European Journal of Molecular & Clinical Medicine

ISSN2515-8260 Volume 09, Issue 06, 2022

A COMPARATIVE STUDY OF THE SAFETY AND EFFICACY OF SECOND-TRIMESTER MEDICAL ABORTION – MIFEPRISTONE PREINDUCTION FOLLOWED BY MISOPROSTOL VERSUS FOLEY CATHETER AND MISOPROSTOL

1st Author – Dr. V. Radha Lakshmi, Professor, Department of OBG, Shanthi Ram Medical College, Nandyal, A. P, India.
2nd Author – Dr. C. Sunitha, Associate Professor, Department of OBG, Siddhartha Medical College, Vijayawada, A. P, India.
3rd Author – Dr. C. Sudhakar, Assistant Professor, Department of OBG, Kurnool Medical College, Kurnool, A. P, India.
4th Author – Dr. N. Mounika, Senior Resident, Department of OBG, Narayana Medical College, Nellore, A. P, India.
Corresponding Author – Dr. N. Mounika, Senior Resident, Department of OBG, Narayana Medical College, Nellore, A. P, India.

Abstract

Introduction: The term "abortion" refers to the natural or artificial termination of a pregnancy prior to foetus viability. The second trimester, which is divided again into early and late periods, lasts from 13 to 28 weeks of gestation. Because of foetal abnormalities such as chromosomal aneuploidy, structural defects, and oligohydramnios discovered by antenatal screening programmes, many second trimester abortions are medically induced (resulting in intrauterine foetal demise). The combination of antiprogestin (mifepristone) and PGE1 analogue Misoprostol seems to be the most effective medical technique for ending a pregnancy in the second trimester.

Aims and Objectives: To evaluate the safety and effectiveness of two medical procedures for an abortion in the second trimester: preinduction with mifepristone followed by a misoprostol regimen (group 1), and preinduction with a foley cather followed by a misoprostol regimen (group 2). (Group 2). In order to make a comparison between the length of time that passed between the induction and the abortion in both groups, we will compare the length of time

that passed. In order to provide an accurate assessment of the disparity in abortion rates between the two populations:

Methods: This study is a prospective randomized trial involving sixty healthy women who chose to have their pregnancies terminated at a tertiary care center's Department of Obstetrics and Gynecology. The women's ultrasounds confirmed an intrauterine gestational age ranging from thirteen to twenty-six weeks of pregnancy.

Results and discussion: Group 1's average induction abortion time was 8.93 hours, whereas group 2's was 8.75. None was statistically significant. 42 women who used mifepristone and misoprostol had IAIs under 6 hours, according to Bijeta et al. The average IAI for Mifepristone + Misoprostol was 8.6 hours and 15.5 hours for Misoprostol. Hourly comparison of mifepristone-misoprostol induction abortion studies: Neha Agarwal et al. found a 6-hour IAI. Sin Eh Goh et al. found a 6.7-hour average IAI. Kulakarni Kranti's average IAI was 8.15 hours. Tang et al. found a 10.5-hour IAI. Ashok et al. found a 6.25-hour IAI. In Subha et altrial, the foley catheter termination group received misoprostol after 13.84 5.37 hours.

Conclusion: Both the mifepristone preinduction with misoprostol and the foley catheter preinduction with misoprostol procedures are risk-free and simple ways for terminating a pregnancy in the second trimester. There was no statistically significant difference between the two groups in terms of the mean induction-abortion interval, the mean doses of misoprostol required, the side-effect profile, or the rate of women who experienced a complete abortion. In the group that used mifepristone and misoprostol, the success rate was 100%, while in the group that used foley bulb induction, the success rate was 96.7%. In this particular trial, the group that received mifepristone and misoprostol had a significantly lower level of pain intensity and a shorter length of time spent in the hospital. This difference was statistically significant. Therefore, it is possible to utilise either of these approaches to stop a pregnancy in the second trimester, although this will rely on whether or not mifepristone is readily available.

Keywords: Comparative study, trimester, safety, efficacy, misoprolol,

Introduction

Abortion is defined as spontaneous or induced termination of pregnancy before foetal viability.[1] Second trimester is a period ranging from13 to 28 weeks of gestation age,again

divided into early (13-20 weeks) and late period (20-28 weeks).[2] Many second trimester abortions are medically induced because of foetal abnormalities detected by antenatal screening programme for chromosomal aneuploidy, structural defect and oligohydramnios (resulting in intrauterine foetal demise).[3] The most efficacious medical method for second trimester termination of pregnancy appears to be the combination of antiprogestin(mifepristone) followed by PGE1 analogue Misoprostol.[5]

