



## **To Evaluate Shorter Versus Standard Mifepristone To Misoprostol Interval for Second Trimester Medical Method of Termination of Pregnancy**

<sup>1</sup>Dr. Rudrakshi, SMS Medical College, Jaipur.

<sup>2</sup>Dr. Devendra K Benwal, SMS Medical College, Jaipur.

<sup>3</sup>Dr. Babita, SMS Medical College, Jaipur.

<sup>4</sup>Dr. Navneet, SMS Medical College, Jaipur.

**Corresponding Author:** Dr. Rudrakshi, SMS Medical College, Jaipur.

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### **Abstract**

**Background:** Second-trimester abortion (13–24 weeks) is vital in women’s healthcare but carries higher risks than first-trimester procedures. Medical methods of abortion with mifepristone followed by misoprostol is a highly effective and safe option than any surgical approaches. Traditionally, a 48-hour interval is advised, but shorter intervals may improve efficiency, reduce hospital stay, and enhance patient comfort.

**Aim:** To evaluate the effectiveness of a shorter versus a standard mifepristone-to-misoprostol interval for second-trimester medical termination of pregnancy.

**Methods:** A prospective hospital-based study at SMS Medical College randomized women into 24-hour and 48-hour mifepristone-to-misoprostol groups. Standard examinations, investigations, and informed consent were obtained. Abortion outcomes were assessed after administering mifepristone 200 mg orally and misoprostol vaginally, with subsequent dosing as required. Statistical analysis compared efficacy and safety between groups.

**Results:** The study compared 24-hour and 48-hour mifepristone-to-misoprostol intervals for second-trimester abortion. Both regimens showed similar efficacy, side effects, parity distribution, misoprostol dose requirements, and induction-to-abortion intervals. However, the 48-hour group had a significantly longer mifepristone-to-abortion interval, suggesting the 24-hour protocol may be more time-efficient without compromising safety or outcomes.

**Conclusion:** Both 24-hour and 48-hour regimens were comparable in efficacy, safety, and side effects, but the 24-hour interval ensured faster abortion completion, making it a more time-efficient yet equally effective protocol.

**Keywords:** Termination of Pregnancy, Misoprostol Interval, mifepristone-to-misoprostol Interval, pregnancy loss.

### **Introduction**

Pregnancy is often considered a joyful phase, but not all result in favorable maternal and fetal outcomes. Abortion, the termination of pregnancy before fetal

viability, may be medical or surgical, with medical methods increasingly preferred for their effectiveness and procedural advantages. Second-trimester abortion (13–26 weeks) is an important aspect of women's healthcare, performed for reasons including late pregnancy detection, severe fetal anomalies, and complications such as preeclampsia, preterm premature rupture of membranes, or fetal demise.<sup>1</sup> Data remain underreported; only 64% of providers offer services beyond 12 weeks and 23% beyond 20 weeks. Globally, 10–15% of induced abortions occur in this period, often due to delayed diagnosis, limited access, financial constraints, or stigma (Drey 2006).<sup>2</sup> In India, the MTP Act (2021) extended the gestational limit from 20 to 24 weeks under specific conditions. Second-trimester procedures carry higher morbidity. Surgical abortion risks uterine perforation, hemorrhage, and sepsis, whereas medical abortion is safer with fewer infrastructure needs.<sup>3</sup> WHO recommends mifepristone–misoprostol up to 9 weeks,<sup>4</sup> while misoprostol alone achieves 97.2% success for later terminations. Medical methods are preferred where D&E is unavailable or when the woman wishes to view the fetus. Protocols involve mifepristone pretreatment followed by misoprostol after 24–48 hours.<sup>4</sup> Mifepristone primes the uterus for misoprostol-induced contractions.<sup>8</sup> The combination shortens expulsion time compared to misoprostol alone,<sup>5</sup> which needs higher doses and causes more side effects. A 3-hour dosing interval is more effective than 6 hours. A common regimen is 200 mg oral mifepristone followed by up to 800 mcg vaginal misoprostol. Mifepristone may be given 1–2 days before misoprostol, with vaginal administration more effective than sublingual, which often requires stronger analgesia.<sup>6</sup> Although a 36–48 hour interval is traditional (Gemzell-Danielsson and Lalitkumar, 2008), shorter intervals could improve efficiency and reduce patient anxiety.

