparison of our results with previous findings. A large multicentric Cochrane database analysis conducted by WHO reviewed 58 trials. All showed greater effectiveness. These variations maybe due to different regimens, routes of administration and definition of success rate.<sup>9</sup>

Type of Expulsion	Our Study (%)	Demotroulis et al <sup>10</sup> (%)	Crenin et al <sup>11</sup> (%)	Tanq et al <sup>12</sup> (%)
Complete expulsion	89	82.5	92.9	84-93
Incomplete expulsion	11	17.5	7.1	16-7

**Table 2. Comparison of Outcome in Different Studies**

In our study, we used misoprostol alone, because it is reported that addition of mifepristone offers no advantage compared with misoprostol as initial management.<sup>13</sup> Our study showed parity and gestational age are important determinants of success rate in medical management. Incidence of incomplete abortion increases with parity and gestational age. This was also observed in a retrospective analysis of medical abortions conducted in University of Edinburgh.<sup>14</sup> In that study, surgical intervention was higher at gestational age more than 7 weeks. Another observation was that parous women had more incomplete expulsion than nulliparous (5.4% vs. 2%).

Majority of patients in our study had an induction delivery interval of 6-12 hours (78%). In the study of Rizwan and Uddin (2014), it was 15.6 hrs.<sup>15</sup> In our study, only 4% of the patients had bleeding more than 14 days and all of them had incomplete expulsion. Hence, longer duration of bleeding was a sign of incomplete expulsion. Heavy bleeding was not observed in any of them. The study of Dempsey and Davis observed moderate bleeding, which persist as spotting for 2 weeks or more.<sup>16</sup>

Side effects like vomiting, diarrhoea, headache and fever were observed only in a minority in our study. Only 9% of patients had more than 1 side effect. Adverse effects vary based on route of administration since the drug can be given orally, vaginally and sublingually.<sup>17</sup> Patients receiving vaginal misoprostol have decreased gastrointestinal side effects and prolonged action.<sup>18</sup>

A study conducted by Shuaib and Alharazi in 2013 found that infection rate in medical abortion was higher than in surgical group.<sup>19</sup> Our study showed a different result from this. Fever was observed in 9% of our study population, it was misoprostol induced and subsided. None

of the patients had features of sepsis and pelvic inflammatory disease.

### CONCLUSION

Our study analysed the outcome of medical management with vaginal misoprostol alone in patients with missed miscarriage less than 12 weeks. Main outcome was successful resolution without surgical intervention. The outcome was also analysed with respect to age, parity, previous mode of delivery, gestational age and duration of bleeding. Induction expulsion interval and side effects were analysed.

From the above study, we could observe that medical management of first trimester missed miscarriage is safe, economic, convenient and successful with very minimal complications. Complete expulsion is more among women aged above 30 years. As gestational age and parity advances, possibility of successful outcome decreases. Success rate is more among those having previous normal deliveries. Majority of women experienced an induction expulsion interval of 6-12 hours. Duration of bleeding is more among those with incomplete expulsion. Other complications like fever, vomiting, headache and diarrhoea were seen in minority of patients who were relieved without any medications. No serious complications were observed in the study.

As a whole, this study had shown safety, tolerability and a better success rate. Patients feel that medical management is more natural, private and under their control. The cost savings to the patient is also important. Hence, we recommend that all patients with missed miscarriage should be given this option. However, patient's decision regarding the treatment should be given the primary preference. Only limitation of this study is that treatment cannot be used for noncompliant patients and those who don't have access to 24 hours emergency services. Women and healthcare system worldwide could significantly benefit from this noninvasive treatment option. Medical miscarriage indirectly reduces maternal morbidity and mortality by reducing the complications due to surgical abortion.

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