Prostaglandins were used for induced second trimester abortions in the last 20 years. When Misoprostol alone is used, the mean induction - abortion interval (IAI) can be as long as 12-16 hrs. Induction abortion interval can be defined,as the time from the first dose of misoprostol to the expulsion of the products of conception.[3] Mifepristone RU-486 is a synthetic steroidal antiprogestogen acts as a competitive progesterone receptor agonist blocking progesterone receptors, resulting in the conversion of quiet pregnant uterus into an organ of spontaneous activity with its maximal effect at 36-48 hrs,after administration.[9] The peak concentration is reached in 1.3 hrs. The priming of uterus with mifepristone, results in, reduction of Induction Abortion Interval, the total dose of prostaglandins required,analgesia requirement, failure rate and the hospital stay.[3] Direct mechanical dilatation and endogenous release of prostaglandins are the mechanisms of cervical ripening by foley catheter induction.[6] This effect is enhanced, when the traction is applied.Apart from the direct mechanical dilatation,it stimulates the paracervical plexus of nerves resulting in release of endogenous prostaglandins and increases the excitability of uterus resulting in cervical ripening and uterine contractions.[6] To compare the safety and efficacy of medical methods of second trimester abortion– mifepristone preinduction followed by misoprostol regimen (group 1) versus foley cather preinduction followed by misoprostol (group 2). Objectives are to compare the induction- abortion interval in both groups. To compare the complete – abortion rates in both groups. This is a comparative study of two medical methods of second-trimester abortion, that is mifepristone and misoprostol regimen versus foley catheter induction followed by misoprostol. The advantages of mifepristone – misoprostol regimen over foley bulb induction are – it's a op based non- invasive method with less hospital stay, high efficacy, less mean dosage of misoprostol requirement,decreased pain severity and decreased rate of intrauterine infection.[3,9]

Methodology

Patients and Methods

This is a prospective randomised trial of 60 healthy women opting for termination of pregnancy,Department of Obstetrics and Gynaecology, tertiary care center with ultrasound confirmed intrauterine gestational age from 13 to 26 weeks of gestation

Study Design: Prospective Randomised Control Trial

Study Place: Department of Obstetrics and Gynaecology, tertiary care centre

Study Population: Women requesting abortion from 13- 26 weeks of gestation, in the Out-patient room at Department of Obstetrics and Gynaecology, tertiary care centre

Study Period: December 2019 to December 2021

Sample Size: 60 (random allocation to either group)

Group 1: Mifepristone preinduction followed by misoprostol group -30

Group 2: Foley catheter preinduction followed by misoprostol group-30

Inclusion Criteria:

1. 15-45 years of age
2. 13 to 26 weeks of gestation
3. HB->10 gm/dl
4. Gross IUGR
5. Gross oligohydramnios
6. Congenital anomalies of the foetus,not compatible with life
7. Upto gravid 4
8. Failed contraceptives
9. Singleton pregnancy
10. No regular uterine contractions

Exclusion Criteria:

1. Women with hypersensitivity to misoprostol or mifepristone
2. Scarred uterus
3. Grand multipara
4. Congenital uterine anomalies
5. Women with renal disease, heart disease, severe anemia, chronic renal failure, porphyrias, epilepsy

6. Ruptured membranes
7. Multiple pregnancy

Methodology:

Group 1: Mifepristone 200 mg is given orally, then after 24 hours, the misoprostol (the dose is given according to gestationl age) is inserted into the posterior fornix of the vagina,for every four hours up to 4 doses.

< 24 weeks of gestation – 400 µg of misoprostol

>24 weeks of gestation – 200 µg of misoprostol

Group 2: Foley catheter induction – 18 size catheter is introduced into the cervix beyond the internal os, under direct visualization with speculum examination. Once it passed the internal os, the balloon is then inflated with 60 CC normal saline,then the catheter is firmly attached to the inner side of thigh for continuous traction. After 24 hours or foley bulb expulsion, the misoprostol is inserted into the posterior fornix depending on the gestational age up to 4 doses. Oxytocin infusion was started at 3cm dilatation in both groups. Intravenous antibiotic coverage is given to both groups. Pain management was done with analgesics such as ibuprofen. Additional measures are followed in patients with incomplete abortion like instrumental evacuation and oxytocin infusion. Check ultrasound of pelvis was done the next day, to assess for the completeness of the abortion .

Outcome:

Complete: When the products of conception are expelled (in 48 hours)

Incomplete: When either placenta or foetus is retained

Failed: When neither placenta nor foetus was expelled

Parameters Studied:

1. Induction abortion interval.
2. Complete abortion rate.
3. Total number of misoprostol doses required.
4. Need for surgical intervention.
5. Side – effect observed- pain, fever, vomiting, nausea, diarrhoea, infection.
6. Pain score-visual analog scale.

