Original Article

Comparison of Two Different Intervals of Misoprostol Administration in Second Trimester Abortions

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Abstract

Objective: Comparison of two different intervals of misoprostol administration after mifepristone in second trimester abortions.

Materials and methods: This 12-month prospective study was conducted at a tertiary care facility. Only pregnancies with congenital deformity or sterilisation failure were included in the study's recruitment of 100 women who visited the hospital for a second trimester abortion between 12 and 20 weeks; cases with scarred uteri were omitted. In a systematic random selection of 50 women in each group, the administration of 200 mg of mifepristone orally was followed by two distinct intervals of intravaginal misoprostol administration at 24- and 48-hour intervals. After 24 hours, group A women received intravaginal 400 mcg misoprostol three hourly, up to a maximum of five doses, while group B received the same doses after 48 hours. Induction abortion interval noted on various parameters and paired t test and chi square test applied.

Results: The mean IAI following misoprostol administration was 8.14 2±.03 hours in group A and 7.71 ±2.56 hours in group B. This difference was statistically insignificant. Average misoprostol doses for group A were 1.68±0.71 and for the group, B were 1.68±0.84; both doses were found to be statistically insignificant when used to induce abortion. All women aborted successfully in each group. There was no significant difference in side effects in both groups.

Conclusion: Based on the results it was observed that shorter interval between mifepristone and misoprostol i.e., 24 hours can be chosen to decrease the hospital stay as there was no significant difference was seen after intravaginal misoprostol in terms of induction abortion interval, number of doses and side effects.

Keywords: Mifepristone; Misoprostol; Second Trimester Abortion

Introduction

Second-trimester abortion accounts 10 to 15% of all induced abortions performed worldwide and is also the cause of two thirds of the most serious complications associated to abortion (1).

The ideal procedure for second trimester abortion is still up for debate, and finding it is crucial because second trimester abortions are disproportionately more likely to result in morbidity and mortality from abortion than other types of abortion.

In the past, intraamniotic infusion of hypertonic

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saline or urea or the administration of oxytocin were the two most prevalent procedures used to end pregnancies in the second trimester. However, both procedures increase morbidity and can cause hypernatremia and water intoxication, respectively (2). Dilatation and evacuation have been linked to uterine haemorrhage, uterine perforation, and cervical damage, necessitating the assistance of competent gynaecologists (3, 4).

The management of second-trimester abortions was altered when prostaglandin analogues were introduced in the late 1970s (5). The oral, sublingual, intramuscular, vaginal, and rectal modes of administration for prostaglandin analogues are all acceptable; however, the vaginal route is the most favoured due to its great efficacy and few side effects (6).

Misoprostol is the most popular prostaglandin analogue as it is inexpensive, convenient to store at room temperature, and has few systemic side effects, The ideal dose, dosing interval, and methods, however, have not been well analysed and differ globally (7).

Misoprostol is used in a variety of studies at doses ranging from 200 to 800 micrograms at intervals of 3 to 12 hours. While higher doses, like 600 or 800 mcg, have shown comparable success rates for abortion, they are also more likely to cause side effects like fever, diarrhoea, nausea, and vomiting (8).

When mifepristone, a progesterone agonist-antagonist, became introduced in the 1980s, second-trimester abortion success rates increased even more. Mifepristone softens the cervical tissue and makes the uterus more sensitive to prostaglandins (9, 10) Myometrial sensitization occurs within 24 hours of mifepristone administration, and the impact is greatest when misoprostol is administered 36 to 48 hours after mifepristone (11).

Mifepristone can lower the amount of misoprostol required and shorten the period between induction and abortion. if taken between 36 and 48 hours prior to misoprostol treatment. This period, however, has several disadvantages because the patient can decide against taking the medication or she might not follow up after taking it. To determine the appropriate window of time between the two drug administrations, research is still being done in this area.

The goal of the current study is to identify an appropriate regimen that is efficient and shortens the induction abortion interval for medical abortion in the second trimester of pregnancy while having few adverse effects.

In the current study, we examined the effectiveness of misoprostol administered 24 and 48 hours after mifepristone in causing second-trimester abortions.

Materials and methods

A prospective study was performed on 100 women who presented to the Department of Obstetrics and Gynaecology, Pt BD Sharma PGIMS, Rohtak for medical termination of pregnancy during the second trimester of pregnancy due to congenital anomalies or with failed sterilization surgery. Abortion is carried out according to the PNDT law. After obtaining their appropriate written consent for MTP and inclusion in the study.

