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Use of mifepristone plus misoprostol vs cerviprime plus misoprostol for second trimester abortion: A prospective comparative study

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Abstract
Background: The complications of abortion increase with the advancing gestational age. The search for the best and most reliable method for second trimester abortion is still ongoing. A prospective comparative study was conducted at a tertiary care hospital in Delhi from 01 Sep 2017 to 31 Aug 2018 with an aim to find out an effective method of second trimester abortion within reasonable time and fewer complications.
Study: A total of 70 patients were studied to compare combination of Mifepristone and misoprostol Vs cerviprime and misoprostol for second trimester abortion. The end point of the study was complete abortion with expulsion of placenta. The Induction abortion interval, success rate, side effects and complications were compared between the two groups.
Results: There was a significant difference in the IAI in both the groups. The mean Induction to abortion interval was 10.7 hrs in the Mifepristone + misoprostol group and 13.7 hrs in the Cerviprime + misoprostol group. The success rate was 100% in each arm, none of the patients required hysterotomy. More side effects were seen in the cerviprime + misoprostol group.
Conclusions: Mifepristone followed by misoprostol and Cerviprime followed by misoprostol are effective methods for second trimester abortion, but mifepristone + misoprostol has the advantage of having lesser Induction to abortion interval and fewer side effects.

Keywords: mifepristone, misoprostol, cerviprime, mid trimester abortion, induction abortion interval

Introduction
Unplanned pregnancies are one of the major problems with which patient present to our clinic. Most of the patients present in the first trimester and they are managed by the medical method of abortion. But few patients require to undergo second trimester abortion for indications such as fetal anomalies, missed abortion, unwanted pregnancy which was missed in the first trimester, victim of rape. Second trimester abortion contribute significantly to maternal morbidity and mortality especially in places where access to safe second trimester abortion is limited.
Globally, over 42 million abortions are performed annually and 10-15% of the cases take place in second trimester period, over half of which are considered unsafe, and disproportionately contribute to maternal deaths [1].
Second trimester abortion methods have undergone a sea change in the last five decades. In the early 1970s, the most commonly used methods were vacuum aspiration (VA), dilatation and curettage, hysterotomy (Sectio parva), intra-amniotic injection of hypertonic saline or hyperosmolar urea, intra- or extra-amniotic administration of ethacryidine lactate, intra-amniotic or extra-amniotic administration of prostaglandin (PG) analogues and i.v. or i.m. administration of oxytocin [2].
With the introduction of prostaglandin analogues, the efficacy of medical abortion has improved drastically, and the risk for complications and side effects have reduced. Among prostaglandins, PGE1 and PGE2 have been used in different doses and by various routes for second trimester abortion [3, 4] The method of medically induced abortion has further improved with usage of mifepristone [5]. With mifepristone, the induction-to-abortion interval has shortened, and the dose of PG analogues required has reduced. Today, medical abortion has become the method of choice in many centres [6]. This study was done to compare the efficacy of vs mifepristone and

misoprostol Vs cerviprime and misoprostol regime.

Methods

This was a prospective, comparative clinical study undertaken in the department of obstetrics and gynecology at a Tertiary care Army hospital in Delhi, India over a period of one year from 1st September 2017 to 31st August 2018. A total of 70 women fulfilling the inclusion criteria were enrolled for this study. They were randomly distributed as case (A group - Mifepristone) and control (B group- Cerviprime) having 35 women in each group.

Inclusion criteria

1. Gestational age more than 13 weeks but less than 24 weeks.
2. Women fulfilling indications of MTP Act of India.

Exclusion criteria

1. Grand multipara.
2. Heart disease.
3. Hb < 7 gm %.
4. Known contraindication to mifepristone or misoprostol.

After proper counseling, written consents were taken. Women in the group A received mifepristone 200 mg orally, followed 36-48 hours later by misoprostol 800 micrograms vaginally and thereafter by repeated doses of 400 micrograms misoprostol vaginally, every 4 hours, to a maximum of 4 doses. Whereas women in group B received vaginal Dinoprostone gel at 1200 hrs and 1800 hrs, followed by 800 mcg misoprostol at 0100 hrs and 400 mcg every 4 hours, to a maximum of 4 vaginal doses. The induction abortion interval (IAI) was defined as time from administration of first dose of misoprostol (800 mcg) to abortion of foetus. Maternal side effects of drugs were observed and treated accordingly. All patients were given one dose of Inj Tramadol once they started having pain. Any patient needing more analgesia support were added in the group showing side effect of pain and was given a repeat inj of either tramadol or inj pethidine 50 mg IM.

