

Efficacy of Vaginal Misoprostol versus Sublingual Misoprostol in the Management of Early Miscarriage

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ABSTRACT

Aim: To compare the effectiveness of vaginal with sublingual misoprostol in the management of early miscarriage.

Study Design: Randomized controlled trial

Place and Duration of Study: Department of Gynaecology and Obstetrics, Unit-I, Sandeman Provincial Hospital Quetta from 1st February 2018 to 31st July 2018.

Methodology: One hundred and eleven patients with clinical diagnosis of missed miscarriage confirmed by ultrasound receiving per vaginal misoprostol (800 µg) were named as group "A" and those receiving sublingual misoprostol were labeled as group "B". Clinical outcome was assessed as the complete expulsion of the products of conception either successful or unsuccessful confirmed by a repeat pelvic ultrasound after the treatment.

Results: The mean age of patients in group-A was 25.89±5.7 years and in the group-B was a 26.38±5.5 year. The mean gestational age in group-A was 9.44±1.58 weeks and in group-B was a 9.45±1.52 week. The overall miscarriage rate was 67.5%. 72% of women in group-B and 63% in the group-A had complete miscarriage. The mean induction to expulsion interval was 13.55 hours in group-A and 13.22 hours in group-B. The rate of complete expulsion of products of conception was high in group- A compared to the group- B.

Conclusion: Sublingual misoprostol is as effective as vaginal misoprostol in management of the early miscarriage.

Key words: Miscarriage, Misoprostol, vaginal, sublingual

INTRODUCTION

Early miscarriage is a major health problem worldwide with an incidence of 15-20%. In Pakistan 890,000 women annually present with missed or incomplete miscarriage with an annual miscarriage rate of 29 per 1000 women aged 15-49 years¹. Management of early miscarriage includes expectant, medical and surgical. Traditionally the primary treatment for early miscarriage has been Dilatation and Curettage (DNC). DNC is though considered safe in the hands of skilled personnel but requires a trained personnel, operating room and an anesthetist². Recent studies have questioned the need for routine DNC suggesting that medical management might be more appropriate^{3,4}.

Medical management using misoprostol is a safe and cost effective method for early miscarriage having a high level of patient satisfaction⁴ and a success rate around 80%.⁵ Misoprostol is a synthetic prostaglandin E₁ analogue available in the form of tablets administered through oral, sublingual, rectal and vaginal routes, with a reported effectiveness of 85% with vaginal route⁶. Sublingual route is though associated with more side effects, most common of which is an unpleasant taste but has a success rate of 95% and is more convenient, avoids painful vaginal administration and gives more privacy⁷.

Nonsurgical alternatives expand a woman's treatment options and, in turn, the quality of care.⁸ Moreover, in some settings, surgical options are not available to women or are not medically feasible. In first trimester abortion, combined treatment by misoprostol with mifepristone appears to be

more effective than misoprostol-alone regimens and thus are considered the gold standard for medical induction. However, misoprostol-alone regimens may be the treatment of choice in settings in which mifepristone is not available or is too costly⁹.

Medical management of missed abortion is less practiced in our area because of doubts regarding its efficacy. Similarly sublingual route of administration is also less popular due to the same reason though Sublingual route is gaining popularity worldwide. Considering the magnitude of early miscarriage and the clinical burden on hospitals in our setup the authors wanted to conduct this study to remove doubts regarding efficacy of sublingual administration of misoprostol as a cost effective method.

PATIENTS AND METHODS

This randomized controlled trial study was conducted at Gynaecology and obstetrics department, Unit-I, Sandeman provincial hospital, Quetta from first February 2018 till 31st July 2018. Randomization was done by lottery method. Approval to conduct the study was taken from the medical superintendent of the Sandeman provincial hospital, Quetta. Sample size calculated was 222 (111 for each group), keeping anticipated population proportion for complete uterine evacuation with vaginal misoprostol as 85% and anticipated population proportion for sublingual misoprostol as 95%, power of test 80% and level of significance 5%. All the patients having early miscarriage fulfilling the inclusion criteria were included in the study. Patients with suspected ectopic pregnancy, severe anemia (Hb<7g/dl), severe blood loss at admission soaking > 2 large pads in an hour for 2 hours in a row, known allergy to prostaglandin, patients with intrauterine contraceptive device, evidence of cardiac, hepatic or renal disease,

