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Comparative Study of Combination of Mifepristone And Misoprostol Regimen With Misoprostol Only Regimen For Mid Trimester Abortion

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ABSTRACT:
BACKGROUND:
Abortion is defined as spontaneous or induced termination of pregnancy before fetal viability less than 500 gm or less than 20 weeks gestation age. Midtrimester abortion is mostly done for fetal abnormalities and anatomical defects after ultrasound screening.
AIM:
To compare the effect of oral mifepristone and misoprostolwith misoprostol alone in cervical ripening and induction of labor in mid trimester abortion.
MATERIAL AND METHOD:
This was a randomized comparative analysis and prospective study conducted in Department of Obstetrics and Gynecology of Dhiraj hospital .it was conducted from 1stJan 2019 to 1stJune 2020.
RESULTS:
160 Cases of antenatal patients admitted in obstetric ward in gestational age of >12 weeks and < 20 weeks who came with specific indications of abortion were selected for study. All patients were willing for medical induction of labour.80 patients were induced with combination of vaginal misoprostol(400 microgram) and oral mifepristone(200 mg) and 80 patients were given vaginal misoprostol(400 microgram) alone .
It was found that in 60% mifepristone added 48 hours before misoprostol produced cervical dilation in shorter time interval compared with misoprostol alone.In 40% patients misoprostol given alone produced cervical dilation in shorter time interval hence producing earlier induction of labor leading to abortion.
CONCLUSION:
Patients with indication of mid trimester abortion induced with combination of misoprostol and mifepristone delivered early with greater response as compared to those with misoprostol alone.over all combination resulted in lesser complications and early induction and termination of pregnancy.
KEYWORD: induction of mid trimester abortion , misoprostol , mifepristone.

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I. INTRODUCTION

For abortion at 13–20 weeks of gestation, medical abortion with mifepristone followed by a prostaglandin (PG) analogue is an appropriate method and has been shown to be safe and effective. The combination of mifepristone and misoprostol has synergistic effects and stimulates expulsion of the pregnancy.
The most commonly used combination is:

- mifepristone, taken first
- misoprostol, 24–48 hours later

Mifepristone is a 19-norsteroid, which binds with high affinity to the progesterone receptor, thus inhibiting the effect of progesterone. Progesterone is a key hormone in maintaining pregnancy by keeping the uterus in a quiescent state. It prevents softening and dilatation of the cervix, reduces PG output from the decidua

and suppresses uterine contractions. Thus, the blocking of progesterone receptors by mifepristone results in vascular damage, decidual necrosis and bleeding, which leads to cervical softening, increased uterine sensitivity to PG and conversion of the quiet pregnant uterus into an organ of spontaneous activity with maximal effect at 36–48 hours.

Misoprostol is a synthetic PGE-1 analogue which induces cervical ripening as well as strong uterine contractions and leads to expulsion of a pregnancy. Prostaglandins play an important role in the regulation of uterine contractility during pregnancy. The receptors are present throughout the pregnancy; hence, PGs and PG analogues are effective for termination of pregnancy.

Combination of mifepristone with misoprostol is a common method for mid trimester pregnancy termination. Priming of the uterus with mifepristone makes it more sensitive to prostaglandins. It binds with the progesterone receptors and antagonizes the actions of progesterone on prostaglandin synthesis and metabolism resulting in increase in production and decreased deactivation of prostaglandins. It also induces cervical softening thus, enhancing the efficacy of the prostaglandins as an abortifacient.

II. METHODOLOGY

This was a randomized comparative analysis and prospective study conducted in Department of Obstetrics and Gynecology of Dhiraj hospital .it was conducted from 1stJan 2019 to 1stJune2020.
SAMPLE SIZE : 160 patients
DURATION: 1stJan2019 to 1stJune 2020.

