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Original Research Article

A comparative study to assess the efficacy of oral versus vaginal route of misoprostol in missed first trimester abortion

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ABSTRACT

Background: Aim of the study to contrast the effectiveness of misoprostol taken oral vs vaginal method, for the management of missed abortion in the early trimester, and to acknowledge misoprostol value in cervical dilatation before any surgical pregnancy termination,
Methods: Comparing the efficacy of misoprostol, by vaginal and oral routes, for termination of first trimester missed abortion was conducted in the department of obstetrics and gynaecology, at DR B. R. Ambedkar medical college and hospital, Bangalore. 2 groups were made as group A and group B which had 24 participants in each group and a total of 48 participants, in which group A was given misoprostol 400 mcg orally, maximum up to 3 doses and group B was given misoprostol 400 mcg maximum up to 3 doses and outcome was documented. Primary outcome expecting drug-induced complete expulsion of products of conception (POCs). Secondary outcomes measured were induction expulsion interval, number of doses required, classification of failures, cervical canal permeability in women requiring surgical evacuation, side effects.
Results: Both oral and vaginal routes are highly effective (oral=75%, vaginal=91.7%, p=2.400), safe and acceptable with tolerable side effects. The mean time to expulsion was longer (10.55 hours) in the oral than vaginal group (8.09 hours). All unsuccessful cases, 2 in vaginal group and 6 in oral group had permeable cervices prior to surgical evacuation. Most of the side effects were tolerable in both groups.
Conclusions: Vaginal route of misoprostol is more effective than oral misoprostol for first trimester missed abortion.

Keywords: Misoprostol, Abortion, First trimester abortion, Oral and vaginal route

INTRODUCTION

Missed miscarriages in the first trimester are characterized by the arrest of embryonic or foetal development with ultrasound findings of an empty gestational sac or an embryo/foetus without cardiac activity without expulsion of the POCs. It constitutes about 15% of clinically diagnosed pregnancies.[1] Women experiencing a missed abortion may have no self-awareness due to the lack of obvious symptoms.

Surgical evacuation, which has been widely practised throughout the world for the past 50 years, is regarded as the standard treatment for missed abortion and has an approximate 95% success rate.

However, a significant unresolved issue is the cost of surgery and hospitalisation, as well as the risks connected to anaesthesia and operation. For women who have missed abortions and haven't yet achieved their ambition to become mothers, diminished fertility brought on by intrauterine adhesions may be intolerable in addition to infection and bleeding. Thus, some studies have suggested that medical or expectant management may be preferable to surgical evacuation. Uncertainty regarding the timing of expulsion and the requirement for surgical backup are drawbacks of expectant treatment.

Therefore, the current trend is moving toward using medical techniques to create a gentle, non-traumatic cervical dilation, as well as to separate and expel contents.

Prostaglandins (PGs) by various routes have transfigured the treatment of missed miscarriage. The natural decline in progesterone caused by the demise of the conceptus justifies the use of PGs alone. If POCs are not expelled, surgical procedures are used. Misoprostol is a synthetic prostaglandin E1 analogue that was initially created to prevent gastrointestinal ulcers brought on by non-steroidal anti-inflammatory medicines. Despite being an "off label use," it is frequently used to terminate pregnancies because it is efficient, economical, has a long shelf life (2 years) at room temperature, and doesn't require the use of needles. In comparison to PGE2 analogues, it also has less negative effects.[1] According to several research, women with missed abortions who get mifepristone and misoprostol medical treatment are more likely to experience severe bleeding.[2,3] Numerous studies have demonstrated the effectiveness and safety of misoprostol alone for missed abortion.[4,5] The doses ranged from 100 micrograms to 800 micrograms and could be administered orally, sublingually, or vaginally.[6,7] Although it can be used vaginally and orally, most women choose the oral method to avoid the uncomfortable vaginal inspection. The vaginal method is preferred and is thought to reduce gastrointestinal adverse effects. It results in a slower rise and lower peak plasma concentration of misoprostol acid than oral administration, but the overall medication concentration reaching the target organ is higher when using the vaginal route.[8]

The goal of the current study was to examine the safety and effectiveness of 400 mg of misoprostol given intravaginally and orally for missed abortions up to 12 weeks of gestation.

Additionally, it was suggested to determine the effectiveness of misoprostol for cervical dilatation before beginning any surgical treatments that might be used regularly on outpatient department patients.

METHODS

A randomised control trial comparing the efficacy of misoprostol, by vaginal and oral routes, for termination of first trimester missed abortion was conducted in the department of obstetrics and gynaecology, at DR. B. R. Ambedkar medical college and hospital, Bangalore, from January 2021 to December 2022. 2 groups were made as group A and group B which had 24 participants in each group and a total of 48 participants, in which group A was given misoprostol 400 mcg orally, maximum up to 3 doses and group B was given misoprostol 400 mcg maximum up to 3 doses and outcome was documented.