Types of outcome measures

Primary outcomes

i. Rate of complete abortion.
ii. Induction-to-abortion interval.

Secondary outcomes

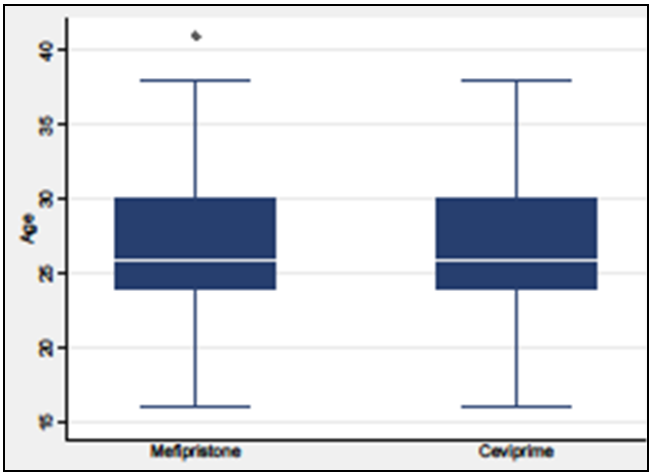
i. Excessive blood loss either measured or estimated by a clinically relevant drop in haemoglobin.
ii. Pain resulting from the procedure, reported by the women or measured by use of analgesics.
iii. Post-abortion curettage required in women with medical abortion method.
iv. Side effects such as pyrexia, nausea, vomiting and diarrhoea.
v. Uterine rupture.
vi. Infectious morbidity.
vii. Mortality
viii. Any other grave complication.

Results

The distribution of patients in Group A and B were similar and maximum patients were in the range of 26 -30 years (Table 1). In group a, mean age is 27, SD 5.5, whereas in group B mean age is 26.6, SD 4.4.

Table 1: Age of women

Age (Yrs)	Group A (Mifepristone) No. of women	Percentage	Group B (cerviprime) No. of women	Percentage
<20	02	5.7	03	8.5
20-25	13	37.1	12	34.2
26-30	14	40	12	34.2
31-35	05	14.2	05	14.2
36-40	01	2.8	02	5.7
>40	-	-	01	2.8



Most of the cases were second gravida in both the groups (Group A - 40% (n=14), Group B - 37.1% (n=13)) (Table 2).

Table 2: Gravida distribution of women

Gravida	Group A (Mifepristone) No. of women	Percentage	Group B (cerviprime) No. of women	Percentage
Primi	10	28.5	10	28.5
Second Gravida	14	40	13	37.1
Third Gravida	09	25.7	11	31.4
Fourth Gravida	02	5.7	01	2.8

The mean gestational age was 17.1 weeks SD 2.2 in group A (Mifepristone) and 17.4 weeks SD 2.5 in Group B (Cerviprime) (Table 3).

Table 3: Period of gestation

POG (wks)	Group A (Mifepristone) No. of women	Percentage	Group B (cerviprime) No. of women	Percentage
12- 14	5	14.3	6	17.1
15-17	16	45.7	19	54.1
18-20	10	28.6	8	22.8
21-24	4	11.4	2	5.7

