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Comparison of Prostaglandin E2 And Misoprostol for Induction in Second Trimester Miscarriage in Patients Presented in Independent University Hospital Faisalabad

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ABSTRACT

Objectives: To compare the efficacy of Misoprostol and Prostaglandin E2 (PGE-2) for induction in second-trimester miscarriage, considering demographic and clinical factors. Study Settings: This randomized controlled trial was conducted at the Department of Gynecology, Independent Medical University, Faisalabad, over six months. Duration of Study: The study was conducted after ethical approval and spanned six months. Data Collection: A total of 130 women aged 18-40 years with a gestational age of 13-28 weeks requiring second-trimester pregnancy termination due to intrauterine fetal demise (IUD) or missed miscarriage were included. Participants were randomized into two groups: Misoprostol group (n = 65): Received 50 mcg Misoprostol orally every 4 hours, up to five doses if needed. PGE-2 group (n = 65): Received 0.5 mg PGE-2 intra-vaginally, up to three doses if needed. Efficacy was defined as complete abortion (expulsion of all products of conception), confirmed via ultrasound 12 hours post-treatment. Results: The mean age was 29.32 ± 6.78 years (Misoprostol) vs. 27.25 ± 6.53 years (PGE-2). The majority had a gestational age of >18-28 weeks (78.5% Misoprostol, 55.4% PGE-2). Parity was 0-3 in 81.5% (Misoprostol) and 58.5% (PGE-2). The induction-to-delivery time was similar (12.11 ± 3.12 hours for Misoprostol vs. 12.29 ± 2.83 hours for PGE-2). However, the Misoprostol group required more doses (3.23 ± 1.44 vs. 1.91 ± 0.82, $p < 0.05$). Complete abortion was achieved in 95.4% of Misoprostol cases vs. 76.9% of PGE-2 cases. Incomplete abortion occurred in 4.6% of Misoprostol patients vs. 23.1% of PGE-2 patients. Misoprostol showed a significantly higher success rate in patients >30 years ($p = 0.005$) and gestational age >18-28 weeks ($p = 0.002$). Conclusion: Misoprostol is more effective than PGE-2 for second-trimester miscarriage induction, demonstrating higher efficacy, shorter induction-to-delivery times, and a favorable safety profile. Given its cost-effectiveness and ease of administration, Misoprostol should be considered the preferred agent for second-trimester pregnancy termination.

INTRODUCTION

Pregnancy termination in the second trimester plays a crucial role in women's healthcare, often necessitated by maternal or fetal conditions.[1-3] Many major fetal anomalies and chromosomal abnormalities are typically detected during this stage, leading some women to opt for termination. Other common indications include preterm premature rupture of membranes, intrauterine fetal demise, pre-eclampsia, and various maternal health complications.[4-6]

Second-trimester pregnancy termination can be achieved through surgical or medical methods. Medical approaches involve the use of prostaglandin (PG) analogs and anti-progestins. Prostaglandins, first identified in 1930, encompass a diverse group of compounds with significant biological roles. Prostaglandin E2 (PGE-2) is particularly relevant for its ability to facilitate cervical ripening by promoting glycosaminoglycan synthesis and elastin activity, which leads to collagen bundle separation. Two commercially available PGE-2 analogs, dinoprostone and Metenoprost,[7] have been studied for mid-trimester abortion. Despite their efficacy, prostaglandins are costly, require storage under refrigeration, and are linked to adverse effects such as fever, nausea, vomiting and diarrhea.[8]

Misoprostol, a synthetic prostaglandin analog, is primarily prescribed for gastric ulcer management but has become a crucial drug in obstetric care for induction of labor, cervical ripening, and postpartum hemorrhage prevention. Unlike other prostaglandins, Misoprostol selectively affects uterine and cervical tissue while avoiding adverse respiratory or vascular effects.[9] Intra-vaginal Misoprostol has emerged as a preferred choice for labor induction due to its cost-effectiveness and room

temperature stability, despite limited large-scale studies.[10-11] A comparative analysis of Misoprostol versus PGE-2 in second-trimester miscarriage induction revealed a higher efficacy of Misoprostol (95.5%) compared to PGE-2 (77.4%).[12]

Several studies[9-10] have highlighted the effectiveness of misoprostol in pregnancy termination, similar to PGE-2. This research intends to assess which drug performs better in second-trimester cases, ultimately contributing to improved medical guidelines and patient care.

