INTRODUCTION

Miscarriage is the most common complication of early pregnancy. Its effects are both physical and psychological and may be an immediate or long term in their nature. The incidence of clinical miscarriage is around 10 - 15 percent. The risk of miscarriage is highest in the first trimester of pregnancy and decreases to 2 - 7.5 % once a viable fetus is identified.1,2

The management of miscarriages should be individualized, taking into account the wishes of the women as well as the clinical situation. In most instances expectant, medical, or surgical management will be appropriate, although availability of these managements will depend on local provision. If patient is hemodynamically unstable, or the pain cannot be adequately controlled, or there are concerns about infection/sepsis, then surgical management is usually indicated.1,2

The recommended management in early pregnancy loss is to reduce morbidities like pelvic inflammatory disease (PID), hemorrhage, blood coagulation defects, chronic pelvic pain and infertility. Medically, pregnancy loss is usually described as incomplete or early fetal demise. An “incomplete abortion” is usually diagnosed when the woman has an open cervix and has passed some, but not all the products of conception. An “early fetal demise” is diagnosed when a woman has a closed cervix, a uterus which does not increase in size and a nonviable embryo or fetus (an embryonic pregnancy or an embryonic/fetal demise). Terminology is embryo (0 to 8 weeks) and fetus (9 to 12 weeks).1

MEDICAL MANAGEMENT OF THE COMPLICATIONS OF EARLY PREGNANCY WITH MISOPROSTOL

Nuzhat Amin, Himasa Gull
Department of Gynecology, Bacha Khan Medical College, Mardan, Pakistan

ABSTRACT

Objective: The objective of the study was to determine the effectiveness of misoprostol in patients with the complication of early pregnancy. And to avoid surgical evacuation in these patients.

Material & Methods: This experimental study was conducted at the department of obstetrics and gynaecology unit A, Mardan Medical Complex Hospital Mardan in 2015 and 2017. A total of 200 women with early pregnancy complications were recruited for treatment with misoprostol. The inclusion criteria were patients with complications of early pregnancy having gestational age less than 15 weeks and hemodynamically stable. The exclusion criteria were patients with the history of hypersensitivity to prostaglandin, ectopic pregnancy, gestational trophoblastic disease, high risk of uterine rupture, hemodynamically unstable and hemoglobin less than 9 g. Main outcome measures were the successful resolution of miscarriages without surgical intervention. Secondary outcomes were the incidence of pain, vaginal bleeding, infection, pyrexia and gastrointestinal side effects.

Results: A total of 200 women were included in the study. Age ranged from 16 to 45 years and primigravida to grand multigravida. Early fetal demise was found in 88 (44%), Incomplete abortion was found in 82 (41%), an embryonic pregnancy in 30 (15%). 140 (70%) women completely expelled the conceptual products on treatment with misoprostol alone, while 60 (30 %) patients required surgical evacuation due to the incomplete expulsion of conceptual products and heavy bleeding. Mean induction to expulsion interval was 16 h. Main side effects noted were a pain, pyrexia, nausea, vomiting, and diarrhea. More than one side effect was noted in 14 patients.

Conclusion: Treatment of early pregnancy loss with misoprostol is effective and acceptable for patients with early pregnancy complications. It is also cheap and heat stable and can be stored at room temperature.

Key Words: Misoprostol, medical treatment, miscarriage.
Expectant management is to wait for a spontaneous abortion, but the success rate with the use of this approach for embryonic or fetal death or an embryonic gestation is suboptimal (ranging from 25 to 76%). The interval to spontaneous expulsion is unpredictable, and it may take a month. The uncertainty and anxiety, along with the sadness resulting from pregnancy loss, often make expectant management less appealing to patients. It is an appropriate for women diagnosed with a pregnancy of uncertain viability, where the diagnosis is unclear.1,2

Surgical management is the treatment of choice for patients who are hemodynamically unstable, who show signs of sepsis, or who are not suitable for medical or expectant management either through patient’s preference or other medical or co morbidity.1,2

Medical management involves the use of prostaglandin analog misoprostol to induce uterine contractions, resulting in the delivery of pregnancy vaginally. Misoprostol (15 deoxy-16 hydroxyl 16 methyl PGE1) is a stable, synthetic form of prostaglandin E1 analogue. It was originally developed in 1970’s for the prevention of non-steroidal anti-inflammatory drugs (NSAID) induced peptic ulcers. Several clinical trials have evaluated the use of misoprostol alone for termination of early pregnancy failure.3

In the last two decades, medical termination of pregnancy has become a safe alternative to vacuum aspiration and dilatation and curettage. The cost savings to the patient and family is extremely important, even if the misoprostol administration did not lead to uterine evacuation. It would soften the cervix and make surgical evacuation an easier procedure.4

The objective was to study the effectiveness of misoprostol in women with the complication of early pregnancy and to avoid surgical management and its complications in these patients.

METHODOLOGY

After the consent from the patients, a total of 200 women with early pregnancy failure were recruited for treatment with misoprostol. The women were given detailed information regarding different treatment options available, only women who accepted the medical treatment with misoprostol were selected. The inclusion criteria were gestational age of fewer than 15 weeks and hemodynamically stable. The exclusion criteria were patients with a history of hypersensitivity to prostaglandin, ectopic pregnancy, gestational trophoblastic disease, high risk of uterine rupture, hemoglobin less than 9 g and hemodynamically unstable. Gestational age and early pregnancy complication were determined by clinical examination and ultrasound.