By using a systematic randomization method, the women were divided into two groups of 50 each. Group, A included 50 pregnant women with an odd number of enrolments who had been induced with mifepristone 200 mg orally and misoprostol 400 mcg intravaginally every three hours, up to five doses in a 24-hour period. Group B included 50 pregnant women with an even number of enrolments who had been induced with mifepristone 200 mg orally and misoprostol 400 mcg intravaginally every three hours, up to five doses in a 48-hour period. Only singleton pregnancies with gestations between 12 and 20 weeks with either congenital malformations or failed sterilisation surgeries were included in this study.

Exclusion criteria

Women with scarred uterus (history of LSCS, myomectomy, hysterectomy)

Multiple gestation

Haemoglobin < 8 gm%

Inherited porphyria

Contraindication for use of Mifepristone or misoprostol like

Glaucoma

Epilepsy

Sickle cell anaemia

Heavy smoking

Long term corticosteroid therapy

Known hypersensitivity to misoprostol or mifepristone

Deranged coagulation

Heart disease

Grand multipara

Before being admitted to the hospital, the gestational period was confirmed by ultrasound, and

management details were explained to the patient and attendant along with informed written consent. This was done after obtaining a thorough history and examination and sending the necessary blood tests in accordance with hospital protocol. The candidate received treatment in accordance with their group assignment. In all the women following outcomes were measured:

Number of misoprostol doses required

Induction abortion interval (IAI) from the start of misoprostol

IAI from the start of Mifepristone

Expulsion of foetus within 24 hours of initiation of misoprostol

Intensity of side effects were noted

Evacuation required or not

The chi-square test and paired t-test were used to gather and analyse the data of various parameters of this randomised investigation. The success of induction was determined by the vaginal evacuation of the abortus within 24 hours.

Results

The age, parity distributions, booking statuses, and localities of the patients were comparable. (Table 1).

Table 1: Demographic characteristics of studied cases

	Group A		Group B		P Value
	n	%	n	%	
Age (years)					>0.05
<20	13	26	11	22	
21-25	30	60	31	62	
26-30	5	10	8	16	
31-35	2	4	0	0	
>35	0	0	0	0	
Parity					>0.05
P0	30	60	27	54	
P1	14	28	17	34	
P2	5	10	6	12	
P3	1	2	0	0	
>P3	0	0	0	0	
Booking status					>0.05
Booked	15	30	10	20	
unbooked	35	70	40	80	
Locality					>0.05
Rural	39	78	38	76	
urban	11	22	12	24	

The mean induction abortion interval (IAI) after mifepristone in group A is 32.14 ±2. 06 hours, while it is 55.7 4±.25 hours in group B. Table 2 illustrates this difference, which was judged to be significant (0.001).

Table 2: Bishop Score before and after administration of Mifepristone

Bishop score (Mean ±SD)	Group A	Group B	P value
Before Administration	1.32 ±058	1.44 ±0.72	>0.05
After Administration	1.72 ±0.72	1.78 ±081	>0.05
P value	<0.005	<0.005	

The mean IAI following misoprostol administration was 8.14 2±.03 hours in group A and 7.71 ±2.56 hours in group B. This difference was statistically insignificant. Average misoprostol doses for group A were 1.68±0.71 and for the group, B were 1.68±0.84; both doses were found to be statistically insignificant when used to induce abortion. No difference of parity was observed while pregnancy <16 weeks aborted earlier than >16 weeks pregnancy (Table 3, Table 4).

All the females in both groups aborted successfully in 24 hours (Figure 1).

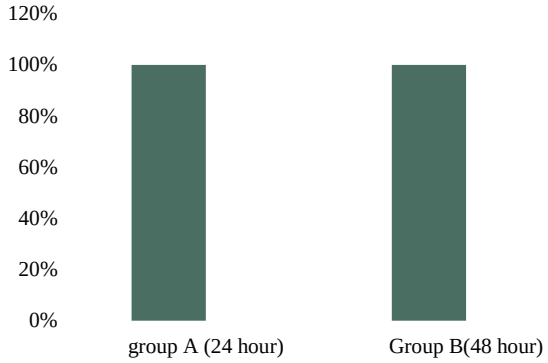

Figure 1: Success rate of induced abortion (expulsion of abortus within 24 hours)

There were no statistically significant changes in the side effects across the intervals at which misoprostol was administered (Table 5.) When the administration of Misoprostol was changed from 24 to 48 hours, the length of the women's hospital stays changed significantly (p-value 0.001) (Table 6).