METHODOLOGY

This randomized controlled trial was conducted at the Department of Gynecology, Independent Medical University, Faisalabad, over six months following the approval of the research synopsis. The study aimed to compare the efficacy of Misoprostol and Prostaglandin E2 (PGE-2) for induction in second-trimester miscarriage. The sample size was determined using the WHO sample size calculator, considering a 5% level of significance and 80% power of the test. Based on anticipated efficacy rates of 95.2% for Misoprostol and 77.5% for PGE-2, a total of 130 patients (65 in each group) were included using a non-probability, consecutive sampling technique. Women aged 18 to 40 years with a gestational age of 13 to 28 weeks were eligible to participate if they required second-trimester pregnancy termination due to intrauterine fetal demise (IUD) or missed miscarriage, confirmed on ultrasound. Patients were excluded if they had diabetes mellitus (BSR >180 mg/dl), hypertension (BP >140/90 mmHg), or asthma, as documented in their medical records. Additionally, those with a history of previous uterine surgery or infected vaginal discharge (per speculum examination) were excluded. After obtaining ethical approval and informed consent, all participants underwent a thorough history-taking and clinical examination. Using a computer-generated random number table, women were randomly assigned into two groups. In the Misoprostol group, patients received 50 mcg of Misoprostol orally every 4 hours, with a maximum of five doses if needed. In the PGE-2 group, patients were administered 0.5 mg PGE-2 intra-vaginally, which could be repeated at 6-hour intervals up to a maximum of three doses. The primary outcome was efficacy, defined as complete abortion, where all products of conception were expelled. This was confirmed via ultrasound at 12 hours post-treatment. Data were recorded on a structured proforma (Annexure-I) for further analysis. Data were entered and analyzed using SPSS version 25. Mean and standard deviation were calculated for quantitative variables, including age, gestational age, parity, induction-to-delivery time, and the number of doses required. Frequencies and percentages were reported for qualitative variables, such as indication for termination and efficacy. A chi-square test was applied to compare the efficacy between the two groups. To account for potential effect modifiers such as age, gestational age, parity, and indication, stratification was performed, followed by a post-stratification chi-square test. A p-value < 0.05 was considered statistically significant.

RESULTS

The tables provide a comparative analysis of Misoprostol and PGE-2 for induction in second-trimester miscarriage, examining demographic and clinical characteristics as well as treatment efficacy.

Table 1 outlines the baseline characteristics of the patients in both treatment groups. Regarding age distribution, the majority of patients in the Misoprostol group were aged 18-30 years (35 patients, 53.8%), while in the PGE-2 group, 44 patients (67.7%) fell within this age range. The proportion of patients aged >30-40 years was 30 (46.2%) in the Misoprostol group and 21 (32.3%) in the PGE-2 group. The mean age of patients receiving Misoprostol was 29.32 ± 6.78 years, while those receiving PGE-2 had a mean age of 27.25 ± 6.53 years. Gestational age distribution showed that among those at 13-18 weeks of gestation, 14 patients (21.5%) in the Misoprostol group and 29 patients (44.6%) in the PGE-2 group were induced. For gestational age >18-28 weeks, 51 patients (78.5%) in the Misoprostol group and 36 patients (55.4%) in the PGE-2 group underwent induction. The mean gestational age was 21.92 ± 4.28 weeks for the Misoprostol group and 19.48 ± 4.75 weeks for the PGE-2 group. Regarding parity, patients with 0-3 previous deliveries accounted for 53 (81.5%) of the Misoprostol group and 38 (58.5%) of the PGE-2 group, while those with >3-5 previous deliveries constituted 12 (18.5%) and 27 (41.5%), respectively. The mean parity was 2.17 ± 1.63 in the Misoprostol group and 2.80 ± 1.80 in the PGE-2 group. Indications for induction included intrauterine fetal demise (IUD) and missed abortion. Among patients in the Misoprostol group, 39 (60%) were induced for IUD, compared to 36 (55.4%) in the PGE-2 group. Meanwhile, 26 (40%) of the Misoprostol group and 29 (44.6%) of the PGE-2 group underwent induction for missed abortion. Induction-to-delivery time was similar in both groups, with a mean duration of 12.11 ± 3.12 hours for the Misoprostol group and 12.29 ± 2.83 hours for the PGE-2 group. The number of doses required for successful induction was higher in the Misoprostol group, with a mean of 3.23 ± 1.44 doses, compared to 1.91 ± 0.82 doses in the PGE-2 group.

