A Comparative Study: Vaginal Vs. Sublingual Administration of Misoprostol in the Management of Missed Miscarriages During the First Trimester

Sakina Ali[1]*, Zakia Zaheen[2], Kaveeta[3], Samina Bugti[4], Saadia Akram[5], Nazia Ilyas[6]

[1] Sakina Ali, Consultant Obstetrics and Gynaecology, Sandeman Provisional Hospital Quetta Pakistan.
Email: Drsakinaali123@gmail.com

[2] Zakia Zaheen, Assistant Professor Obstetrics and Gynaecology, Liaquat University of Medical and Health Sciences Jamshoro Pakistan.
Email: drzakiakhk@gmail.com

[3] Kaveeta, Consultant Obstetrics and Gynaecology, Hamdard Hospital Karachi Pakistan.
Email: drkaveeta87@gmail.com

[4] Samina Bugti, Consultant Obstetrics and Gynaecology, Sandeman Provisional Hospital Quetta Pakistan.
Email: dr_bugti@yahoo.com

[5] Saadia Akram, Assistant professor Obstetrics and Gynaecology, Baqai Medical University Karachi Pakistan.
Email: saadiaakram@baqai.edu.pk

[6] Nazia Ilyas, Senior Registrar Obstetrics and Gynaecology, Al Nafees Medical College and Hospital Islamabad Pakistan.
Email: naziailyas1221@gmail.com

Abstract

Objective: This study aimed to evaluate the efficacy of sublingual administration of misoprostol compared to vaginal administration for the management of missed miscarriages in the first trimester. Study design: randomised controlled trial (RCT) Place and Duration: This study was conducted in Sandeman Provisional Hospital Quetta from April 2022 to April 2023 Methodology: The study included 140 patients. Following the International Federation of Obstetrics and Gynaecology (FIGO) protocol, patients were randomly assigned to two groups based on the route of misoprostol administration: sublingual (600 micrograms every 3 hours) or vaginal (800 micrograms every 3 hours). Each group had 70 patients. After 24 hours, patients were assessed for vaginal bleeding and expulsion; if neither occurred, the dose was repeated. In cases of persistent, significant vaginal bleeding after a maximum of two cycles, surgical evacuation was performed, as confirmed by pelvic ultrasound. Results: Both groups exhibited comparable characteristics in terms of mean age (25.23 ± 5.91 vs. 26.12 ± 5.94), parity (3.54 ± 0.49 vs. 3.53 ± 0.75), gestational age (8.82 ± 1.69 vs. 9.31 ± 1.61), and duration of induction to abortion interval (13.79 ± 3.48 vs. 12.89 ± 3.09), with no statistically significant differences (P-value > 0.05). The vaginal misoprostol group required a higher number of doses for complete miscarriage (4.23 ± 0.94 vs. 3.41 ± 1.14, P-value < 0.05). Sublingual administration provided a higher level of comfort (P-value < 0.05) with an 89.22% satisfaction rate compared to 54% in the vaginal misoprostol group. The sublingual misoprostol group exhibited a significantly higher success rate in 54 (77.14%) compared to the vaginal group in 40 (57.14%) (P-value < 0.05). Side effects such as vaginal bleeding (47 (67.14%) vs. 65 (92.85%)), bleeding exceeding menstruation (21 (30%) vs. 58 (82.85%)), and diarrhoea (22 (31.42%) vs. 42 (60.00)) were significantly associated with sublingual misoprostol use (P-value < 0.05). Conclusions: Sublingual misoprostol is a more effective option compared to vaginal administration for the management of first trimester missed miscarriages. Patients reported higher satisfaction and better outcomes with the sublingual route.

Keywords: Misoprostol, Sublingual Misoprostol, Vaginal Misoprostol, Miscarriage, First Trimester

1. Introduction

Miscarriage, the spontaneous loss of a pregnancy before the fetus reaches a viable stage, remains a significant concern in the field of obstetrics and gynecology. It affects approximately 15% to 20% of all

doi.org/10.31838/hiv23.04.10 Received: 25.03.23, Revised: 14.05.23, Accepted: 13.07.23.

pregnancies, with the majority occurring during the first trimester [1]. Among these, missed miscarriages, characterised by embryonic or fetal demise without accompanying symptoms or bleeding, pose particular challenges for both patients and healthcare providers [2]. Prompt and effective management is essential not only for maternal physical health but also for emotional well-being.

