



**ORIGINAL RESEARCH PAPER**

**Obstetrics And Gynaecology**

**PROSPECTIVE STUDY ON EFFICACY OF MIFEPRISTONE AND MISOPROSTOL VS MISOPROSTOL ALONE IN 1ST TRIMESTER MTP.**

**KEY WORDS:** Mifepristone, Misoprostol, MTP, Medical Termination of Pregnancy.

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**Background:** Unsafe abortions are the third leading cause of maternal mortality in India, close to 8 women die from unsafe abortion each day. (1) MMR in India is 103/100,000 live births (2017-2019), unsafe abortion account for 8% of the MMR. Both MTP act of 1971 and MTP amendment act 2021, which expanded the scope of the act and provides impetus for safer abortions, are progressive and encouraging. Each year 4.7-13.2% of maternal death attributed due to unsafe abortions (2). Unsafe abortion accounts for 13% of maternal deaths worldwide of which 19% occurs in South East Asia (3, 4). Medical methods of abortion has become preferable method with availability of prostaglandin analogue misoprostol and antiprogesterone mifepristone. There are many studies for both drugs and each study claims its schedule to be superior and safer than others. (5, 6, 7)

**AIM:** This study mainly aims to compare efficacy of Mifepristone and Misoprostol combination versus Misoprostol alone in procuring complete abortions in first trimester by comparing their Need for Manual /electric vacuum aspiration.

**OBJECTIVES:**

- To compare efficacy in relation to gestational period.
- To compare the Success rate of combination drugs with misoprostol alone.
- To compare Induction to abortion time intervals.
- To evaluate the Safety.

This is a prospective observational study conducted at Government Victoria hospital, Department of Obstetrics & Gynaecology, Andhra Medical College, Visakhapatnam, and Andhra Pradesh

Total no. of patients – 100  
No. of women who were given Mifepristone & Misoprostol combination 50  
No. of women received Misoprostol alone -50

Observations of this study

1. Maternal age was compared in both the groups. Majority of patients belongs to 21 to 25 years age group.
2. Majority are multigravida in both groups
3. Majority (64%) have opted for termination before 45days in mifepristone +misoprostol group, where as in misoprostol group 60% between 45-63 days
4. In both major indication for termination is unwanted pregnancy.
5. In mifepristone and misoprostol group 46 cases had complete abortion whereas 4 cases required electric vacuum aspiration
6. when comparing induction and abortion interval mifepristone and misoprostol group mean interval is 4.31 hours whereas misoprostol group is 16.18 hours and p value is <0.0001 showing induction abortion interval is less in mifepristone and misoprostol group
7. Unwanted symptoms were noted in both groups but significantly more with misoprostol only group but the p value was not significant.
8. There were no statistically significant major complications in both groups, none required blood transfusion
9. Although Mifepristone and Misoprostol combination is costly but more effective with higher rate of complete expulsion, should be preferred over Misoprostol alone where cost is not a restraining factor.

**CONCLUSION**

Based on findings from this study it can be concluded that

1. Mifepristone plus vaginal misoprostol combination group is associated with shorter induction abortion interval and 96% success rate when compared to misoprostol group alone.
2. Mifepristone plus vaginal misoprostol combination group is associated with complete abortion rate compared to misoprostol alone group. Vaginal misoprostol alone group is cost effective.
3. Routine use of Mifepristone-Misoprostol combination is an effective option for early MTP where cost is not a consideration and is ideal for home management.
4. Complication are less in Mifepristone-Misoprostol combination The only confounding factor is the cost involved which is about 20 times that of Misoprostol alone.

**ABSTRACT**

**INTRODUCTION**

MTP Act permits abortions if the continuation of the pregnancy would involve a risk to the life or of grave injury to mother's physical or mental health or there is a substantial risk if the child were born both physically and mentally as such a serious problem.

**Study Design:**

Prospective randomized observational study.

**Study Period:** January 2019 to September 2020

**Study Sample:** All pregnant women who attended

GOVERNMENT VICTORIA HOSPITAL, VISAKHAPATNAM family planning OPD seeking MTP are included as per inclusion and exclusion criteria, and given informed consent for study.

