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EFFICACY OF ORAL VS VAGINAL MISOPROSTOL IN FIRST TRIMESTER MISSED MISCARRIAGE

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ABSTRACT

Background: *First-trimester missed miscarriage is commonly managed with misoprostol, either orally or vaginally. While vaginal misoprostol is thought to be more effective, controversy exists regarding the comparison of oral versus vaginal forms, with inconsistent findings in the literature. Additionally, data on this issue in local population is scarce. This study was conducted to assess and compare the efficacy of oral and vaginal misoprostol in a local population.*

Objective: *To compare the efficacy of misoprostol by vaginal and oral route, for the management of first trimester missed abortion.*

Duration: *Six months.*

Methodology: *A total of 140 patients with of patients with missed abortion, 18 to 45 years of age were included. Patients with signs of allergy to or C/I to misoprostol use, anemia, active lactation, bleeding disorder, deranged coagulation profile and infection were excluded. In group A, 400µg vaginal misoprostol was given, while in group B patients, 400µg oral misoprostol was done. All patients were monitored for vitals, vaginal bleeding and expulsion of POCs. Over the next 18-30 hours, complete, incomplete or no expulsion was documented.*

Results: *The study sample consisted of 140 participants, with a mean age of 27.71 ± 4.31 years. The mean gestational age at the time of enrollment was 7.63 ± 2.35 weeks. In terms of parity, the mean was 3.29 ± 1.15. Both groups were statistically comparable with each other for all baseline variables, as indicated by the p-values greater than 0.05. In terms of efficacy, Group A demonstrated a higher success rate, with 65 participants (92.86%) achieving a successful outcome, compared to 53 participants. Stratification of efficacy between the groups based on age, gestational age, and parity revealed a consistent superiority of Group A over Group B across all subgroups. However, in certain subgroups, statistical significance could not be achieved due to the small sample sizes.*

Conclusion: *The study demonstrated that vaginal misoprostol (Group A) was more effective than oral misoprostol (Group B) in the management of first-trimester missed*

miscarriage, with a significantly higher success rate observed in Group A. Stratification by age, gestational age, and parity consistently showed the superiority of vaginal misoprostol across all subgroups. However, statistical significance was not achieved in some subgroups due to small sample sizes. Overall, vaginal misoprostol appears to be a more effective treatment for missed miscarriage in the first trimester.
Keywords: *1st trimester miscarriages, vaginal or oral misoprostol, complete uterine evacuation.*

INTRODUCTION

Miscarriage is a common and distressing complication during early pregnancy, affecting 20% to 25% of all pregnancies worldwide. In the first trimester, approximately 11% to 15% of pregnancies end in spontaneous miscarriage.[1,2] A missed abortion is a particular form of spontaneous miscarriage, where the embryo or fetus has died but remains retained in the uterus for days or even weeks with a closed cervical os. Missed abortion is observed in approximately 8% to 20% of clinically confirmed intrauterine pregnancies and is typically diagnosed using ultrasonography.[3,4]

The traditional management of missed abortion often involves surgical intervention, specifically dilatation and curettage (D&C). While effective, this method is invasive and carries risks, including uterine perforation, cervical injury, and anesthesia-related complications. Additionally, one of the most concerning long-term complications associated with D&C is intrauterine adhesions (IUAs), which can affect subsequent fertility and cause menstrual irregularities, potentially leading to infertility.[5] Given the risks associated with surgical management, medical management of missed abortion using misoprostol has become an increasingly popular alternative. Misoprostol is a synthetic prostaglandin analogue that can be administered through various routes, including oral, sublingual, buccal, or vaginal. The drug works by inducing myometrial contractions, helping to expel pregnancy tissue from the uterus. It is cost-effective and widely available, making it an attractive option for the medical management of miscarriage.[1,6,7] Despite its effectiveness, there is ongoing debate in the literature regarding the optimal route of misoprostol administration for the treatment of missed miscarriage.[7]

Studies comparing oral and vaginal misoprostol have shown mixed results. Marwah et al. (2016) found vaginal misoprostol more effective (92.0% vs. 74.0%, p-value<0.05), while Aman et al. (2022) reported no significant difference (77.0% vs. 82.0%, p=0.19). Souizi et al. (2020) observed a higher success rate with vaginal misoprostol (96.8% vs. 84.9%), though not statistically significant (p=0.051). These conflicting findings highlight the ongoing debate over the efficacy of both routes.[8,9,10]

Given these inconsistencies, this study was designed to provide stronger evidence regarding the efficacy of oral versus vaginal misoprostol in a local population. The findings could inform clinical decision-making and improve the management of missed abortion in future practice.