INCLUSION CRITERIA:

- pregnancy >12 to < 20 weeks
- no contraindication for use of prostaglandin
- singleton pregnancy
- live fetus
- cervical os closed
- no bleeding
- willing for induction
- fetus with congenital anomaly

Exclusion Criteria:

- history of allergy to prostaglandin
- cervical os dilated
- incomplete abortion
- suspected ectopic pregnancy
- coagulopathies
- chronic systemic use of corticosteroids
- chronic adrenal failure
- inherited porphyria

Participants were randomized to one of two study groups; women in the first group received pretreatment of 200 mg mifepristone to take orally followed by 400 micrograms misoprostol orally. Those in the second group received only the first dose of 400 micrograms misoprostol to be taken orally. Doses were repeated every 4 hours, up to 3 doses, until the expulsion of the fetus and the placenta occurred. After administration of the first misoprostol dose, blood pressure, temperature, side effects, and bleeding were monitored every 3 hours.

The procedure was considered complete if the products of conception were passed and appeared complete (including the placenta) within 14 hours of the first misoprostol dose and no further interventions were given. The induction was considered a failure and the woman was offered standard evacuation if fetal expulsion did not occur within 14 hours from the first misoprostol dose (4 hours after the final dose). if the fetus was expelled but the placenta remained in the uterus after an additional 30 minutes, the woman could be given an additional 400 micrograms of misoprostol buccally to help evacuate the placenta and wait an additional 6 hours for expulsion (21.5 hours after the first misoprostol dose). If placental expulsion still did not occur, the remaining products were removed surgically.

III. RESULTS

One hundred and sixty women were enrolled from Jan 2019 to June 2020 .Participants were equally randomized between the two study groups.