**Inclusion Criteria:**

1. Confirmed pregnancy up to 9 weeks
2. Both primigravida and multigravida
3. Confirmed intrauterine gestation
4. Single intrauterine pregnancy
5. Women fulfilling indications as per MTP act
6. Those who gave informed consent

**Exclusion Criteria:**

Patients were excluded for medical management if they had any of the following

1. Gestational age more than 9 weeks
2. Missed / incomplete / inevitable abortion
3. Patient on chronic corticosteroid Administration or with adrenal disease as Mifepristone is contraindicated
4. Patient with glaucoma, mitral stenosis, sickle cell anemia, poorly controlled seizure disorder, or known allergy to prostaglandin as misoprostol is contraindicated
5. inherited porphyria
6. known or suspected extra uterine pregnancy or adnexal mass
7. Known clotting defect or receiving anticoagulants; and systemic disorders.
8. History of previous attempts to terminate the present pregnancy

**METHODOLGY:**

**Cases Are Randomized**

**Group A:** 50 cases received Combination regimen  
 DAY 1: oral Mifepristone 200 Mg given and informed about warning symptoms and were asked to report to hospital if warning symptoms arises .

Day 3: 800µg misoprostol kept vaginally in posterior fornix  
 If fetus has not expelled advised to come back after 24-48hours and admit in hospital till abortion is complete.

**GROUP B:** Single 800µg misoprostol kept in posterior fornix, explained about warning symptoms and were asked to report to hospital if warning symptoms arises

If abortion process is not completed Manual / electric vacuum aspiration is done.

All these women were clinically evaluated and investigated including TVS.

Proper Counseling including the follow up contraceptive methods was made.

Informed Consent was taken from the patient to participate in the study.

All mandatory forms were filled as per the MTP Act guidelines.

As medical termination of pregnancy can be done as outpatient procedure, all women informed that she required making at least 2 visits to hospital. If the woman wishes to stay in hospital, she monitored for her pulse rate and blood pressure, time of onset of bleeding and expulsion of products, side effects of drugs if any are noted.

Pelvic examination was done before the patient leaves the hospital and if cervix is open and if products felt through the os removed by electric vacuum aspiration and follow up ultrasonography done for confirmation of complete abortion.

**Ethical Considerations:**

Prior permission was taken from Institutional Ethics

Committee, Andhra Medical College, Visakhapatnam. A Written informed consent was taken from each individual of the study.

The results observed, subjected to statistical analysis by **independent't' test and chi-square test, a p value <0.05** is considered statistically significant.

**Conflict Of Interest-NONE**

**OBSERVATION AND RESULTS**

Total number of cases studied for first trimester MTP was 100 cases. All 100 cases are randomized and double blinded. 50 cases provided with 200mg mifepristone and 800µg misoprostol regime and other 50 cases with 800µg misoprostol alone.

**Table 1: Comparison Of Age Groups**

Age groups	Number of cases	Percentage%
18-20	6	6.0
21-25	46	46.0
26-30	33	33.0
>30	15	15.0
Total	100	100.0

In the present study, most of the patients belong to age group 21-25 yrs (46%), 33% of the cases belong to 26-30 yrs whereas only 15% belongs to >30 and only 6% belongs to 18-20 yrs .p value >0.05.(8-10)

**Table 2: Comparison Of Parity**

Parity	Number of cases	Percentage%
Primigravida	5	5.0
G2	18	18.0
G3	69	69.0
G4	8	8.0
Total	100	100.0

In the present study, 69% of cases were in G3 and only 5% of the cases in primigravida.

**Table 3: Comparison Of Gestational Age**

Gestational Age (In Days)	Number of cases	Percentage
<45	63	63.0
45-61	28	28.0
>61	9	9.0
Total	100	100.0

In present study 63% cases belong to gestational age of <45 day, 28% belongs to 45-61 days of gestational age and 9% in the gestational age > 61 days.

**Table 4: Indications For Termination**

Cause for Termination	Number of cases	Percentage%
Unwanted pregnancy	81	81.0
Contraception failure	9	9.0
Hyperemesis	1	1.0
Epilepsy	4	4.0
Psychiatric Illness	5	5.0
Total	100	100.0

Out of 100 cases most common cause for termination is unwanted pregnancy in 81% of cases 9% of cases contraception failure, 5% of cases with psychiatric illness, 4% cases epilepsy complicating 1% for hyperemesis.

