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EVAULATION OF ROLE OF INTRAVAGINAL ISOSORBIDE MONONITRATE IN INDUCTION OF SECOND TRIMESTER ABORTION

Prof Dr. Shikha Singh Professor and Head of the Department, Sarojini Naidu Medical College, Agra

Dr. Deepti Tyagi* Senior Resident, Sarojini Naidu Medical College, Agra *Corresponding Author

ABSTRACT **Introduction:** Second-trimester pregnancy termination is a challenging procedure requiring effective and safe methods. Isosorbide mononitrate , widely used for medical abortions, to improve outcomes. The addition of ISMN enhances cervical ripening and reduces the induction-abortion interval, making the process more efficient and tolerable. This study examines the effectiveness of this approach in managing second-trimester terminations. **Aim:** To study the role of intravaginal misoprostol with and without isosorbide mononitrate (ISMN) in the induction of second-trimester abortion. **Methods:** This randomized clinical trial included 72 pregnant women (12-28 weeks) undergoing second-trimester abortion. Participants were divided into two groups of 36: Group A received intravaginal misoprostol with ISMN, and Group B received Misoprostol alone. Primary outcomes included the induction-abortion interval, misoprostol doses needed for complete expulsion, and adverse events such as bleeding, headache, pelvic pain, hypotension, backache, fever, nausea, and vomiting, offering insight into the efficacy and safety of these methods. **Results:** The study demonstrated that the combination of misoprostol and ISMN significantly improved cervical consistency, dilatation, and effacement. The induction-abortion interval was shorter, and fewer misoprostol doses were required in Group A compared to Group B. Additionally, Group A experienced fewer side effects, with a lower incidence of abdominal pain and other adverse events. These findings highlight the synergistic effect of combining misoprostol with ISMN, enhancing efficacy and tolerability. **Conclusion:** Misoprostol is an effective cervical ripening agent, but combining it with ISMN provides better outcomes, including shorter induction times, fewer doses, and improved patient comfort with minimal side effects. This combination offers a safe, efficient alternative for second-trimester abortion. Further studies are essential to validate these findings and refine clinical guidelines for broader implementation.

KEYWORDS : Second-Trimester Abortion, Misoprostol, Isosorbide Mononitrate, Cervical Ripening, Induction-Abortion Interval, Medical Abortion, Pregnancy Termination, Adverse Effects

INTRODUCTION

Mid-trimester abortion refers to the termination of a pregnancy between the 13th and 28th week of fetal development. This period is subdivided into an early phase (13-20 weeks) and a late phase (20-28 weeks)[1,2]. Second-trimester abortions are an integral component of comprehensive women's healthcare, addressing medical, social[3], and psychological factors that influence decisions to terminate pregnancies at this stage. Globally, between 2015 and 2019, approximately 73.3 million intentional pregnancy terminations occurred annually, with 45% conducted under unsafe conditions[4]. Developing nations accounted for the majority of unsafe abortions, with over 98% occurring in these regions[5]. While most abortions are performed during the first trimester, an estimated 10-15% occur in the second trimester, often associated with two-thirds of major complications arising from pregnancy terminations[6].

In India, medically supervised abortion services are a vital aspect of the Reproductive and Child Health program[7], enabling women to access safe procedures for unplanned pregnancies. However, abortions performed outside medical settings contribute significantly to maternal health risks, accounting for 8% of maternal deaths and a 12% increase in pregnancy-related illnesses. Globally, unsafe abortion procedures during the second trimester are a major contributor to maternal deaths, comprising 13% of all maternal fatalities[8]. The burden is particularly evident in sub-Saharan Africa, where the number of abortions doubled from 4.3 million to 8.0 million between 1995–1999 and 2015–2019[9,10]. Compared to first-trimester abortions, second-trimester procedures carry higher financial costs and greater risks of morbidity and mortality.