METHODOLOGY

This randomized controlled trial was conducted at the Department of Gynaecology and Obstetrics, SPH Quetta, over a duration of six months after approval form ethical review committee. The sample size was calculated, assuming a success rate of 92% in Group A and 74% in Group B, with a power of 80%.[8] A total of 140 women, 70 in each group, were required for this study. The sampling technique used was non-probability, consecutive sampling. The study included females aged 18-45 years with a gestational age of ≤ 12 weeks, as determined by the last menstrual period (LMP), and a confirmed diagnosis of missed abortion through ultrasound (USG). Participants in the study were required to have no history of inflammatory bowel disease, asthma, liver disease, or any contraindications to misoprostol use. Women with molar pregnancy, cervical dilatation, excessive uterine bleeding, hemoglobin concentration <9 g/dL, hemodynamic instability, blood pressure ≥140/90 mmHg, poor general health, abnormal coagulation profile (PTI ≤85%), infection, anticoagulant use, or bleeding disorders were excluded. Additional exclusion criteria included known allergy to misoprostol, active lactation, prior treatments for pregnancy termination, and twin gestations. Baseline investigations were conducted, and Rh-negative women received 50µg of prophylactic anti-D immunoglobulin intramuscularly. Participants were randomly assigned to one of two groups using computer-generated sequentially numbered envelopes. Group A received 400µg of vaginal misoprostol, inserted into the posterior

fornix every six hours up to three doses. Vaginal cleansing was performed with 10% povidone iodine before insertion, and women were asked to remain in a recumbent position for three hours after insertion. Group B received 400µg of oral misoprostol every six hours for a maximum of three doses. All patients were monitored for vital signs, vaginal bleeding, and expulsion of products of conception (POCs). Expulsion status was documented over 18-30 hours, with further doses administered if necessary. Data were collected on a pre-designed pro-forma for statistical analysis.

RESULTS

The study sample consisted of 140 participants, with a mean age of 27.71 ± 4.31 years. The majority of participants were between 18 and 30 years old (68.57%), while 31.43% were aged 31-45 years. The mean gestational age at the time of enrollment was 7.63 ± 2.35 weeks, with 40.0% of participants having a gestational age of 1-6 weeks and 60.0% falling within the 7-12 week range. In terms of parity, the mean was 3.29 ± 1.15. A little more than half of the participants (55.0%) had a parity of 0-3, while 45.0% had a parity of 4-5, as given in Table 1.0. Both groups were statistically comparable with each other for all baseline variables, as indicated by the p-values greater than 0.05, as shown in Table 2.0. This suggests that there were no significant differences between the groups at baseline. In terms of efficacy, Group A (vaginal misoprostol, n=70) demonstrated a higher success rate, with 65 participants (92.86%) achieving a successful outcome, compared to 53 participants (75.71%) in Group B (oral misoprostol, n=70), as given in Table 3.0. Stratification of efficacy between the groups based on age, gestational age, and parity revealed a consistent superiority of Group A (vaginal misoprostol) over Group B (oral misoprostol) across all subgroups. However, in certain subgroups, statistical significance could not be achieved due to the small sample sizes, limiting the ability to draw definitive conclusions in those specific categories. Data is given in Table 4.0.

Table 1.0 Baseline Characteristics of Study Sample

Characteristics	**Study Sample n=140**
Age (years)	27.71±4.31
• **18-30 years**	96 (68.57%)
• **31-45 years**	44 (31.43%)
Gestational Age (weeks)	7.63±2.35
• **1-6 weeks**	56 (40.0%)
• **7-12 weeks**	84 (60.0%)
Parity	3.29±1.15
• **0-3**	77 (55.0%)
• **4-5**	63 (45.0%)

Table 2.0 Baseline Characteristics of Study Groups

Characteristics	**Group A (Vaginal Misoprostol) n=70**	**Group B (Oral Misoprostol) n=70**	**p-value**
Age (years)	27.73±4.05	27.50±4.84	>0.05 *
• **18-30 years**	52 (74.29%)	44 (62.86%)	>0.05 **
• **31-45 years**	18 (25.71%)	26 (37.14%)	
Gestational Age (weeks)	7.96±2.46	7.54±2.31	>0.05 **
• **1-6 weeks**	25 (35.71%)	31 (44.29%)	>0.05 **
• **7-12 weeks**	45 (64.9%)	39 (55.71%)	
Parity	3.27±1.19	3.44±1.14	>0.05 *
• **0-3**	41 (58.57%)	36 (51.43%)	>0.05 **
• **4-5**	29 (41.43%)	34 (48.57%)	

*Independent sample t-test, ** Chi square test, taking p-value≤0.05 as significant

Table 3.0 Comparison of Efficacy between the Groups

	Group A (n=70)	Group B (n=70)	P-value
Efficacy			0.005
• **Success**	65 (92.86%)	53 (75.71%)	
• **Failure**	5 (7.14%)	17 (24.29%)	

Chi square test, taking p-value≤0.05 as significant

Table 4.0 Comparison of Efficacy between the Groups Stratified for Various Sub Groups

