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Original Article

Outcomes of Early Pregnancy Loss Induced by Sublingual Misoprostol: A Clinical Evaluation

Marzina Begum[1*], Shahinara Islam[2], Farzana Afroze[3], Afsana Sarker[4]

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*Corresponding author

ABSTRACT

Background: 15-20% of pregnancies diagnosed are lost in early pregnancy loss, and management can be expectant, medical, or surgical. The study aimed to evaluate the effectiveness and safety of sublingual misoprostol in the treatment of early pregnancy loss. **Methods & Materials:** The prospective observational study was carried out at Shaheed Suhrawardy Medical College Hospital, Dhaka, from January 2025 to June 2025. One hundred women between 18 and 45 years with ultrasound-diagnosed missed miscarriage at ≤13 weeks gestation were included. Participants were given 600 micrograms of sublingual misoprostol, repeated every 3 hours as required. Complete expulsion was checked by ultrasound on the seventh day after the first treatment. Demographic details, clinical parameters, treatment outcomes, and side effects were recorded and analyzed using SPSS version 20.0. **Results:** Successful expulsion was achieved in 80% of patients, and most of the expulsions (56%) were between 13-18 hours from initial dosing. The majority of them (61%) required three or more doses of misoprostol, and only 3% were responsive to a single dose. Of the failed ones, 90% had porous services despite incomplete expulsion. The most frequent side effects were nausea (69%), severe pain (40%), and diarrhea (14%), and rare serious adverse effects were excessive bleeding (6%) and hyperpyrexia (5%). The risk factors identified were PCOS (22%), thyroid disease (21%), hypertension (16%), and antiphospholipid antibody syndrome (16%). **Conclusion:** Sublingual misoprostol offers a safe and less invasive option compared to surgery in the treatment of early pregnancy loss, particularly useful in low-resource settings where surgical facilities are not readily available. Multiple doses are typically required, with expulsion typically 7-18 hours after administration.

Keywords: *Early pregnancy loss, Misoprostol, Sublingual administration.*

1. *Consultant, Department of Gynecology & Obstetrics, Popular Diagnostic Centre, Barisal, Bangladesh (ORCID: 0009-0008-0240-2659)*
2. *Junior Consultant, Department of Gynecology & Obstetrics, Sylhet Mag Osmani Medical College Hospital, Sylhet, Bangladesh*
3. *MBBS, DGO, FCPS, OSD, DGHS, Attachment! Bangladesh Medical University, Dhaka, Bangladesh*
4. *Registrar, Department of Gynecology & Obstetrics, ZH Sikder Women's Medical College, Dhaka, Bangladesh*

