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A prospective comparative study of 3 different regimens involving mifepristone and oral/ vaginalmisoprostol combination in medical termination of pregnancy at less than 9 weeks gestation

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Abstract
Background and Objectives: Medical abortion with a combination of mifepristone and a prostaglandin analogue (Misoprostol) is a well-established and adequately studied as an alternative to surgical abortion in early pregnancy for many years now but still no consensus has been reached regarding superiority of one route and dosage. This study is an attempt to compare efficacy in terms of rate of complete abortion, side effects and women's perceptions of three mifepristone/misoprostol regimens and to study the effect of continued oral misoprostol for one week in medical termination of pregnancies of less than nine weeks gestation.
Materials and Methods: Abortion seeking women of less than nine weeks period of gestation were included in this study and were divided into three groups: GROUP I also referred as O+O group, GROUP II the V+O group, and GROUP III referred as V ONLY group. This is an outpatient regimen requiring minimum three visits on day 1, 3 and 15. Initially, tablet mifepristone 200 mg was administered orally in all three groups on day 1. This was followed on day 3 by oral misoprostol 0.8 mg in group I and vaginal 0.8 mg misoprostol in group II & III. It was placebo controlled. Patients were sent home after 4 hour observation period. The oral group and one of the vaginal groups i.e. group I and II continued 0.4 mg of oral misoprostol twice daily for 7 days. Final assessment was done on day 15.
Results: All three groups were comparable in terms of rates of complete abortion: Group I 93.06%; II 94.44% and group III 93.06%. Incomplete abortion occurred in 9.72% women in group I, 5.52% in group II and 6.94% women in group III. 73.61 % of women in group I, 76.38% women in group II and 77.76% in group III suffered from lower abdominal pain & cramping. 100% women cited oral route as their preferred route and overall 199 (92%) women were satisfied with treatment, 12(5.6%) were unsure and 5(2.4%) were dissatisfied. For future purposes 100 % women cited medical abortion to be their preferred mode compared to surgical one
Conclusion: In light of previous studies establishing superiority of vaginal route over oral, continuation of misoprostol for 7 days possibly improved the efficacy for oral misoprostol group(group I) but it did not seem to further increase the efficacy for vaginal Misoprostol (group II) as all three groups were of comparable efficacy. Additional misoprostol did not shorten the duration of bleeding or induction abortion interval compared to group not continuing additional one week misoprostol. Successful abortion was associated more with lower gestational age,multigravidas and multiparas.Oral group had higher frequency of nausea, vomiting and diarrhea than vaginal administration. Statistically insignificant but still lower number of women were satisfied in the end with the treatment in the oral group compared to vaginal groups despite oral mode being the preferred mode. Additional larger studies are required on initial oral misoprostol administration and its continuation to establish its equivalence to vaginal route.

Keywords: Mifepristone, oral, vaginal, misoprostol

Introduction
Induced abortion is the third commonest means of fertility control next to sterilization and oral contraceptives [1]. According to latest available worldwide data, around 121 million unintended pregnancies occurred each year, 61% (73.3 million) of which, ended in abortion [2]. In India alone 15.6 million annual abortion were estimated to occur [3].

This data makes one realize the importance of dealing with unplanned pregnancies in a proper manner.

Over the past few decades, numerous studies have been conducted for exploring medical methods of inducing abortion [4]. Abortifacient agents such as antiprogesterone (Mifepristone) and prostaglandins (Misoprostol) were approved by United States Food & Drug Administration in 2000 for first trimester abortions [5].

Misoprostol is established and proven to be preferred over gemeprost [6]. Misoprostol alone was also explored as an alternative but combination of mifepristone along with misoprostol has established itself as gold standard in various routes and regimens over the decades [7].

After pretreatment with mifepristone, both oral and vaginal routes of misoprostol have been tried successfully. A high patient acceptance rate was seen using outpatient oral misoprostol [8] as it can avoid uncomfortable per vaginal examination and provides more privacy during abortion process, but vaginal route offers advantage of increased effectiveness, shorter induction abortion time and lesser side effects [9].

