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A Comparative Study on the Effectiveness of Misoprostol Moistened with Acetic Acid versus Saline for Second-Trimester Pregnancy Termination

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Abstract: ***Introduction**: Second-trimester pregnancy termination presents significant medical challenges, requiring safe and effective methods. Misoprostol, a prostaglandin E1 analog, is widely used due to its affordability, ease of administration, and efficacy. Recent research suggests that moistening misoprostol with acetic acid may enhance its absorption and effectiveness. This study compares the effectiveness of misoprostol moistened with acetic acid versus saline in second-trimester pregnancy termination. **Methods**: A prospective hospital-based interventional study was conducted at a Tertiary healthcare centre, from December 2022 to January 2024. Sixty women aged 18-40 years with singleton pregnancies of 14-24 weeks were randomly allocated into two groups: Group A received misoprostol moistened with saline, while Group B received misoprostol moistened with acetic acid. The primary outcome measured was the induction-abortion interval. Secondary outcomes included mean misoprostol dose, side effects, complications, and hospital stay duration. **Results**: The mean induction-abortion interval was significantly shorter in Group B (18.01 ± 3.1 hours) compared to Group A (21.96 ± 2.5 hours, $p < 0.0001$). Group B also demonstrated a higher success rate of pregnancy termination (93.3% vs. 86.7%). No significant differences were found in the occurrence of side effects between the two groups. The mean duration of hospital stay was shorter in Group B (2.33 ± 0.95 days) than in Group A (3 ± 1.11 days, $p = 0.01$). **Conclusion**: Misoprostol moistened with acetic acid significantly shortens the induction-abortion interval and hospital stay without increasing adverse effects. These findings suggest that misoprostol moistened with acetic acid may be a more effective option for second-trimester pregnancy termination.*

Keywords: Misoprostol, Second-trimester abortion, Acetic acid, Saline, Induction-abortion interval

1. Introduction

Second-trimester pregnancy termination presents significant medical challenges due to the increased risks associated with surgical procedures and prolonged induction times. Medical abortion, particularly with misoprostol, has emerged as a safer and more effective alternative to surgical methods since the 1970s. Misoprostol, a synthetic prostaglandin E1 analog, has been widely adopted due to its affordability, ease of administration, and effectiveness in inducing uterine contractions. However, optimizing its absorption and efficacy remains an area of ongoing research.

Previous studies have explored various methods to enhance the effectiveness of misoprostol, including different routes of administration and combination therapies. One area of interest is the role of vaginal pH in drug absorption. Some studies suggest that acidifying the vaginal environment may improve misoprostol's pharmacokinetics, potentially leading to a shorter induction-abortion interval and improved outcomes.

The need for this study arises from the inconsistent findings regarding the role of acidified misoprostol in pregnancy termination. While some studies suggest that an acidic medium enhances the drug's effectiveness, others report no significant difference compared to saline-moistened misoprostol. Our study aimed to assess the induction-abortion interval, hospital stay duration, and side effects, and seeks to provide clarity on whether modifying the vaginal environment with acetic acid enhances misoprostol's efficacy.

2. Methods

This was a prospective, hospital-based, interventional study conducted at tertiary healthcare centre designed to assess the effectiveness of misoprostol moistened with acetic acid versus saline for second-trimester pregnancy termination. 60 Participants included women aged 19-30 years with singleton pregnancies of 14-24 weeks, who met inclusion criteria and provided informed consent Primary objective was to compare the induction-abortion interval between misoprostol moistened with acetic acid and misoprostol moistened with saline in second-trimester pregnancy termination. Secondary objectives were to evaluate the mean misoprostol dose required, the frequency of side effects, the occurrence of complications, and the duration of hospital stay between the two study groups.

Inclusion and Exclusion Criteria:

The inclusion criteria of the study were as follows: 1) Singleton pregnancy with a gestational age of 14-24 weeks with intra-uterine fetal demise. 2) Singleton pregnancy with a gestational age of 14-24 weeks with a live fetus having complex fetal structural abnormalities or chromosomal abnormalities. 3) Willing for admission for induced abortion.

The exclusion criteria were as follows:1) Patients with a history of allergies or increased sensitivity to prostaglandins. 2)Patients with increased risk of uterine rupture (e.g., known scarred uterus of previous caesarian or myomectomy). 3)Hemodynamically unstable patients. 4)Contraindication for medical termination (e.g., placenta previa) before the intervention. 5)Patients with active vaginal bleeding, and ruptured membranes. 6) Patients with congenital uterine anomalies.