INTRODUCTION

Early pregnancy loss miscarriage or spontaneous abortion is a significant public health problem in 15-20% of clinically diagnosed pregnancies [1]. In the past, management of early pregnancy loss has largely been surgical evacuation with all its attendant risks of uterine perforation, cervical trauma, infection, and anesthetic complications [2]. However, recent advances in medical management have offered less invasive alternatives, particularly for women who desire to avoid surgical evacuation [3]. Misoprostol, a prostaglandin E1 analog, has emerged as a very effective pharmacological agent in the management of early pregnancy loss due to its uterotonic effect leading to uterine contractions and cervical ripening [4]. Initially developed to prevent and treat gastric ulcers, misoprostol is now widely used in obstetric practice for various indications like labor induction, postpartum hemorrhage, and management of early pregnancy failure. The drug may be administered using various routes like oral, vaginal, sublingual, and buccal, all of which have varying pharmacokinetic profiles and success rates [5]. Misoprostol has been of particular interest when administered sublingually because it possesses some advantages. Sublingual administration provides very rapid absorption through the highly perfused mucosa of the tongue, leading to higher peak plasma levels and bioavailability than oral or vaginal administration [6]. This pharmacokinetic profile can be equivalent to enhanced clinical efficacy as well as reduced dosage requirement and resultant side effects [7]. Sublingual administration is also more acceptable and convenient for the patient since it avoids the discomfort as well as privacy concerns sometimes associated with vaginal insertion [8]. Despite the increased clinical application of sublingual misoprostol, robust evidence of its efficacy, safety profile, optimal dosing regimens, as well as outcomes in various groups of patients is limited [9]. Variabilities in treatment regimens like dose, frequency, and duration of treatment also render it challenging to quantify its actual effectiveness [10]. Furthermore, patient-specific variables such as gestational age, previous obstetric history, and sociodemographic status can influence treatment outcomes and must be seriously taken into consideration during clinical decision-making [11]. The objective of this study is to evaluate the clinical outcome of treating early pregnancy loss with sublingual misoprostol, focusing on complete expulsion rates, time to expulsion, need for additional interventions, and safety profile. Through the observation of a cohort of 100 women with early pregnancy loss treated with sublingual misoprostol in Shaheed Suhrawardy Medical College Hospital, Dhaka, this study seeks to contribute to the evidence base proving medical management as an effective, safe, and alternative option to surgical evacuation. Furthermore, this study examines possible predictors of treatment response, such as demographic variables, gestational age, and clinical variables, in order to more accurately identify those patients most likely to benefit from this strategy. The findings of this study have important implications for clinical practice, particularly in resource-constrained settings where operating theater resources may be scarce. By validating the effectiveness of sublingual misoprostol as a cost-effective, non-surgical option for the management of early pregnancy loss, this study will apprise the development of evidence-based clinical guidelines and add to the repertoire of therapeutic options that are available for women experiencing this frequent but distressing reproductive health event.

METHODS & MATERIALS

This prospective observational study evaluated the efficacy and safety of sublingual misoprostol in treating missed

miscarriage at the Department of Obstetrics & Gynecology, Shaheed Suhrawardy Medical College Hospital in Dhaka, Bangladesh from January 2025 to June 2025. The duration of the study was six months and applied purposive sampling for the recruitment of 100 women suffering from early pregnancy loss (initially calculated as 196, but reduced due to constraints in time and resources). Inclusion criteria were women between the ages of 18-45 years with gestational age ≤13 weeks, missed abortion diagnosed by ultrasound, mild vaginal spotting/bleeding, closed cervix, and hemoglobin level ≥9g/dl. Excluded were women who did not meet this age group, gestational age >13 weeks, cervical dilatation, heavy bleeding, hemodynamic instability, infection symptoms, or contraindication to misoprostol. Students took 600 micrograms of sublingual misoprostol as the starting dose, dosed every 3 hours PRN, based on standard treatment for first-trimester missed abortion. Sonographic assessment at least seven days after the initiation of the first dose was undertaken to confirm the status of expulsion. Success was assessed as spontaneous gestational product expulsion without surgery and failure as the presence of retained products despite medication. The trial was preceded by side effects like fever, chills, nausea, vomiting, abdominal pain, and diarrhea. The patients' data were analyzed using SPSS 20.0 with continuous data expressed as means with standard deviations and categorical data as frequencies and percentages. Statistical analysis for group comparisons used chi-square tests for the categorical variables and independent t-tests for the continuous variables, with $p<0.05$ being significant. Ethical approval was obtained from the Hospital Ethical Review Board and signed informed consent from all participants. Confidentiality of patient information was ensured during the study process.

RESULT

Table I shows the demographic information of 100 patients who underwent sublingual misoprostol treatment for early miscarriage. Most of the patients (64%) were between 28-37 years old, 30% were between 18-27 years old, and only 6% were between 38-45 years old. Education levels varied widely, with 15% having no education, 27% having primary education, 19% having SSC, 23% having HSC, and 16% having graduate or above degrees. Nearly half (48%) were housewives, while others were day laborers (23%), service workers (15%), or students (14%). Socioeconomically, most of the participants (49%) were middle-income classes, 33% were poor, and 18% were wealthy. The study population was made up of slightly more urban residents (58%) than rural residents (42%). These demographic factors provide important context for the interpretation of treatment outcomes and can influence such factors as treatment adherence, ability to access follow-up care, and overall treatment success rates across income groups.

