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Comparative study of "mifepristone plus vaginal misoprostol" versus "vaginal misoprostol" for second trimester (13-20 weeks) abortion at a tertiary care centre in Western India

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Abstract
Aims: To compare the abortifacient efficacy of vaginal misoprostol with mifepristone (mife+miso) and vaginal misoprostol alone (miso) in second trimester (13-20 weeks) pregnancy termination. To compare the induction-abortion intervals, side effects and complications in both groups. To eventually identify the suitable method for second trimester (13-20 weeks) abortion by comparing the various parameters.
Methodology: This prospective randomized comparative study was conducted to compare the efficacy of mifepristone +misoprostol combination with misoprostol alone as a method of second trimester abortion who presented at our tertiary care centre in western India, over a period of one and a half year.
Results: Mean age distribution was similar in both groups, with majority of patients between 21-25 years of age. 52% of patients of mife+miso group and 50% of patients of miso group were gravida three and above. Most of the pregnancies were terminated in 17-20 weeks of gestation in both groups. Maximum of the patients in both study groups belonged to anomalous group followed by missed abortion group. In my study, a significant difference was found in induction-abortion interval in both groups. It was significantly lower in mifepristone + misoprostol Group with a p value of <0.0001. Dose required to terminate second trimester pregnancy along with number of repeat doses required was statistically significantly lower in mifepristone + misoprostol group than miso group. The most common side effect among both the groups was diarrhoea followed by nausea. Outcomes were almost complete in both the groups. The number of successful abortions in Mifepristone + Misoprostol group was 100% and that in misoprostol group was 98%.
Conclusion: In our study it was observed that Mifepristone +misoprostol combination group is associated with shorter induction abortion interval and >95% success rate. The complete abortion rate, success rate and side effects were comparable in both groups. Vaginal misoprostol alone group can also be considered as an effective alternative for Mife+miso combination group.

Keywords: Ruptured ectopic pregnancy, COVID-19, hemoperitoneum, laparotomy, medical abortion, lock-down

Introduction
Pregnancy is a blissful period that gives one the pleasure of experiencing motherhood. Unfortunately, the dilemma is it does not always lead to a good maternal and foetal outcome. Abortion is one of the curses to the beautiful events of pregnancy. And it has been one of the most controversial topics in the field of obstetrics and gynaecology. Worldwide, about 40-50 million women have abortions each year and second trimester abortion constitutes about 10-15% of all induced abortions, but it is related to two thirds of abortion related complications and morbidities1. The Guttmacher Institute, New York, International Institute for Population Sciences (IIPS), Mumbai and Population Council, New Delhi conducted the first study in India to estimate the incidence of abortion. The results from this study were published in Lancet Global Health journal in December 2017 in the form of a paper titled "The incidence of abortion and unintended pregnancy in India, 2015".2 This study estimated that 15.6 million abortions took place in India in 2015.2 3.4 million (22%) of these took place in health facilities, 11.5 million (73%) were done through medical methods outside facilities, and 5% were expected to have been done through other methods. The study further found the abortion rate at 47 abortions

per 1000 women aged 15-49 years. The study highlighted the need for strengthening public health system to provide abortion service delivery. This would include ensuring availability of trained providers, including non-allopathic providers by amending the MTP Act and expanding the provider base as well as streamlining availability of drugs and supplies. Another strategy was to streamline the process of approving private-sector facilities to provide CAC services and strengthening counselling and post-abortion contraception services in efforts to strengthen quality of care for women seeking CAC services. MTP act can have an impact on reduction of maternal mortality and morbidity through safe abortion. Where abortion is legal, it is generally reasonably safe, where it is illegal, Complications are common, and about 78, 000 women die every year from these complications. Worldwide, about 56 million women have abortions each year, and about half (45%) of these procedures are illegal and considered "unsafe" by the World Health Organisation.1 Second trimester pregnancy can be terminated by both surgical and medical methods. Medical (pharmacological) methods have superseded surgical methods in termination of second trimester of pregnancy. The pharmacological abortion induced by the drugs mifepristone and/or misoprostol represents the most commonly used procedure for medical intervention during second trimester of pregnancy and is effective in 90% of cases. This study was conducted to compare the abortifacient efficacy of vaginal misoprostol with mifepristone (mife + miso) and vaginal misoprostol alone (miso) in second trimester (13-20 weeks) pregnancy termination. To compare the induction - abortion intervals, side effects and complications in both groups. To eventually identify the suitable method for second trimester (13-20 weeks) MTP by comparing the various parameters.

Methodology

This prospective randomized comparative study was conducted to compare the efficacy of mife + miso combination with miso alone as a method of second trimester abortion who presented at our tertiary care centre in western India, over a period of one and a half year.