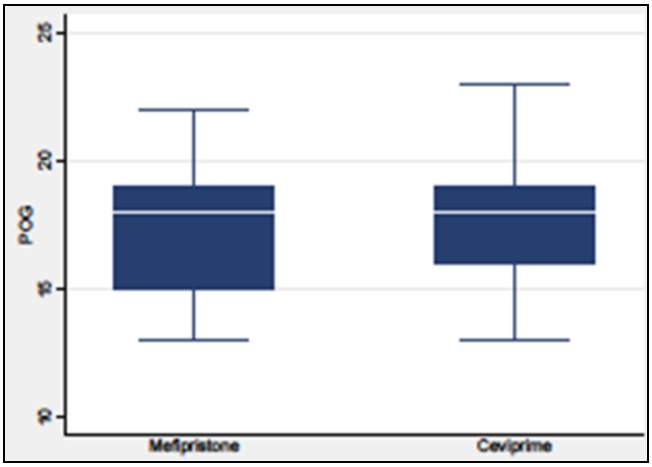


Table 4: Indications for TOP (Termination of pregnancy)

Indication	Group A (Mifepristone) No. of women	Percentage	Group B (Cerviprime) No. of women	Percentage
Anomalies	09	25.7	12	34.2
Missed abortion/early IUD	12	34.2	10	28.5
Unwanted Pregnancy	09	25.7	09	25.7
PPROM	05	14.2	05	14.2

The most common indication for termination of pregnancy was missed abortion in Group A (Mifepistone group) with 34.2% and congenital anomalies in Group B (Cerviprime Group) with 34.2% patients.

Table 5: Complicated Cases

Complication	Group A (Mifepristone) No. of women	Percentage	Group B (cerviprime) No. of women	Percentage
Post LSCS	2	5.7	2	5.7
Placenta previa	3	8.5	-	-
Twins	3	8.5	41 was conjoint twin at 22 wks	11.2

There were two cases of post LSCS pregnancies in both the groups. There were three cases (8.5%) of placenta previa in Group A (Mifepristone). There were 3 cases (8.5%) of twin pregnancy in Group A (Mifepristone) and 4 cases (11.2%) of twin pregnancy one being a case of conjoint twin in Group B (Cerviprime Group).

Table 6: Side effects/complications

Complications	Group A (Mifepristone) No. of women	percentage	Group B (Cerviprime) No. of women	percentage
Exessive loss of blood	1*	2.8	2	5.7
Pain	3	8.5	3	8.5
Check Curettage	2*	5.7	2	5.7
Side effects	1	2.8	2	5.7
Fever Vomiting	2	5.7	3	8.5
Any other complication	1 (Uncontrolled PPH, managed with Internal Iliac ligation)	2.8	-	-
Infectious Morbidity	1*	2.8	-	-

*This was the same patient who needed check curettage for excessive bleeding, and developed sepsis and needed internal artery ligation.

80% of patient in group A had no complications. 71.4% of patients in group B patient had no complication. There was no incidence of uterine rupture. There was no incidence of failure and none of the patients required to undergo hysterotomy.

There were two cases of excessive blood loss requiring check curettage and blood transfusion in each group. However one case in Mifepristone group required check curettage followed by internal iliac Artery ligation for severe PPH and required transfusion of 8 FFP and 5 PRBC and ventilator support for one day and two day ICU stay, She had developed infectious morbidity (Sepsis) and was managed with high grade antibiotics for 7 days.

Two patients in both the group (11.4%) required surgical curettage.

The incidence of pain requiring added analgesia was similar in both group, three patients (8.5%) in each group. The incidence of fever and vomiting was more in the cerviprime group but was not of much significance.

The induction abortion interval (IAI) was defined as time from administration of first dose of misoprostol (800 mcg) to abortion of foetus (Table 7).

The induction to abortion interval was 10.7 hrs SD 2.3 in group A (Mifepristone Group) and 13.7 hrs SD 4.4 in Group B (Cerviprime group) which was statistically significant with p value of 0.0008.