Dilation and curettage (D&C), a surgical method introduced in the 1930s for first-trimester termination, has potential adverse effects, including uterine perforation, excessive bleeding, cervical damage, and infections. To mitigate these risks, various cervical preparation methods have been developed, including physical techniques and pharmacological agents like misoprostol and nitric oxide-releasing drugs[11,12,13]. Misoprostol, a prostaglandin E1 analog, is widely used for cervical softening, labor induction, therapeutic abortions, and postpartum hemorrhage management[14].

Nitric oxide, a gaseous free radical, acts as a potent endothelium-dependent relaxant in smooth muscles, including those in the uterus and cervix. Its biological messenger properties have found applications in obstetrics, such as managing preterm labor, facilitating uterine relaxation, and improving fetal blood circulation. Research has shown that nitric oxide donors, applied vaginally, effectively prepare the cervix for labor induction by directly and indirectly promoting prostaglandin release, cytokine activity, and collagen reorganization. These mechanisms enhance cervical readiness for childbirth while minimizing adverse effects like fetal stress[15].

Studies comparing second-trimester abortion methods have highlighted combinations of pharmacological agents, such as Misoprostol with mifepristone or methotrexate, and mechanical techniques like Foley's catheter. Mifepristone, a progesterone antagonist, prepares the uterus for contractions, while misoprostol induces uterine activity through prostaglandin-mediated mechanisms. Misoprostol's pharmacokinetics vary by administration route, with vaginal application yielding slower clearance and more localized effects, while sublingual routes offer rapid absorption but increased gastrointestinal side effects. Recent research has also examined isosorbide mononitrate, a nitric oxide donor, as an effective and economical option for cervical ripening. Its uterine first-pass effect ensures high local absorption with minimal systemic exposure, making it a preferred candidate for pre-abortion preparation[16].

The use of nitric oxide donors in combination with prostaglandins has demonstrated synergistic effects, achieving effective cervical ripening while reducing adverse outcomes associated with high doses of either agent alone. This combination approach offers a promising solution for optimizing second-trimester abortion procedures. Despite these advancements, concerns such as uterine artery dilation and potential hypotension remain, necessitating further research to refine administration protocols.

MATERIALAND METHODS

A randomized, controlled, prospective clinical study was conducted at the Department of Obstetrics and Gynaecology, S.N. Medical College, Agra, over a period of 18 months, from September 2022 to March 2024. The study was initiated after receiving ethical clearance from the Institutional Ethics Committee, ensuring adherence to ethical standards in human research.

Participants and Eligibility Criteria:

A total of 72 antenatal women, all within the gestational age range of 12 to 20 weeks and requiring medical termination of pregnancy, were recruited for the study. The inclusion criteria were clearly defined: participants were women aged between 18 and 35 years, with singleton pregnancies, an unscarred uterus, and a closed cervical os.

Exclusion criteria were applied to ensure patient safety and data integrity. Women were excluded if they had:
Gestational age outside the 12–20 weeks range,
A history of uterine surgery (i.e., scarred uterus)
Known bleeding disorders
Use of anticoagulants or corticosteroids
Known hypersensitivity to either Mifepristone or Misoprostol
Severe underlying medical conditions that could complicate the termination process.

Intervention and Study Groups:
Participants were randomly assigned into two groups for the intervention.
Group 1 received a combination of 400 mcg misoprostol along with 40 mg isosorbide mononitrate (ISMN), administered intravaginally every 4 hours, up to a maximum of four doses.
Group 2 received 400 mcg misoprostol alone intravaginally every 4 hours, up to four doses.

All participants in both groups were pre-treated with 200 mg of oral Mifepristone, administered 36 to 48 hours before the vaginal induction, in line with standard medical abortion protocols to enhance cervical ripening and improve efficacy.

Data Collection and Outcome Measures:
Comprehensive clinical data were collected for each patient, including baseline investigations, vital signs, and any adverse effects experienced during the procedure. Patient satisfaction with the treatment was also evaluated. These data points were essential to assess both the effectiveness and safety of the treatment regimens.

Statistical Analysis:
Data analysis was performed using IBM SPSS Statistics software, version 23.0. The results were interpreted with a significance level set at $p < 0.05$, indicating statistical significance. This analytical approach allowed for robust comparison of outcomes between the case and control group.