Informed consent was taken from the patients who were included in this study and ethical committee approval was taken from the college for the conduction of study.

Criteria for inclusion of study participant were 13-20 weeks gestation, Woman full-filing the MTP indications as per the MTP act, Single fetus demise, congenital malformation Present with closed cervical os, No vaginal bleeding and Patients consenting to this procedure only. Patients were equally divided in two groups (50 in each group).

First group was given 200mg mifepristone orally and 800 mcg misoprostol vaginally 6 hrs later followed by misoprostol 400 mcg vaginally every 6 hrs until delivery (or total of 4 doses). If undelivered 6 hrs after 4th dose, then repeat dose of 200mg mifepristone was given and induction was resumed next day or surgical abortion was considered.

Second group was given only vaginal mifepristone 800 mcg moistened with saline inserted in posterior vaginal fornix followed by misoprostol 400mcg vaginally every 6hrs until delivery or total of 4 doses. Additional measures were adopted in patients with incomplete abortion like instrumental evacuation and oxytocin infusion which was followed by a check ultrasonography (USG) on the next day after expulsion to exclude any retained products of conception. If any retained products were found further management was done.

Various parameters were studied including: Induction - Abortion Interval; Complete abortion rate; Success rate; side Effect Profile of the drug like Vomiting, Diarrhoea, Fever, Headache, Rigor, Haemorrhage, Infection; Total Number of Misoprostol Doses Required ; Need for Additional Procedures like Curettage, Misoprostol or Oxytocin and Requirement of blood transfusion. Data was analysed using SPSS software using ANOVA, Independent sample test and Chi- Square test and significant p value being less than 0.05.

Results

Mean age distribution was similar in both groups, with majority of patients between 21 – 25 years of age.

52% of patients of mifepristone +misoprostol group and 50% of patients of misoprostol group were gravida three and above. Most of the pregnancies were terminated in 17-20 weeks of gestation in both groups. Maximum of the patients in both study groups belonged to anomalous group followed by missed abortion group.

In my study, a significant difference was found in induction-abortion interval in both groups. It was significantly lower in mifepristone + misoprostol Group with a p value of <0.0001.

Table 1: Induction-Abortion interval

Induction-Abortion (in hrs.)	Mifepristone +Misoprostol	Only Misoprostol
Mean interval	10.78	19.12
Std. deviation	7.70	7.89

t value 5.341, P value <0.0001 (S)

There was no significant difference in between the induction abortion interval of both groups when compared according to parity. There was a significant difference statistically in between both the groups when compared according to gestational age in 13-16 weeks age group.

Table 2: Gestational AGE –Induction Abortion-interval

Gestational age	Mife +Miso (Mean±SD)	Miso (Mean±SD)	t value	p value
13-16 weeks	8.14±7.94	21.37±7.41	3.658	**0.001**
17-18 weeks	11.57±8.34	17.42±6.20	2.635	**0.011**
19-20 weeks	10.92±7.27	20.1±10.46	3.184	**0.003**

Dose required to terminate second trimester pregnancy along with number of repeat doses required was statistically significantly lower in mifepristone+ misoprostol group than misoprostol group.

Table 3: Dose required

Method group	Total dosage		
	N	Mean	STD. Deviation
Mifepristone+Misoprostol	50	1355.1	558.66
Misoprostol only	50	1912.0	437.35

t value 5.530, P value <0.0001 (S)

The data also showed significant difference with mifepristone +misoprostol requiring less no. of repeat doses to terminate second trimester pregnancy as compared to Misoprostol group alone.

Table 4: Repeat dose of misoprostol required for abortion

Mode	Number of doses				
	0	1	2	3	4
Mifepristone +Misoprostol	17	15	6	6	6
Misoprostol	2	2	16	14	16

Chi square 34.07, df 4, P value <0.0001 (S)

The most common side effect among both the groups was diarrhoea followed by nausea.

Table 5: Analysis of symptoms

Sr. No	Symptoms	Mife+Miso group		Miso group		P value
		N	%	N	%	
1.	Diarrhoea	18	36%	13	26%	0.279
2.	Nausea	15	30%	15	30%	1.000
3.	Vomiting	7	14%	7	14%	1.000
4	Pain	7	14%	11	22%	0.297
5.	Fever	3	6%	8	16%	0.110
6.	Excessive bleeding PV	2	4%	9	18%	0.025
7.	Rigor	1	2%	0	0%	1.000

Outcomes were almost complete in both the groups.

Table 6: Outcomes in both groups

Outcomes		MIFE+MISO		MISO
	N	%	N	%
Complete	50	100%	49	98%
Incomplete(RPOC)	0	0%	1	2%
Failure	0	0%	0	0%

Fisher exact test, odd ratio 3.061, P value 1.000 (NS)
The number of successful abortions in Mifepristone + Misoprostol group was 100% and that in miso group was 98%.