Subgroups	Facial Nerve Weakness n/n (%)		P-value
	Group A (n=70)	Group B (n=70)	
Age (years)			
• **18-30 years**	48/52 (9.1%)	35/44 (39.1%)	0.069
• **31-45 years**	17/18 (5.6%)	18/26 (35.3%)	0.041
Gestational Age (weeks)			
• **1-6 weeks**	24/25 (8.3%)	25/31 (40.0%)	0.084
• **7-12 weeks**	41/45 (6.3%)	28/39 (33.3%)	0.021
Parity			
• **0-3**	38/41 (9.5%)	25/36 (40.0%)	0.008
• **4-5**	27/29 (5.3%)	28/34 (35.0%)	0.201

Chi square test, taking p-value≤0.05 as significant

DISCUSSION

First-trimester missed miscarriage is a common obstetric complication, often requiring medical intervention to expel the fetus.[11] Traditionally, surgical intervention or oral misoprostol have been used to manage this condition.[12,13] However, vaginal misoprostol has emerged as a potentially more effective alternative, offering higher success rates in expulsion.[12,14] Despite the growing use of vaginal misoprostol, controversy exists in the literature regarding the comparative efficacy of oral versus vaginal misoprostol, with some studies showing varying results.[8-10] Furthermore, there is a scarcity of data on this topic in local populations. This study was therefore designed to evaluate the efficacy of oral versus vaginal misoprostol in a local setting.

In this study, mean age of the patients was 27.71±4.31 years. Previously a similar mean age of the patient's undergoing first trimester missed carriage was reported as 27.018±2.09 years by Roshan et al. (2023) in Pakistan.[15] However, some other studies reported mean age of their participants as 32.41±3.52 years and 29.2±6.0 years by Mohammadi et al. (2019) in India and Souizi et al. (2020) in Iran.[16,10] A lower mean age was reported by Vijaykumar et al. (2023) in India as 25.9±1.7 years and by Aman et al. (2022) in Pakistan as 23.9±3.7 years.[17,9]

The mean gestational age at the time of enrollment was 7.63±2.35 weeks. Our findings closely match with results of Souizi et al. (2020) who reported mean age of the patients as 8.4±2.2 weeks.[9] Some other authors reported it differently as 15.53±2.26 weeks by Rohsan et al. (2023), 9.35±1.34 weeks by Mohammadi et al. (2019) and 68.8±1.6 days by Aman et al. (2022).[15,16,9] In terms of parity, the mean was 3.29 ± 1.15 in this study. Previously a mean parity of 2.47±0.90 was reported by Mohammadi et al. (2019) as 2.47±0.90.[16]

In terms of efficacy, Group A demonstrated a higher success rate, with 65 participants (92.86%) achieving a successful outcome, compared to 53 participants (75.71%) in Group B; p-value=0.005. Previously, similar findings were reported by Roshan et al. (73.6% vs. 64.1%; p-value=0.022), Saeed et al. (60.0% vs. 40.0%; p-value=0.046) and Marvah et al. (92.0% vs. 74.0%) where efficacy in group A was significantly higher than group B.[15,18,8] However, insignificantly higher efficacy in group A than group B was also reported by some authors. Vijaykumar et al. (2023) reported efficacy as 91.7% vs. 75.0%; value>0.05 and Sozuizi et al. (2020)

reported efficacy as 96.8% vs. 84.9%; p-value=0.051, respectively between group A and B.[17,10] It is important to mention that insignificantly less efficacy in Group A than group B was also reported by Aman et al. (2022) and Mohammadi et al. (2019) as 77.0% vs. 82.0%; p-value=0.19 and 78.57% vs. 79.31%; p-value=0.928.[9,16] Stratification of efficacy between the groups based on age, gestational age, and parity revealed a consistent superiority of Group A over Group B across all subgroups. However, in certain subgroups, statistical significance could not be achieved due to the small sample sizes, limiting the ability to draw definitive conclusions in those specific categories.

CONCLUSION

The study demonstrated that Group A was more effective than Group B in the management of first-trimester missed miscarriage, with a significantly higher success rate observed in Group A. Stratification by age, gestational age, and parity consistently showed the superiority of vaginal misoprostol across all subgroups. However, statistical significance was not achieved in some subgroups due to small sample sizes. Overall, vaginal misoprostol appears to be a more effective treatment for missed miscarriage in the first trimester.

LIMITATIONS & RECOMMENDATIONS

The strengths of this study include its clear comparison of oral versus vaginal misoprostol in a local population, addressing a gap in existing literature. It provides valuable insights into the efficacy of both treatments for first-trimester missed miscarriage. However, limitations include small sample sizes in certain subgroups, which may affect statistical significance. Future research should focus on larger, multicenter studies, including a detailed comparison of side effects, long-term outcomes, and patient preferences to enhance the generalizability, safety, and clinical applicability of the findings.

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