Table I

Demographic and Socio-Economic Profiles of the Study Population (*n*=100).

Demographic Profiles	(n)	(%)
Age		
18-27	30	30%
28-37	64	64%
38-45	6	6%
Educational status		
No formal education	15	15%
Completed primary	27	27%
Completed SSC	19	19%
Completed HSC	23	23%
Graduate or above	16	16%
Occupation		
Student	14	14%
Housewife	48	48%
Day labor	23	23%
Service	15	15%
Socio-economic status		
Rich	18	18%
Middle-income	49	49%
Poor	33	33%
Residence		
Urban	58	58%
Rural	42	42%

Table II shows the clinical presentation of 100 sublingual misoprostol-treated subjects for early pregnancy loss. Most (86%) were 6-12 weeks pregnant, while the rest (14%) were less than 6 weeks pregnant. Nearly two-thirds (65%) had their first pregnancy (primigravida), while the rest (35%) had experienced previous pregnancies (multigravida). The most common presenting symptoms were per-vaginal bleeding (52%) and lower abdominal pain (45%), which are typical clinical presentations of early pregnancy loss. Fever was noted in approximately one-quarter (24%) of the cases, possibly indicating infection which could complicate management. Of special note, 9% of the respondents required blood transfusion, pointing to severe hemorrhage in such cases. These clinical characteristics enable to establishment of the baseline severity of pregnancy loss cases in the study and define important parameters for clinicians to consider while evaluating the efficacy of sublingual treatment with misoprostol compared to typical presenting symptoms and patient demographics.

Table II
Clinical Features and Presenting Symptoms of the Study Population (*n*=100).

Clinical Features and Presenting Symptoms	(n)	(%)
Gestational age (in weeks)		
< 6 weeks	14	14%
6-12 weeks	86	86%
Gravidity		
Primigravida	65	65%
Multigravida	35	35%
Presenting Symptoms		
Per-vaginal bleeding	52	52%
Lower abdominal pain	45	45%
Fever	24	24%
Blood transfusion	9	9%

Table III presents the frequency of various risk factors among the 100 study women receiving sublingual misoprostol for early pregnancy loss. The most frequent was Polycystic Ovary Syndrome (PCOS) (22%), followed by thyroid abnormalities (21%), showing a significant correlation of hormonal imbalance and early pregnancy loss. Hypertension (16%) and antiphospholipid antibody syndrome (16%) were of the same frequency and are well-established risk factors for pregnancy complications. Diabetes mellitus was observed in 8% of the subjects, while endometriosis was observed in 10%. Systemic lupus erythematosus (SLE), an autoimmune condition known to influence pregnancy outcome, was observed in 5% of cases. History of previous abortion was noted in 11% of subjects, reflecting recurrence risk. Physical conditions such as trauma and travel history were each noted in 5% and 8% of cases respectively. This distribution of risk factors is of significant value in determining potential predisposing conditions for early pregnancy loss and can influence the effectiveness of misoprostol treatment.

Table III
Distribution of the Respondents by The Presence of Risk Factors (*n*=100).

Risk factors*	(n)	(%)
HTN	16	16%
DM	8	8%
Thyroid abnormalities	21	21%
PCOS	22	22%
Endometriosis	10	10%
SLE	5	5%
Antiphospholipid antibody syndrome	16	16%
History of trauma	5	5%
History of travel	8	8%
H/o previous abortion	11	11%

Table IV presents clinical symptoms and physiological signs found in the 100 volunteers: anemia, in 28% of the subjects, may perhaps be attributed to blood loss accompanying pregnancy loss or accompanying disease. The table further presents mean values of vital parameters with standard errors: patients had a pulse rate of mean = 79 ± 13 per minute, most presumably within a standard range. Blood pressure readings showed a mean systolic blood pressure of 108±13 mmHg and diastolic blood pressure of 73.76±11.25 mmHg, indicating that most participants had normal to low-normal blood pressure during treatment. The mean body temperature was 36.47±0.68°C, which is within normal limits. These physiological parameters are important baseline clinical indices against which the condition of a patient must be compared during and after misoprostol, particularly for monitoring complications such as uncontrollable bleeding (expressed in increasing pulse in relation to decreasing blood pressure) or infection (expressed by fever).