Somehow efficacy of oral route can be increased, and amount of vaginal bleeding decreased post medical abortion without markedly increasing side effects, the acceptability of medical abortion can be further increased by leaps and bounds. My study is an attempt to find an effective, simple and safe mifepristone/misoprostol regimen for medical termination of pregnancy up to 9 weeks of gestation.

Materials and Methods

In this comparative study done between September 2019 and May 2021, based on inclusion-exclusion criteria, we included 216 OPD based willing and consenting pregnant females requesting legal MTP. As per inclusion criteria healthy pregnant women of age 18 years or above with good general health with confirmed single intrauterine pregnancy up to 9 weeks(as per ultrasound) were included. Inclusion criteria also required hemoglobin of more than 10g/dl with no other medical or surgical contraindications for the procedure and ladies willing to use contraception other than hormonal or intrauterine contraceptive devices until the first menses after abortion. After explaining the study to them and making sure they're willing and able to participate, they were included in the study.

We excluded patients with gestation age > 9 weeks, missed abortions / incomplete abortions/ inevitable abortions, suspected case of ectopic pregnancy, any previous attempts at terminating the present pregnancy, pregnancies with IUD in situ, medical conditions contraindicating the use of mifepristone (e.g. adrenal disease), medical conditions contraindicating the use of misoprostol (e.g. hypertension, mitral stenosis, bronchial asthma, glaucoma, sickle cell anaemia, hypotension), allergy to mifepristone or misoprostol, any history or evidence of thromboembolism, liver disease or pruritus of pregnancy, previous surgery of uterine cervix. Breast-feeding ladies and women smoking >10 cigarettes over the past two years or refusing consent for the study were also left out.

All these women were thoroughly investigated before MTP. The workup included: details of patient, investigations including urine pregnancy test, viral markers, complete blood counts, Examination of vital signs, abdominal and pelvic examination, USG for period of gestation and Counselling regarding type of contraceptive. The women who were included in the study were explained the study and provided with patient information sheet, after which they were asked to sign an informed consent form. The patients were divided into three groups randomly.

GROUP I or O + O group: It is the Mifepristone-Oral Misoprostol group. In this group, on Day 1 - 200 mg of tablet Mifepristone was given orally. Patient was counselled about symptoms and asked to come to the hospital if the symptoms were severe. On Day 3-800 µg of Misoprostol tablet was given orally along with vaginal placebo. Further for one week i.e., Day 4-10 Oral misoprostol 400 µg twice daily was continued. Patient was asked to return to hospital on Day 15 for final evaluation.

GROUP II i.e V +O Group:It is the Mifepristone -Vaginal Misoprostol with continued Oral misoprostol group. On Day 1 -- 200 mg of Mifepristone was given orally to patients. They were counselled about symptoms and asked to return to the hospital if the symptoms are severe. On Day 3 -- 800µg of tablet Misoprostol was kept vaginally along with oral placebo tablet. Patients in this group were further continued with daily oral misoprostol 400ug for one week i.e., Day 4-10. Patients were asked to return to hospital on day 15 for final evaluation.

GROUP III: V ONLY group: It is also a Mifepristone - Misoprostol Group but without continued oral misoprostol. On Day 1 -- 200 mg of Mifepristone was given orally. They were counselled about symptoms and asked to return to the hospital if the symptoms are severe. On day 3 -800 µg of Misoprostol was kept per vaginally along with oral placebo. Analgesics were not routinely administered. Further for one-week i.e., day 4-10 they continued oral placebo twice a day.