This study aims to evaluate the effectiveness of a shorter versus a standard mifepristone-to-misoprostol interval for second-trimester medical termination of pregnancy.

## Materials and Methods

**Type of Study:** Interventional

**Design:** Prospective comparative study

**Place:** Dept. of Obstetrics & Gynaecology, SMS Medical College, Jaipur

**Duration:** Data collection began Oct 2023 after ethics approval; analysis completed within two months

**Universe:** All women attending Obstetrics & Gynaecology OPD

**Population:** Women undergoing second-trimester termination with mifepristone + misoprostol

**Sample Size:** 60 women (30/group), based on previous study (mean induction-abortion time 23.4 hrs, SD 2.56, 95% CI, 80% power)

**Sampling:** First-come, first-serve basis

**Ethical Clearance:** Obtained prior to study

**Inclusion:** Women  $\geq 18$  years with intrauterine pregnancy (12–20 weeks), requesting MTP as per Act, and giving informed written consent.

**Exclusion:** Women with uterine scar, drug allergy, systemic illnesses, or on corticosteroid/ anticoagulant therapy.

**Methodology:** History, examination, and investigations were done; participants randomized into two groups; given mifepristone followed by misoprostol (24/48 hrs); repeat doses until expulsion; vitals monitored, CBC repeated, alternatives used if failure. 24-hr contact provided for follow-up

**Statistical Analysis:** Data were analyzed using SPSS; categorical variables expressed as frequencies and percentages; Fisher's exact test applied;  $p < 0.05$  considered significant; all analyses performed at a 95% confidence level.

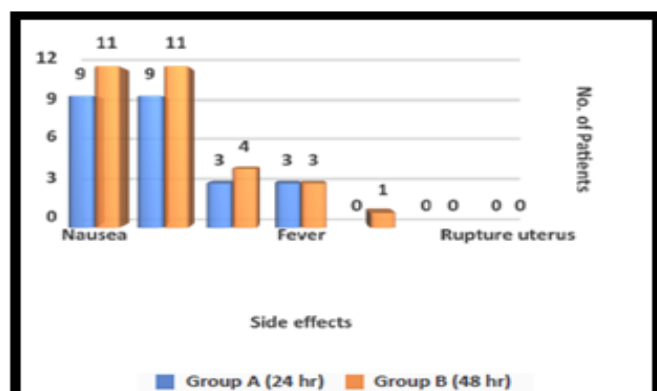
**Result and observations** In Group A (24-hour) and Group B (48-hour), mean ages were  $24.23 \pm 4.15$  vs.  $24.9 \pm 3.80$  years ( $p=0.51$ ). Nulliparity was 60% vs. 66.67% ( $p=0.59$ ). Complete outcomes occurred in 80% vs. 76.67% ( $p=0.75$ ). Mean repeat misoprostol doses were  $2.16 \pm 4.1$  vs.  $2.3 \pm 1.17$  ( $p=0.85$ ). Induction-abortion intervals among nulliparas were 5.46 vs. 7.3 h ( $p=0.34$ ) and among multiparas 4.35 vs. 4.15 h ( $p=0.004$ ).

Table 1: Distribution of patients according to Gestational age (in weeks)

Gestational age (in weeks)	Group A (24 hr)		Group B (48 hr)	
	No. of Patients	Percentage	No. of Patients	Percentage
Nulliparous	18	60.00	20	66.67
Multiparous	12	40.00	10	33.33
Total	30	100	30	100
Mean $\pm$ SD	$19.16 \pm 2.56$		$20.4 \pm 2.34$	
P-value	0.05			

Group A (24-hour) had a mean gestational age of  $19.16 \pm 2.56$  weeks, while Group B (48-hour) showed  $20.4 \pm 2.34$  weeks. Both groups comprised nulliparous and multiparous patients, with nulliparous slightly more common. The difference in gestational age was borderline statistically significant ( $p=0.05$ ).

