e-ISSN: 0976-822X, p-ISSN:2961-6042

Available online on http://www.ijcpr.com/

International Journal of Current Pharmaceutical Review and Research 2023; 15(8); 197-202

Original Research Article

A Prospective Observational Study Assessing the Efficacy and Acceptability of Medical Abortion with Mifepristone and Misoprostol in Early Pregnancy

Rashmi Kumari[1], Priti Kumari[2], Krishna Sinha[3]

[1]Senior Resident, Department of Obstetrics and Gynaecology, JLNMCH, Bhagalpur, Bihar, India
[2]Senior Resident, Department of Obstetrics and Gynaecology, JLNMCH, Bhagalpur, Bihar, India
[3]Associate Professor, Department of Obstetrics and Gynaecology, JLNMCH, Bhagalpur, Bihar, India

Received: 14-01-2023 / Revised: 10-03-2023 / Accepted: 25-04-2023

Corresponding author: Dr. Priti Kumari

Conflict of interest: Nil

Abstract

Aim: The current study was planned to evaluate the efficacy and acceptability of medical abortion with low dose mifepristone (200mg) and oral or vaginal 400 mcg misoprostol in early pregnancy (≤ 7weeks of gestation) in Indian women.

Methods: A prospective observational study was conducted in the Department of Obstetrics and gynaecology, JLNMCH, Bhagalpur, Bihar, India in between the duration of 1 year. A total of 100 early pregnancy abortion seeking women with amenorrhoea of less than or equal to 7 weeks (49 days) from the first day of last menstrual period were taken and counselled to participate in the study.

Results: There were no significant differences in baseline characteristics between groups in age or parity. The complete abortion rate did not differ significantly between the groups. In the early group complete abortion rate was 92% and in the late group 94%. The majority of women in both groups were satisfied with the treatment. The participants were also satisfied with sufficient information received before the abortion and the pain medication. In both groups, most of the women answered that they were either very satisfied or satisfied with feeling calm and safe during the abortion, the treatment and the bleeding met their expectations. No significant difference was observed in experienced pain and duration of bleeding.

Conclusion: Nevertheless, medical abortion is a revolutionary technique and our study results indicate that mifepristone-misoprostol medical abortion can complement available surgical services and help meet the long-standing need for safe abortion.

Keywords: Medical Abortion, Mifepristone, Misoprostol, Methods of Abortion.

This is an Open Access article that uses a funding model which does not charge readers or their institutions for access and distributed under the terms of the Creative Commons Attribution License (http://creativecommons.org/licenses/by/4.0) and the Budapest Open Access Initiative (http://www.budapestopenaccessinitiative.org/read), which permit unrestricted use, distribution, and reproduction in any medium, provided original work is properly credited.

Introduction

Medical methods for pregnancy termination have become the method of choice for many women worldwide. [1] In order to improve women's reproductive health every effort should be made to reduce unwanted pregnancies. Yet, every year, millions of women are exposed to unprotected intercourse or encounter contraceptive failure, involving risk of unwanted pregnancy. These huge numbers of unwanted pregnancies are terminated by induced abortions. [2] Unsafe abortion which can cause severe illness and death should be prevented at every cost. The safety and efficacy of induced abortion is therefore of global public health importance. Termination of such an unwanted pregnancy has been legal in India (MTP Act, 1971) for more than three decades. [3] Though safe in hands of expert, the surgical abortion performed by the untrained practitioner under unhygienic conditions, is associated with high maternal morbidity and mortality. Medical methods emerged as an alternative to surgical abortion with the discovery of prostaglandins in the early 1970s. [4,5,6] Their use has evolved in the last two decades and various drugs have been used for first trimester medical abortion. Several studies have explored utilization of mifepristone, methotrexate and various prostaglandins with different doses, routes and intervals of administration. [7] The administration of mifepristone, a powerful antiprogestin, coupled with a prostaglandin is a highly effective medical method of terminating pregnancy. [8] Of the most widely used prostaglandins, misoprostol shows the greater promise for use in developing countries. It can be administered orally and inexpensive stable at ambient temperature and widely available. [9]

Currently, antiprogesterone mifepristone orally followed two days later by prostaglandin analogue misoprostol (orally/vaginally) for this purpose is very promising. [2] This combination is registered as a non-surgical alternative to surgical termination of early intrauterine pregnancy. The recommended dose of mifepristone in USA is 600mg, but it has been shown by the World Health Organization and others that a lower dose of mifepristone (200 mg) is just as effective as the 600-mg dose. [10,11]

This is especially important for reducing the cost of medical abortions, as it would mean taking only one 200-mg tablet instead of three 200-mg tablets. Nevertheless, medical abortion is a revolutionary technique and our study results indicate that mifepristone-misoprostol medical abortion can complement available surgical services and help meet the long-standing need for safe abortion. The current study was planned to evaluate the efficacy and acceptability of medical abortion with low dose mifepristone (200mg) and oral or vaginal 400 mcg misoprostol in early pregnancy (≤ 7weeks of gestation) in Indian women.