Discussion

The various methods used for second trimester termination of pregnancy are undergoing critical appraisal worldwide. Misoprostol, although being used routinely for second trimester MTP has the disadvantages of long induction-abortion interval, more chances of incomplete abortion and high failure rate. Recently, Mifepristone and Misoprostol combination has been found to be very effective in the termination of second trimester pregnancy with short induction-abortion interval and high success rate in spite of its high cost. The present study evaluated the time-trusted method of instilling Vaginal Misoprostol with Mifepristone versus vaginal administration of Misoprostol alone in second trimester pregnancy termination.

The present study done at Dept. of Obstetrics and Gynaecology at a tertiary care centre in western India was a randomized comparative study of 100 patients with gestational age between 13-20wks admitted for unwanted pregnancy or anomalous fetus mostly. Group I (50 patients) received 200 mg of Mifepristone and 800 mcg vaginal misoprostol after 24 hours, followed by 400 mcg vaginal misoprostol every 6 hours (maximum of four doses) or until delivery and Group II (50 patients) received 800 mcg vaginal misoprostol followed by 400 mcg vaginal misoprostol every six hours (maximum of four doses) or until delivery for induction of abortion.

Patient characteristics

Age: In this study, the mean age of patients in mifepristone + misoprostol group was 27.4years with a range of 16-35 years and the mean age of patients in misoprostol group was 26.3 years with a range of 18-36 years. There was no association between advancing maternal age and induction abortion rates or complete abortion rates in our study.
This was comparable to the study of KAPP, NATHALIE MD, MPH3 the mean age of mifepristone + misoprostol was 25.7 years and that in misoprostol was 25.5years.
In the study of JAN E DICKINSON4 the mean age of mifepristone + misoprostol was 32 years and that of misoprostol was 32 years.

Gravida: In the present study at least one prior delivery accounted for 76% in the mifepristone + misoprostol group and 78% in the misoprostol group.
In the study of JAN E DICKINSON4 mifepristone + misoprostol group was 57.8% and misoprostol group was 60.3%

Gestational age: In the present study, the mean gestational age in mifepristone + misoprostol group was 18.06 weeks while that in misoprostol group was 17.62 weeks.
In the study of JAN E DICKINSON4 the mean gestational age was 19.1 weeks in mifepristone + misoprostol group and 19.6 weeks in misoprostol group.

Indication: In this study, the most common indication for pregnancy termination was anomalous pregnancy and it accounts for 67% in both groups and it is comparable with other studies.

Parameters studied

Induction-Abortion: In the present study the mean induction abortion interval was 10.7 hrs for mifepristone + misoprostol group and 19.12 hrs for misoprostol group which showed statistically significant difference.
In the study of JAN E Dickinson the mean induction abortion interval was 8.6hrs for mifepristone + misoprostol group and 15.5hrs for misoprostol group.

Dose of Misoprostol in Misoprostol Group Alone

The total dose of misoprostol required to terminate second trimester abortion in misoprostol group alone was 1912 microgram in my study. It was comparable to Jan E Dickinson study in which the amount required was 1600 microgram. In study by Chaudhri *et al.* the dose required was 760 microgram.

Table 7: dose of misoprostol in misoprostol group alone

Study	Misoprostol Mean Dose (mcg)
Chaudhri *et al.* [5]	760
Jan E Dickinson [4]	1600
Present study	1912.0

Dose of vaginal misoprostol used in various studies in mifepristone+ misoprostol group: The total dose of vaginal misoprostol required to terminate second trimester abortion in mifepristone+ misoprostol group was 1355.1 microgram in my study. It was comparable to Jan E Dickinson in which the dose required was 1600 microgram. In Sukwai Ngai Oi Shan Tang and Pak Chang study the dose required was 812 microgram. And in Rose SB *et al.* study the dose required was 1200 microgram.

Table 8: Dose of vaginal misoprostol used in various studies in mifeprestone+misoprostol group

Study	Misoprostol dose (mcg) mean
Sukwai ngai oi shan tang and pak chang 6	812
Rose sb, shang c, simmons a7	1200
jan e dickinson4	1600
Present study	1355.1

Studies have shown that pre-treatment with mifepristone results in shorter induction-abortion intervals compared to misoprostol group alone and also dose of misoprostol req. is reduced.

Outcome in various studies (miso only)

The outcome in my study with miso only was with success rate of 98% in 48 hours of induction with misoprostol. It was comparable to studies done by Chaudri *et al*. and Tang *et al*. in which the success rate was 95%.