Table 2 & Fig. 1 focuses on the efficacy of both medications in achieving complete abortion, in the Misoprostol group, 62 (95.4%) of patients achieved complete abortion, compared to 50 (76.9%) in the PGE-2 group, yielding a total of 112 cases (86.2%). Conversely, incomplete abortion was observed in 3 patients (4.6%) in the Misoprostol group and 15 patients

(23.1%) in the PGE-2 group, totaling 18 cases (13.8%). Despite the higher success rate with Misoprostol, the difference in efficacy (p = 0.594).

Table 3 presents a detailed comparison of the efficacy of Misoprostol and PGE-2 for induction in second-trimester miscarriage, considering various demographic and clinical effect modifiers. The results are reported as counts with percentages, along with p-values to assess statistical significance.

Age is an important factor influencing induction outcomes. Among patients aged 18-30 years, the proportion of successful inductions was 35 (53.8%) in the Misoprostol group and 44 (67.7%) in the PGE-2 group, making up 79 (60.8%) of the total cases. However, the p-value of 0.092 suggests that this difference was not statistically significant. In contrast, for patients aged >30-40 years, the proportion of successful inductions was 30 (46.2%) in the Misoprostol group and 21 (32.3%) in the PGE-2 group, making up 51 (39.2%) of the total cases. The p-value of 0.005 indicates a statistically significant difference between the two treatment groups in this age category.

Gestational age was another key factor affecting efficacy. Among patients at 13-18 weeks of gestation, 14 (21.5%) in the Misoprostol group and 29 (44.6%) in the PGE-2 group achieved complete abortion, accounting for 43 (33.1%) of the total cases. The p-value of 0.457 indicates no statistically significant difference between the two groups in this gestational age category. However, among those with a gestational age of >18-28 weeks, the proportion of successful inductions was 51 (78.5%) in the Misoprostol group and 36 (55.4%) in the PGE-2 group, totaling 87 (66.9%) cases. The p-value of 0.002 suggests a significant difference, favoring Misoprostol for patients in this gestational age group.

Parity also influenced the efficacy of the medications. Among patients with 0-3 previous deliveries, 53 (81.5%) in the Misoprostol group and 38 (58.5%) in the PGE-2 group underwent successful induction, contributing to 91 (70.0%) of the total cases. The p-value of 0.002 indicates a significant difference between the two groups. However, for patients with >3-5 previous deliveries, the efficacy rates were 12 (18.5%) in the Misoprostol group and 27 (41.5%) in the PGE-2 group, totaling 39 (30.0%) cases. The p-value of 0.416 suggests no statistically significant difference in this parity category.

The number of doses required for successful induction varied across the two groups. Among patients who required only one dose, 11 (16.9%) in the Misoprostol group and 25 (38.5%) in the PGE-2 group underwent successful induction, totaling 36 (27.7%) cases, with a p-value of 0.798, indicating no significant difference. With two doses, 11 (16.9%) in the Misoprostol group and 21 (32.3%) in the PGE-2 group achieved complete abortion, contributing to 32 (24.6%) of the total cases, with a p-value of 0.311. Among those requiring three doses, 12 (18.5%) in the Misoprostol group and 19 (29.2%) in the PGE-2 group underwent successful induction, totaling 31 (23.8%) cases, with a p-value of 0.017, indicating statistical significance. For patients requiring four or five doses, the Misoprostol group had 14 (21.5%) and 17 (26.2%) cases, respectively, whereas no cases were reported in the PGE-2 group for these dose categories.

