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To compare the effectiveness of medical termination pills in early and late first trimester abortion in a tertiary care center

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Abstract

Background: MTP has been legalized in India since 1971. MTP pill combination of Mifepristone and Misoprostol used in early pregnancy termination (≤ 9-week gestation). Present study aims to measure its effectiveness and safety as an abortifacient drug.

Methods: Prospective and Comparative study of 60 cases, conducted at OBGY Department, J.K. Hospital, Bhopal from September 2020 to September 2021. This study involves two groups, Group 1 involving patients with Intra uterine gestational age < 7 weeks and Group 2 involving patients with Intra uterine gestational age 7- 9 weeks, who needed termination of pregnancy, confirmed by ultrasound and justified by indication. They were administered orally 200 mg of Mifepristone followed by Misoprostol 800 µg after 48 hours sublingually/ vaginally by MTP protocol.

Results: Majority of Women in both groups, seeking for 1st trimester MTP were of age 26-30 years (46.7% and 40%). Majority of women in the Group 1 were Gravida 3 (53.3%) whereas in Group 2 second Gravida (40%) were more. Efficacy outcome by different routes, out of 30 women in vaginal route group (25)83.3% had complete abortion as compared to (27) 90% in sublingual route group. Patients with GA < 7 weeks had high rate of successful abortion (93.3%) compared to 7-9 weeks (80%). Only 6.7 % of cases from group 1 needed surgical intervention due to incomplete abortion as compared to 16.7% of cases from group 2.

Conclusions: The present observational study demonstrates that Mifepristone and Misoprostol

combined therapy is a more effective and well tolerated medication up to 7 weeks as compared to ≥7 weeks in Indian adult women requiring MTP up to 63 days' gestation.

Keywords: Abortion, MTP, MTP pill Mifepristone and Misoprostol, Sublingually, vaginally.

Introduction

MTP has been legalized in India since 1971 to prevent unsafe and illegal abortion. [1]

Abortion is the termination of a pregnancy before the fetus has attained viability, i.e., becomes capable of independent extra-uterine life. Medical methods emerged as an alternative to surgical abortion with the discovery of prostaglandins in the early 1970s [2, 3, 4]. The term medical abortion refers to early pregnancy termination (usually before 9 weeks' gestation) performed without primary surgical intervention and resulting from the use of abortion-inducing medications. When performed as per guidelines with success rate of 95 to 99%. [5]

Drug Controller General of India approved the use of Mifepristone (in April 2002) and Misoprostol (in December 2006) for termination of pregnancy up to 49 days gestation period. In December 2008, Mifepristone + Misoprostol (1 tab of Mifepristone 200mg and 4 tab of Misoprostol 200 mcg each). Combi pack was approved by the Central Drugs Standard Control Organization, Directorate General of Health Services for the medical termination of intrauterine pregnancy (MTP) for up to 63 days gestation. [6] As per the MTP law of India, abortion pills can only be prescribed by registered medical practitioner. [1] Mifepristone acts by binding to the progesterone receptor, thus inhibiting the effect of progesterone. The sensitivity of myometrium to exogenous prostaglandins is also increased by administration of Mifepristone. [7]

Misoprostol is a synthetic prostaglandins E1 analogue and because of its uterotonic and cervical-ripening actions. [8] Prostaglandins causes powerful contraction of uterus. [9]

The regimen of 200 mg Mifepristone followed 48 hours later by Misoprostol is recommended for the early termination of pregnancy, at the dose of 800 mcg misoprostol buccal, vaginally or sublingually for pregnancies up to 12 weeks. [10] With oral administration of Misoprostol the efficacy decreases sharply when the duration of pregnancy is over 7 weeks. [11] In an attempt to find an effective alternative to vaginal administration, misoprostol tablets have been given sublingually (under the tongue) [12] or buccally (between the gum and the cheek), [13] with better efficacy results than orally (swallowing).

Aims & Objectives

1) To compare the effectiveness of Mifepristone & Misoprostol as an abortifacient drug at gestational age <7 weeks & 7-9 weeks.