RESULTS

The study included 72 patients equally divided into Group A and Group B, with 36 patients in each group. The mean age of patients in Group A was 25.89 years (±4.30), while in Group B, it was 26.64 years (±4.86), with no statistically significant difference observed between the groups (p=0.490). Most participants in both groups were aged between 26-30 years.

Table 1: Comparative Analysis of Demographic, Clinical, and Socioeconomic Characteristics Between Group A and Group B

Parameter	Group A (n=36)	Group B (n=36)	p-value
Mean Age (±SD)	25.89 ±4.30	26.64 ±4.86	0.49
Gestational Age			
12-16 weeks (%)	61.1	41.7	0.099
16-20 weeks (%)	38.9	58.3	
Parity			0.684
Primiparous (%)	58.3	44.4	
Multiparous (%)	41.7	55.6	
BMI			0.617
Normal (%)	69.4	63.9	
Overweight (%)	30.6	36.1	
Indication			>0.05
Anomalous Baby (%)	25	33.3	
IUFD (%)	19.4	11.1	
Medical Indications (%)	8.3	16.7	
Social Causes (%)	25	19.4	
Socioeconomic Status			>0.05
Lower Class (%)	33.3	27.8	
Semi-Urban (%)	36.1	41.7	0.758
Rural (%)	38.9	30.6	

Gestational age distribution showed that in Group A, 61.1% of patients had a gestational age of 12-16 weeks, while 38.9% had 16-20 weeks. In contrast, Group B had 41.7% of patients in the 12-16 weeks range and 58.3% in the 16-20 weeks range. This difference was not statistically significant (p=0.099) (Table 1)

There were no statistically significant differences between Group A and Group B in terms of parity (primiparous vs. multiparous), BMI (normal vs. overweight), indications for pregnancy termination, socioeconomic status, or living area. Group A had slightly higher proportions of primiparous women, normal-weight individuals, and patients from lower socioeconomic classes, but these differences were not significant. The most common termination reason in both groups was fetal anomaly.(Table 1).

In Group A, 16.7% (6 patients) required one dose, 61.1% (22 patients) required two doses, 19.4% (7 patients) required three doses, and 2.8% (1 patient) required four doses. In Group B, 8.3% (3 patients) required one dose, 36.1% (13 patients) required two doses, 41.7% (15 patients) required three doses, and 13.9% (5 patients) required four doses. There was a statistically significant difference in the number of doses required between the groups (P = 0.031) (Figure 1).

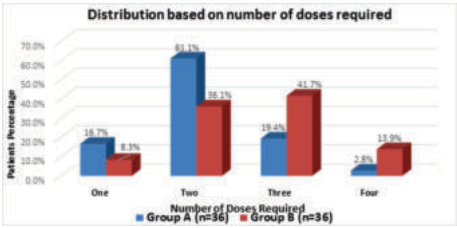

Figure 1: Distribution of the Studied Patients Based on the Number of Doses Required

The mean dose of misoprostol was significantly higher in Group B (1044.44 ± 335.04 µg) compared to Group A (833.33 ± 276.72 µg) (P = 0.005) (Figure 2).

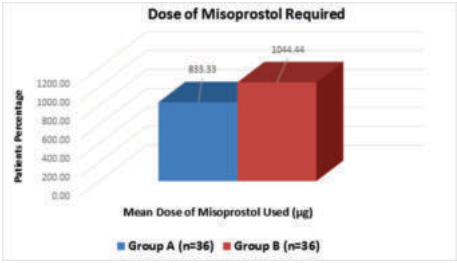

Figure 2: Distribution of the Studied Patients Based on Dose of Misoprostol Required

Primiparous patients required higher mean doses compared to multiparous patients within each group, and Group B had significantly higher doses for both categories. For Group A, the mean dose was 971.43 ± 239.05 µg for primiparous patients and 640.00 ± 202.84 µg for multiparous patients (P < 0.001). In Group B, the mean dose was 1275.00 ± 262.05 µg for primiparous patients and 860.00 ± 268.33 µg for multiparous patients (P < 0.001) (Table 2).