**Table 5: Method For Termination**

Method	Number of cases	Percentage%
Mifepristone + Misoprostol	50	50.0
Misoprostol	50	50.0
Total	100	100.0

Out of 100 cases 50 cases belongs to Mifepristone and Misoprostol combination group and 50 cases belong to Misoprostol alone group.

**Table 6: Comparison Of Complete And Incomplete Abortions**

Result	Number of cases	Percentage%
complete	83	83.0
Incomplete	17	17
Total	100	100.0

In the present study, 83% of the cases result in complete abortion, and in 17% of cases incomplete abortion

**Table 7: Side Effects**

Side effects	Frequency	Percentage
Nil	72	72.0
Abdominal Pain	9	9.0
Fever	6	6.0
Excessive Blood	6	6.0
Nausea	5	5.0
Diarrhea	2	2.0
Total	100	100.0

In the present study, 9% of cases had severe abdominal pain, 6% of cases had fever and in 6% of cases had excessive bleeding 5% had nausea and vomiting and, only 2% cases had diarrhea and remaining 72% cases had no side effects.

**Table 8: Analysis Of Both Methods Of Abortion Based On Age Groups**

Age groups	Mifepristone + Misoprostol	Misoprostol alone	Total	Fishers Exact Value	p value
18-20	4(8%)	2(4%)	6(6%)	0.89	0.87
21-25	22(44%)	24(48%)	46(46%)		
26-30	16(32%)	17(34%)	33(33%)		
>30	8(16%)	7(14%)	15(15%)		
Total	50(100%)	50(100%)	100(100%)		

**Using Fishers Exact Test**

In the present study, comparing of abortion based on age group in Mifepristone + Misoprostol and in Misoprostol alone, 44% cases belong to 21-25 age group in Mifepristone + Misoprostol and 48% in misoprostol alone. In 18-20 years age group 8% cases belong to Mifepristone + Misoprostol and 4% Misoprostol alone

**Table 9: Analysis Of Both Methods Of Abortion Based On Parity**

Parity	Mifepristone + Misoprostol	Misoprostol	Total	Fishers Exact Value	p value
Primi	2(4%)	3(6%)	5(5%)	2.64	0.44
G2	12(24%)	6(12%)	18(18%)		
G3	32(64%)	37(74%)	69(69%)		
G4	4(8%)	4(8%)	8(8%)		
Total	50(100%)	50(100%)	100(100%)		

**Using Fishers Exact Test**

In the present study, 63% of the cases in mifepristone and misoprostol and 74% in misoprostol alone belongs G3

**Table 10: Analysis Both Methods Based On Gestational Age**

Gestational Age (In Days)	Mifepristone + Misoprostol	Misoprostol	Total	Fishers Exact Value	p value
<45	32(64%)	31(62%)	63(63%)	0.13	0.93

45-63	14(28%)	14(28%)	28(28%)		
>63	4(8%)	5(10%)	9(9%)		
Total	50(100%)	50(100%)	100(100%)		

**Using Fishers Exact Test**

In comparing gestational age in Mifepristone + Misoprostol group 64% had < 45 days of gestational age where as in misoprostol only group 62% 45-61 days, 14% in mifepristone and misoprostol and 14% in misoprostol alone belong to 45-63 days gestational age groups. Beyond 63days 8% are in mifepristone and misoprostol group and 10% in misoprostol alone group.

**Table 11: Analysis For Causes For Termination**

Cause For Termination	Mifepristone + Misoprostol	Misoprostol	Total	Fishers Exact Value	p value
Unwanted	42(84%)	39(78%)	81(81%)	6.46	0.69
Contraception failure	4(8%)	5(10%)	9(9%)		
HYPERTENSIS	0	1(2%)	1(1%)		
Epilepsy	1(2%)	3(6%)	4(4%)		
Psychiatric Illness	3(6%)	2(4%)	5(5%)		
Total	50(100%)	50(100%)	100(100%)		

**Using Fishers Exact Test**

In most of the cases the cause for termination is unwanted pregnancy accounting 81%.