Table IV
Distribution of the Respondents by the Signs (*n*=100).

Signs	(%)
Anemia	28%
Physiological parameters	Mean±SD
Pulse (beats/min)	79±13
SBP (mmHg)	108±13
DBP (mmHg)	73.76±11.25
Temperature (°C)	36.47±0.68

Table V also shows the dosing regimen and outcome of sublingual misoprostol treatment in 100 patients. The majority of patients (61%) required three or more doses of misoprostol to become effective, 36% required two doses, and only 3% responded to a single dose. This suggests that multiple dosing is extremely frequently necessary for effectiveness. For treatment success, there was a complete expulsion of pregnancy tissue in 80% of cases, indicating a success rate for this non-surgical procedure. For 20% of patients, there was an incomplete expulsion or no expulsion, indicating treatment failure and the possible need for additional procedures such as surgical evacuation. These findings demonstrate that while sublingual misoprostol is extremely

effective as a medical treatment of early pregnancy loss, a significant minority of patients will still require further treatment. The success rate was good and this validates the use of misoprostol as a first treatment option before resorting to more invasive procedures.

Table V
Treatment Administration and Success Rates.

Doses	(n)	(%)
1	3	3%
2	36	36%
3 or more	61	61%
Expulsion		
Complete	80	80%
Incomplete or no	20	20%

Table VI is a study of the timing of expulsion following misoprostol administration and cervical appearance in incomplete success treatment cases. Induction-expulsion interval data show that the majority of the expulsions (56%) occurred between 13-18 hours of administration, 35% between 7-12 hours, 2% within 6 hours, and 7% more than 18 hours. This distribution highlights that patients typically need to be monitored for at least 18 hours in order to capture most expulsion events. In the 20 instances where complete expulsion did not occur, cervical examination revealed that 90% of them had permeable cervices, and only 10% had non-permeable cervices. The frequency of cervical permeability at this high level after incomplete expulsion means that problems other than resistance within the cervix can cause failure of treatment in these cases, such as insufficient uterine contractions or anatomical differences. These are worth knowing for establishing the expected timeline of treatment effect and what can cause treatment failure.

Table VI
Time of Expulsion and Cervical Status in Unsuccessful Cases.

Induction-expulsion interval (in hours)	(n)	(%)
≤ 6	2	2
7-12	35	35
13-18	56	56
>18	7	7
Permeability of cervix		
Permeable	18	90%
Not permeable	2	10%

Table VII documents side effects experienced by the patients who received sublingual misoprostol treatment. Nausea was the most frequent side effect, affecting 69% of patients, and therefore a near certainty of treatment. Severe pain was experienced by 40% of patients, and this highlights the need for adequate analgesia as part of the treatment process. Gastrointestinal side effects were also common, with diarrhea in 14% and vomiting in 11% of patients. Shivering was observed in 8% of the subjects, and a bad taste was reported by 7%, as would be expected by the sublingual route of administration. More significant complications were uncommon but clinically important: 6% experienced uncontrolled blood loss, and hyperpyrexia (fever) occurred in 5%. This side effect profile is predictable based on the anticipated pharmacologic effect of misoprostol and is useful for patient counseling and management of expectations. Its occurrence ought to be balanced with the advantages of avoiding surgical treatment in instances where misoprostol is utilized to treat early pregnancy loss (*Table VII*).

Table VII
Distribution of the Respondents by the Side Effects and Complications (*n*=100).