ISSN2515-8260 Volume 09, Issue 06, 2022

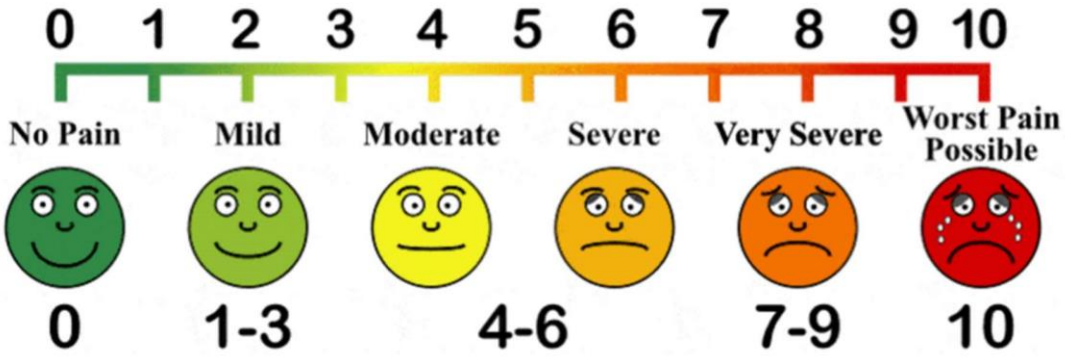

Figure1 – visual analog scale

Observation and Results:

This study is a comparative study to assess the safety and efficacy of medical methods of mid- trimester abortion.

Group 1 - Mifepristone followed by misoprostol

Group 2 - Foley bulb induction followed by misoprostol

Table 1: Distribution of cases by Age

Age category (in years)	**Mifepristone + Misoprostol group**		**Foley bulb induction + Misoprostol group**	
	Number	**Percentage**	**Number**	**Percentage**
<20	4	13.3	9	30
21 – 25	19	63.3	17	56.6
26 – 30	7	23.3	2	6.7
>30	0	0	2	6.7
Total	30	100	30	100
Chi-square = 6.812, p = 0.078				

In this study, majority, i.e. 63.6% and 56.6% cases in group 1 and group 2 were from the age group of 21 to 25 years. The distribution of cases among the both groups was not statistically significant.

Table 2: Distribution of cases by Mean age

	Mifepristone + Misoprostol group		**Foley bulb induction + Misoprostol group**	
Age	**Mean**	**Standard deviation**	**Mean**	**Standard deviation**
	23.57	2.763	23.17	4.602
Independent Sample t test, F = 1.496, p = 0.228				

In this study, the average age of the cases was 23.57 years and 23.17 years in group 1 and group 2 respectively.

Table 3: Distribution of cases by Gestational age

Gestational age in weeks	**Mifepristone + Misoprostol group**		**Foley bulb induction + Misoprostol group**	
	Number	**Percentage**	**Number**	**Percentage**
12 – 16	6	20	5	16.5
17 – 20	6	20	6	20
21– 24	16	53.6	14	46.7
>24	2	6.7	5	16.7
Total	**30**	**100**	**30**	**100**
Chi-square = 1.51, p = 0.680				

In this study, 21 – 24 weeks of gestation was noted in majority i.e. 53.6% in group 1 and 46.7% in group 2 ,followed by 17 to 20 weeks of gestation in 20% in group 1 and 20% in group 2.

Table 4: Distribution of cases by mean Gestational age

	Mifepristone + Misoprostol group		**Foley bulb induction + Misoprostol group**	
	Mean	**Standard deviation**	**Mean**	**Standard deviation**
Gestational age	20.60	4.005	20.90	3.809
Independent Sample t test, F = 0.905, p = 0.345				

In this study, the average gestational age of cases was 20.60 in group 1 and 20.90 in group 2 weeks.

Table 5: Distribution of cases by Gravida

Gravida	**Mifepristone + Misoprostol group**		**Foley bulb induction + Misoprostol group**	
	Number	**Percentage**	**Number**	**Percentage**
1	10	33.3	10	33.3
2	13	43.3	13	43.3
3	4	13.3	5	16.7
4	3	10	2	6.7
Total	30	100	30	100
Chi-square = 0.311, p = 0.958				

In this study, majority i.e. 43.3% cases in group 1 and group 2 each were of gravida 2, followed by 33.3% cases in group 1 and group 2 each of gravida 1.

Table 6: Distribution of cases by Indication for termination

Indication for termination	Mifepristone + Misoprostol group		Foley bulb induction + Misoprostol group	
	Number	Percentage	Number	Percentage
Anomalous baby	28	93.3	25	83.3
Severe Oligohydramnios	2	6.7	5	16.7
Total	30	100%	30	100%
Chi-square = 1.456, p = 0.243				

In the present study, the indication for termination was anomalous baby in 93.3% and 83.3% of the cases from group 1 and group 2 respectively, severe Oligohydramnios in 6.7% and 16.7% of cases from group 1 and group 2 respectively.

Table 7: Distribution of cases by Induction abortion interval

	Mifepristone + Misoprostol group		Foley bulb induction + Misoprostol group	
Induction abortion interval	Mean	Standard deviation	Mean	Standard deviation
	8.93	3.81	8.75	2.95
Independent Sample t test, F = 1.25, p = 0.345				

In this study, the average IAI was 8.93 hours in the group of Mifepristone + Misoprostol and 8.75 hours in the group of Foley bulb induction + Misoprostol group and there was no statistically significant difference.