Figure 1: Distribution of patients according to Side effects.



In Group A (24-hour), 30% of patients reported nausea and pain, compared to 36.67% in Group B (48-hour). Rigor and fever occurred in fewer patients, while weakness was noted in one patient (3.33%) of Group B.

No cases of giddiness or uterine rupture were observed. Overall, side-effect incidence showed no significant difference ( $p=0.9$ ).

Table 2: Distribution of patients according to Mifepristone to Abortion interval

Mifepristone to Abortion interval	Group A (24 hr)		Group B (48 hr)	
	No. of Patients	Percentage	No. of Patients	Percentage
<15 hrs	1	3.33	0	0.00
15-25 hrs	5	16.67	1	3.33
25-35 hrs	24	80.00	1	3.33
35-45 hrs	0	0.00	1	3.33
45-55 hrs	0	0.00	22	73.33
>55 hrs	0	0.00	5	16.67
Total	30	100.00	30	100.00
Mean $\pm$ SD	$25.03 \pm 9.99$		$51.45 \pm 8.09$	
P-Value	<0.0001			

In Group A (24-hour), 80% aborted within 25–35 hours, with a mean interval of  $25.03 \pm 9.99$  hours. In Group B (48-hour), 73.33% aborted within 45–55 hours, mean  $51.45 \pm 8.09$  hours. Few patients aborted outside these ranges. The difference was highly significant ( $p<0.0001$ ), showing delayed abortion with the 48-hour regimen.

Table 3: Distribution of patients according to Induction abortion interval (in hrs)

Induction abortion interval (in hrs)	Group A (24 hr)		Group B (48 hr)	
	No. of Patients	Percentage	No. of Patients	Percentage
0-3 hrs.	7	23.33	7	23.33
3-6 hrs.	12	40.00	10	33.33
6-9 hrs.	6	20.00	9	30.00
9-12 hrs.	5	16.67	4	13.33
Total	30	100.00	30	100.00
Mean $\pm$ SD	$4.95 \pm 3.18$		$5.2 \pm 3.06$	
P-Value	0.75			

In Group A (24-hour), 40% aborted within 3–6 hours and 23.33% within 0–3 hours, while in Group B (48-hour), 33.33% aborted within 3–6 hours and 23.33% within 0–3 hours. Mean induction-abortion intervals were  $4.95 \pm$

3.18 hours (Group A) and  $5.2 \pm 3.06$  hours (Group B).

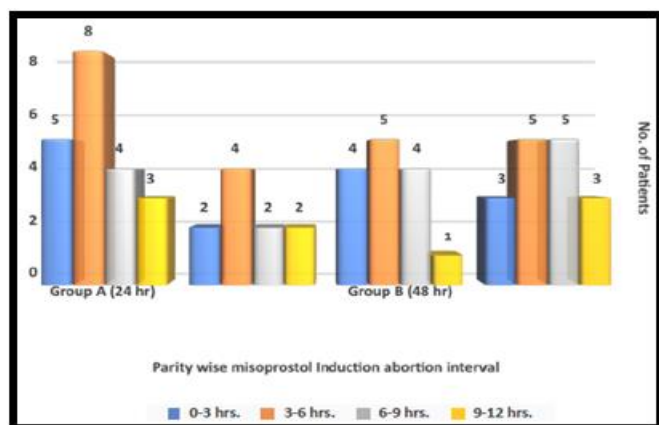
No significant difference was observed ( $p=0.75$ ).

Table 4: Distribution of patients according to Total dose of misoprostol

Parameter	Group A (24 hr)		Group B (48 hr)		P-value
	Mean	SD	Mean	SD	
Total dose of misoprostol	866.66	493.63	920	471.53	0.67

Group A (24-hour) required a mean misoprostol dose of  $866.66 \pm 493.63$   $\mu$ g, while Group B (48- hour) required  $920 \pm 471.53$   $\mu$ g. The difference was not statistically significant ( $p=0.67$ ), indicating that extending the interval between mifepristone and misoprostol did not affect total dose requirement.