Since the Mifepristone – Misoprostol protocol is an out-patient procedure, admission was done only if required (if the patient requests admission or on medical grounds). Patients were administered Tab mifepristone 200 mg orally on day one in all 3 groups. They were required to stay in the hospital for 4 hours observation period, during which vitals were monitored hourly including blood pressure and pulse rate. At the end of observation period females were allowed to go home after per vaginal examination and were asked to return to hospital for next visit on day 3 for misoprostol administration. All the women were given same hospital supply of sanitary pads to be brought to hospital for review of bleeding on next visit in addition to an entry sheet to record the days and amount of vaginal bleeding (in comparison with their usual menstrual periods), timing of expulsion of products of conception and any side-effects experienced. In case the woman was illiterate, any literate attendant was asked to note down the required details. Analgesics were not routinely administered.

Patients were asked to follow up on day 15. Vital charting including blood pressure and pulse rate, physical examination including vaginal examination and ultrasound of pelvis.

Blood tests only if required were carried out.

Treatment was considered successful if on Day 15 follow up visit if : ultrasound showed a well-defined endometrial line with a maximum thickness of < 15 mm and absence of any significant retained products of conception, there was absence of vaginal bleeding, uterus felt empty on a per-vaginal examination. If evacuation was not complete even after 15 days, it was considered as failure of method and the patients were offered alternative methods of termination like suction evacuation.

Results

All three groups were comparable in terms of rate of complete Abortion: Group I 67 (93.06%); II 68(94.44%) and group III 67(93.06%). Incomplete abortion occurred in 9.72% women in group I, 5.52% in group II and 6.94% women in group III.(p-value=0.5726)

The mean age of subjects (n=216) across 3 groups of our study was 32 years with age range of 22-37 years. Mean age in group I was 32 years; 31 years in group II and 33 years in group III.

Out of 216 subjects, 2 (0.92%) study subjects belonged to upper class; 60(27.7%) to upper middle-class group, 115(53.24%) to middle class, 29(13.4%) to lower middle class and 10 (4.6%) were from lower class of socioeconomic status

Total number of primigravida women in our study was 11 while multigravida was 205. In group I (n=72) and II, primigravida were 5.56% while multigravida was 94.44%. In group III (n=72), primigravida were 4.17% and multigravida were 95.83%.When gravidity was compared against the number of successful abortions, the p-value was 0.0005 which was significant at significance level of 0.05 i.e., there was a significant difference between primigravida and multigravida in terms of successful abortion with medical methods. Out of total women in our study (n=216), 13 were nulliparous and 203 were parous. In group I, 6.94% were nulliparous while 93.06% patients were parous. In group II, 5.56% patients were nulliparous while 94.44% were parous. In group III, number of nulliparous and parous were same as that of group II. The p-value is 0.88662 when parity was compared with abortions which was not significant at significance level of 0.05 i.e., there is no significant difference between nulliparous and parous patients in terms of successful abortion with medical methods.

Mean gestational age in our study was 6.75 weeks with minimum of 5 weeks and maximum of 9 weeks. In group I, mean gestational age was 6.8 weeks while in group II it was 6.73 weeks. In group III mean gestational age was 6.72 weeks. The p-value is significant at significance level of 0.05 i.e., there is a significant difference between the groups in terms of successful abortion. Women with gestational age ≤ 7 weeks have significantly higher rates of complete abortion with medical methods as compared with patients with gestational age >7 weeks.

The mean duration of induction-abortion interval in our study was 7.63 hours with minimum of 2 hours and maximum of 48 hours. In group I, mean was 9.67 hours. In group II it was 6.27 hours and in Group III it was 6.94 hours.

Mean duration of bleeding in women in our study (n=216) was 6.33 days with minimum value of 4 days and maximum of 16 days. In group I, mean duration of bleeding days were 6.21 days while in group II, it was 6.29 days. In group III, mean duration of bleeding was 6.51 days. The p value is 0.56322. The result is not significant at p < 0.05. This concludes that there is no significant difference between three groups in terms of duration of bleeding and additional one week of oral misoprostol doesn't result in lesser duration of bleeding.