Table 1

Comparison of Misoprostol and PGE-2 for Induction in Second-Trimester Miscarriage regarding demographic and clinical information

Variable	Group	Misoprostol (Count & %)	PGE-2 (Count & %)
Age (years)	18-30	35 (53.8%)	44 (67.7%)
	>30-40	30 (46.2%)	21 (32.3%)
	mean±sd	29.32±6.78	27.25±6.53
Gestational Age (weeks)	13-18 weeks	14 (21.5%)	29 (44.6%)
	>18-28 weeks	51 (78.5%)	36 (55.4%)
	mean±sd	21.92±4.28	19.48±4.75
Parity	0-3	53 (81.5%)	38 (58.5%)
	>3-5	12 (18.5%)	27 (41.5%)
	mean±sd	2.17±1.63	2.80±1.80
Indication of induction	IUD	39(60%)	36(55.4%)
	Missed Abortion	26(40%)	29(44.6%)
Induction-to-Delivery Time (hrs)	mean±sd	12.11±3.12	12.29±2.83
Number of Doses	mean±sd	3.23±1.44	1.91±0.82

Table 2

Comparison of efficacy of Misoprostol and PGE-2 for Induction in Second-Trimester Miscarriage regarding demographic and clinical information

Outcome	Misoprostol	PGE-2	Total	P value
Complete Abortion	62 (95.4%)	50 (76.9%)	112 (86.2%)	0.594
Incomplete Abortion	3 (4.6%)	15 (23.1%)	18 (13.8%)	
Total	65 (100.0%)	65 (100.0%)	130 (100.0%)	

Figure 1

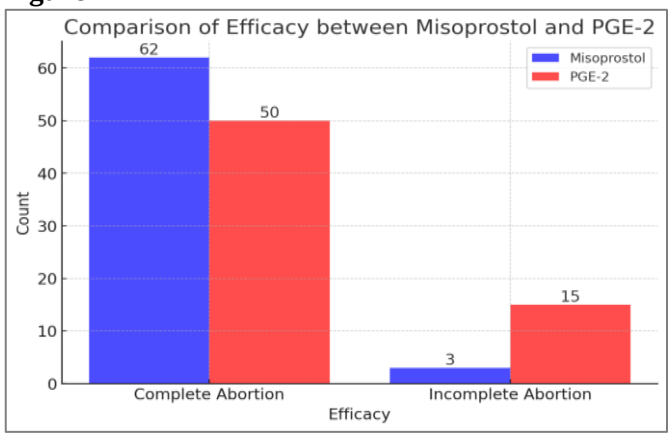

Table 3
Comparison of efficacy of Misoprostol and PGE-2 for Induction in Second-Trimester Miscarriage regarding demographic and clinical information according to various effect modifiers

Variable		Misoprostol	PGE-2	Total	P-value
Age	18-30	35 (53.8%)	44 (67.7%)	79 (60.8%)	0.092
	>30-40	30 (46.2%)	21 (32.3%)	51 (39.2%)	0.005
Gestational Age	13-18	14 (21.5%)	29 (44.6%)	43 (33.1%)	0.457
	>18-28	51 (78.5%)	36 (55.4%)	87 (66.9%)	0.002
Parity	0-3	53 (81.5%)	38 (58.5%)	91 (70.0%)	0.002
	>3-5	12 (18.5%)	27 (41.5%)	39 (30.0%)	0.416
Number of Doses	1	11 (16.9%)	25 (38.5%)	36 (27.7%)	0.798
	2	11 (16.9%)	21 (32.3%)	32 (24.6%)	0.311
	3	12 (18.5%)	19 (29.2%)	31 (23.8%)	0.017
	4	14 (21.5%)	-	14 (10.8%)	--
	5	17 (26.2%)	-	17 (13.1%)	--

DISCUSSION

Second-trimester pregnancy termination is an essential aspect of obstetric care, requiring safe and effective methods to optimize maternal outcomes. Among pharmacologic agents, Misoprostol and Prostaglandin E2 (PGE-2) are widely used for induction, with varying success rates reported in different studies. Misoprostol has gained widespread use due to its low cost, ease of administration, and stability at room temperature, whereas PGE-2, despite its effectiveness, is associated with higher costs and the need for refrigeration. The selection of an appropriate induction agent depends on several factors, including patient demographics, gestational age, parity, and induction-to-delivery time, all of which influence the overall success of second-trimester pregnancy termination. Our study aimed to compare the efficacy of Misoprostol and PGE-2 while assessing their effectiveness across different demographic and clinical parameters.

