

A COMPARATIVE STUDY ON THE EFFICACY OF ORAL AND VAGINAL ADMINISTRATION OF MISOPROSTOL

Qamar un Nisa[✉], Seema Gul¹, Sadaf Zohra²

ABSTRACT

BACKGROUND: Different doses, routes and regimens of misoprostol for medical termination of pregnancy during second trimester have been studied for effective termination.. Misoprostol can be administered through various routes i-e orally, buccally, sublingually, rectally and vaginally. Objective of this study was to compare the efficacy of oral with vaginal misoprostol for termination of pregnancy in second trimester missed miscarriage.

METHODS: This Randomized Controlled Trial (RCT) was conducted in the Department of Obstetrics & Gynaecology, Combined Military Hospital, Rawalpindi from 1st October 2016 to 31st March 2017. A total of 152 women were sampled through non-probability consecutive sampling. Patients with 13-24 weeks gestation presenting to the antenatal clinic or emergency with missed miscarriage were included. Patients within complete miscarriage, retained products of conception and twin pregnancy were excluded. All selected cases were randomly divided into two groups. Women in group A received 400mcg of misoprostol orally whereas group B received 400mcg of misoprostol vaginally.

RESULTS: The mean age of women in group A was 28.04 ± 3.37 years and in group B was 30.18 ± 6.05 years.. Efficacy in Group A (oral misoprostol) was seen in 63 (82.89%) while in Group B (vaginal misoprostol) was seen in 41 (53.95%) patients ($p = 0.0001$).

CONCLUSION: This study concluded that efficacy of oral misoprostol is better as compared to vaginal misoprostol for termination of pregnancy in second trimester missed miscarriage.

KEYWORDS: Miscarriage, Second trimester, Misoprostol.

✉ Registrar - Deptt of Gynae & Obs, Watim Medical & Dental College Rawalpindi, Pakistan.

@ doc.qamar@hotmail.com

📞 0345-4778221

1. Deptt of Gynae & Obs, Watim Medical & Dental College, Rawalpindi, Pakistan.

2. Deptt of Gynae & Obs, CMH Rawalpindi, Pakistan.

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INTRODUCTION

Miscarriage (early pregnancy loss) is defined as the spontaneous loss of pregnancy before the fetus reaches viability i.e. 24 weeks of gestation. Clinically the overall miscarriage burden constitutes approximately 12% of pregnancies¹. Pregnancy loss whether early or in second trimester, particularly in couples affected by recurrent miscarriage can have a significant impact on the woman's

physical health, mental health and emotional wellbeing as well as her partner and family. Maternal age (≥ 35 years of age) and number of previous miscarriages are two independent risk factors for a further miscarriage².

Second trimester miscarriage occurs between 13 and 24 weeks of gestation and it complicates approximately 1% of pregnancies. Clinically missed miscarriage includes gestational sac containing dead embryo

or fetus before 24 weeks gestation without having clinical symptom of expulsion³.

Various management protocols are used for second trimester pregnancy termination which include surgical technique (dilatation and evacuation) and medical methods such as intra-amniotic Prostaglandin F2 Alpha instillation, Prostaglandin E2 vaginal suppositories, Prostaglandin E1 and high dose oxytocin³. Misoprostol is a synthetic prostaglandin E1 (PGE) analogue used for prevention and treatment of peptic ulcer disease⁴. It has become an important drug in obstetric practice due to its uterotonic and cervical ripening effect³. It has been studied for medical abortion, induction of labor at term and for cervical priming before surgical abortion. It is easily available, easy to administer, cost effective, stable at room temperature, has fewer side effects and is suitable for settings with limited resources⁴.

Different doses, routes and regimens of misoprostol for medical termination of pregnancy during second trimester have been studied for effective termination i.e. acceptable success rate, short induction-termination interval and minimum side effects. Misoprostol can be administered through various routes i-e orally, buccally, sublingually, rectally and vaginally.

The standard treatment for missed miscarriage has been dilatation and evacuation which is typically done in an operating room, thus significantly increasing the costs. Medical evacuation of missed abortion is an effective, safe and cost effective alternative to surgical evacuation of the uterus and is particularly suited to women not wanting hospital admission or a surgical procedure under general anaesthesia⁵. On the other hand medical complications of surgical abortion is related to serious morbidity in 2.1% cases, and there is a risk of mortality in 0.5/100000 population⁴.