Informed and written consent from women was taken before the study. A complete history was taken and a general & obstetrics examination were done. Subjects were informed about the benefits, adverse effects, and possible risks. Subjects were told that in case of failure to abort completely,

surgical methods would be performed. Before the start of therapy, a blood sample was taken to determine CBC, ABORh, GCT, HIV, HBsAg, VDRL, Anti-HCV, S.TSH, LFT, RFT, HBA1c, RBS, coagulation profile, Urine routine & microscopy, and USG for fetal wellbeing was done. Vitals were recorded. Randomization was done to allocate women in each group using computer generated random numbers and patients were divided into two groups. Women in the first group were given 400mcg misoprostol intra-vaginally moistened with 3ml of 0.9% normal saline simultaneously and misoprostol was repeated 6 hourly to a maximum of 5 doses. Women in the second group were given 400mcg misoprostol intra-vaginally moistened with 3ml of 5% Acetic Acid simultaneously and misoprostol was repeated 6 hourly to a maximum of 5 doses. Misoprostol was placed in the posterior fornix of the vagina by the doctor in 6-hour intervals and repeated to a maximum of 5 doses. No additional misoprostol was repeated if the patient was in an active phase of labour or the cervix was at least 70% effaced with 2 cm dilatation. After an abortion, all patients received 20IU of oxytocin in 500ml RL and we determined whether products of gestation (that is, fetus and placenta) had been successfully removed. Any products of the placenta if not delivered spontaneously within 1 hour after delivery were removed manually with ovum forceps. After delivery, the subject's vitals were recorded and repeat CBC was sent.

Statistical Analysis: The collected data were analyzed using SPSS version 25. Quantitative variables were expressed as mean ± standard deviation (SD), and qualitative variables were presented as percentages. Comparisons between the two groups were performed using an independent t-test for continuous variables and the chi-square test for categorical variables. A p-value of less than 0.05 was considered statistically significant.

3. Results

3.1 Demographic and Clinical Characteristics

The study population had a mean age of 24.3 years. No significant differences were observed between groups in age, socioeconomic status, BMI, gravidity, or gestational age.

Table 1: Distribution of cases according to Age

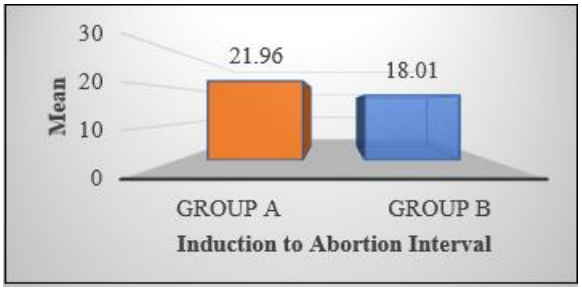
Age Distribution (in years)	Group A		Group B	
	No. of Patients	Percentage	No. of Patients	Percentage
19-22	9	30.0	12	40.0
23-26	11	36.7	14	46.7
27-30	10	33.3	4	13.3
Total	30	100.0	30	100.0
Mean±SD	25.1±3.44		23.46±2.60	
P-Value	0.05			

3.2 Induction to Abortion Interval

The mean induction-abortion interval was significantly shorter in Group B (18.01 hours) than Group A (21.96 hours) ($p < 0.0001$).

Table 2: Distribution of cases according to Induction to Abortion Interval (In hours).

Parameter	Group A (N.S.)		Group B (Acetic Acid)		P-Value
	Mean	SD	Mean	SD	
Induction to Abortion Interval (Hours)	21.96	2.5	18.01	3.1	<0.0001

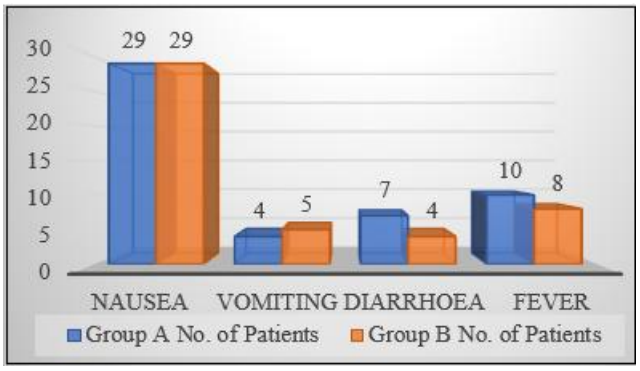


3.3 Side Effects and Complications

Both groups exhibited similar rates of nausea (96.7%), vomiting (13.3%-16.7%), diarrhea (13.3%-23.3%), and fever (26.7%-33.3%).