Table 9: Outcome in various studies (miso only)

Study	Success rates of			
	12hrs	24hrs	36hrs	48hrs
Chaudri *et al.* [5]	35%	75%	88%	95%
Tang *et al.* [8]		86%		95%
Present study	12%	68%	96%	98%

Outcome in various studies (Mife+Miso)

The outcome in my study was 100% in 36 hours of induction. It was comparable to Jan E Dickinson study in which 98% success rate within 36 hours. It was 95% in Rose SB Shand c study.

Table 10: Outcome in various studies (mife+miso)

Study	Success Rate			
	12hrs	24hrs	36hrs	48hrs
Sukwai Ngai Shan Tang and Pak Chang [6]	70.4%	81.4%	99.5%	97%
Rose SB Shand C [7]		95%		
Jan E Dickinson [4]	70.4%	91.5%	98%	99.5%
Present Study	60%	88%	100%	

Side Effects

In the study of Tang *et al*. 12 and HO *et al.* 23 where dosing interval was frequent the incidence of side effects was more, but in the present study it is comparable with other studies. In my study most common side effect was diarrhoea followed by nausea.

Table 11: Side effects in various studies (miso only group)

Study	Nausea	Vomiting	Diarrhoea	Fever	Bleeding	Rigor
Chauduri e*t al.* [5]		15%		13.3%		
Jain *at al.* [10]		4%	4%	11%		
Bebbington *et al.* [9]				24%		
Tang *et al.* [8]	48%		26%	59%		64%
Present study	30%		26%	16%	18%	14%

Table 12: Side effects in various studies (mife+miso group)

Study	Nausea	Vomiting	Diarrhoea	Fever	Excess bleeding	Rigor
Sukwai Ngai o Shan Tang and PAK Chung [6]			40%			
ROSE SB Shang C Simon A [7]					8.1%	
Jan E Dickinson [4]				43.7%		
Present study	30%	2%	36%	6%	4%	14%

The most common side effect was diarrhoea followed by nausea overall.

Conclusion

In our study it was observed that Mife +miso combination group is associated with shorter induction abortion interval and >95% success rate. The complete abortion rate, success rate and side effects were comparable in both groups. Mife +miso combination is associated with less adverse effects as compared to miso alone group.

Vaginal misoprostol alone group can also be considered as an effective alternative for Mife+miso combination group.

References

1. Sedgh, Gilda; Bearak, Jonathan; Singh, Susheela; Bankole, Akinrinola; Popinchalk, Anna; Ganatra, Bela; Rossier, Clémentine; Gerdts, Caitlin; Tunçalp, Özge; Johnson, Brooke Ronald; Johnston, Heidi Bart; Alkema, Leontine (May). Abortion incidence between 1990 and 2014: global, regional, and subregional levels and trends. The Lancet. 2016;388(10041):258-67.
2. Singh Susheela, Shekhar Chander, Acharya Rajib, Moore Ann M, Stillman Melissa, Pradhan Manas R, *et al*. The incidence of abortion and unintended pregnancy in India, 2015. The Lancet Global Health. 2018;6(1):e111-e120.
3. Kapp N, Borgatta L, Stubblefield PG, Vragovic O, Moreno N. Mifepristone in midtrimester medical abortion: a randomized controlled trial. Obstet Gynecol. 2007;110:1304-10.
4. Jan Dickinson E, Phoeha Brownell, Kaitlin Ginnis MC, Elizabeth Nathan A. Australian and New Zealand Journal of Obstetrics and Gynaecology. 2010;50(1):60-64.
5. Chauduri S, Mitra SN, Chauduri N, Chattopadya D, Banerjee D. Bose S. A comparison of intravaginal misoprostol with extraamnic. -ethacricline lactate for second trimester MTP. J Obstet Gynecol India. 2006;56:518-521.
6. Chauduri S, Mitra SN, Chauduri N, Chattopadya D, Banerjee D. Bose S. A comparison of intravaginal misoprostol with extraamnic'. -ethacricline lactate for second trimester MTP. J Obstet Gynecol India. 2006;56:518-521.
7. Rose SB, Shand C, Simmons A. Department of Primary Health Care and General Practice, Wellington School of Medicine and Health Sciences, and Level F Unit, Wellington Hospital, Capital and Coast Health Ltd., Wellington, New Zealand Mifepristone and misoprostol-induced mid-trimester termination of pregnancy: a review of 272 cases.
8. 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.
9. Bebbington MW, Kent N, Lim K, Gagnon A, Delisle MF, Tessier F, *et al*. 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.
10. Jain KJ, Kuo J, Mishell DR. A comparison of two dosing regimens of intravaginal misoprostol for second trimester pregnancy termination. Obstet Gynecol. 1999;93:571-575.