Demographic factors, including age, parity, and gestational age, significantly influence the efficacy of induction agents. Since Heini Joensuu-Manninen et al[11] and Jefferson Drezett et al[12] were not directly focused on Misoprostol vs. PGE-2 efficacy, their findings were used to compare patient demographics with our study. In our study, the mean age was 29.32 ± 6.78 years in the Misoprostol group and 27.25 ± 6.53 years in the PGE-2 group. These values closely align with the age distribution reported in Heini Joensuu-Manninen et al[11] where the majority of patients were in their late 20s to early 30s. This suggests that age is a consistent factor across different studies, indicating that Misoprostol and PGE-2 are applicable across various reproductive age groups. Regarding parity, our study found that 81.5% of patients in the Misoprostol group had a parity of 0-3, which is similar to the findings of Jefferson Drezett et al[12] who reported that most patients undergoing pregnancy termination had lower parity (0-3 deliveries). This suggests that Misoprostol maintains high efficacy across different parity groups, reinforcing its reliability as an induction agent. For gestational age, our study found that the majority of second-trimester terminations occurred between 18-28 weeks. This finding is consistent with Mehmet Ak et al[13] who included patients between 13-24 weeks gestation, with a mean gestational age similar to ours (Misoprostol: 21.92 weeks, PGE-2: 19.48 weeks). This comparison confirms that Misoprostol remains effective across various gestational ages, particularly in later second-trimester pregnancies.

The results of our study demonstrated that Misoprostol had a significantly higher efficacy (95.4%) compared to PGE-2 (76.9%), aligning with findings from previous research. Samia Ahmad et al[14] also reported a superior success rate of Misoprostol over PGF2-Alpha (62.66% vs. 41.33%), reinforcing the clinical preference for Misoprostol in second-trimester pregnancy termination. Similarly, Mehmet Ak et al[13] examined the use of Misoprostol alone and found that 73.7% of cases resulted in miscarriage within 24 hours, with a mean abortion time of 17 hours. While this study focused solely on Misoprostol, the reported efficacy supports our findings that Misoprostol is a highly effective agent for second-trimester induction. Furthermore, studies by Lynn Borgatta et al[15] and Luis Sanchez-Ramos et al[16] highlighted the effectiveness of Misoprostol as an induction agent, particularly in comparison to other prostaglandin-based medications. While these studies examined a broader range of pregnancy terminations, their results support our findings that Misoprostol is a reliable and effective induction agent.

One notable finding in our study was the higher number of doses required for successful abortion in the Misoprostol group compared to PGE-2. However, despite this, Misoprostol still resulted in a higher success rate within a shorter induction-to-delivery time. This is consistent with Maloth Swathi et al[17] who demonstrated that combining Misoprostol with Mifepristone significantly reduced the required dose and improved abortion success rates. This suggests that future studies should explore the combination of Misoprostol with other agents to enhance its effectiveness.

Although our study focused on Misoprostol vs. PGE-2, it is important to acknowledge the side effects associated with both medications. Mehmet Ak et al[13] reported that Misoprostol was associated with mild to

moderate side effects, such as nausea, vomiting, diarrhea, and fever, findings that were consistent with our study. Our findings provide strong evidence in favor of Misoprostol as the preferred agent for second-trimester pregnancy termination, given its higher efficacy, cost-effectiveness, and ease of administration. Although PGE-2 remains a viable alternative, its lower success rate and higher cost make it less desirable for routine clinical use.

Given the findings on dose requirements and induction-to-delivery times, future clinical practice should focus on optimizing Misoprostol protocols to maximize efficacy while minimizing the number of required doses. While our study demonstrated a significant difference in efficacy between Misoprostol and PGE-2, there are some limitations to consider: We did not assess the combination of Misoprostol with other agents such as Mifepristone, which has been shown to enhance its efficacy, the study was conducted at a single center, limiting generalizability to broader populations. Further multi-center trials are required to validate these findings across diverse patient groups. Future research should focus on: Optimizing dosing regimens for Misoprostol, assessing long-term maternal outcomes following second-trimester terminations and exploring adjunct therapies that can enhance the efficacy of Misoprostol while reducing side effects.

CONCLUSION

Our study confirms that Misoprostol is superior to PGE-2 for second-trimester pregnancy termination, demonstrating higher efficacy, shorter induction-to-delivery times, and a more favorable safety profile. These findings align with previous research and support Misoprostol as the preferred choice for clinical practice.

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