Complete abortion rates in group I was 93.06%, in group II were 94.4% and in group III were 93.06%. Incomplete abortion occurred in 9.72% women in group I, 5.52% in group II and 6.94% women in group III. Only one woman in the study had missed abortion and this occurred in group I. The p-value is 0.5726. The result is not significant at $p<.05$ i.e., there is no statistical difference between three groups in terms of efficacy (successful abortion)

Overall, 53(73.61 %) of women in group I, 55 (76.38%) women in group II and 56(77.7%) group III suffered from lower abdominal pain & cramping. 38 women in group I started with pain abdomen at ≤ 3 hours observation period and 15 more women started with pain abdomen after 3 hours. Similarly, in group II, 26 women initially experienced pain and cramping at ≤ 3 hours, while 29 new patients were added to the list >3 hours later. In group III 28 each patient complained of pain and cramping at both these instances.

41.66 % of women in group I, 36.12% women in group II and 22.22% in group III suffered from nausea in our study. (Table 10.2 and Figure 3)26.77 % of women in group I, 26.38% women in group II and 8.33% in group III suffered from vomiting in our study.(Table 10.3)34.72 % of women in group I, 30.55% women in group II and 13.89% in group III suffered from diarrhoea in our study. Risk of diarrhoea increased 2.2 times in the vaginal V Only group of continuing with oral misoprostol (V/O group).

4.16% of women in group I, 6.94% women in group II and 5.55% in group III suffered from fever in our study.

100% of the women stated oral route to be their preferred route of drug administration at the initiation of treatment. Lower numbers of women were satisfied (88.89%) with the treatment in the oral group (Group I) compared to vaginal groups: group II (94.44%) and III (93.05%) but the results were not statistically significant. Number of people not satisfied with treatment were comparable in all three groups i.e., 2.77% each in group I and II; 1.38% in group III. Women who couldn't decide on treatment satisfaction were 8.33%, 2.77% and 1.38% respectively in the three groups. All the women enrolled in the study regardless of the outcome suggested that they would still prefer medical method instead of surgical one, if such a need must arise in future

Discussion

In our study complete abortion rates in group I, II and III were 93.06%, 94.4% and 93.06%, respectively. Incomplete abortion occurred in 5.56 % women in group I, 5.52% in group II and 6.94% in group III. Only one woman in the study had missed abortion and this occurred in group I, which was mostly comparable to study by Von hertzen H *et al*. (2003) [10] where complete abortion percentages were 92.3%, 94.7% and 93.5% in the O/O, V/O and V-only group respectively when all the undetermined cases were treated as failure.

El Refaey (1995) [9], Sudip Mukhopadhyay *et al*. (2020) [11], Dalenda c *et al*. (2009) [12], Farhadifar *et al*. (2016) [13], Jyoti shetty (2016) [14] and other studies have already established vaginal route of misoprostol to be more efficient than oral in this regard. But in our study the efficacy in the form of complete abortion rates in three groups were comparable (p=0.5726).

Out of total 13 nulliparous women, only 11(84.61%) resulted in successful abortion, while 2 women (15.38%) landed with incomplete abortion; however out of total 191 multiparous 191(94.09%) had complete abortion and 11women (5.42%) had incomplete abortion. Similar observations were made in systematic reviews by Abubekaer (2020) [15] and Ian ferguson (2020) [16] that the

complete abortion rate, both crude and adjusted for gestational age, was higher in parous women.

In the present study women with ≤ 7 weeks gestation had significantly higher rates (98.46%vs 47.61%) of complete abortion as compared to ones with gestational age > 7weeks.There is statistically significant difference between the two groups in terms of successful abortion. Singh D *et al* (2017) [17], Mukhopadhyay (2020) [11] observed similar trend of lower gestational age being associated with better out comes in terms of complete abortion.