2) To compare the safety and efficacy of Mifepristone & Misoprostol as an abortifacient drug by different routes

Material and Methods

This is a prospective and comparative study of 60 cases, conducted at Obstetrics and Gynecology Department, J.K. Hospital, Kolar Road, Bhopal. This study involves two groups of women, Group 1 involving patients seeking medical termination with Intra uterine gestational age < 7 weeks and Group 2 involving patients with Intra uterine gestational age 7 to 9 weeks, confirmed by ultrasound. Patient counseling was done regarding options for the termination, risks and benefits

of medical methods, the possible side effects and need for treatment. Informed consent and MTP consent (as per indication) was taken from patients enrolled in the study & case record was maintained including maternal age, obstetric history, past medical/surgical history, socioeconomic status, gestational age (by ultra sound), clinical examination findings. Hemoglobin%, Blood grouping and RH typing, Bleeding time, Clotting time, were recorded. The women was given combi pack of Mifepristone and Misoprostol and was instructed to swallow tab Mifepristone 200 mg took in the presence of doctor. Out of 60 women, 30 women were selected randomly took 800 mcg Misoprostol by sublingual route, whereas remaining 30 women took 800 mcg Misoprostol by vaginal route on Day 3 at home (48 hour).

The woman was advised to come to hospital at any time if they had excessive bleeding or vomiting or fever or foul-smelling discharge. Patient was given a follow up card (14) where she was supposed to note the time when the bleeding starts and duration of bleeding. Patient was also asked to note the side effects and whether the medication was required or not for the management of same. The second visit is a follow-up appointment, usually scheduled about 2 weeks after the dose completion. Efficacy rates were determined as complete abortion rate, incomplete abortion rate or no response rate observed at Day 15.

Protocol for MMA for upto 9 Weeks

Mifepristone on Day 1 200 mg (1 tablet) orally (available as 200 mg tablet)	Misoprostol on Day 3		Day 15
	Dose	Route	• Confirm and ensure completion of the process • Contraception
	400 mcg-800mcg	Oral/vaginal/ sublingual/buccal *(WHO, 2012)*	

Inclusion Criteria

This study involves two groups of women, seeking MTP as per guidelines. Group 1 involving patients with intra uterine pregnancy < 7 weeks gestational age and Group 2 involving patients with intra uterine pregnancy 7- 9 weeks gestational age, confirmed by ultrasound.

Exclusion Criteria

- Pregnant women more than 9 weeks of gestation
- Previous allergic reaction to the drugs involved
- Severe anemia
- Pre-existing heart disease
- Undiagnosed adnexal mass /confirmed or suspected ectopic pregnancy
- Intrauterine device in place
- Chronic adrenal failure
- Renal or hepatic failure
- Porphyria and Hemorrhagic disorders
- With concurrent anticoagulant therapy
- Long-term corticosteroid therapy.

Results

Table 1: Age distribution

Age (years)	Group 1 (<7 weeks) No. = 30 (%)	Group 2 (7- 9 weeks) No. = 30 (%)
<19	0 (0%)	0 (0%)
20-25	9 (30%)	8 (26.7%)
26-30	14 (46.7%)	12 (40%)
31-35	5 (16.6%)	6 (20%)
>36	2 (6.7%)	4 (13.3%)

Table 1 shows majority of women in both groups were seeking for MTP pill are of 26-30 years of age (46.7% and 40%).

Table 2: Gravida status

Gravida	Group 1 (< 7 weeks) No. =30 (%)	Group 2 (7- 9 weeks) No. =30 (%)
Primi	4 (13.4%)	6 (20%)
G2	9 (30%)	12 (40%)
G3	16 (53.3%)	9 (30%)
G4	1 (3.3%)	2 (6.7%)
G5/more	0 (0%)	1 (3.3%)

Table 2 shows majority of women in the Group 1 (< 7 weeks) were Gravida 3 (53.3%) compared to 30% women in the Group 2 (7- 9 weeks). Most of women in Group 2 (7- 9 weeks) were Gravida 2 about 40 %.

Table 3: Gestational age (weeks)

Gestational age	No =60 (%)
< 7 weeks	30 (50%)
7- 9 weeks	30 (50%)

According to table 3, Gestational age were equally divided in both groups like 60 pregnant women were equally divided in both groups. Group 1 belonged to 30 pregnant women, whereas 30 pregnant women belonged to group 2.

Table 4: Time of Onset of Bleeding (hrs.)

Time of onset of Bleeding	Group 1 (< 7 weeks) No. =30 (%)	Group 2 (7- 9 weeks) No. =30 (%)
Bleeding after Mifepristone and before Misoprostol	1 (3.3%)	2 (6.7%)
Bleeding after Misoprostol		
<2 hour	10 (33.4%)	8 (26.7%)
2-4 hours	16 (53.3%)	15 (50%)
>4 hours	3 (10%)	5 (16.6%)

Most of the women had started bleeding between 2-4 hours of Misoprostol intake in both groups (53.3% belonged to group 1 and 50% belonged to group 2).