Table 8: Distribution of cases by Induction abortion interval and Gravida

Gravida	Mifepristone + Misoprostol group		Foley bulb induction + Misoprostol group	
	Mean	Standard deviation	Mean	Standard deviation
1	11.70	3.02	10.90	2.96
2	8.85	3.15	8.54	1.61
3	6.50	2.88	5.90	2.88
4	3.33	0.57	6.50	3.53
One way ANOVA test	F = 64.803, p = 0.001		F = 32.51, p = 0.005	

In this study the average Induction abortion interval among gravida 1 was high i.e. 11.7 hours and 10.90 hours in Mifepristone + Misoprostol group and Foley bulb induction + Misoprostol group respectively. The average Induction abortion interval in gravida 4 was low i.e. 3.33 hours and 6.5 hours in Mifepristone + Misoprostol group and Foley bulb induction + Misoprostol group respectively and the difference was statistically significant in both groups.

Table 9: Distribution of cases by Induction abortion interval and gestational age

Gestational age	Mifepristone + Misoprostol group		Foley bulb induction + Misoprostol group	
	Mean	Standard deviation	Mean	Standard deviation
12 – 16 weeks	11.83	5.38	11.80	2.16
17 – 20 weeks	7.17	2.31	8.42	2.49
21 – 24 weeks	8.75	3.37	7.43	2.10
>24 weeks	7.00	1.41	9.80	4.14
One way ANOVA test	F = 25.733, p = 0.148		F = 25.713, p = 0.022	

In this study, the average Induction abortion interval in cases with gestational age 12 – 16 weeks was high i.e. 11.83 hours and 11.80 hours in Mifepristone + Misoprostol group and Foley bulb induction + Misoprostol group respectively. The average Induction abortion interval in cases with gestational age >24 weeks was low i.e. 7.0 hours and 9.8 hours in Mifepristone + Misoprostol group and Foley bulb induction + Misoprostol group respectively.

Table 10: Distribution of cases by mean doses of Misoprostol required

	Mifepristone + Misoprostol group		**Foley bulb induction + Misoprostol group**	
Doses of Misoprostol required	**Mean**	**Standard deviation**	**Mean**	**Standard deviation**
	2.40	0.894	2.53	0.860
Independent Sample t test, F = 0.055, p = 0.815				

In this study, the average doses of Misoprostol required in the Mifepristone + Misoprostol group and Foley bulb induction + Misoprostol group were 2.4 and 2.5 respectively and there was no statistically significant difference.

Table11: Distribution of cases by requirement of misoprostol doses

Doses of Misoprostol required	**Mifepristone + Misoprostol group**		**Foley bulb induction + Misoprostol group**	
	Number	**Percentage**	**Number**	**Percentage**
1	5	16.7	3	10
2	11	36.7	12	40
3	11	36.7	11	36.7
4	3	10	4	12.3
Total	30	100	30	100
Chi-square = 0.686, p = 0.876				

In this study, the doses of Misoprostol required was 2 in 36.7% and 40% of the cases required in the Mifepristone + Misoprostol group and Foley bulb induction + Misoprostol group respectively. The number of doses of Misoprostol required was 3 in 36.7% and 36.7% of the cases of both groups. The number of doses of Misoprostol required was 4 in 10% of cases in group 1 and 12.3% of the cases in group 2.

Table 12: Distribution of cases by Outcome

Outcome	Mifepristone + Misoprostol group		Foley bulb induction + Misoprostol group	
	Number	Percentage	Number	Percentage
Complete	27	90	25	83.3
Incomplete	3	10	4	13.3
Failed	0	0	1	3.3
Total	30	100	30	100
Chi-square = 1.220, p = 0.543				

In this study, the outcome of the abortion was complete in 90% and 83.3%, Incomplete in 10% and 13.3% and failed in 0% and 3.3% of the cases belonging to the Mifepristone + Misoprostol group and Foley bulb induction + Misoprostol group respectively.

Table 13: Distribution of cases by need for surgical intervention

Surgical intervention	Mifepristone + Misoprostol group		Foley bulb induction + Misoprostol group	
	Number	Percentage	Number	Percentage
Yes	4	13.3	5	16.7
No	26	86.7	25	83.3
Total	30	100	30	100
Chi-square = 0.718, p = 1.00				

In this study, surgical intervention was needed in 13.3% and 16.7% of the cases belonging to Mifepristone + Misoprostol group and Foley bulb induction + Misoprostol group respectively.

Table 14: Distribution of cases by side effects

Side effects	Mifepristone + Misoprostol group		Foley bulb induction + Misoprostol group	
	Number	Percentage	Number	Percentage
Pain	30	100	30	100
Fever	5	16.7	4	13.3
Vomiting	8	100	8	100
Nausea	13	43.3	6	20
Diarrhoea	0	0	0	0

In this study, Pain and Vomiting were the side effects seen in 100% and 100% of the cases belonging to Mifepristone + Misoprostol group and Foley bulb induction + Misoprostol group respectively. Fever was present in 16.7% and 13.3% and nausea was present in 43.3% and 20% of the cases belonging to Mifepristone + Misoprostol group and Foley bulb induction + Misoprostol group respectively.