Lower abdominal pain and cramping was seen more in Group I in the initial 3 hours, however overall incidence was comparable in three groups. Nausea was associated more with oral group (Group I) starting from first three hour period itself compared to the two vaginal groups (groups II and III),however later at the 15th day follow up visit rate of nausea was comparable in the two groups continuing with oral misoprostol for 7 more days(Groups I and II). Group III didn't witness any significant rise in nausea at the follow up visit. This was statistically significant result (p-value=0.032317). Vomiting too, followed the same trend of having higher association with oral route of misoprostol (group I) than vaginal groups (groups II and III) at 3-hour period and later the rates being comparable and higher in group I and II, while the vaginal group without any additional 1-week misoprostol maintained approximately same rate of nausea even at day 15.This was statistically significant too. In case of Diarrhea same findings were repeated and were statistically significant. These findings are in line with results from previous studies by El-Refaey *et al*. (1995) [9]; Honkanen H *et al*. (2004) [18]; Tang *et al*. (1998) [98]. This is also in line with the pharmacokinetics of misoprostol since oral route is associated with faster absorption and higher peak concentration and hence higher side effects.

Honkanen H *et al*. (2004) [18] who had reported higher association of fever with vaginal route. Deepika Nautiyal *et al*. (2015) [19], also found side effects comparable in all the groups except diarrhea being more in the oral groups and fever being significantly higher in the vaginal group.

A strong preference for oral route was observed in my study prior to treatment initiation. All the 216 women (100%) stated oral route to be their preferred route over vaginal owing to it being less painful and offering more privacy. This preference was more than in study by Ngai SW *et al*. [20] where 90% subjects preferred oral route and Kumar mistri (2020) [11] where 88.8% females had chosen oral route.

Out of total 195 women in the present study who were of gestational age 7 weeks or lower,190 i.e. 97.43% were satisfied with their treatment experience; whereas out of total 21 females of more than 7 weeks gestational age, only 9 were satisfied which is equivalent to42.85%. Lower gestational ages were associated with increased patient satisfaction too in the multicenter study, by Honkanen H *et al*. (2004) [18] and other studies. The majority of women, majority of women stated that they would choose medical abortion again should the need arise, which is in accordance with other studies (Mehta *et al*. 2019; Mistri 2000; Honaker H *et al*.) [21, 11, 18]

Table 1: Distribution of induction-abortion interval

S. No.	Induction Abortion	Group-I {O+O}		Group-II {V+ O}		Group-III {VONLY}	
	Interval (IN HRS.)	No of patients	%age	No of patients	%age	No of patients	%age
1	1-2	09	12.6	14	19.44	12	16.67
2	3-4	40	55.33	49	68.06	50	69.44
3	5-24	03	4.22	08	11.11	08	11.11
4	>24	19	26.76	01	1.39	02	2.78
	Total	71		72		72	

Table 2: Distribution of induction-abortion interval

S. No.	Induction Abortion	Group-I {O+O}		Group-II {V+ O}		Group-III {VONLY}		p-Value
	Interval	No of patients	% age	No of patients	%age	No of patients	%age	
1	<4hours	49	68.05	63	87.5	62	86.11	0.585624
2	≥4 hours	22	30.55	9	12.5	10	13.88	
p-value=0.585624								

Table 8: Distribution of duration of bleeding

S. No.	Duration of	Group-I {O+O}		GROUP-II {V+ O}		GROUP-III {VONLY}		p-Value
	Bleeding	No of patients	% age	No of patients	%age	No of patients	%age	
1	4-7days	55	76.39	60	83.33	62	86.11	
2	8-10days	10	13.89	08	11.11	05	6.94	
3	>10days	07	9.72	04	5.56	05	6.94	**0.56322**
	TOTAL	72		72		72		

p-value=0.56322

Table 3: Efficacy of three regimens of medicalabortion in women

S. No.	Results	Group-I {O+O}7DAYS		Group-II {V + O}7DAYS		Group-III {VONLY}		p-Value
		No of patients	%age	No of patients	%age	No of patients	%age	
1	Complete Abortion	67	93.06	68	94.44	67	93.06	
2	Incomplete Abortion	04	5.56	04	5.56	05	6.94	0.5726
3	Missed Abortion	01	1.389	00	00	00	00	
	TOTAL	72		72		72		