Materials & Methods

A prospective observational study was conducted in the Department of Obstetrics and gynaecology, JLNMCH, Bhagalpur, Bihar, India in between the duration of 1 year (Feb 2020 Jan 2021). A total of 100 early pregnancy abortion seeking women with amenorrhoea of less than or equal to 7 weeks (49 days) from the first day of last menstrual period were taken and counselled to participate in the study. All women received standardized counseling about the procedure and their most common side effects. An informed consent form was signed regarding participation in the study. Once they decided regarding the choice of method (medical or surgical) the abortion procedure was carried out according to the chosen method. Those who accepted medical method were given a choice regarding route of administration of misoprostol (vaginal or oral) and the reason for choosing a particular route of administration was recorded. The participants were also explained about the types of surgical abortion available at the clinic and that this method was nearly 100% effective. Explicit comparisons between medical and surgical abortion were avoided, however, so as not to bias women's selection.

The inclusion criteria were ultrasound-confirmed intrauterine pregnancy up to 70 days of gestation, willingness to administer misoprostol at home, age 18 years or older, hemoglobin >100 g/L, ability to understand the instructions, and absence of any known health problems or clinical findings that could affect the patient's safety during the study. Concerning own choice, the study was not designed as a randomized trial. Exclusion criteria were any contra- indication to receive mifepristone or misoprostol (anemia, breast- feeding, liver disease, bleeding disease) and pregnancy length of

>70 days of GA. Women declining to participate in the study were not recorded.

All women included in the study were allocated into two groups by GA. The first group included women pregnant with a GA up to 63 days and the second group included women with a GA between 64 and 70 days.

Procedure

Specially trained midwives provided information, and doctors were responsible for the inclusion of women in the study in all clinics. During the first visit to the abortion clinic, women swallowed 200 mg of mifepristone (Mifegyne®, Exelgyn®) on site and were provided with 1200 µg of misoprostol (6 tab- lets of 0.2 mg of misoprostol Cytotec®, Pfizer), pain medication and a subject diary to log bleeding, pain and side effects that occurred during the treatment. Women were instructed to fill in the diary daily, starting on the day of mifepristone intake, to avoid recall bias. The participants were instructed to take four tablets of misoprostol vaginally at home 24– 48 hours after mifepristone administration. If bleeding had not started within 3 hours after misoprostol administration, women were instructed to take an additional two misoprostol tablets sublingually.

All women were scheduled for a second visit to one of the study sites approximately 4 weeks after the first appointment. For this visit, women were asked to return unused misoprostol tablets and/ or empty blisters and the diary. Women were asked about ongoing bleeding, any other symptoms and possible adverse events. Complete abortion was assessed using a low-sensitivity urine pregnancy test (1000 mIU/mL human chorionic gonadotropin) or transvaginal ultrasound examination to evaluate the treatment outcome. Ongoing pregnancy, heavy uterine bleeding or retained products of conception were treated according to the local guidelines of the study site. At follow-up, all women were asked to fill in questionnaires regard- ing satisfaction and their perceptions about the abortion procedure and preferred method of contraception. The questionnaire included seven statements on satisfaction such as: "I am satisfied with the treatment" and "I was given enough information before the procedure", where participants were to indicate their experience on a 5- point Likert Scale: 1—Very unsatisfied, 2—Unsatisfied, 3—Neutral, 4—Satisfied, and 5—Very satisfied. The statements in the questionnaire were analyzed individually and divided into three categories: 1 and 2 represented "not agreeing with the statement", 4 and 5 "agree- ing with the statement" and 3 was considered neutral. In addition there was

also one yes-or-no statement: "I would recommend home abortion to a friend in the same situation". The worst pain experienced during the abortion procedure was assessed on a scale from 1 to 10.