All women were given detailed information about the protocol of medical termination of pregnancy and were then admitted. Routine physical examination and investigations were carried out. Investigations included full blood count, urine routine examination, random blood sugar, blood group and Rhesus factor, hepatitis screening, liver function tests, renal function tests and blood coagulation profile.

Main outcome measures were the successful resolution of miscarriages without surgical intervention; secondary outcomes were the incidence of pain, vaginal bleeding, infection, pyrexia and gastrointestinal side effects.

After taking informed consent, misoprostol was inserted intravaginally in posterior fornix in a dose of 800 mcg (4×200 mcg) with repeat dose every 6 h for a total of 4 doses. Vaginal bleeding and abdominal pain were assessed and adverse effects were recorded. Induction to expulsion interval was defined as the time in hours from initiation of therapy until the expulsion of products of conception. The complete expulsion had been confirmed by ultrasound examination. Medical treatment was considered unsuccessful if there would be no complete expulsion of the products 24 hours after the last dose, and in those patients, surgical management has been performed.

RESULTS

A total of 200 women were included in the study. Age range from 16 to 45 years and from 0 to grand multigravida (Table 1).

<table>
<thead>
<tr>
<th>Age (years)</th>
<th>No. of patients</th>
<th>Percentage</th>
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</thead>
<tbody>
<tr>
<td>16-20</td>
<td>44</td>
<td>22%</td>
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<tr>
<td>21-30</td>
<td>98</td>
<td>49%</td>
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<tr>
<td>31-40</td>
<td>38</td>
<td>19%</td>
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<tr>
<td>40-45</td>
<td>20</td>
<td>10%</td>
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Early fetal demise was 88 (44%), incomplete abortion was 82 (41%) and an embryonic pregnancy was 30 (15%). 140 (70%) patients completely expelled products with misoprostol alone, while 60 patients (30%) required surgical evacuation due to the incomplete expulsion of the products and heavy bleeding.

Mean induction to expulsion interval was 16 h. Main side effects noted were a pain, pyrexia, nausea, vomiting, and diarrhea. More than one side effect was noted in 14 patients (Table 3).

### DISCUSSION

Management of early pregnancy complications is a common obstetrical problem. Medical management of early pregnancy loss needs effective care and observation and longer time. However maternal mortality and morbidity increase significantly by surgical methods. The medical method has become a safe alternative to vacuum aspiration and dilatation and curettage.

Misoprostol is the prostaglandin of choice as it is cheap and stable at room temperature. Different doses of oral, sublingual or vaginal misoprostol have been used. A Cochrane review of 19 randomized controlled trials indicated that vaginal route is the best option with no significant difference in side effects. The regimen using repeated doses of misoprostol alone that can be finished within one day have the advantage of requiring fewer hospital visits and ultrasound examinations.

In our study treatment with misoprostol resulted in the complete expulsion of products of conception in 70% of the cases, which is in accordance with other studies conducted nationally and internationally.

In a study conducted by Sultan Qaboos in Oman University in 2015. They used 800 ug misoprostol vaginally every 24 hours and max of 3 doses. Their success rate was 62.4%. In their study, 38.6% required surgical evacuation. These results are near to our results but this 8% difference may be because they used 3 doses and we in our study used 4 max doses.

In a study conducted in Pakistan by Nowshaba R, Syed Farhan in 2014 on the use of misoprostol in first trimester abortions. They also used 800ug dose but initially, they have given 600ug orally and then started vaginal 800ug dose at 4 hours interval and used a max of 4 doses. They repeated the 4th dose after 4 days if the products were not expelled with advice for follow up on 7th day.

Their success rate is also near to ours one. It’s 62.7% success rate in their study. This may be because they initially used only 3 doses. They also used a very long protocol, this usually results in patients dissatisfaction and refusal of the management.

In a randomized trial published in BJOG in 2006, it is concluded that with a dose of 800ug success rate is better than low doses of 600ug and 400ug. They also concluded that doses requirement and treatment duration also decreases with increasing misoprostol dose to 800ug in early pregnancy complications as compared to 600ug and 400ug regimens.

In our study, the vaginal route was used for administration of misoprostol. The vaginal route appears to be the most effective, followed by sublingual with oral being the least effective. Sublingual misoprostol needs a more frequent administration, that is, every 3 h to achieve a similar effectiveness to the vaginal route.

The incidence of pyrexia (7%), nausea (15%), vomiting (12%), diarrhea (2%), and heavy vaginal bleeding (16%), respectively. This is comparable to the study conducted by Mazhar et al. (2013).

Oral and sublingual administration of misoprostol is associated with more gastrointestinal side effects than a vaginal route. Abdominal pain was noted in 41%
of women. It was much high in comparison to other studies (Wood and Brain, 2002; Neilsen et al., 1999) none of the patients had pelvic inflammatory disease.12

CONCLUSION

Treatment of early pregnancy loss with misoprostol is efficient, acceptable and cost effective for patients with complications of early pregnancy. And it prevents the patients from the surgical interventions and its complications.

REFERENCES

1) Obstetrics and gynecology an Evidence based Text. 3rd ed. 2015; 679-84.
2) Khan et al. 2007; Albertman, 1992; Macrow and Elstein 1993.