Table 2: Distribution of the Studied Patients Based on Parity and Mean Dose of Misoprostol

	Parity		P value
	<2	≥2	
Group A (Mean Dose of Misoprostol)	971.43±239.05	640.00±202.84	<0.001
Group B (Mean Dose of Misoprostol)	1275.00±262.05	860.00±268.33	<0.001
P value	<0.001	<0.001	

The induction abortion interval differed significantly between groups (P < 0.05). In Group A, 30.6% of patients had an interval of 0-4 hours, 58.3% had 4-8 hours, 11.1% had 8-12 hours, and none had 12-16 hours. In Group B, 16.7% had 0-4 hours, 41.7% had 4-8 hours, 38.9% had 8-12 hours, and 2.8% had 12-16 hours (Figure 3).

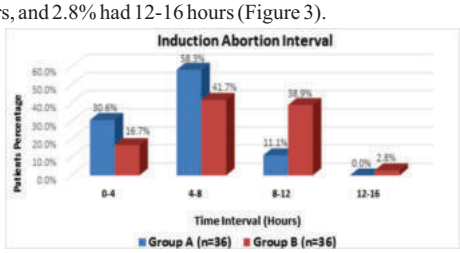

Figure 3: Distribution of the Studied Patients Based on Induction Abortion Interval

In Group A, primiparous patients had shorter induction intervals than multiparous patients (P = 0.003). In Group B, primiparous patients also had significantly shorter intervals compared to multiparous patients (P = 0.004) (Table 3).

Table 3: Distribution of the Studied Patients Based on Parity and Induction Abortion Interval in group A

Time Interval (Hours)	Parity	
	Group A (n=36)	
	Primi	Multi
0-4	2 (5.6%)	9 (25.0%)
4-8	15 (41.7%)	6 (16.7%)
8-12	4 (11.1%)	0 (0.0%)
12-16	0 (0.0%)	0 (0.0%)
p-value	0.003	

Side effects were more common in Group B compared to Group A. Overall, 66.7% of patients in Group B experienced side effects, compared to 38.9% in Group A (P = 0.018). Specifically, abdominal pain was significantly more frequent in Group B (63.9%) than in Group A (38.9%) (P = 0.034). Other side effects, such as fever, nausea, diarrhea, shivering were observed at similar rates in both groups and were not statistically significant(Figure 4).

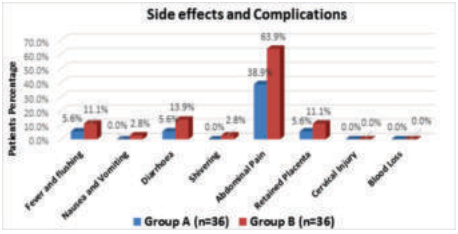

Figure 4: Distribution of the Studied Patients Based on Side Effects and Complications

The rate of complete abortion was slightly higher in Group A (94.4%) compared to Group B (80.6%), while incomplete abortions were more frequent in Group B (19.4%) than in Group A (5.6%). No cases of abortion failure were reported in either group. However, the differences were not statistically significant (P = 0.07) (Table 4).

Table 4: Distribution of the Studied Patients Based on Status of Abortion in Group A and B

Outcome	Group A (n=36)	Group B (n=36)	P value
Complete Abortion	34 (94.4%)	29 (80.6%)	0.07
Incomplete Abortion	2 (5.6%)	7 (19.4%)	
Failure	0 (0.0%)	0 (0.0%)	

Satisfaction levels were comparable between the two groups. In Group A, 50% of patients were very satisfied, while 52.8% of patients in Group B reported the same. The proportions of satisfied, neutral, and dissatisfied patients were also similar, with no statistically significant differences (P > 0.05) (Figure 5).