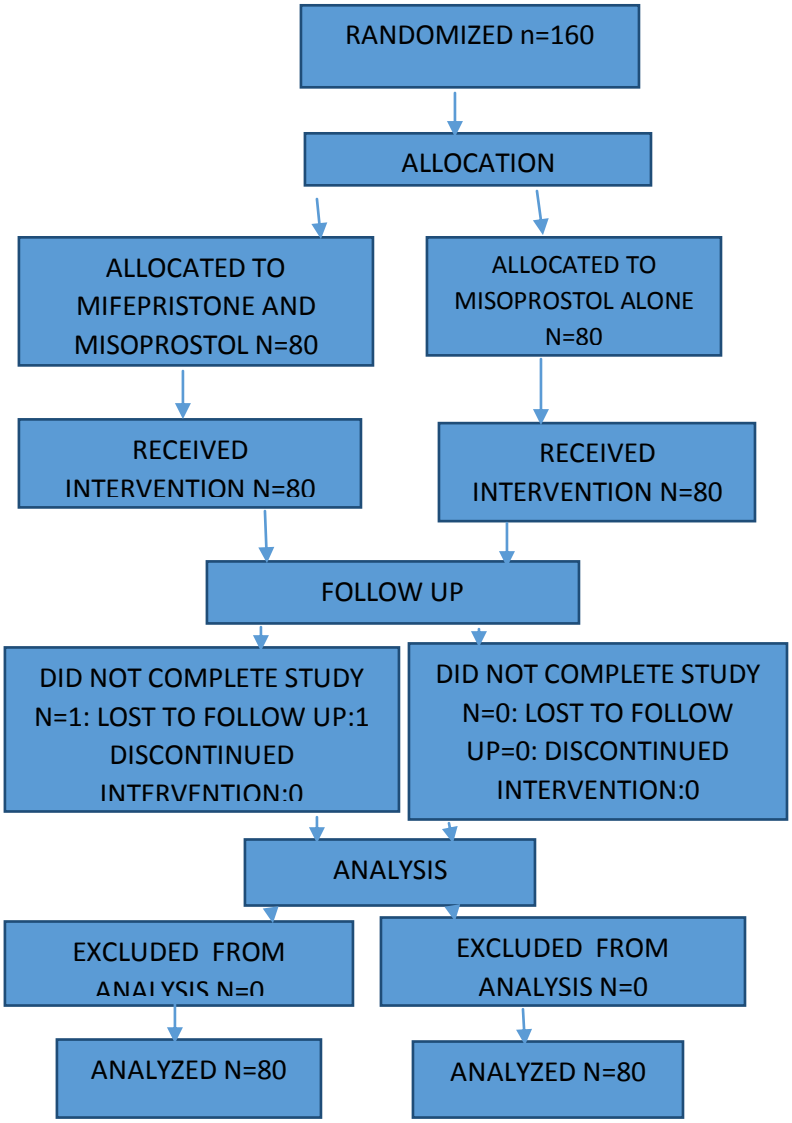

Fig. 1:

Flow of patients through the study. Fig. 1. *Medical Abortion in the Second Trimester*

Table 1:

Participants' Characteristics*

PARTICIPANT CHARACTERSTICS	GROUP 1: MIFEPRISTONE PLUS MISOPROSTOL N=80	GROUP 2: MISOPROSTOL ALONE N=80
MATERNAL AGE	25+-6.5 (13-43)	25+-6.5(15-49)
GESTATIONAL AGE	16.6+-2.1(14-21)	17.2+-2.3(14-21)
EDUCATION LEVEL		
NO EDUCATION	2.5(2)	2.5(2)
PRIMARY	22.5(18)	20(16)
SECONDARY	30(48)	29(47)
TECHNICAL	5(4)	5(4)
UNIVERSITY/COLLEGE	10(8)	13.75(11)

MARITAL STATUS		
SINGLE	2.5(2)	2.5(2)
MARRIED	98(78)	98(78)
DIVORCED	0.5(1)	0.5(1)
PREGNANCY HISTORY		
GRAVIDA	2.0+-1.6(1-5)	1.9+-1.6(1-5)
PARITY	0.5+-0.9(O-3)	0.5+-0.9(0-3)
PRIMIGRAVIDA	75(60)	80(64)
PRIOR INDUCED	25(20)	20(16)

We examined the characteristics of the participants, including maternal age, gestational age, education, marital status, and pregnancy, and abortion history. The average age of participants was 25 years. More than half (98%) were married, and only (30%) had completed secondary school as their highest level of education (data not shown). These characteristics were compared by study group (Table 1). The only statistically significant difference between arms 1 and 2 was mean gestational age (16.6 and 17.2 weeks, respectively; *P*<.03).

Table 2:
Rates of Complete Uterine Evacuation and Time to Expulsion

	Mifepristone and misoprostol n=80	Misoprostol n=80	RR
Complete uterine evacuation with initial study regimen, all participants by gestation age weeks	80(64)	37.5(30)	2.13
14-15	40(32)	37.5(30)	1.07
16-17	31.25(25)	26.25(23)	1.08
18-19	17.5(14)	10(8)	1.75
20-21	11.25(9)	23.75(19)	0.47
Time to complete abortion in hours median	81+-2.8(2.5-14.8)	10.6+-25(6.5-15.5)	
median	7.5	10.8	
No of doses for complete abortion	3.1+-0.9(1-5)	3.9+-0.8(2-5)	
median	3	4	
Complete fetal expulsion	85(68)	40(32)	2.12
Time to fetal expulsion hrs	7.3	10.5	
median			
Additional call given for fetal expulsion			
oxytocin	7.35 (5/68)	6.35(2/32)	
Sponge forceps removal	2.94(2/68)	0(0/32)	
Dilation curettage	1.47(1/68)	3.12(1/32)	
Additional 400 microgram	4.41(3/68)	0(0/32)	