Table 15: Distribution of cases by mean hospital stay in days

	Mifepristone + Misoprostol group		Foley bulb induction + Misoprostol group	
Mean hospital stay (days)	Mean	Standard deviation	Mean	Standard deviation
	1.27	0.45	2.00	0.000
Independent Sample t test, F = 104.16, p = 0.000				

In this study, the mean hospital stay was 1.27 days and 2.0 days for the cases belonging to Mifepristone + Misoprostol group and Foley bulb induction + Misoprostol group respectively and there was no statistically significant difference.

Table 16: Distribution of cases by Pain intensity

Pain intensity	Mifepristone + Misoprostol group		Foley bulb induction + Misoprostol group	
	Number	**Percentage**	**Number**	**Percentage**
Mild	9	30	2	6.7
Moderate	19	63.3	21	70
Severe	2	6.7	7	23.3
Total	30	100	30	100
Chi-square = 7.332, p = 0.026				

In this study, the pain intensity was moderate in 63.3% and 70%, was mild in 30% and 6.7% of the cases and was severe in 6.3% and 23.3% of the cases of the cases belonging to Mifepristone + Misoprostol group and Foley bulb induction + Misoprostol group respectively and a statistically significant difference noted with the degree of pain intensity in both groups.

Discussion

Second trimester pregnancy has a global incidence of 10 -15 %.[4] There is a progressive rise in incidence because of increased awareness of antenatal diagnostic procedures. The best method for mid- trimester abortion appears to be mifepristone and misoprostol regimen with 97-99% success rate in first 24 hours. The combination of mifepristone with misoprostol, renders the procedure, a op based non- invasive method with less hospital stay, high efficacy, less mean dose of misoprostol requirement, decreased pain severity and decreased rate of intrauterine infection. This study was done in Government general hospital Kurnool,tertiary care centre. It was a prospective comparative study of 60 patients with 13-28 weeks of gestation, opting for second trimester abortion. The patients were selected based on the inclusion criteria of the study and divided into two groups by random allocation method. The patients were comparable with age, parity and gestational age in both the groups.

In the first group- 200 mg of mifepristone was given orally and misoprostol (200-400 µg) was given after 24 hours and the doses were repeated 4th hourly in the vaginal route. In the second group -after foley bulb induction, misoprostol doses were repeated 4th hourly after foley bulb

expulsion or after 24 hours of foley catheter induction. The misoprostol doses were given depending on the gestational age and the side- effects observed were noted in all the patients. Vitals of all the patients were monitored.

Visual analog scale method was used to measure the pain intensity in both the groups. Oxytocin infusion was started at 3cm dilatation after cervical reassessment. The induction-abortion interval was calculated from the first dose of administration of misoprostol to the expulsion of products of conception. Later, the two groups were reassessed for completeness of the abortion either clinically or with ultrasonography. The average age of patients opting for termination in GROUP 1 is 23.57 years in GROUP 2 is 23.17 years.63.6 % women in group1 and 56.6% in group 2 were from the age group of 21 to 25 years. In the study conducted by Fonseca MN et al, the mean age is 27 years in mifepristone and foley bulb induction groups.[7]

Comparison of Mean age in years :

In this study, the mean gestational age in group 1 was 20.60 weeks and 20.90 years in group B. 53.6 % in group 1 and 46.7 % in group 2 were in 21-24 weeks of gestation. In the study of Fonseca MN et al, most of the pregnancies were terminated between 16- 20 weeks in both groups.[7] In the study conducted by Kulakarni Kranti, the average gestational age was between 16- 17 weeks.[13]

Comparison of mean gestational age in weeks in mifepristone and misoprostol regimen studies: The multiparous women contributed more when compared to primi gravida - 66.7 % in both groups. In a study conducted by Fonseca MN et al, majority of the women contributed are multigravida (88.8%).[7]

comparison of contribution of multiparous women in percentage :

In this study, the most common indication for termination is anomalous foetus, not compatible with life- 93.3 % in group 1 and 83.3% in group 2. It was similar to the the studies conducted by Fonseca MN et al, where the indication for termination in their study was congenital malformation of foetus (47.22%) followed by contraceptive failure in multiparous women (38.88%).[7]

In this study, the average induction abortion interval was 8.93 hours in group 1 and 8.75 hours in group 2. There was no statistically significant difference noted. The IAI was smaller than 6 hours in 42 women who took mifepristone followed by misoprostol in a study conducted by

Bijeta et al.[9] In the study of JAN E DICKINSON et al, the average IAI was 8.6hrs for Mifepristone + Misoprostol group and 15.5hrs for Misoprostol group.[16]

Comparison of Induction abortion interval in hours in various studies of mifepristone – misoprostol regimen:

In the study conducted by Neha Agarwal et al, the average IAI was 6 hours.[11] In the study conducted by Sin Eh Goh et al, the average IAI was 6.7 hours.[15] In the study conducted by Kulakarni Kranti, the average IAI was 8.15 hours.[13] In the study conducted by Tang et al, the average IAI was 10.5 hours.[22]