Figure 2: Distribution of patients according to Gestational age wise misoprostol Induction abortion interval



In Group A (24-hour), the mean induction-abortion interval was  $4.77 \pm 3.13$  hours (12–20 weeks) and  $5.3 \pm 3.42$  hours (>20 weeks), with no significance ( $p=0.67$ ). In Group B (48-hour), it was  $7.3 \pm 2.83$  hours (12–20 weeks) and  $5.75 \pm 3.36$  hours (>20 weeks), also not significant ( $p=0.19$ ), showing gestational age had no effect.

## Discussion

Second-trimester medical termination commonly uses mifepristone followed by misoprostol, with a 48-hour interval traditionally recommended. Shorter intervals

may reduce abortion duration, hospital stay, and improve convenience, though concerns about efficacy and safety remain. This study compares shorter versus standard intervals at SMS Medical College, Jaipur, to evaluate outcomes.

The mean gestational age was  $19.16 \pm 2.56$  weeks in Group A and  $20.4 \pm 2.34$  weeks in Group B ( $p=0.05$ ). Jaya T et al<sup>7</sup> reported gravidity with 36.7% primigravida, 26.7% Gravida 2, and 36.6%  $\geq 3$  in Group 1, while Group 2 showed 30%, 25%, and 45%. Nilas L et al<sup>8</sup> noted parity increased with gestational age (median 0, range up to 2). Nausea and pain were most common (30% Group A, 36.67% Group B), with no significant difference ( $p=0.9$ ). Chaudhuri S et al<sup>9</sup> observed nausea in 15% and vomiting in 13.3%, with no diarrhea, fever, or rigor. Conversely, Tang O S et al<sup>6</sup> reported higher rates: nausea 48%, vomiting 26%, diarrhea 59%, and fever 64%. Most abortions occurred within 3–6 hours in both groups, with similar mean induction–abortion times ( $4.95 \pm 3.18$  vs.  $5.2 \pm 3.06$  hours;  $p=0.75$ ). Khairnar M M et al<sup>10</sup> reported shorter intervals with mifepristone–misoprostol ( $6.22 \pm 2$  hours) versus misoprostol alone ( $10.82 \pm 2$ ). Similarly, Nagaria T et al<sup>11</sup> observed reduced intervals ( $6.72 \pm 2.26$  vs.  $12.29 \pm 3.14$  hours). Most abortions occurred within 3–6 hours in both groups, with comparable mean induction–abortion times ( $4.95 \pm 3.18$  vs.  $5.2 \pm 3.06$  hours;  $p=0.75$ ). Patil N G et al<sup>12</sup> reported a mean induction–abortion interval of 9.3 hours in the combination group, while Arora C et al<sup>13</sup> observed moderate induction intervals, indicating variability based on dosage schedules and clinical practices.

The mean misoprostol dose was comparable in both groups ( $866.66 \pm 493.63$   $\mu$ g vs.  $920 \pm 471.53$   $\mu$ g;  $P=0.67$ ). Jan E. Dickinson<sup>14</sup> reported a higher cumulative requirement of 1600  $\mu$ g, likely due to misoprostol-only regimens, while Sharma N et al<sup>15</sup> observed reduced doses

with mifepristone pre-treatment ( $1247.06 \pm 191.07 \mu\text{g}$  vs.  $1405.71 \pm 280.69 \mu\text{g}$ ;  $P=0.003$ ). The mean gestational age was  $19.16 \pm 2.56$  weeks in Group A and  $20.4 \pm 2.34$  weeks in Group B ( $p=0.05$ ). Jaya T et al<sup>7</sup> reported Group 1 with 36.7% primigravida, 26.7% Gravida 2, and 36.6%  $\geq 3$ , while Group 2 had 30%, 25%, and 45% respectively. Nilas L et al<sup>8</sup> noted parity tended to increase with gestational age (median 0, range up to 2).

### Conclusion

The study found 24-hour and 48-hour mifepristone-to-misoprostol intervals comparable in demographics, parity, booking, locality, completeness, side effects, dosage, and induction-to-abortion time. The 24-hour interval achieved significantly earlier abortion completion without added risks. Parity influenced timing in the longer regimen, while gestational age showed minimal effect, favoring the shorter protocol.

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