Pretreatment with mifepristone resulted in more than twice the chance of a complete uterine evacuation compared with misoprostol alone (relative risk 2.16, 95% CI 1.70–2.75). Approximately 80% (79.8%) of the mifepristone–misoprostol group had complete abortions compared with 37.5% of the misoprostol-alone group (Table 2). For instance, by 10 hours, almost 60% of women in the mifepristone–misoprostol group had complete uterine evacuation compared with fewer than 20% in the misoprostol-only group. some women experienced complete uterine evacuation after the 15 hours stipulated in the protocol but before any additional interventions were provided. If we reclassify these women, we achieve moderately higher efficacy rates: 81.4% with mifepristone–misoprostol and 41.5% with misoprostol alone. Gestational age did not appear to affect evacuation rates among women pretreated with mifepristone; however, the rate of complete evacuation did vary by gestational age among women given misoprostol only (13.0–56.3%) resulting in a wide range of risk ratios between the two regimens.

Fetal expulsion occurred for 80% of the mifepristone–misoprostol participants and for 37.5% of misoprostol-alone recipients (relative risk 2.19; 95% CI 1.75–2.75). The mean times to fetal expulsion among participants who had a complete uterine evacuation were similar to the mean times to complete evacuation for both study regimens (Table 2). Additional care given to women who expelled the fetus but not the placenta included administration of oxytocin, removal with sponge forceps, dilation and curettage, and additional doses of misoprostol (Table 2).

The mean induction-to-abortion interval for complete uterine evacuation was statistically significantly shorter among participants who were pretreated with mifepristone compared with those who took misoprostol alone (8.1 and 10.6 hours, respectively; $P<.001$). Among participants who experienced complete uterine evacuation with the study regimen, the median number of doses of misoprostol received was significantly lower among the mifepristone–misoprostol group (three) as compared with the misoprostol-alone group (four) ($P<.001$; Table 2). The side-effect profiles for the two study regimens did not differ significantly. Pain was the most commonly reported side effect, Other side effects associated were nausea, vomiting, diarrhea, chills, and headache. Women were inquired about severity of their side effects; the only significant differences in severity between the two groups were diarrhea and chills, both lesser in the mifepristone plus misoprostol arm.

IV. DISCUSSION:

This studycompares misoprostol alone with combination of mifepristone pretreatment and misoprostol for medical abortion with a live fetus in the mid trimester. This method shows the true efficacy of both .The oral misoprostol was effective and found to be easy to use by participants.

The results confirm that treatment with mifepristone leads to a higher completion rate as well as a shorter time-to-abortion interval with same side-effects and acceptance. As seen in this study, mifepristone can be taken at home by women. Hence, mifepristone should be included in mid-trimester abortion regimens.

The cutoff time for outcome assessment (15 hours after the first misoprostol dose) is much shorter than cutoff times reported in other studies (24–48 hours). A majority of women with successful fetal expulsion within 15 hours also expelled their placenta within this time. Although our protocol allowed for an additional dose of misoprostol (and additional time of 6 hours) for placental expulsion to avoid additional intervention, there were few women who expelled their placenta more than 30 minutes after fetal expulsion..

It is possible that given its better efficacy and shorter time-to-abortion interval, regimens with mifepristone pretreatment will be less expensive for delivery. Although mifepristone is more expensive than misoprostol, women given the combined regimen appear to complete their abortion earlier and need a shorter duration of hospitalization, thus reducing the expenses.

V. CONCLUSION:

The study was performed to compare the effect of two regimes which included mifepristone with misoprostol and misoprostol alone in induction of labor in mid trimester abortion and it was concluded that though both regimens are effective but better results with shorter induction abortion time was seen with the combination of mifepristone and misoprostol regimen. Hence it produced better results.

VI. SUMMARY

This study included 160 cases of antenatal women over a period of 1.5 years performed at Dhiraj hospital which had indications for abortion. The women were explained and consent was taken for medical abortion. 2 groups were formed of 80 cases each. Group A was induced with combination regimen of mifepristone and misoprostol and Group B was induced with misoprostol alone. The cases were monitored for induction abortion interval and side effects along with complete uterine evacuation. It was clearly noted that the group of women induced with combination regimen of mifepristone and misoprostol had shorter abortion induction interval producing better results.

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