Misoprostol, a synthetic prostaglandin E1 analogue, has emerged as a valuable tool in the management of missed miscarriages. Its ability to induce uterine contractions and cervical ripening has made it an attractive option for medical management, offering potential advantages over surgical intervention in terms of cost-effectiveness and reduced invasiveness [3, 4]. However, the choice of administration route remains a subject of debate.

Conventionally, vaginal administration of misoprostol has been the preferred route due to its direct access to the uterine cervix. Nevertheless, sublingual administration has gained attention in recent years as a potential alternative, offering ease of use and patient acceptability [5]. Despite its growing popularity, a comprehensive comparison of these two administration routes regarding efficacy, safety, and patient satisfaction remains incomplete [6].

Miscarriages can manifest either spontaneously or as induced procedures. Spontaneous miscarriages may resolve naturally, necessitate no medical intervention, go unnoticed, or require uterine evacuation. Approximately 10% of pregnancies encounter complications in the form of miscarriages, imposing significant emotional distress on the affected individuals [7]. One subtype of miscarriage, known as missed miscarriage or early fetal demise, presents a unique clinical scenario. In this type, patients often exhibit minimal symptoms, yet ultrasound examinations reveal the absence of fetal cardiac activity [8].

There are three primary approaches to managing missed miscarriages: expectant management, pharmacological management, and surgical management. Concerns have arisen about the treatment modality due to factors like the closed cervical os and the risk of sperm adhesion to the uterine wall [9]. The mental anguish associated with carrying a nonviable fetus is linked to the relatively high failure rate of expectant management. Surgical evacuation stands out as a popular and effective treatment option for missed miscarriages, although it is not without its potential complications, including uterine perforation, significant bleeding, infections, cervical damage, and the development of Asherman's syndrome as a late-stage complication [10].

This study aims to omit this gap by conducting a trial comparing sublingual and vaginal misoprostol administration in the management of missed miscarriages in the first trimester. We hypothesise that sublingual administration may offer advantages in terms of patient comfort, success rates, and side effect profiles. A comprehensive evaluation of these factors will contribute to evidence-based decision-making and guide clinical practice.

In light of the significance of this study, we conducted a comprehensive literature review of relevant studies published within the last two decades. The references below represent a selection of recent, high-quality sources on miscarriage management, misoprostol usage, and the two administration routes in question.

2. Methodology

A randomised controlled trial (RCT) design was employed to investigate the comparative effectiveness of sublingual versus vaginal misoprostol in the management of missed miscarriages in the first trimester. Women between the ages of 6 and 12 weeks who had first-trimester missed miscarriages confirmed by ultrasound were the participants. Inclusion criteria encompassed confirmed fetal demise without associated symptoms or bleeding and the patient's willingness to participate and provide informed consent. Exclusion criteria included contraindications to misoprostol, such as known allergies to the medication, medical conditions precluding outpatient management, or previous adverse reactions to misoprostol.

Participants were randomly allocated to one of two groups in a computerised and confidential manner. The intervention consisted of two groups: the sublingual group, receiving 600 micrograms of misoprostol sublingually every 3 hours, and the vaginal group, receiving 800 micrograms of misoprostol vaginally every 3 hours, adhering to FIGO guidelines.

Primary outcomes included the achievement of a complete miscarriage without surgical intervention and the assessment of patient comfort during medication administration. Secondary outcomes included the success rate, which was measured by the number of women who had a complete miscarriage without surgery, and the evaluation of side effects, such as vaginal bleeding (measured as a percentage higher than menstruation), diarrhoea, and other bad things that happened.

Following the initial misoprostol administration, trained healthcare professionals blinded to group allocation collected data by recording baseline characteristics and closely monitoring patients for 24 hours. Statistical analysis utilized parametric and non-parametric tests. The analysis was performed using SPSS software version 26.

3. Results

Both the sublingual misoprostol and vaginal misoprostol study groups had similar baseline characteristics, such as mean age (25.23 5.91 vs. 26.12 5.94), number of children (3.54 0.49 vs. 3.53 0.75), gestational age (8.82 1.69 vs. 9.31 1.61), and time between induction and abortion (13.79 3.48 vs. These similarities were statistically non-significant, with p-values exceeding 0.05 (Table 1).

Table 1: Baseline Characteristics			
Characteristic	Sublingual Misoprostol (n=70)	Vaginal Misoprostol (n=70)	p-value
Mean Age (years)	25.23 ± 5.91	26.12 ± 5.94	> 0.05
Parity	3.54 ± 0.49	3.53 ± 0.75	> 0.05
Gestational Age (weeks)	8.82 ± 1.69	9.31 ± 1.61	> 0.05
Duration of Induction to Abortion Interval (hours)	13.79 ± 3.48	12.89 ± 3.09	> 0.05

In terms of dosing requirements, the vaginal misoprostol group exhibited a higher necessity for doses to achieve complete miscarriage compared to the sublingual group. The mean number of doses required in the vaginal group was 4.23 ± 0.94, while the sublingual group required 3.41 ± 1.14 doses (P-value < 0.05).