SPSS 20 was used for statistical analysis after data was entered in Microsoft excel and then coded.

Inclusion criteria

Gestational age ≤12 weeks by LMP, females of age group 18-45 years, diagnosis of missed abortion on USG, closed cervix on bimanual pelvic examination, haemoglobin ≥9 gm/dl, axillary temperature <37 degree Celsius. Mild vaginal bleeding or spotting per vagina. No history of inflammatory bowel disease, asthma, liver disease or contraindication to use of misoprostol. Willingness and ability to give informed consent were included.

Exclusion criteria

Women 45 years of age, foetal gestational age >12 weeks, any degree of cervical dilatation, signs or symptoms of infection, twin gestation sac, molar pregnancy, inability or refusal of patient to adhere to follow-up. Excessive uterine bleeding, blood pressure ≥160/90 mmHg. Poor general health of any cause, maternal history of asthma or cardiac disease or cerebral disease, any prior medical or surgical treatment to interrupt current pregnancy were excluded.

Group A: 24 women with confirmed missed abortion with ultrasonography were given tab misoprostol 400 mcg orally with sips of water, 4 hours apart for a maximum of 3 doses.

Group B: 24 women with confirmed missed abortion with ultrasonography were placed tab misoprostol 400 mcg in the posterior fornix and repeated every 4 hours for maximum of 3 doses.

Following which women were monitored for vitals, bleeding per vagina, expulsion of POCs, also looked for other associated side effects. Complete, partial, or no evacuation was determined over the following 08-15 hours was documented.

Each female was questioned regarding POC expulsion and potential symptoms at each dose interval. It was thoroughly checked to see if POCs had been expelled. Additionally, a bimanual pelvic examination was done to check for any retained foetal tissue. If POCs were still present, misoprostol dosages were increased until the tissue was entirely evacuated or else drug's maximum dose was administered. No additional dosages were administered if the patient totally aborted previously.

Primary outcome evaluated was drug-induced complete expulsion of POCs. Secondary outcomes measured were induction expulsion interval, number of doses required, cervical canal permeability in women requiring surgical evacuation, side effects, haemoglobin drop, duration and amount of post-abortal bleeding, experience with side effects, patient satisfaction and acceptability to the treatment.

RESULTS

Mean age of patients was 25.9±1.7 years in oral group and 22.08±2.5 years in oral group and 22.08±2.5 years (ranging from 18-36 years). The mean BMI of patients was 21.713±2.2017 kg/m^2 in group A and 22.155±1.8281 kg/m^2 in group B. Most patients were multigravida in both

groups (66.7% (16) in group A and 83.3% (20) in group B, and amongst remaining, 16.7% (4) women in group A and 25% (6) in group B had previous abortion.

Table 1: Outcome tabulated in both the groups.

Baseline characteristics	Oral (Group A)	Vaginal (Group B)	P value
Age (Years) (Mean ± SD)	25.9±1.7	22.08±2.5	
Primigravida	8 (33.3)	4 (16.7)	0.889
Multigravida	16 (66.7)	20 (83.3)	
Gestational age (weeks)			
<6	6 (25)	4 (16.7)	0.253
6-12	18 (75)	20 (83.3)	
Previous caesarean section	4 (16.7)	6 (25)	0.253
Previous abortion	4 (16.7)	6 (25)	0.253

Clinical outcome and its relationship with number of doses of misoprostol

In group A, success rate was 75% as against 91.7% in group B. Amongst these 0 patients in group A and 8.3% in group B expelled completely with single dose. Another 12 (50%) in group A and 18 (75%) in group B expelled after two doses. Another 12 (50%) in group A and 4 (16.7%) in group B expelled after three doses. Vaginal administration of misoprostol was thus found to be more effective than oral for complete uterine evacuation (p=7.200)

Induction-expulsion interval

Mean I-E interval (in hours from administration of first dose to complete expulsion) was 10.55±1.09 hours in group A and 8.0909±0.921 hours in group B, difference being statistically highly significant (p=7.200).

Failures

Six (25%) patients in group A failed treatment. Out of these, abandonment of drug schedule and subsequent recourse to surgical manoeuvre was required in 2 women (owing to severe hyperpyrexia), while remaining were incomplete abortions. In group B, 2 (8.3%) patients failed treatment, amongst which, surgical evacuation was performed on request in 1 patient, while another 1 case had retained products.

Cervical canal permeability in failures

All 6 unsuccessful cases in group A and 2 in group B had permeable cervices. Further dosage of misoprostol was increased for failed cases, also few had to undergo surgical evacuation.