Table 7: Induction to abortion interval

I- A interval	Group A (Mifepristone) No. of women	Percentage	Group B (Cerviprime) No. of women	Percentage
< or equal 8hrs	7	20	2	5.7
8.1 -12hrs	22	62.8	20	57
12.1 -16hrs	6	17.1	10	28.5
>16hrs	-		3	8.56

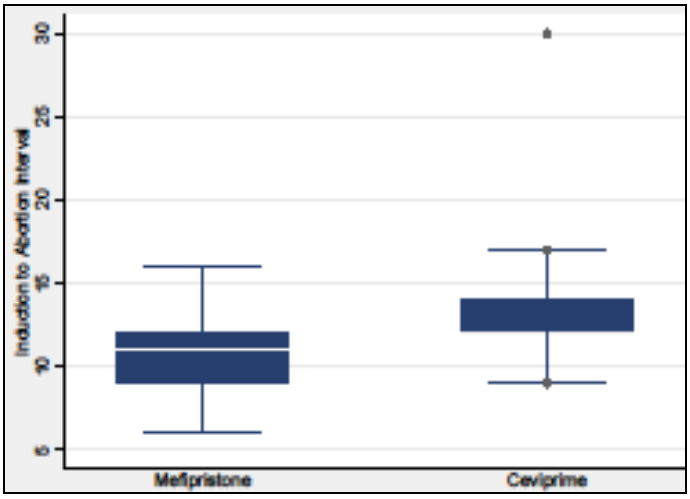


Table 8: Characterstic of the patients

Characterstic	Mifepristone (N=35)	Cerviprime (N=35)	P value*
Age, mean (SD)	27 (5.5)	26.6 (4.4)	0.8
POG	17.1 (2.2)	17.4 (2.5)	0.6
Induction to abortion interval	10.7 (2.3)	13.7 (4.4)	0.0008

*Unpaired "T" Test Interpretation

There is no statistical significant difference between age and POG. But there is statistical significant difference in Induction to abortion interval, with Cerviprime group taking considerable more time mifepristone group.

Discussion

This study compared combination of Mifepristone and misoprostol with combination of cerviprime and misoprostol. The mean age of patient was 27 years in mifepristone group and 26.6 years in cerviprie group which was also the case in other studies [6, 7].

Mean gestational age was 17.1 weeks in Mifepristone group and 17.4 weeks in Cerviprime group as seen in the study by Singh V and Carbonella [6, 8].

The mean induction abortion interval was 10.7 hrs in Mifepristone group and 13.7 hrs in Cerviprime group which is comparable to study by Jahagirdar SS [7] and Chai J [9]. IA interval was lesser in the Mifepristone group and is statistically significant with p value of 0.0008.the similar findings were seen in study by Patel [10] and Kapp N [11].

Both the regimens were 100% successful as none of the patient required to undergo hysterotomy as seen in other study [7]. In Mifepristone group 82% aborted in 12hrs and 100% in 16 hrs. In cerviprime group 63% aborted in 12hrs and 91% aborted in 16 hrs and 100% aborted in 30 hrs. These results show better efficacy of the regime of miferpristone and misoprostol as compared to results of largest cohort study of 1,002 women having second-trimester medical abortion using the recommended Mifepristone and misoprostol regimen (24-36 hrs.) interval between both drugs where the complete expulsion rate was 98.3 percent at 24 hours and 99.2 percent at 36 hours [12].

In our study we had three patients of placenta previa who successfully aborted by Mifepristone regime. Similar safety data was seen in the study of cases of mid trimester abortion without any significant difference in the blood loss by Daisuke Nakayama [13].

Three case had excessive blood loss needing blood transfusion. One in Mifepristone and two in cerviprime group. One case had severe PPH and developed sepsis, but she was a case of prolpnged PPROM and chorioamnionitis and had developed atonic PPH which required 8 FFP and 5 PRBCs transfusion and internal Artery ligation and high grade antibiotics.

In our study we had 4 cases of post LSCS pregnancy, 2 in each group and all the case aborted successfully without any significant complication. There was no incidence of uterine rupture in our study. It is comparable to previous study by Chikkagowdra [14].

Thus, both the regimens used in our study were effective method for termmination of pregnancy with Mifepristone group having statistically signifiant induction abortion interval. The side effects were also lesser in the mifeprisone group but this was of not much significance.

Conclusions

Mifepristone followed by misoprostol and Cerviprime followed by misoprostol are effective methods for second trimester abortion, but mifepristone + misoprostol has the advantage of having lesser Induction to abortion interval and fewer side effects.

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