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patients with previous caesarean section were excluded from the study to avoid confounding factors and biasness during the study. Informed consent was taken from the patients. Baseline investigations were sent to laboratory for blood complete count, blood grouping, Hepatitis B surface antigen, anti-hepatitis C antibodies and blood sugar level for optimizing management accordingly. Patient's privacy and comfort were kept in consideration. Patients were given misoprostol vaginally and sublingually by lottery method to remove personal biasness. Patients labeled as Group-A received intra vaginal misoprostol 800 micrograms at the time of admission, in case of failure to abort two further doses of 400 microgram were repeated at 3 hourly intervals. Patients named as Group-B received 600 microgram of misoprostol sublingually and were advised to keep the saliva in mouth until the tablet absorbed. In case of failure to abort or incomplete abortion 400µg misoprostol was repeated at three hourly intervals for a maximum of two doses and a total of three doses. An ultrasound was carried out to confirm uterine evacuation after the patient expelled the products of conception. Cervical status, amount of vaginal blood loss and vitals were monitored. Women with heavy vaginal bleeding and incomplete miscarriage needing emergency surgical evacuation by dilatation and curettage were considered as treatment failure. Women requiring analgesia were given injection tramadol intramuscularly. Following the evacuation all patients were followed for 6 hours for vaginal bleeding and were discharged with advice of follow-up 1 week later. Rh-anti D immunoglobulin was given to Rh-negative women who underwent surgical evacuation on emergency basis due to treatment failure. The data were entered and analyzed on SPSS version 20. For efficacy of both routes of administration of misoprostol as complete evacuation, percentages were calculated and Chi-square test was applied. P-value of <0.05 was considered significant.

RESULTS

A total of 222 patients were included in the study. One-hundred and eleven patients each were included in group-A and group-B. The mean age of patients in group-A was 25.89±5.7 years. The mean age of patients in group-B was 26.38±5.5 years. Mean gestational age of subject in vaginal group was 9.44±1.58 weeks and in sublingual group 9.45±1.52 weeks. Mean gestational age of the study group was 9.4±1.55 weeks; mean gestational age in the vaginal group was 9.4±1.58 weeks and in the sublingual group was 9.45±1.52 weeks. Effect of maternal age, parity and gestational age with the risk of the occurrence of early miscarriage is given in Table 1.

The miscarriage rate overall was 67.5%. 72% of women in the sublingual group and 63% in the vaginal group had complete miscarriage as represented in Table 2. Mean induction to abortion interval was 13.55 hours in vaginal group and 13.22 hours in sublingual group. No statistical difference between the outcome of miscarriage and induction to abortion interval was observed between the sublingual and vaginal group.

Table 1: The demographic characteristics of the women diagnosed with early miscarriage

Variables	Vaginal Misoprostol n=111	Sublingual Misoprostol n=111	p-value
Mean Age (years)	25.89±5.7	26.38±5.52	0.36
Parity, median (range)	3.29±0.51	3.33±0.58	0.41
Mean gestational age (Weeks)	9.44±1.58	9.45±1.52	0.17

Table 2: Comparison of efficacy between vaginal with sublingual misoprostol in the treatment of early miscarriage

Complete miscarriage	Vaginal Misoprostol n=111	Sublingual Misoprostol n=111	Total
Successful (Efficacy Yes)	70(63.06%)	80(72.07%)	150(67.56%)
Unsuccessful or required DNC (Efficacy No)	41(36.94%)	31(27.93%)	72(32.43%)

DISCUSSION

With the availability of prostaglandins in the early 1970s, medical termination has become an alternative method for managing the early pregnancy miscarriage and misoprostol is the drug of choice worldwide^{10,11}. Misoprostol is a potent uterotonic agent, stable at room temperature and is considerably cheaper, thus cost-effective for our low economic resource setup with high environmental temperature¹².

Most of the cases were between 19 to 30 years of age in both groups. Mean age, gravidity, parity and gestational age were not significant between groups. Vaginal misoprostol of 800ug was recommended for missed miscarriage by the NICE and some clinical guidelines.¹³ In this study rate of successfully complete miscarriage was 72.07% in sublingual group and 63.06% in vaginal group with no statistical difference between the two routes (p<0.5). Similar is true about induction to abortion interval. Treatment failure needing surgical evacuation was required in about 30% of cases in sublingual group versus 40% in vaginal group.

The results of the study are comparable to a study from Bahawalpur which reported a success rate of 73.3% in sublingual group and 66.7% in vaginal group¹⁴. However it is much less comparable to similar studies reported from China and India which used 600 µgm of sublingual and vaginal misoprostol and reported an overall success rate of 87.5% and 86% respectively.¹⁵ This higher success rate may be related to the higher dose 600 ugm of misoprostol used in those studies. According to the Systematic Review of the Cochrane database, sublingual misoprostol is as effective as vaginal misoprostol in causing complete miscarriage but is associated with more frequent diarrhoea.¹⁶ More frequent side effects with sublingual use of misoprostol are due to its high peak concentration and great bioavai

CONCLUSION

In conclusion, sublingual 600 µg or vaginal 800 µg misoprostol is a non-invasive, effective and safe agent so it can be used for management of early pregnancy loss. Sublingual route of administration is as effective as vaginal group, with more convenient dosage and privacy and side effects that are easily manageable.

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