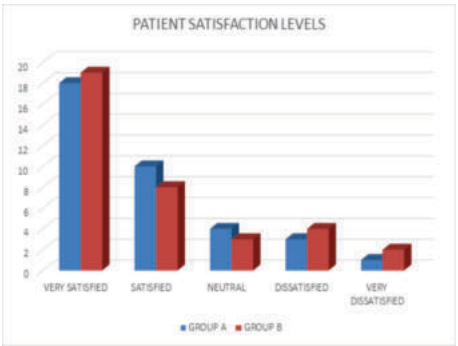

Figure 5: Distribution of the Studied Patients Based on the Satisfaction Level in Group A and B

DISCUSSION

Second-trimester pregnancy termination is a challenging and emotionally taxing process that often requires effective medical protocols to minimize complications and psychological distress. This study aimed to compare the effectiveness of intravaginal misoprostol along with its combination with isosorbide mononitrate (ISMN) for second-trimester pregnancy terminations, focusing on key parameters such as induction-abortion interval, misoprostol dosage, side effects, and success rates.

The mean age of participants in Group A (Misoprostol with ISMN) was 25.89±4.30 years, while Group B (misoprostol alone) had a mean age of 26.64±4.86 years. These findings were not statistically significant (p>0.05) and are consistent with prior studies, such as those by Atalla et al.[17]and Sivakumar S et al which reported similar age distributions among participants seeking second-trimester terminations. The gestational age distribution showed that most participants in Group A were between 12-16 weeks (61.1%), whereas Group B had a higher proportion of cases between 16-20 weeks (58.3%), with no statistically significant differences (p>0.05). This aligns with findings from Atalla et al [17]. and Sivakumar S et al., which highlighted comparable gestational age distributions in similar cohorts.

A significant difference was observed in the number of misoprostol doses required between the two groups (p=0.031). Group A required fewer doses, with a mean dose of 833.33±276.72 µg, compared to 1044.44±335.04 µg in Group B (p=0.005). These results align with studies by Atalla et al. and Sivakumar S et al., which demonstrated that the addition of ISMN significantly reduces the required misoprostol dose. Furthermore, Group A exhibited a shorter induction-abortion interval, with 58.3% achieving abortion within 4-8 hours, compared to 41.7% in Group B. These findings are supported by Mousiolis et al, who reported significantly shorter induction-abortion intervals with combination therapy (12.4 hours) compared to misoprostol alone (20.4 hours).

The incidence of side effects was significantly lower in Group A (38.9%) compared to Group B (66.7%, p<0.05). Abdominal pain was the most prevalent side effect, affecting 38.9% of Group A patients and 63.9% of Group B patients. Other side effects, such as fever, nausea, and diarrhea, were comparable between the groups. These findings align with those of Atalla et al [17]. and Sivakumar S et al., which highlighted fewer side effects with combination therapy. No severe complications, such as cervical injury or excessive blood loss, were observed in either group, consistent with prior studies.

Complete abortion was achieved in 94.4% of Group A and 80.6% of Group B cases, with no reported failures in either group. While the difference was not statistically significant (p=0.07), the higher success rate in Group A aligns with studies by Atalla et al[17] and Sivakumar S et al, which demonstrated superior outcomes with combination therapies. The addition of ISMN likely enhances cervical ripening and uterine contractility, contributing to the observed trend.

This study's findings align closely with prior research by Atalla et al[17] Sivakumar S et al [18], and Mousiolis et al, which reported similar benefits of combining ISMN with misoprostol. The reduction in misoprostol dosage, shorter induction-abortion intervals, and lower incidence of side effects in the combination group highlight the clinical advantages of ISMN as an adjunct in second-trimester terminations.

The study's modest sample size and single-center design may limit generalizability. Additionally, factors such as long-term outcomes and psychological impacts were not assessed.This study provides valuable insights into optimizing medical protocols for second-trimester terminations. The findings support the efficacy and safety of combining ISMN with misoprostol, offering a practical alternative to surgical methods.