Systemic bioavailability of misoprostol has been found to be efficacious⁶. A recent study by Shah N et al reported complete evacuation of 52% and 48% with oral and vaginal

misoprostol respectively⁵. Another study by Diop A and colleagues found out 80% complete evacuation with oral misoprostol⁷. Some studies have even shown 100% evacuation with misoprostol given either orally, sublingual or vaginal.

We planned to conduct a randomized controlled trial to compare the efficacy of oral and vaginal misoprostol in women having second trimester missed miscarriage.

MATERIAL & METHODS

This Randomized Controlled Trial (RCT) was conducted in the Department of Obstetrics & Gynaecology, Combined Military Hospital, Rawalpindi from 1st October 2016 to 31st March 2017.

With the help of WHO sample size calculator, 152 patients, through non-probability, consecutive sampling, were selected and then randomized in 1:1 i.e 76 to each of the two groups. Women with 13-24 weeks gestation presenting to the antenatal clinic or emergency with missed miscarriage were included. Patients having incomplete miscarriage, retained products of conception (RPOCs), previous caesarean section scars, twin or triplet pregnancies or those who refused to participate were excluded from the study.

Ethical approval was obtained from hospital ethical committee of the CMH Rawalpindi. Written informed consent was taken from eligible participants. Women in group A received 400mcg of misoprostol orally every four hours for a maximum of 5 doses whereas group B received 400mcg of misoprostol vaginally every four hours for a maximum of 5 doses. Missed miscarriage was defined as gestational sac containing dead embryo or fetus before 24 weeks gestation (no heart beat) and not having clinical symptom of expulsion like vaginal bleeding while efficacy was defined as complete evacuation of pregnancy (miscarriage) in the second trimester following oral or vaginal misoprostol confirmed on ultrasound with no retained products of conception.

Women were told to inform the

duty doctor if they experienced any abdominal pain, vaginal bleeding, passed the gestational sac or developed any side effects like fever or shivering. Information regarding age, gestational age, ultrasound diagnosis, number of doses, and induction to abortion interval, side effects and success or failure of treatment was recorded on structured proforma. All the information was collected by the researcher herself to reduce selection bias and maintenance of quality of data.

Data was entered in SPSS software version 16. Frequencies and percentages were calculated for categorical variables while mean and standard deviation were calculated for numerical variables. The proportions of study outcome i.e. efficacy was compared among two groups using chi-square test to test null hypothesis; no difference of efficacy between oral and vaginal administration of misoprostol. P-value ≤0.05 was considered significant.

TABLE 1: COMPARISON OF EFFICACY BETWEEN TWO GROUPS = 152 (%)

Efficacy	Group A	Group B	Chi Sq	P value
Yes	63(82.9%)	41(53.9%)	14.7	0.0001**
No	13(17.1%)	35(46.0%)		

** result highly significant

DISCUSSION

Missed abortion is defined as unrecognized intrauterine death of the embryo or fetus without expulsion of the products of conception. It constitutes approximately 15% of clinically diagnosed pregnancies⁸. Women experiencing a missed abortion may have no self-awareness due to the lack of obvious symptoms. With around 95% 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 years⁹. However, the costs of surgery and hospitalization, as well as the complications associated with surgery and anaesthesia are a major unresolved concern. Besides infection and bleeding, decreased fertility caused by intrauterine adhesions may be unacceptable for women with

RESULTS

Age range in this study was from 18 to 38 years with mean age of 27.93 ± 3.41years. The mean age of women in group A was 28.04 ± 3.37years and in group B was 30.18 ± 6.05 years. Majority of the patients 119 (78.29%) were between 18 to 30 years of age. Gestational age ranged from 13-24 weeks with mean gestational age of 17.16 ± 2.62weeks. The mean gestational age in group A was 17.37 ± 2.67weeks and in group B was 16.96 ± 2.61weeks. Majority of the patients 96 (63.16%) were between 13 to 18 weeks of gestation.

missed abortion, who have not yet fulfilled their motherhood desires. Some studies have thus suggested that expectant or medical management might be more suitable instead of surgical evacuation¹⁰.