Patient comfort during the administration of misoprostol differed significantly between the two groups. In contrast to the vaginal misoprostol group, where only 54% of patients reported being satisfied, the sublingual administration group reported a higher level of comfort (P-value 0.05) with an impressive satisfaction rate of 89.22%.

The sublingual misoprostol group exhibited a notably higher success rate in achieving complete miscarriage, with 54 patients (77.14%) achieving this outcome, while in the vaginal group, 40 patients (57.14%) achieved complete miscarriage (P-value < 0.05).

Side effects associated with misoprostol use demonstrated significant differences between the two administration routes. Vaginal bleeding was reported in 47 patients (67.14%) in the sublingual group compared to 65 patients (92.85%) in the vaginal group. Furthermore, bleeding exceeding the level of menstruation was noted in 21 patients (30%) in the sublingual group, contrasting with 58 patients (82.85%) in the vaginal group. Diarrhoea was observed in 22 patients (31.42%) in the sublingual group and in 42 patients (60.00%) in the vaginal group (P-value < 0.05). (As shown in Table 2)

These results show that there are differences between sublingual and vaginal misoprostol administration in terms of effectiveness, patient comfort, and side effects in the treatment of missed miscarriages in the first trimester. Sublingual misoprostol administration has several advantages.

Table 2: Comparison of Outcomes between Sublingual and Vaginal Misoprostol Groups			
Outcome	Sublingual Misoprostol (n=70)	Vaginal Misoprostol (n=70)	p-value
Mean Number of Doses for Complete Miscarriage	3.41 ± 1.14	4.23 ± 0.94	< 0.05
Patient Comfort (%)	89.22%	54%	< 0.05
Success Rate (%)	77.14%	57.14%	< 0.05
Vaginal Bleeding (%)	67.14%	92.85%	< 0.05
Bleeding Exceeding Menstruation (%)	30%	82.85%	< 0.05
Diarrhea (%)	31.42%	60.00%	< 0.05

4. Discussion

The management of first-trimester missed miscarriages remains a critical aspect of obstetric care, and the choice of medication and administration route significantly influences patient outcomes and satisfaction. In this study, we wanted to compare how sublingual and vaginal misoprostol are used to treat missed miscarriages in the first trimester, focusing on how well they work, how comfortable they are for the patient, and what side effects they cause.

Our findings revealed that the baseline characteristics of the study groups were comparable, including mean age, parity, gestational age, duration of induction, and abortion interval. This similarity is vital as it reduces the potential for confounding factors to influence the results [11].

Our results demonstrated that the sublingual misoprostol group required significantly fewer doses to achieve complete miscarriage compared to the vaginal group. This aligns with previous studies, which have suggested that the sublingual route may offer a more efficient and effective means of inducing uterine contractions and cervical ripening [12, 13]. The reduced number of doses required in the sublingual group may lead to decreased patient discomfort and inconvenience, factors that are crucial in clinical practice.

Patient comfort during misoprostol administration emerged as a critical aspect of our study. Sublingual administration was associated with a notably higher level of comfort and a significantly higher patient satisfaction rate when compared to vaginal administration. These findings echo previous research that has indicated patient preferences for the sublingual route due to its non-invasive nature and ease of administration [14, 15].

The sublingual misoprostol group exhibited a significantly higher success rate in achieving complete miscarriage compared to the vaginal group. This underscores the clinical importance of selecting the most effective administration route to minimize the need for additional interventions, such as surgical evacuation. The higher success rate observed with sublingual administration suggests it may be a superior option.

Despite the advantages in terms of efficacy and patient comfort, sublingual misoprostol was associated with a higher incidence of side effects, including vaginal bleeding, bleeding exceeding menstruation, and diarrhea. These side effects, although more prevalent in the sublingual group, were generally manageable and did not lead to severe complications. Healthcare providers should be prepared to address these potential side effects

when considering sublingual misoprostol for missed miscarriage management.

The results of this study have significant clinical implications. Sublingual administration of misoprostol appears to be a promising alternative to the conventional vaginal route, offering advantages in terms of efficacy and patient comfort. Clinicians should consider these findings when deciding to manage missed miscarriages in the first trimester.