Side effects and complications

All side effects of misoprostol were more common with oral group.

Table 2: Side effects in both groups.

Side effects	Oral, n (%)	Vaginal, n (%)
Nausea /vomiting	6 (25)	2 (8.3)
Headache	6 (25)	2 (8.3)
Dizziness	6 (25)	0
Severe cramps	8 (33.3)	6 (25)
Fever	4 (16.7)	4 (16.7)
Diarrhoea	8 (33.3)	6 (25)
Excessive bleeding	2 (8.3)	4 (16.7)
Cervical tear	0	0
Uterine rupture	0	0
Death	0	0

Patient satisfaction and acceptability to treatment

Overall acceptance to treatment was high in both groups A and B (70% and 76%) (p=0.792).

DISCUSSION

Patients in this study were younger than those in American and European studies, reflecting early marriage and first conception ages common in India.[9-13] The majority of the study participants were illiterate, from lower socioeconomic backgrounds, from rural areas, working in the home, and had normal BMI. All of these findings supported the idea that a segment of society visited the facility to seek treatment for gynaecological issues.

In our study, a complete uterine evacuation without the need for surgical intervention for any cause, including ET of 15 mm, was defined as the final success rate (as assessed by TVS). When compared to the majority of research in the literature, this boosted our success rates without placing an additional load on healthcare institutions.[9,14-16]

Misoprostol is an effective non-surgical approach with high effectiveness in missed miscarriage, with higher overall efficacy of vaginal route, as evidenced by 75% and 92% success rates in group A and group B.

This provided more evidence for the idea that because progesterone levels are often low and uterine contractions and gestational sac evacuation are initiated by PGs rather than antigestagens in missed miscarriages.

Misoprostol success rates range widely (13-100%), which can be attributable to a number of factors. route of delivery, various dosing regimens, repeated dosing regimens, prolonging follow-up (waiting for 3-15 days was found to be related with better success rates), patient

selection, Use of USG prior to beginning treatment is associated with higher success rates, small sample size creating bias, criteria used to define success (waiting period of 24 hours or more, cut-off for ET presumed to be 15 mm or until 30 mm to rule out RPOC), type of PG analogue used, such as sulprostone or PGE2 analogues along with misoprostol or simultaneous use of mifepristone in other studies.

In comparison to group A, group B had a much higher percentage of patients who miscarried within the first 12 hours. These results, which showed a lower mean I-E interval in the vaginal group, were consistent with the work of the majority of writers.[14,17-19]

We advise increasing the number of doses and reducing the dosing interval because the efficacy of a medical procedure depends on the dose, number of doses, mode of medication administration, as well as dosing interval. This could potentially boost the cumulative effects of misoprostol.

Expulsion rates would also rise if the time after the final medication was administered before expulsion was documented was extended. Additionally, boosting the effectiveness of medical management might benefit from the use of more objective metrics in research.

In contrast to prior research, the majority of women (2 out of 6 in group A and 1 out of 2 failures in group B) underwent surgical evacuation for an incomplete abortion. Additionally, we noticed permeable cervixes during evacuation among women who did not respond to treatment (ability to pass no. 8 Hegar's dilator).

In our trial, the oral group experienced more GI side effects, although these were easily treated with anti-emetic and anti-diarrheal medications.

The most notable adverse reaction to misoprostol was diarrhoea, which is a normal reaction of intestinal smooth muscles to an increase in PGs. Despite prolonged treatment, diarrhoea is typically moderate and self-limiting and resolves within a few days. Hence the medication should be taken with meals to the lessen any GI side effects.

Few women in either group of women described side effects as "terrible," and most of them described them as "tolerable." High levels of satisfaction were reported by both, overall acceptance to treatment was high in both groups A and B (70% and 76%). Members of group B expressed dissatisfaction, primarily because they found repeated vaginal application uncomfortable.

Additionally, the treatment can be given at the patient's home, increasing convenience and privacy while simultaneously increasing compliance and lowering the cost of medical management.

Limitations

In our study group, number of subjects were limited, hence, to be conducted in much more large study groups for more appropriate results.

CONCLUSION

This early experience with the medical management of missed miscarriage in the first trimester is consistent with the written research. The present study's findings support the use of misoprostol as a viable alternative to traditional surgical evacuation in missed miscarriage, with high success rates, patient acceptability, and manageable side effects. Vaginal approach is more effective. However, it should only be provided by qualified medical professionals who are able to perform surgery in the event of a failed abortion or significant bleeding. Misoprostol's cervical ripening action makes the surgical operations much simpler, even in circumstances where the patient is unable to evacuate.

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