Side effects/ complications*	(n)	(%)
Nausea	69	
Vomiting	11	
Diarrhea	14	
Severe pain	40	
Hyperpyrexia	5	
Shivering	8	
Excessive blood loss	6	
Unpleasant taste	7	

**Multiple responses considered*

DISCUSSION

This prospective observational study evaluated the efficacy and safety of sublingual misoprostol in the management of early pregnancy loss in 100 women. Our findings demonstrate an 80% complete expulsion rate, which is in agreement with reports of 67-91% success rates of medical management of early pregnancy loss [12]. Our fairly high success rate in favor of sublingual misoprostol is a testament to the drug as a good substitute for surgical evacuation in the management of early pregnancy loss. Demographic factors appeared to influence the outcomes of treatment in our cohort. Most participants (64%) were 28-37 years of age, of predominantly urban origin (58%), and of

middle-income socioeconomic status (49%). Our study was not powered to ascertain significant correlations between these demographic factors and treatment success, but the study by Zeteroglu et al. has shown maternal age, parity, and gestational age to influence the efficacy of misoprostol [13]. Kamlungkuea et al. were more successful in women with lower gestational age and previous vaginal deliveries, which is partly in agreement with our finding that 86% of our participants were between 6-12 weeks gestation [14]. The time to expulsion data showed that most subjects (56%) experienced complete expulsion 13-18 hours after first-dose administration, while an additional 35% experienced expulsion between 7-12 hours. The timing setting provides helpful clinical information for patient counseling and monitoring protocols. Another similar finding was documented by Schreiber et al., where they documented median expulsion at 9 hours (range 3-27 hours) following the administration of misoprostol [15]. Interestingly, 61% of our subjects required three or more doses of misoprostol for successful expulsion, as opposed to only 3% that responded with one dose. This observation underscores the need to develop proper dosing regimens and to have realistic expectations regarding the length of treatment. Zieman et al. have shown that sublingual delivery leads to faster absorption and higher peak plasma levels than oral or vaginal delivery and may justify more frequent dosing intervals with the sublingual administration [16]. The side effect profile in our study was in accordance with the known pharmacologic effects of misoprostol. The most common were nausea (69%), severe pain (40%), and diarrhea (14%). These agree with Tang et al., who showed that sublingual had more frequent gastrointestinal side effects but greater patient acceptability than vaginal administration [17]. The incidence of more serious complications such as uncontrolled bleeding (6%) and hyperpyrexia (5%) was very low, considering the safety profile of the treatment regimen. Our study found several risk factors among the participants, including PCOS (22%), thyroid disease (21%), hypertension (16%), and antiphospholipid antibody syndrome (16%). They have been associated with an increased risk of pregnancy complications and may also affect treatment outcomes. Schreiber et al. demonstrated that women with certain medical comorbidities may have worse success rates for medical management of early pregnancy loss, hence the need for specific treatment approaches [18]. The 20% of patients who experienced partial or no expulsion underscore the failure of medical management and the residual place of surgery in judiciously selected cases. In such cases, cervical exams revealed that 90% of them had friable cervices in spite of partial expulsion, suggesting causes of failure other than cervical resistance. Chen and Creinin proposed that factors such as uterine contractility, gestational site within the uterine cavity, and individual variation in drug metabolism could influence treatment [19]. From a public health perspective, our findings are of particular relevance to resource-poor settings. By validating the efficacy of sublingual misoprostol, our study promotes greater access to non-surgical treatment, which may reduce the burden on surgical facilities and improve patient autonomy.

LIMITATIONS

The study is limited by the observational study design with no control group to compare with, and the sample size was smaller than initially calculated due to resource constraints. Follow-up was also only for seven days post-treatment, and delayed complications or late expulsions may have been missed.

CONCLUSION

Sublingual misoprostol is highly effective (80%) for complete expulsion in early pregnancy loss with most expulsions within 7-18 hours of administration. While repeated doses are typically required, therapy offers a safe, non-surgical means of management with acceptable side effects. It is particularly valuable in resource-limited settings and in patients who prefer to avoid surgery.

FUTURE RECOMMENDATIONS

Future studies must include randomized controlled trials comparing different routes of misoprostol administration with standard dosing regimens. Investigation into predictive factors for success of treatment would be helpful in defining individualized management regimens for early pregnancy loss, with possible improvement in outcomes and patient satisfaction.

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CONFLICT OF INTEREST

None declared

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