The primary objective of the study was to study efficacy in gestations up to and above 63 days with home use of misoprostol. Efficacy was defined as a complete abortion without any need for surgical or medical intervention due to incomplete abortion or on- going pregnancy. Secondary objectives included pain, bleeding, side effects and women's satisfaction and perception of home use of misoprostol.

Statistical Analyses

Continuous data were presented as means ± SD, range, and discrete data were presented as median and range. The normality of distribution was tested with the Shapiro–Wilk test. A com- parison of means between groups was performed using a Mann– Whitney U test. A comparison of categorical variables was made with Fisher's exact test. The significance level was set to a p-value ≤0.05.

Result

Table 1: Patient characteristics

	Gestational age	
Characteristic	**≤63 days**	**64–70 days**
Age in years, median (range, IQR; no. of women)	27 (18–46)	28 (18–47)
BMI, mean ± SD (no. of women)	23.57 ± 3.57	24.06 ± 3.77
Parity, median (range, IQR; no. of women)	0 (0–3)	0 (0–5)
Gravidity, median (range, IQR; no. of women)	2 (0–9)	3 (0–10)
Pregnancy length, mean ± SD (no. of women)	46.84 ± 6.74	68.42 ± 1.8
Number of previous abortions, median (range, IQR; no. of women)	0 (0–5)	1 (0–7)
Miscarriage, median (range, IQR; no. of women)	0 (0–5)	0 (0–2)

There were no significant differences in baseline characteristics between groups in age or parity.

Table 2: Primary outcome

Success rate	**≤63 days (n = 50)**	**64–70 days (n = 50)**	**p**
Complete abortion, n (%)	46 (92)	47 (94)	0.710
Incomplete abortion			
Treated medically, n (%)	3 (6)	1 (2)	0.68
Treated surgically, n (%)	1 (2)	1 (2)	1
Ongoing pregnancy			
Treated surgically, n (%)	0 (0)	1 (2)	1

The complete abortion rate did not differ significantly between the groups. In the early group complete abortion rate was 92% and in the late group 94%.

Table 3: Secondary outcome—experience and perception of the abortion treatment

Gestational age	**≤63 days (n = 50)***	**64–70 days (n = 50)***	**p**
Satisfied with the chosen treatment			
Agreeing with the statement, n (%)	45 (90)	43 (86)	
Neutral, n (%)	3 (6)	5 (10)	
Not agreeing with the statement, n (%)	2 (4)	2 (4)	
Total score 1–5, mean ± SD	4.7 ± 0.72	4.38 ± 0.92	0.210
Feeling calm and safe during the abortion			
Agreeing with the statement, n (%)	40 (80)	36 (72)	
Neutral, n (%)	6 (12)	10 (20)	
Not agreeing with the statement, n (%)	4 (8)	4 (8)	
Total score 1–5, mean ± SD	4.11 ± 0.98	3.92 ± 1.11	0.220
Provided with sufficient information before the abortion			
Agreeing with the statement, n (%)	46 (92)	44 (88)	
Neutral, n (%)	3 (6)	4 (8)	
Not agreeing with the statement, n (%)	1 (2)	2 (4)	
Total score 1–5, mean ± SD	4.58 ± 0.62	4.46 ± 0.7	0.473
Treatment matching patient's expectations			
Agreeing with the statement, n (%)	39 (78)	38 (76)	
Neutral, n (%)	7 (14)	6 (12)	

Not agreeing with the statement, n (%)	4 (8)	6 (12)	
Total score 1–5, mean ± SD	4.19 ± 0.99	3.95 ± 1.14	0.136
Experienced bleeding matching patient's expectations			0.1
Agreeing with the statement, n (%)	19 (38)	25 (50)	
Neutral n (%)	20 (40)	16 (32)	
Not agreeing with the statement, n (%)	11 (22)	9 (18)	
Total score 1–5, mean ± SD	3.19 ± 1.25	3.48 ± 1.11	0.1
Experienced pain matching patient's expectations			
Agreeing with the statement, n (%)	18 (36)	27 (54)	
Neutral, n (%)	14 (28)	12 (24)	
Not agreeing with the statement, n (%)	18 (36)	11 (22)	
Total score 1–5, mean ± SD	2.98 ± 1.35	3.52 ± 1.15	0.01
Provided with sufficient pain medication			
Agreeing with the statement, n (%)	45 (90)	43 (86)	
Neutral, n (%)	4 (8)	5 (10)	
Not agreeing with the statement, n (%)	1 (2)	2 (4)	
Total score 1–5, mean ± SD	4.55 ± 0.84	4.47 ± 1	0.805
Recommendation of home abortion to a friend in the same situation			0.467
Agreeing with the statement, n (%)	48 (96)	46 (92)	
Not agreeing with the statement, n (%)	2 (4)	4 (8)	

The acceptability was similarly high in both groups (Table 3).