Discussion

The availability of cutting-edge diagnostic tools for foetal malformations contributes to an increase in both first- and second-trimester abortions (12).

Table 3: Induction abortion interval after mifepristone and Misoprostol in Hours (Hr)

Induction abortion interval	Group A (n=50)	Percentage (%)	Group B (n=50)	Percentage (%)	P value
Induction abortion interval after mifepristone					<0.001
21-30 Hr	9	18	-		
31-40 Hr	41	82	1	2	
41-50 Hr	.-		1	2	
51-60 Hr	-		42	84	
61-70 Hr	-		6	12	
Mean± SD	32.2±2.04		55.64±4.02		
Induction abortion interval after Misoprostol					>0.05
0-5 Hr	4	8	7	14.2	
6-10 Hr	39	78	37	75.5	
11-15 Hr	7	14	5	10.2	
Mean± SD	8.14±2.03		7.71±2.56		
Parity wise Induction abortion interval after Misoprostol					
IAI after Misoprostol	Group A		Group B		
	Nulliparous	Parous	nulliparous	Parous	
1-5 Hr	2	2	4	3	
6-10 Hr	23	16	21	16	
11-15 Hr	5	2	2	3	
Mean± SD	8.35 ±2.07	7.90 ±1.97	7.55± 2.88	7.56± 2.67	
p-value	>0.05 Nonsignificant		>0.05 Nonsignificant		
Gestation wise distribution of IAI after Misoprostol					
IAI after Misoprostol	Group A (Gestational age)		Group B (Gestational age)		
	12-16 week	17-20 week	12-16 week	17-20 week	
0-5 Hr	3	1	4	5	
6-10Hr	8	31	3	34	
11-15 Hr	0	7	0	4	
Mean SD	7.09± 1.86	8.43 ±1.99	5.42 ±2.76	7.95 ±2.59	
P value	<0.05 Significant		<0.05 Significant		

Couples who undergo an induced abortion generally experience psychological anguish, therefore they want to spend as little time in the hospital as possible.

This study was conducted to determine whether shortening the typical 48-hour window following mifepristone to 24 hours resulted in any modifications to the abortion procedure.

The best method for inducing abortion for pregnancies greater than 12 weeks involves 200 mg of mifepristone taken orally, followed by a prostaglandin, 1-2 days later, according to WHO recommendations on abortion treatment (13). The main disadvantage of second-trimester abortions is that they require a lengthier hospital stay since the cervix needs 36 to 48 hours to ripen after taking mifepristone.

To test the effectiveness of combination of mifepristone and misoprostol given 24 and 48 hours apart, the current study was conducted on 100 pregnant women who came for second-trimester abortions. They were separated into two groups of 50 women each. Women in group A received 200 mg of mifepristone followed by misoprostol after 24 hours, while those in group B received misoprostol after 48 hours.

Table 4: Number of doses of Misoprostol

Number of doses of Misoprostol	Group A (n=50)	Percentage (%)	Group B (n=50)	Percentage (%)	P value
0	-	-	1	2	>0.05
1	23	46	25	50	
2	20	40	13	26	
3	7	14	11	22	
Mean± SD	1.68± 0.71		1.68±0.84		

Table 5: Side effects of Misoprostol

Side effects	Group A	Group B	P value
Nausea	1	-	>0.05
Vomiting	2	3	
Headache	-	-	
Pain abdomen	-	-	
Fever	2	-	
Diarrhoea	2	2	
Weakness	-	-	
Giddiness	-	-	
Shivering	1	-	
Rupture Uterus	-	-	

In our study, both groups received maximum 5 doses of 400 mcg of misoprostol spaced 3 hours apart, and they were similar in terms of age, parity booking status, and locality (rural vs. urban), which indicates a nonsignificant p value of >0.5.

Table 6: Hospital stay duration in two groups

Hospital stays (in hours)	Group A	Group B	P value
31-40	49	1	<0.001
41-50	1	-	
51-60	-	33	
61-70	-	16	
Mean± SD	36.16±2.05	59.66±4.08	

Bishop score was compared in both groups after mifepristone administration, and both groups showed improvement. However, the change seen after 24 hours and 48 hours was nearly similar, 1.72 ± 0.72 vs. 1.78 ± 081, and on comparison of this p-value received >0.05. Similarly, a single arm study conducted by Chikkagowdra S et al. for second-trimester abortion in previous LSCS females also showed improvement in Bishop score (14).