Table 3: Distribution of cases according to Side Effects

Side Effects	Group A		Group B		P-Value
	No. of Patients	Percentage	No. of Patients	Percentage	
Nausea	9	30.0	19	63.3	-
Vomiting	18	60.0	10	33.3	0.71
Diarrhoea	3	10.0	1	3.3	0.32
Fever	30	100.0	30	100.0	0.58

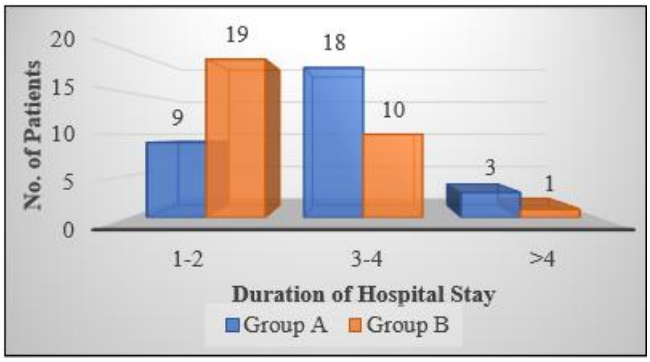


3.4 Hospital Stay and Termination Success

Successful termination was achieved in 93.3% of Group B cases compared to 86.7% in Group A. Hospital stay was significantly shorter in Group B ($p = 0.01$).

Table 4: Distribution of cases according to Duration of Hospital Stay (In Days).

Duration of Hospital Stay (In Days).	Group A		Group B	
	No. of Patients	Percentage	No. of Patients	Percentage
1-2	9	30.0	19	63.3
3-4	18	60.0	10	33.3
>4	3	10.0	1	3.3
Total	30	100.0	30	100.0
Mean±SD	3±1.11		2.33±0.95	
P-Value	0.01			



4. Discussion

Misoprostol is extensively utilized for initiating first-trimester abortion, a procedure that carries potential risks. Current research predominantly focuses on enhancing the effectiveness of misoprostol by evaluating different dosages, dosing intervals, routes of administration, and optimal dissolving media. The administered dosages of misoprostol varied between 100 and 800µg, while dosing intervals ranged from 3 to 12 hours. Misoprostol tablets are not specifically formulated for vaginal use, and the local conditions in the vaginal environment may significantly impact their effectiveness. To maintain a consistent plasma profile, it becomes crucial to alter the medium for vaginal misoprostol, ensuring thorough dissolution of the tablets for optimal efficacy. It is worth noting that misoprostol tablets exhibit improved liquefaction in an acidic medium. This study demonstrated that misoprostol moistened with acetic acid significantly reduced the induction-abortion interval compared to saline-moistened misoprostol. The mean induction-abortion interval in the acetic acid group was 18.01 hours, significantly shorter than the 21.96 hours observed in the saline group ($p < 0.0001$). These findings align with previous research indicating that acidifying the vaginal environment enhances misoprostol absorption and effectiveness. The higher termination success rate (93.3%) in the acetic acid group compared to the saline group (86.7%) suggests that modifying the vaginal pH may improve misoprostol's pharmacokinetics.

Both groups exhibited comparable side effects, including nausea, vomiting, and fever, indicating that acidification does not increase adverse reactions. The shorter hospital stay in the acetic acid group ($p = 0.01$) suggests potential benefits in reducing healthcare costs and patient discomfort.

The results of this study demonstrate that misoprostol moistened with acetic acid significantly reduces the induction-abortion interval compared to saline-moistened misoprostol. This aligns with previous studies suggesting that an acidic medium enhances drug absorption, leading to improved efficacy. The higher success rate in Group B further supports the hypothesis that acetic acid increases the bioavailability of misoprostol, contributing to faster pregnancy termination.

The similarity in adverse effects between the two groups suggests that modifying the vaginal environment with acetic acid does not introduce additional risks. The reduced hospital stay in Group B is a notable advantage, as it may lower healthcare costs and improve patient comfort.

Our study aligns with previous research indicating that acidifying agents can enhance misoprostol effectiveness. Acetic acid-moistened misoprostol led to a shorter induction-abortion interval and reduced hospital stay without increasing adverse effects. The findings support its potential as a superior option for second-trimester pregnancy termination.

5. Conclusion

Misoprostol moistened with acetic acid is more effective than saline in reducing the induction-abortion interval and hospital stay duration while maintaining a similar safety profile. Further large-scale studies are recommended to confirm these findings and guide clinical practice.

6. Recommendations

Based on the findings of this study, the following recommendations are proposed:

1) Acetic acid-moistened misoprostol should be considered as an alternative to saline-moistened misoprostol for second-trimester pregnancy termination due to its shorter induction-abortion interval and reduced hospital stay.
2) Further large-scale, multicenter studies are needed to validate these findings and assess long-term safety and patient satisfaction.
3) Future research should explore the optimal concentration of acetic acid for enhancing misoprostol efficacy without increasing adverse effects.
4) Healthcare providers should receive training on the benefits and administration protocols for misoprostol moistened with acetic acid to improve clinical outcomes.
5) Cost-effectiveness analysis should be conducted to evaluate the economic impact of using acetic acid-moistened misoprostol in different healthcare settings.

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