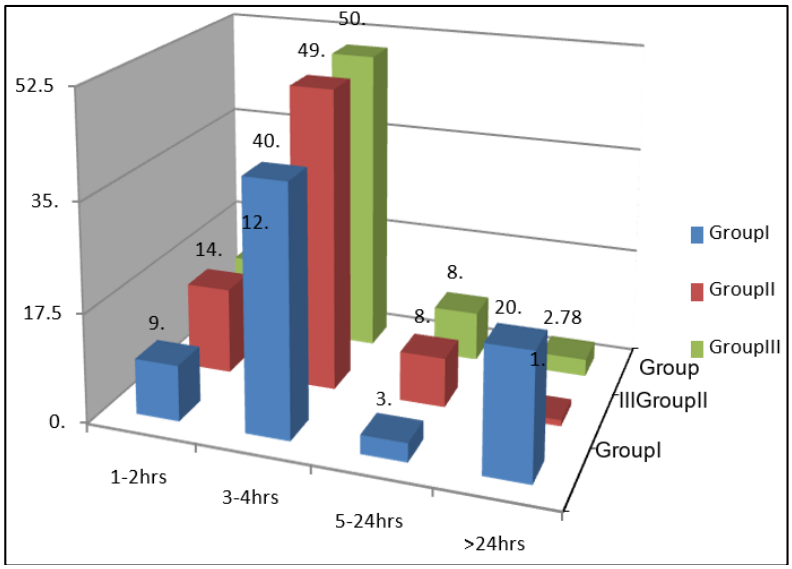

Fig 1: Induction-abortion interval (INHRS)

Conclusion

Additional 0.4 mg of oral misoprostol twice daily for one week seems to increase the efficacy of oral route (Group I) to reach at par with the vaginal one (group II and III). For pregnancies ≤ 7 weeks gestations, no difference in efficacy was observed between the three treatment regimens and had better rates of complete abortion compared to women with pregnancies >7 weeks (98.46% vs. 47.61%).

All three methods in the present study were found to be highly efficacious. Even if improved results with oral route could be at the cost of higher side effects but none of the side effects were serious enough for any subject to return to hospital and hence can be considered acceptable. Hence, it seems fair to provide women with adequate information and let her decide for herself which route is suitable to her, without compromising on efficacy. Larger scale studies to establish equivalence of oral route to vaginal route with lowest required additional dosing of misoprostol could be undertaken in future