Table 5: Adverse Effects

Adverse Effects	Group 1 (< 7 weeks) No. =30 (%)	Group 2 (7- 9 weeks) No. =30 (%)
Abdominal pain	24 (80%)	26 (86.7%)
Nausea	10 (33.3%)	13 (43.3%)
Vomiting	7 (23.3%)	9 (30%)
Diarrhea	5 (16.7%)	7 (23.3%)

According to Table 5, Almost all the patients had abdominal pain in both groups were 80 % in group 1 & 86.7% in group 2; where nausea occurred in 33.3% patients of group 1 & 43.3% in group 2 patients, whereas vomiting occurred in 23.3% patients of group 1 & 30% in group 2 patients, and diarrhea occurred in 16.7 % patients of group 1 & 23.3 % in group 2 patients after administration of Misoprostol. So, majority of adverse effects were belonged to group 2 compared to group 1.

Table 6: Duration of bleeding (days)

Duration of bleeding	Group 1 (< 7 weeks) No. =30 (%)	Group 2 (7- 9 weeks) No. =30 (%)
<5 days	2 (6.7%)	2 (6.7%)
5-7 days	14 (46.7%)	9 (30%)
7-10 days	11 (36.6%)	14 (46.7%)
>10 days	3 (10%)	5 (16.6%)

Table 6 shows Most of women in group 1 (< 7 weeks) had bleeding for 5-7 days about 46.7% of women compared to 30 % women in the group 2 (7- 9 weeks). Most (46.7%) of women in group 2 had bleeding for 7-10 days. Bleeding was severe for first 2 days then it was moderate or just spotting was present. On an average, duration of bleeding was 5 to 10 days in most of the cases.

Table 7: Gestational age/route

Gestational age /Route	Vaginal(n =30)	Sublingual (n = 30)
< 7 weeks	15	15
7- 9 weeks	15	15

According to table 7, out of 60 women, 30 women were administered Misoprostol by vaginal route and 30 by sublingual route.

Table 8: Efficacy outcome by Route

Outcome	Vaginal (n=30)	Sublingual (n=30)
Complete abortion	25 (83.3%)	27 (90%)
Failure to complete abortion	5 (16.7%)	3 (10%)
All	30 (100%)	30 (100%)

Table 8 shows efficacy outcome by different routes, out of 30 women in vaginal route group (25)83.3% had complete abortion as compared to (27) 90% in sublingual route group.

Table 9: Results of Abortion by Gestational age

Duration of gestation	No. of patients N=60 (%)	No. of patients successful aborted	No. of patients of incomplete abortion	No effect
< 7 weeks	30 (50%)	28 (93.3%)	2 (6.7%)	0 (0%)
7- 9 weeks	30 (50%)	24 (80%)	5 (16.7%)	1 (3.3%)

Patients with conception of < 7 weeks have high rate of successful abortion (93.3%) compared to 7- 9 weeks (80%). Only 6.7 % of cases belonged to < 7 weeks of gestational age required surgical intervention due to incomplete abortion as compared to 16.7% of cases 7- 9 weeks of gestational age. Only 3.3 % cases of 7- 9 weeks of gestational age had no response to combi pack (MTP Pill), hence surgical evacuation done.

Discussion

In India, MTP act was passed in 1971 to prevent unsafe and illegal abortion. [1] As per the guidelines for medical abortion in India, medical abortion is only offered only to those patients, who are ready for minimum three follow-up visits, can understand the instruction, ready for surgical procedure if failure or excessive bleeding, good family support and easy access to appropriate healthcare facility.[15]

In our study shows majority of women in both groups were seeking for MTP pill are of 26-30 years of age (46.7% and 40%). Whereas no patients were less than 19 years, compare to study by Sarojini et al 3.8% patients were less than 19 years of age. [16] Here, majority of women in the Group 1 (< 7 weeks) were Gravida 3 (53.3%) compared to 30% women in the Group 2 (7- 9 weeks). Most of women in Group 2 (7- 9 weeks) were Gravida 2 about 40%. 13.4% and 20% patients were primigravida respectively in group 1 and group 2. Whereas in the study by Sarojini majority of patients were multigravida. [16]