Mean IAI following Mifepristone administration was 32.14 ±2.06 in group A (21-40 hours), while it was 55.7± 4.25 in group B. (51-70 hours). 82% of women in group A had abortions within 10 hours (31-40 hours), while 90% of women in group B had abortions within the same time (i.e., 10 hours), indicating that this difference was significant with a p-value of 0.001. (51-60 hours). When this was analysed, it was discovered that, if the intervals after the administration of mifepristone were omitted, most of the study group (Both A and B groups) had an abortion within around 10 hours of taking misoprostol, in our study there was no significant difference was observed in nulliparous versus multiparous females in IAI most of them aborted in 6 to 10 hours.

A similar study conducted by Heikenheimo et al and they found IAI after misoprostol was found to be 8:20 hours (2:05-16:45) in primi and 7.30 hours in parous females in the 24-hour interval group, while in the 48-hour group it was 6.45 hours for nulliparous and 5.20 hours in parous females, and the results were non-synchronous to our study and .In our study, there was no significant difference found between nulliparous and multiparous individuals both type of parity females aborted in 6 to 10 hours. The mean time for abortion in this study IAI from mifepristone consumption was 28 hours and 25 minutes in the 1-day group and 52 hours and 43 minutes in the 2-day group, which is nearly identical to our study (15).

One hundred women who chose to end their pregnancies voluntarily between 13 and 16 weeks of gestation participated in a prospective randomised cohort research by Hou et al. Patients were randomised to receive 200 mg of oral mifepristone, 600 mcg of vaginal misoprostol one day (group 1) or two days later (group 2), and 400 mcg of oral misoprostol every six hours for a maximum of two doses. Their mean misoprostol to abortion interval (7.0 ± 3.0 Hr vs 6.8 4±.3 Hr, P = 0.744, NS) was comparable in both groups and parallel to our study's mean misoprostol to abortion interval (8.14 2. ±03 vs 7.71± 2.56 Hr, p-value >0.05), although the route and dosage of misoprostol differ from their study (16).

Women with gestational ages between 12 and 16 weeks had abortions earlier than those between 17 and 20 weeks in both groups when the red to those data. Significant difference was observed (p = 0.005). In a study conducted in a similar manner, Nilas et al. and Heikenheimo et al. discovered that the time to abortion was much shorter in pregnancies under 16 weeks (15, 17).

In our investigation, we found that the mean number of misoprostol dosages needed in groups A and B was 1.68 ±0.71 and 1.68 ±0.84, respectively, with a p-value >0.05 nonsignificant. Heikenheimo et al. similarly discovered that the mean number of misoprostol dosages needed in group 1(24 hr) and group 2 (48 hr) was comparable. A mean of 3 doses was administered to the one-day interval and two-day interval groups (15).

In our study, the success of induction of abortion was determined by the vaginal expulsion of the abortus within 24 hours of administration of the first dose of misoprostol, and all women in both groups had abortions within the allotted time without any abortion failure. In a retrospective analysis, Nilas et

al. examined the effects of a 1- and 2-day interval between the administration of 200 mg of mifepristone and 400 mcg of vaginal misoprostol every 3 hours they found 98% women aborted within 24 hours of start of misoprostol. Hou et al. also received results of successful 24 hours abortion rate (16, 17).

Like the study conducted by Hou et al. where vomiting, diarrhoea, and chills and rigours were the predominant adverse effects, no significant difference was discovered when the side effects of misoprostol were compared in both groups in the current investigation (16).

Since compliance was a big problem for the majority of the women in our research who came from rural backgrounds, every woman was admitted after the mifepristone administration. Hospital stays were longer in Group B compared to Group A, which was statistically significant (p value > 0.001; 36.16 ± 2.05 vs. 59.66 ± 4.08).

The current study demonstrates, based on these results, that a shorter interval (24 hours) is just as beneficial as a traditional 48-hour period.

Conclusion

Based on these results, the current study's induction abortion interval following mifepristone administration considerably varied between the two groups. However, the time after mifepristone administration was comparable across the two groups, as were the doses of misoprostol that were needed, and 100% success rate was attained in both groups. Although the IAI differed depending on whether the gestational period was 16 weeks or >16 weeks, parity had no effect on the induction abortion interval in either group. IAI was lower in both groups at≤ 16 weeks of gestation. The two groups' side effect profiles were equivalent. Hospital stay was very significantly shorter in 24 hours group than in 48-hour group.

Therefore, we advise choosing a shorter interval to improve the quality of life of women having second trimester abortions by shortening their hospital stay if the patient profile is properly chosen following a comprehensive history and examination.

Conflict of Interests

Authors declare no conflict of interests.

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