The efficacy and safety of misoprostol alone for missed abortion was established in many studies¹¹⁻¹⁴. However, route of administration of misoprostol and success rates varied among the studies. It could be given by oral, sublingual or vaginal, while the doses ranged from 100 micrograms to 800 micrograms¹¹. The most suitable route and dose of misoprostol for missed abortion is not yet clear. A single dose of 800 micrograms of misoprostol by vaginal or oral for missed abortion was recommended by National Institute for Health and Care Excellence (NICE)¹⁵. However

some studies reported converse opinion, by pointing out that a lower dose or different routes of misoprostol may be equally effective^{16,17}.

A recent study by Shah N et al reported complete evacuation of 52% and 48% with oral and vaginal misoprostol respectively⁵. Another study by Diop A and colleagues found out 80% complete evacuation with oral misoprostol⁷. Some studies have even shown 100% evacuation with misoprostol given either orally, sublingual or vaginal.

Another study has shown that there were no statistically significant differences between oral (82.3%) and vaginal (80%) misoprostol groups in terms of response to treatment (the excretion of gestation products)¹⁸. In a study by Behrashi et al, response to treatment in vaginal group was 86.7% and in oral group was 43.3%. In a study by Tale et al, response to the treatment in the oral misoprostol group was 71.1%¹⁹ and in Hassanzadeh's study, response to treatment was 83% in the vaginal misoprostol group²⁰. In a study by Ayati et al, in vaginal misoprostol group 75.6% and in oral misoprostol group 84.6% had excreted gestation products²¹. Mirmohammadi et al demonstrated that in vaginal misoprostol, 44% had excreted gestation products completely and 56% had incomplete excretion²². Ganguly et al have shown that complete abortion in sublingual misoprostol group was more than the oral group (P = 0.0338) and vaginal group (P = 0.562)²³.

In a study, two hundred and one patients who miscarried consented to randomization using computer-generated randomization model prior to treatment. A total of 800 µg of misoprostol was given either vaginally or orally to the randomized subjects. A second dose was repeated 4 h later if the product of conception had not been passed. The incidence of complete uterine evacuation following vaginal and oral misoprostol was similar [(58/95) 61.1% versus (67/103) 64.4%]. There was a significantly decreased incidence of diarrhoea [(12/95) 13.6% versus (62/103) 65.3%, P < 0.01] with the use of vaginal misoprostol²⁴.

A meta-analysis concluded that misoprostol is a non-invasive, effective medical method for completion of abortion in missed abortion. Sublingual misoprostol of 600 µg or vaginal misoprostol of 800 µg may be a good choice for the first dose. The ideal dose and medication interval of misoprostol however needs to be further researched. Another randomized trial comparing the use of oral misoprostol and vaginal misoprostol in the medical evacuation of incomplete miscarriage was performed by Crenin et al²⁵. They found that vaginal misoprostol was associated with a significant improvement in uterine evacuation but at the same time, an increase in systemic side-effects. However, the dosage of vaginal misoprostol used was twice as high as the oral group, therefore making the interpretation of the results difficult²⁵.

Limited articles could be found about the efficacy and tolerability of sublingual or oral misoprostol of 800 µg which made us difficult to evaluate. Only in one study it was compared with vaginal misoprostol of 800 µg, the authors found that sublingual misoprostol was as effective as vaginal misoprostol and most side effects were similar in both groups, but heavy bleeding was more common in the sublingual group²⁶. Two studies reported that oral misoprostol or vaginal of 800 mcg was comparable in terms of efficacy while more side effects were reported in oral misoprostol of 800 mcg in one study^{27,28}.

CONCLUSION

Efficacy of oral misoprostol is better as compared to vaginal misoprostol for termination of pregnancy in second trimester missed miscarriage. So, we recommend that oral misoprostol should be used as a first line surgical method in the treatment of second trimester missed miscarriage in order to reduce maternal morbidity and mortality.

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CONFLICT OF INTEREST

None declared.

GRANT SUPPORT AND FINANCIAL DISCLOSURE

NIL

Authors agree to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.