In our study tested a regimen of Mifepristone 200mg on day1 and patient self-administration at home of the 800µg sublingually/vaginally Misoprostol on day3 by MTP protocol. The results confirm that, this is a safe and effective regimen for early pregnancy termination. The overall success rates for various gestational ages ranged from 80% to 93.3%. Study of Geeta lebageri report the results of study of Mifepristone and Misoprostol in women with pregnancies of up to seven weeks duration, they administered 200mg mifepristone on day 1 with oral Tab Misoprostol 400µg on day3 in 50 patients seeking MTP at Gulbarga in 2004-2005 observed 98% patients aborted safely. [17] Study of Chunni and Chandrashekhar on 112 women for MTP of 63 days

duration with oral Mifepristone 200 mg followed by oral Misoprostol 400 mcg 48 h apart. The rates of complete abortion were 92.8%, 83%, and 80% in the <49 days group, 50–59 days group, and 57–63 days group, respectively.[18] Study of Kant Anitha, Taneja Indu conducted at Department of Obstetrics and Gynecology, Escorts hospital and Research center limited, Faridabad during 2003, included 120 pregnant woman up to 49 days of gestation. They administered 200 mg of Mifepristone on Day I, 400 µg of oral Misorostol on Day III. Success rate were 95.8%. [19] Similarly Schaff et al reported success rate of 97% with 200mg Mifepristone followed by 800 microgram Misoprostol vaginally. [20]

In our study, rates for various gestational ages ranged from 6.7% to 16.7% of cases requiring surgical intervention due to incomplete abortion which is slightly higher than 2-5% reported by Ashok et al. In a study by Sarojini et al, surgical evacuation required in 90.4% and 1-2% required surgical evacuation for heavy bleeding and 2-3% need surgical evacuation due to incomplete abortion.[16] Schaff et al reported 2.4% surgical evacuation rate and spitz IM, and Bardin CW reported 14.65% surgical evacuation rate respectively. [20,21]

In our study, 3.3% cases had no effect. which is higher than the 0.6% rate reported by Ashok et al and Schaff et al reported 0.3% of cases of the same [8,20] Ongoing pregnancy rate with a range of 0.8% to 1.5% has been reported by Spitz IM et al. [21] In our study, pain related side effect like abdominal pain for various gestational ages ranged from 80 to 86.7% in different groups. Where as in study of Schaff et al, the abdominal cramping was reported 36.9% -91.8%. [20]. About nausea, vomiting and diarrhoea, our study reported for various gestational ages in compared groups ranged from 33.3% to 43.3%, from 23.3% to 30% and from 16.7% to 23.3% respectively, whereas in the study of Schaff et al, nausea was reported in 44.6 and 91.8%. [18], also in study of El-Refaey et al, its incidence reported was 70%, 44%, and 36% respectively.[22]

Regarding the route of Misoprostol, the sublingual and vaginal administration routes had similar efficacies. Sublingual administration of Misoprostol induces stronger uterine contractions after a shorter interval than when misoprostol is administered vaginally.[23]

A randomised pilot study compared 800 µg Misoprostol when administered either vaginally or sublingually after Mifepristone pretreatment. [24] The study included 224 women up to 63 days of gestation. The proportions of women with complete abortion were 93.8 and 98.2% after vaginal and sublingual administration, respectively, suggesting that the sublingual route might be superior to the vaginal route in efficacy. Another small study reported a high rate of complete abortion (98.9%) after sublingual administration of 600 µg Misoprostol among 96 women. [25]

Conclusion

Medical abortion is effective and safe if carried out under medical supervision. The standard protocol followed by the hospital was oral administration of 200 mg Mifepristone followed by (48 hours later) oral/ sublingual/ vaginal/buccal administration of Misoprostol 800 mcg. The success rate of the combination was excellent and correlated with gestational age. Medical abortion offers great potential for improving abortion access and safety, as it requires less extensive infrastructure than surgical abortion. Also there is, reduced cost, no need for anesthesia and operation theatre facilities, and maintains patient's need for privacy. The disadvantages are unpredictable outcome in few patients, longer duration of bleeding, and potential

risk of fetal malformation if it fails to cause abortion. The factors that may prevent the women from accepting the medical method of termination of pregnancy is the abdominal cramps and heavy bleeding, duration of bleeding (average 7–10 days), and the need to follow-up after 2 weeks for clinical examination and sonography. Sublingual and vaginal Misoprostol have similar efficacy, but vaginal administration is associated with a lower frequency of adverse effects. Also we would like to suggest that regular use of FOGSI MMA card for follow in medical abortion services should be incorporated in day to day practice.

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