The majority of women in both groups were satisfied with the treatment. The participants were also satisfied with sufficient information received before the abortion and the pain medication. In both groups, most of the women answered that they were either very satisfied or satisfied with feeling calm and safe during the abortion, the treatment and the bleeding met their expectations.

Table 4: Pain and bleeding: median, range and IQR

	Gestational age		p
	≤63 days	64–70 days	
Pain intensity 1–10	7 (3–10, 4; n = 55)	7 (0–14, 4; n = 91)	0.32
Bleeding days	14 (2–28, 6; n = 73)	15 (4–31, 8; n = 114)	0.1
Duration of heavy bleeding, days	2 (0–10, 3; n = 69)	3 (1–14, 3; n = 109)	0.34
Duration of moderate bleeding, days	5 (0–19, 4; n = 70)	5 (1–27, 5; n = 110)	0.70
Duration of spotting	7 (1–20, 5.5; n = 71)	7 (0–24, 7; n = 96)	0.24

No significant difference was observed in experienced pain and duration of bleeding.

Discussion

Estimated annual number of induced abortion of India is 6.7 million. Most of these abortions are performed under unsafe and undesirable conditions, making abortion a vital reproductive health issue for Indian women. Unsafe abortion is a major cause of maternal mortality in India. [3] Medical method of inducing abortion has always fascinated obstetricians. Mifepristone or RU-486 was invented in France in 1980 and has been used as an abortifacient for medical termination of pregnancy for over two decades. [12] The administration of mifepristone, a powerful antiprogestin, coupled with a prostaglandin (misoprostol) is a highly effective medical method of terminating early pregnancy. Provision of safe abortion to the full extent of the law is an important component of reproductive health services. [13] In developing countries, where the demand for abortion services is high, such as India, the need for safe and effective alternatives to surgical abortion is great. The recommended dose of mifepristone in USA is 600mg, but it has been shown by the World Health Organization and others that a lower dose of mifepristone (200 mg) is just as effective as the 600-mg dose. [14] This is especially important for reducing the cost of medical abortions, as it would mean taking only one 200-mg tablet instead of three 200-mg tablets.

There were no significant differences in baseline characteristics be- tween groups in age or parity. The complete abortion rate did not differ significantly between the groups. In the early group complete abortion rate was 92% and in the late group 94%. The majority of women in both groups were satisfied with the treatment. The participants were also satisfied with sufficient information received before the abortion and the pain medication. In both groups, most of the women answered that they were either very satisfied or

satisfied with feeling calm and safe during the abortion, the treatment and the bleeding met their expectations. No significant difference was observed in experienced pain and duration of bleeding. In a recent systemic review with a meta-analysis aiming to identify the potential "cut-off" in gestational length when benefits still outweigh the risk, it was shown that pregnancies up to 63 days of gestation were as safe as pregnancies 64–70 days of gestation. [15] Data on the safety in more advanced pregnancies were, however, not possible to include due to a lack of high-quality studies. There are, however, small prospective and retrospective studies on home abortion also in more advanced pregnancies up to 84 days of gestation showing a high rate of complete abortion. [16]

A combined regimen of mifepristone and misoprostol was found to be more effective in terms of lower rates of ongoing pregnancy and higher rates of successful abortion compared to the misoprostol alone regimen. [17-19] There have been multiple studies that focus on the combination regimen, comparing various misoprostol doses and routes and the interval between mifepristone and misoprostol. When comparing different doses of misoprostol in the combined mifepristone misoprostol regimen, the included studies focused on the dosages of 400 μg and 800 μg. Comparing 400 μg to 800 μg buccal misoprostol [20], treatment with 400 μg misoprostol was found to be more effective (moderate certainty of evidence). On the other hand, administration of 800 μg oral misoprostol demonstrated more effectiveness than 400 μg oral misoprostol. Moreover, there is moderate certainty of evidence that 800 μg sublingual misoprostol is 3 times more effective than 400 μg. [21] High satisfaction with home use of misoprostol in medical abortion has been shown in early gestation. In a study from Singapore, including pregnancies up to 70 days of gestation, satisfaction was reported as very high (94.4%) and successful abortion was observed in 100% of women; however, only 11 women were in the gestational age range 64–70 days. [22]

Conclusion

Nevertheless, medical abortion is a revolutionary technique and our study results indicate that mifepristone-misoprostol medical abortion can complement available surgical services and help meet the long-standing need for safe abortion. As medical abortion is proven to be safe and effective for home use, further development of the online provision of abortion drugs will allow women to have better access to abortion services. However, we strongly support some type of follow-up confirming this result to avoid potential complications.