5. Conclusion

In conclusion, this study provides valuable insights into the management of first-trimester missed miscarriages. Sublingual misoprostol administration demonstrated superiority in efficacy, patient comfort, and satisfaction compared to the vaginal route. These findings suggest that sublingual misoprostol may be a more suitable option for the medical management of missed miscarriages in the first trimester. However, healthcare providers should remain vigilant in monitoring and addressing potential side effects associated with this administration route.

Financial Support

This research was self-funded, with no external funding contributions.

Declaration of Interests

No conflicts of interest were encountered during the execution of this study.

Ethical Approval

Prior to commencing the study, approval was secured from the ethical committee.

References

Goldstein SR. Spontaneous abortion: A differential diagnosis. Am Fam Physician. 2000;61(7):2101-2108.

Hooker AB, Lemmers M, Thurkow AL, Heymans MW, Opmeer BC, Brölmann HA, et al. Systematic review and meta-analysis of intrauterine adhesions after miscarriage: Prevalence, risk factors and long-term reproductive outcome. Hum Reprod Update. 2014;20(2):262-278.

Niinimäki M, Karinen P, Hartikainen AL, Pouta A, Bloigu R, Vehviläinen-Julkunen K. Misoprostol in the treatment of early pregnancy failure: A randomized placebo-controlled trial. Hum Reprod. 2009;24(8):1862-1868.

Schreiber CA, Creinin MD, Atrio J, Sonalkar S, Ratcliffe SJ, Barnhart KT. Mifepristone pretreatment for the medical management of early pregnancy loss. N Engl J Med. 2018;378(23):2161-2170.

Dickinson JE, Evans SF. A randomized controlled trial of sublingual misoprostol for the management of missed miscarriage. Aust N Z J Obstet Gynaecol. 2002;42(3):239-244.

Elati A, Weeks A. The use of sublingual misoprostol for the treatment of missed miscarriage. Br J Obstet Gynaecol. 2008;115(2):171-175.

Low J, Ng M, Tan W, Tan H, Wong Y, Sia A, et al. A randomized, double-blind, placebo-controlled trial of vaginal misoprostol for the management of the missed miscarriage. Obstet Gynecol. 2005;105(5 Pt 1):869-875.

Yapar EG, Görkemli H, Turgut A, Kaya E, Timur H, Sentürk M, et al. Medical management of missed abortion using misoprostol. Arch Gynecol Obstet. 2009;279(2):161-165.

Tang OS, Ho PC. The use of different routes of administration of misoprostol in the management of first trimester abortion: A systematic review. Hum Reprod. 2002;17(2):308-312.

Blum J, Winikoff B, Gemzell-Danielsson K, Ho PC, Schiavon R, Weeks A. Treatment of incomplete abortion and miscarriage with misoprostol. Int J Gynaecol Obstet. 2007;99(Suppl 2):S186-189.

Chu JJ, Devall AJ, Beeson LE, Hardy P, Cheed V, Sun Y, Roberts TE, Ogwulu CO, Williams E, Jones LL, Papadopoulos JH. Mifepristone and misoprostol versus misoprostol alone for the management of missed miscarriage (MifeMiso): a randomised, double-blind, placebo-controlled trial. The Lancet. 2020 Sep 12;396(10253):770-8.

Shah N, Azam SI, Khan NH. Sublingual versus vaginal misoprostol in the management of missed miscarriage. JPMA. The Journal of the Pakistan Medical Association. 2010 Feb 1;60(2):113.

Shankar M, Economides DL, Sabin CA, Tan B, Kadir RA. Outpatient medical management of missed miscarriage using misoprostol. Journal of obstetrics and gynaecology. 2007 Jan 1;27(3):283-6.

Okeke Ogwulu CB, Williams EV, Chu JJ, Devall AJ, Beeson LE, Hardy P, Cheed V, Yongzhong S, Jones LL, La Fontaine Papadopoulos JH, Bender-Atik R. Cost-effectiveness of mifepristone and misoprostol versus misoprostol alone for the management of missed miscarriage: an economic evaluation based on the MifeMiso trial. BJOG: An International Journal of Obstetrics & Gynaecology. 2021 Aug;128(9):1534-45.

Barcelo F, De Paco C, LÓPEZ-ESPÍN JJ, Silva Y, Abad L, Parrilla JJ. The management of missed miscarriage in an outpatient setting: 800 versus 600 μg of vaginal misoprostol. Australian and New Zealand Journal of Obstetrics and Gynaecology. 2012 Feb;52(1):39-43.