In the study conducted by Ashok et al,the average IAI was 6.25 hours.[23] In the study conducted by Subha et al ,the average induction abortion interval was 13.84 ±5.37 hours in the foley catheter termination followed by misoprostol group.[10]

Comparison of induction abortion interval in studies of foley bulb induction and misoprostol:

In this study,the mean IAI in primi gravida was high- 11.7 hours in group 1 and 10.90 hours in group 2 .The mean IAI was low in gravida 4 – 3.33 hours in group 1 and 6.5 hours in group 2, with a statistically significant difference. In a study conducted by Sin Eh Goh et al., nulliparous women took significantly longer time to abort (6.0 h in multiparous women compared to 7.6 h in nulliparous women; $p<.0001$).[15] In a study conducted by Olga Gomez et al., the effect of parity on the induction-to-abortion interval was more modest, with a 20% increase in induction-toabortion interval in nulliparous (10.1 h, SD=9.1), as compared with multiparous women live birth (8.1 h, SD=6.7).[17]

Comparison of induction abortion interval in nulliparous and multiparous women - mifepristone and misoprostol regimen studies:

In the study conducted by Chaudhuri et al.,the nulliparous women had higher induction abortion interval.[18] In this study ,the mean IAI was low with gestational age of more than 24 weeks gestational age i.e.,7 hours in mifepristone group and 9.8 hours in foley bulb induction group. The average IAI was high with 12- 16 weeks of gestation i.e., 11.80 hours in both groups.

In a study conducted by Olga Gomez et al., the mean induction-to-abortion interval was increased by about 50% in patients undergoing termination of pregnancy between 20.0 and 22.6 weeks (12.9 h, SD=8.9), as compared with those at 16.0-19.6 weeks (7.8 h, SD=5.9) and 12.0-15.6 weeks (8.2 h, SD=8.3) ($p<.001$).[17]

Comparison of Induction abortion interval in women with >20 weeks of gestation in mifepristone and misoprostol studies.

In the study conducted by Chaudhuri et al., the women with >16 weeks of gestation had longer induction abortion interval.[18] In this study the average doses of misoprostol required in both groups was 2.4 in group 1 and 2.5 in group 2 and the difference was not found to be statistically different. In the present study, the number of doses misoprostol required was 2 in 36.7 % and 40% of the cases in group 1 and group 2.

In the study conducted by Fonseca MN et al., the average misoprostol doses in the mifepristone group was approximately 300 µg and 800 µg in foley bulb induction group with statistically significant difference. In this study, the misoprostol doses were started after 48 hours of mifepristone administration.[7] In a study conducted by Chaudhuri et al., the mean induction intervals in 24 hours versus 48 hours' interval between mifepristone and misoprostol were., 8.6±4.1hours versus 8.7±3.9hours; P=0.37 and the difference was not statistically significant.[18]

Table 17- comparison of doses of misoprostol and dosage interval in different studies of mifepristone and misoprostol regimen

STUDY	DOSE of misoprostol(µg)	DOSAGEINTERVAL in hours	IAI IN HOURS
Jain et al[19]	200	12	12
Bebbington et al[20]	600-400	4	19.6
Bluementhal et al[21]	200	3	9.5
Tang et al[22]	400	3	10.5
Present study	400(<24 weeks) 200(>24 weeks)	4	8.9

A dose of 200 µg misoprostol was used by Jain et al with a dosage interval of 12 hours and the IAI was 12 hours.[19] Bebbington et al used 600-400 µg of misoprostol,with a dosage interval of 4 hours and the IAI was 19.6 hours.[20] Bluementhal et al ,used 200 µg of misoprostol with a dosage interval of 3 hours and the induction abortion interval was 9.5 hours.[21]

Tang et al., used 400 µg of misoprostol with a dosage interval of 3 hours and the IAI was 10.5 hours.[22] In this study ,complete abortion rate was 90% in group 1 and 83.3 % in group 2 ,no

statistically significant difference noted. In a study conducted by Tang et al.,the complete abortion rate was 82.8 % in mifepristone and misoprostol group.[22] In a study conducted by Ashok et al .,91.9 % was the complete abortion rate.[23] The success rate of this study was 100 % in mifepristone and misoprostol group and 96.4 % in group 2.

TABLE 18 - The success rates in various studies of mifepristone and misoprostol regimen

STUDY	Induction abortion interval in hours	Complete abortion rate (%)	Success rate (%)
Present study	8.93	90	100
Fonseca MN et al[7]	54.77(from mifepristone administration)	83-89	88.88
Deepa Shah et al[8]		70 %	
Neha Agarwal et al[11]	6 hours	100%	100%
Sin Eh Goh[15]	6.7	95	99.8
Kulakarni Kranti [13]	8 hours 15 minutes		100
Tang et al[22]	10.5	85	95
Ashok et al [23]	6.25	91.9	97.1

Comparison of complete abortion rates in different mifepristone and misoprostol studies.