References

1. Kapur K, Joneja G, Biswas M. Medical Abortion-An Alternative to Surgical Abortion. Medical Journal Armed Forces India. 2006;62(4):351-353.
2. Bearak J, Popinchalk A, Ganatra B, Moller A, Tunçalp Ö, Beavin C, *et al*. Unintended pregnancy and abortion by income, region, and the legal status of abortion: estimates from a comprehensive model for 1990–2019. The Lancet Global Health. 2020;8(9):e1152-e1161.
3. Singh S, Shekhar C, Acharya R, Moore A, Stillman M, Pradhan M, *et al*. The incidence of abortion and unintended pregnancy in India, 2015. The Lancet Global Health. 2018;6(1):e111-e120.
4. Kulier R, Kapp N, Gülmezoglu A, Hofmeyr G, Cheng L, Campana A. Medical methods for first trimester abortion. Cochrane Database of Systematic Reviews. 2011.
5. Hausknecht R. Mifepristone and misoprostol for early medical abortion: 18 months experience in the United States. Contraception. 2003;67(6):463-465.
6. Ashok P, Penney G, Flett G, Templeton A. An effective regimen for early medical abortion: a report of 2000 consecutive cases. Human Reproduction. 1998;13(10):2962-2965.
7. Patel A. Medical termination of pregnancy with mifepristone and misoprostol combined therapy: Evaluation of its safety and efficacy in clinical practice in India. Asian Journal of Biomedical and Pharmaceutical Sciences. 2015;05(46):7-12.
8. Ravn P, Rasmussen Å, Knudsen U, Kristiansen F. An outpatient regimen of combined oral mifepristone 400 mg and misoprostol 400 µg for first-trimester legal medical abortion. Acta Obstetricia et Gynecologica Scandinavica. 2005;84(11):1098-1102.
9. El-Refaey H, Rajasekar D, Abdalla M, Calder L, Templeton A. Induction of abortion with mifepristone (RU 486) and oral or vaginal misoprostol. N Engl J Med. 1995 Apr 13;332(15):983-7.
10. Von Hertzen H, Honkanen H, Piaggio G, Bartfai G, Erdenetungalag R, Gemzell- Danielsson K. WHO Research Group on Post-Ovulatory Methods for Fertility Regulation. WHO multinational study of three misoprostol regimens after mifepristone for early medical abortion. I: Efficacy. BJOG. 2003 Sep;110(9):808-18.
11. Kumar Mistri P, Mukhopadhyay S. Efficacy and acceptability of medical abortion with mifepristone and misoprostol in early pregnancy. Indian Journal of Obstetrics and Gynecology Research. 2020;7(1):33-38.
12. Dalenda C, Ines N, Fathia B, Malika A, Bechir Z, Ezzeddine S. Two medical abortion regimens for late first-trimester termination of pregnancy: a prospective randomized trial. Contraception. 2010 Apr;81(4):323-7.
13. Farhadifar F, Shahgheibi S, Moradi G, Memar FM. Comparison of Oral Versus Vaginal Misoprostol for Legal Abortion in Iranian Women. Journal of Clinical Gynecology and Obstetrics. 2016;5(2):59-63.
14. Shetty J MNV. Medical abortion by mifepristone with oral versus vaginal misoprostol. J Obstet Gynecol India. 2006;56(6):529-31.
15. Abubeker FA, Lavelanet A, Rodriguez MI, Kim C. Medical termination for pregnancy in early first trimester (≤ 63 days) using combination of mifepristone and misoprostol or misoprostol alone: A systematic review. BMC Womens Health. 2020 Jul 7;20(1):142.
16. Ferguson I, Scott H. Systematic Review of the Effectiveness, Safety, and Acceptability of Mifepristone and Misoprostol for Medical Abortion in Low- and

Middle-Income Countries. Journal of Obstetrics and Gynaecology Canada. 2020;42(12):1532-1542.e2.
17. Singh D, Sarkar D. Medical Abortion in Early Pregnancy By oral Mifepristone And oral Misoprostol. IOSR Journal of Dental and Medical Sciences. 2017;16(05):19-21.
18. Honkanen H, Piaggio G, Hertzen H, Bártfai G, Erdenetungalag R, Gemzell- Danielsson K. WHO Research Group on Post-Ovulatory Methods for Fertility Regulation. WHO multinational study of three misoprostol regimens after mifepristone for early medical abortion. BJOG. 2004 Jul;111(7):715-25.
19. Nautiyal D, Mukherjee K, Perhar I, Banerjee N. Comparative Study of Misoprostol in First and Second Trimester Abortions by Oral, Sublingual, and Vaginal Routes. J Obstet Gynaecol India. 2015 Jul;65(4):246-50.
20. Ngai SW, Tang OS, Ho PC. Randomized comparison of vaginal (200 microg every 3 h) and oral (400 microg every 3 h) misoprostol when combined with mifepristone in termination of second trimester pregnancy. Hum Reprod. 2000 Oct;15(10):2205-8.
21. Mehta L, Agrawal G. Comparative study of efficiency of vaginal versus oral misoprostol along with mifepristone for first trimester medical termination of pregnancy. International Journal of Reproduction, Contraception, Obstetrics and Gynecology. 2019;8(6):2322.