**Table 12: Analysis Both Methods Based On Induction Abortion Interval**

Method	Induction Abortion Interval hrs		t value	p value
	Mean	SD		
Mifepristone + Misoprostol	4.31	0.83	-36.09	<0.0001
Misoprostol	16.18	2.17		

**Using Independent T Test**

Mean Induction abortion interval in mifepristone + misoprostol group was 4.31hrs where as in misoprostol group was 16.18. Difference between them was found to be statistically significant (p value less than 0.001)

**Table 13: Analysis Of Results In Both Groups**

Result	Mifepristone + Misoprostol	Misoprostol	Total	Fishers Exact Value	p value
Incomplete	4(8%)	13(26%)	17(17%)	5.99	0.01
Complete	46(92%)	37(74%)	83(83%)		
Total	50(100%)	50(100%)	100(100%)		

**Using Fishers Exact Test**

In comparing the analysis of completeness of abortion in Mifepristone and Misoprostol group results 92% cases when compared to in Misoprostol group it is only 74%. Incomplete abortion in both groups is 17% and managed with electric vacuum aspiration and p value is 0.01.

In the present study, out of 100 cases in Mifepristone + Misoprostol and Misoprostol Alone, 83% of the cases results in complete abortion and incomplete abortion mifepristone + misoprostol is 8% and in misoprostol alone group is 13%

alternate method done is electrical vacuum aspiration.

**Table 15: Analysis Of Side Effects In Both Groups**

Side Effects	Mifepristone + Misoprostol	Misoprostol	Total	Fishers Exact Value	p value
No	39(78%)	33(66%)	72(72%)	6.14	0.21
Abdominal Pain	4(8%)	5(10%)	9(9%)		
Fever	1(2%)	5(10%)	6(6%)		
Excessive Bleeding	4(8%)	2(4%)	6(6%)		
Nausea	2(4%)	3(6%)	5(5%)		
Diarrhea	0(0%)	2(4%)	2(2%)		
Total	50(100%)	50(100%)	100(100%)		

**Using Fishers Ex**

In the present study, most of the side effects with misoprostol alone group comparing with mifepristone +misoprostol and the p value is not significant

**DISCUSSION**

The medical methods of abortion are safe and effective, has the advantage over surgical procedures as it is safer with a high success rate, offer more privacy, non-invasive, no instrument or anesthesia requirement, no risk of cervical or uterine injury and it will not affect the future fertility.

Mifepristone acts as antagonist to the progesterone receptors causing necrosis and detachment of placenta. It also ripens the cervix and has synergistic effect with Misoprostol. Misoprostol binds to myometrial cells causing strong myometrial contractions leading to expulsion of fetus from the uterus. (11) NATIONAL ABORTION POLICY 2020(12) recommends medical abortion up to 70 days 200 mg Mifepristone, 48 hours later by 800 µg Misoprostol is given sub lingual, vaginally oral buccal route.

**Table 21: Success Rate For Each Method Comparison With Other Studies**

Success rate Complete abortion	Mifepristone +Misoprostol	Misoprostol
Present study	92%	74%
Dahiya et al (13)	92%	74%
Verma et al (14)	95%	94%
Chawdhary et al (15)	94%	86%

Various studies have shown higher success rate and reduced induction to abortion interval and need for lesser dose of misoprostol when mifepristone is added to Misoprostol (13, 14). Treatment with Mifepristone softness the cervix, increases sensitivity of uterus to prostaglandins. Different studies have shown success rates varying from 73%-97% with combination of mifepristone followed by vaginal Misoprostol (15)

**Table 22: Mean Induction Abortion Interval Comparison With Other Studies**

Mean induction time in Hours	Mifepristone +Misoprostol in hours	Misoprostol in hours
Present study	4.31	16.18
Prasanna Lekha et Al (16)	6.19	10.67
Mukund et al (17)	6.22	10.82
Ashok et al (18)	6.08	8.67
Ngoc et al (19)	8.1	10.6
Dabash R, Chelli et al., (20)	10.4	20.6

The present prospective study analyzes and recommends the usage of combination of Mifepristone and Misoprostol drugs should be preferred over Misoprostol alone for a safe and

effective medical method of abortion in the first trimester of pregnancy.

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