Deepa Shah et al .,study had a complete abortion rate of 70 %.[8] Neha Agarwal et al., study had a IAI of 6 hours ,with a complete abortion rate of 100% and 100 % success rate.[11] Sin Eh Goh et al .,study had a IAI of 6.7 hours , with a complete abortion rate of 95% and a complete abortion rate of 99.8%.[15]

Kulakarni Kranti study had a IAI of 8 hours 15 minutes with a 100% success rate.[13] Tang et al .,study had complete abortion rate of 85 % and 95% success rate.[22] Ashok et al., study had a IAI of 6.25 hours ,with a complete abortion rate of 91.9 % and success rate of 97.1 %.[23].

TABLE 19 - The success rates of various studies with foley catheter induction followed by misoprostol were

Study	Induction Abortion Interval in Hours	Complete Abortion rate (%)	Success rate (%)
Present	8.75	83.3	96.4
Fonseca MN et al[7]	13.84	83-89	83.3
Subha et al[10]	13.84	90	90
Rezk et al[24]	7.5±1.25		100

Fonseca MN et al had a complete abortion rate of 83-89 % and 83.3 % success rate in the foley catheter insertion group.[7] Subha et al ., study had a IAI of 13.84 hours with a complete abortion rate of 90 % and success rate of 90%.[10] Rezk et al.,study had a IAI of 7.5±1.25 with a success rate of 100 %.[24]

Table 20 - need for surgical intervention for various studies of mifepristone -misoprostol group:

STUDY	Need for surgical intervention (%)
Present study	13.3
Fonseca MN et al[7]	13.8
Neha Agarwal et al[11]	0
Sin Eh Goh et al[15]	5
Tang et al[22]	5
Ashok et al[23]	8.1
Ngoc et al[14]	7.3
Kaur et al [12]	8.33

Table 21- Need for surgical intervention in various studies of foley bulb induction and misoprostol:

STUDY	Need for surgical intervention(%)
Present	16.7
Fonseca MN et al[7]	13.8
Subha et al[10]	10

Table 22- comparison of side- effect profile of studies of mifepristone and misoprostol regimen were

Side-effects	Present study(%)	Fonseca MN et al [7](%)
Pain	100	100
Fever	16.7	0
Vomiting	100	16.66
Nausea	43.3	22.22
Diarrhoea	0	0

Fonseca MN et al study, had a side-effect profile of pain in 100 % of cases,fever in 5.55 % of cases,vomitings in 38.88 % of cases,nausea in 55.55 % of cases and diarrhoea in 11.11 % of cases.[7]

Table 23-comparison of the side-effects observed in foley bulb induction and misoprostol group were

Side-effects	Present study (%)	Fonseca MN et al [7] (%)
Pain	100	100
Fever	13.3	5.55
Vomiting	100	38.88

Nausea	20	55.55
Diarrhoea	0	11.11

Table 24 - The degree of pain intensity in studies of mifepristone and misoprostol group

Pain intensity	Mild (%)	Moderate (%)	Severe (%)	Very severe (%)
Present study	30	63.3	6.7	0
Fonseca MN et Al[7]	5.55	72.22	22.22	0

The pain intensity was mild in 30 % of cases , moderate in 63.3 % of cases and severe in 6.7% of cases., in this study. The pain intensity was mild in 5.5 % of cases, moderate in 72.2% of cases and severe in 22.2% of cases.

Table 25 -The degree of pain intensity in studies of foley bulb induction and misoprostol group

Pain intensity	Mild (%)	Moderate (%)	Severe (%)	Very severe (%)
Present	6.7	70.0	23.3	0
Fonseca MN et al [7]	0	16.66	55.55	27.77

Conclusion

The two methods, mifepristone preinduction with misoprostol and foley catheter preinduction with misoprostol are safe and easily accessible methods for mid-trimester pregnancy termination. The mean induction- abortion interval, the mean doses of misoprostol required, the side-effect profile, complete abortion rate was same in both the groups with no statisitically significant difference. The success rate was 100 % in mifepristone and misoprostol group and 96.7 % in foley bulb induction group.The degree of pain- intensity and duration of hospital stay was less in mifepristone and misoprostol group in this study and the

difference was statistically significant. Hence both the methods can be used for termination of pregnancy in second trimester, depending on the availability of the mifepristone.

References:

1. Saini A, Bedi PK, Bhagat N. Comparative effectiveness of simultaneous administration of mifepristone and misoprostol versus interval regimen of mifepristone followed by misoprostol 12 hours apart in second trimester abortion.Int J Reprod Contracept Obstet Gynecol 2018;7:2449-54.
2. Bharti A ,Kumari S.Efficacy of Vaginal Misoprostol in Second Trimester Abortion.Int J Sci Stud 2016;3(12):133-138.
3. Lalitkumar S, Bygdeman M, Gemzell-Danielsson K. Midtrimester induced abortion: a review. Hum Reprod Update. 2007; 13(1): 37–52.
4. American College of Obstetricians and Gynaecologists. Second trimester abortion.Practice Bulletin No.135. Washington,DC: ACOG; 2013.121:13941406.
5. Royal College Of Obstetricians and Gynaecologists.The Care of Women requesting induced abortion.Evidence based Clinical Guideline Number 7.LondonNW14RG:RCOG;2011-14.Available at https://www.rcog.org.uk/globalassets/documents/guidelines/abortion-guideline-summary.pdf
6. Ezimokhai M, Nwabinelli JN. The use of Foley's catheter in ripening of unfavourable cervix prior to induction of labour. Br J Obstet Gynaecol.1980; 87:281-6.
7. Fonseca MN, Sah V. Comparative study between sequential use of Foley catheter with vaginal misoprostol versus sequential use of oral mifepristone with vaginal misoprostol for second trimester medical abortion. Int J Reprod Contracept Obstet Gynecol [Internet]. 2018;7(11):4545. Available from: http://dx.doi.org/10.18203/2320-1770.ijrcog20184505.
8. Shah D, Rijal P, Thakur A, Rai R. Mifepristone and misoprostol vs misoprostol alone in second trimester termination of pregnancy. JNMA J Nepal Med Assoc [Internet].2018;56(213):856–60.Availablefrom: http://dx.doi.org/10.31729/jnma.3690
9. Bijeta, Neelam Nalini. Medical method of second trimester abortion: mifepristone plus misoprostol vs misoprostol alone. International Journal of Contemporary Medical Research 2017;4(12):4-6.
10. Subha, Sarojini, Ipsita, Vivekanand,Ranjan. Comparison of intravaginal misoprostol alone and in combination with intracervical Foley's catheter for termination of second trimester pregnancy - 3 years study at a tertiary care hospital. Perspectives in medical research 2016;4:1:3-8.

11. Singh, N. & Gandhi, G. & Batra, S. & Sharma, R. Role of mifepristone and misoprostol in medical termination of pregnancy between 13 and 20 weeks of gestation. BJOG An International Journal of Obstetrics & Gynaecology. 2014;121. 5-6. 10.1111/1471-0528.12783.
12. Kaur M, Kaur H, Sharma S, Mangla M, Mifepristone followed by Misoprostol for Mid trimester Abortion – A Prospective Study. Indian J Obstet Gynecol Res 2015;2(4):227-231.
13. Kulkarni KK. Pre-induction with Mifepristone for Second Trimester Termination of Pregnancy. J Obstet Gynaecol India. 2014;64(2):102-104.
14. Ngoc NTN, Shochet T, Raghavan S, Blum J, Nga NTB, Minh NTH, Phan VQ, Winikoff B. Mifepristone and misoprostol compared with misoprostol alone for second-trimester abortion: a randomized controlled trial. Obstet Gynecol. 2011 Sep;118(3):601-608.
15. Goh SE, Thong KJ. Induction of second trimester abortion (12-20 weeks) with mifepristone and misoprostol: a review of 386 consecutive cases. Contraception. 2006 May;73(5):516-9.
16. Dickinson JE, Jennings BG, Doherty DA. Mifepristone and oral, vaginal, or sublingual misoprostol for second-trimester abortion: a randomized controlled trial. Obstet Gynecol. 2014 Jun;123(6):1162-1168.
17. Gómez O, Borrás A, Rabanal A, Palacio M, Carceller A, Coll O, Gratacós E. Mifepristone-misoprostol midtrimester abortion: impact of gestational age on the induction-to-abortion interval. Contraception. 2010 Feb;81(2).
18. Chaudhuri, Picklu & Mandal, Apurba & Das, Chandana & Mazumdar, Arindam. Dosing interval of 24 hours versus 48 hours between mifepristone and misoprostol administration for mid-trimester termination of pregnancy. International journal of gynaecology and obstetrics: the official organ of the International Federation of Gynaecology and Obstetrics. 2013;124.
19. Jain A Mishell DR. A comparison of intravaginal misoprostol with prostaglandin E2 for termination of second trimester pregnancy. N Engl J Med 1994; 331:290-293.
20. Bebbington MW, Kent N, Lim K, Gagnon A, Delisle MF, Tessier F, and Wilson RD. A randomized controlled trial comparing two protocols for the use of misoprostol in midtrimester pregnancy termination. Am J Obste t Gynecol 2002; 187: 853- 85.
21. Bluementhal PD. Intravaginal misoprostol vs. prostaglandin E2 for second trimester abortion.Obstet Gynecol 1990; 75:365-368.
22. Tang OS, Ting Lau WN, Wai Chan CC, Ho PC. A prospective randomized comparison of sublingual and vaginal misoprostol in second trimester termination of pregnancy.Br J Obstet Gynecol 2004; 111: 1001-1005.

23. Ashok PW, Templeton A, Wagaarachchi PT and Flett GM . Midtrimester medical termination of pregnancy: a review of 1002 consecutive cases. Contraception .2004;69,51–58.
24. Rezk MA, Sanad Z, Dawood R, Emarh M, Masood A. Comparison of intravaginal misoprostol and intracervical Foley catheter alone or in combination for termination of second trimester pregnancy. J Matern Fetal Neonatal Med. 2015 Jan;28(1):93-96. doi: 10.3109/14767058.2014.905909. Epub 2014 Apr 9. PMID: 24635496.