CONCLUSION

Our findings demonstrate that the combination of Misoprostol and Isosorbide mononitrate (ISMN) significantly shortens the induction-abortion interval compared to misoprostol alone, providing a safer, more efficient, and cost-effective method for mid-trimester pregnancy termination. This combined approach offers a practical alternative, minimizing complications and improving outcomes. Future research should focus on long-term effects, including fertility outcomes, and assess patient satisfaction, acceptance, and convenience. Additionally, studies should evaluate the benefits of reduced cervical dilatation against potential risks to refine clinical guidelines. These insights can help optimize treatment strategies while aligning with WHO recommendations for safe and effective abortion care.

REFERENCES

1. Bygdeman. Mid-trimester induced abortion: a review. Hum Reprod Update. 2007;13:37–52.

2. Mulat A, Bayu H, Mellie H, Alemu A. Induced second trimester abortion and associated factors in Amhara region referral hospitals. BioMed Res Int. 2015;2015:256534.
3. Pranavi B, George N, Saraswathi K. A clinical observational study on second-trimester abortion. 2020;9:1339–46.
4. Bearak J, Popinchalk A, Ganatra B, Moller A-B, Tunçalp Ö, Beavin C, et al. Unintended pregnancy and abortion by income, region, and the legal status of abortion: estimates from a comprehensive model for 1990–2019. Lancet Global Health. 2020;8:1152–61.
5. Gebremedhin M, Semahegn A, Usmael T, Tesfaye G. Unsafe abortion and associated factors among reproductive aged women in Sub-Saharan Africa: a protocol for a systematic review and meta-analysis. Syst Rev. 2018;7:1–5.
6. Kebede K, Gashawbeza B, Gebremedhin S, Tolu LB. Magnitude and determinants of the late request for safe abortion care among women seeking abortion care at a tertiary referral hospital in ethiopia: a cross-sectional study. Int J Womens Health. 2020;12:1223.
7. Bijeta, Neelam Nalini. Medical method of second trimester abortion with Mifepristone and misoprostol vs misoprostol alone: ijcmrvo. 2017; l4(12):77-83.
8. Siraneh Y, Workneh A. Determinants and outcome of safe second trimester medical abortion at Jimma University medical center, Southwest Ethiopia. J Preg. 2019; 2019.
9. Bankole A, Remez L, Owolabi O, Philbin J, Williams P. From unsafe to safe abortion in Sub-Saharan Africa: Slow but steady progress. 2020;10.1363/2020.32446
10. Woyecha . Delay in decision and determinants for safe abortion among women at health facilities in south West Ethiopia: facility based cross sectional study. Int J Equity Health. 2020;19:1–6.
11. Bollagragada S, Mackenzie F. A randomized placebo controlled trial of outpatient cervical ripening with isosorbidemononitrate prior to induction of labour. BMC Pregnancy Childbirth. 2006;6:25.
12. Ekerhovd E, Bullarbo M, Andersch B, Norström A. Vaginal administration of the nitric oxide donor isosorbide mononitrate for cervical ripening at term: a randomized controlled study. Am J Obstet Gynecol. 2003;189(6):1692-7.
13. Tommiska MR. Nitric oxide in the human uterine cervix: endogenous ripening factor. Ann Med. 2008;40(1):45-5.
14. Berghese V et al: Misoprostol for second trimester pregnancy termination in women with previous LSCS- A systematic review: Br. J. obstet Gynecol. 2009; 176:115Ie7.
15. Gynuity Health Project. Map of Misoprostol Approval page, 2008. Available at: https://gynuity. org/downloads. Accessed on 21 January 2022.
16. Meena N, Bindal N, Meena S. Evaluation of isosorbide mononitrate for cervical ripening prior to induction of labor at term pregnancy in an outpatient setting: Int J Reprod Contraception Obstet Gynecol. 2016; 5(3):793-797.
17. Mohamed Atalla EMI. Second Trimester Abortion Induction With Misoprostol Only Versus Misoprostol Plus Isosorbide Mononitrate: A Randomized Controlled Study. OPEN AIMJ. 2022;92-96
18. Sivakumar S, Nalina S, Fathima R, et al. Comparison of misoprostol and misoprostol with isosorbide mononitrate in second trimester termination of pregnancy. J. Evid. Based Med. Healthc. 2016; 3(63), 3424-3429.