References

1. Podolskyi V, Gemzell-Danielsson K, Maltzman LL, Marions L. Effectiveness and acceptability of home use of misoprostol for medical abortion up to 10 weeks of pregnancy. Acta Obstetricia et Gynecologica Scandinavica. 2019 May;102(5):541-8.
2. Mukhopadhyay S, Mistri PK. Efficacy and acceptability of medical abortion with mifepristone and misoprostol in early pregnancy. Indian Journal of Obstetrics and Gynecology Research. 2019;7(1):33-8.
3. Karkal M. Abortion laws and abortion situation in India. Issues Reprod Genet Eng. 1991; 4:223–230.
4. Karim SM. Once-a-month vaginal administration of prostaglandins E2 and F2α for fertility control. Contraception. 1971 Mar 1;3(3):173-83.
5. Karim SM. Use of prostaglandin E2 in the management of missed abortion, missed labour, and hydatidiform mole. Br Med J. 1970 Jul 25;3(5716):196-7.
6. Karim SM, Rao B, Ratnam SS, Prasad RN, Wong YM, Ilancheran A. Termination of early pregnancy (menstrual induction) with 16-phenoxy-ω-tetranor PGE2 methylsulf onylamide. Contraception. 1977 Oct 1;16(4): 377-81.
7. Kahn JG, Becker BJ, MacIsaa L, Amory JK, Neuhaus J, Olkin I, Creinin MD. The efficacy of medical abortion: a meta-analysis. Contraception. 2000 Jan 1;61(1):29-40.
8. Kant A, Taneja I. Low dose mifepristone for early abortion. J Obstet Gynaecol Ind. 2004; 54:173–174.
9. Bygdeman M, Swahn ML. Progesterone receptor blockage: effect on uterine contractility and early pregnancy. Contraception. 1985 Jul 1;32(1):45-51.
10. Raymond EG, Shannon C, Weaver MA, Winikoff B. First-trimester medical abortion with mifepristone 200 mg and misoprostol: a systematic review. Contraception. 2013 Jan 1;87(1):26-37.
11. World Health Organisation Task Force on Post Ovulation Methods of Fertility Regulation. Termination of pregnancy with reduced doses of mifepristone. BMJ. 1993; 307:532–537
12. Bygdeman M, Swahn ML. Progesterone receptor blockage. Effect on uterine contractility and early pregnancy. Contracept. 1985; 32:45–51.
13. Medical Methods of Termination of Pregnancy. WHO Technical Report Series. vol. 871. Geneva: World Health Organization; 1997.
14. World Health Organisation Task Force on Post Ovulation Methods of Fertility Regulation. Termination of pregnancy with reduced doses of mifepristone. BMJ. 1993; 307:532–537.

15. Schmidt-Hansen M, Pandey A, Lohr PA, Nevill M, Taylor P, Hasler E, Cameron S. Expulsion at home for early medical abortion: a systematic review with meta-analyses. Acta Obstetricia et Gynecologica Scandinavica. 2021 Apr;100(4):727-35.
16. Larsson A, Ronnberg AK. Expanding a woman's options to include home use of misoprostol for medical abortion up until 76 days: an observational study of efficacy and safety. Acta Obstetricia et Gynecologica Scandinavica. 2019 Jun;98(6):747-52.
17. Blum J, Raghavan S, Dabash R, Ngoc N, Chelli H, Hajri S, Conkling K, Winikoff B. Comparison of misoprostol-only and combined mifepristone-misoprostol regimens for home-based early medical abortion in Tunisia and Vietnam. Int J Gynaecol Obstet. 2012;118 (2): 166–71.
18. Dahiya K, Ahuja K, Dhingra A, Duhan N, Nanda S. Efficacy and safety of mifepristone and buccal misoprostol versus buccal misoprostol alone for medical abortion. Arch Gynecol Obstet. 2012;285(4):1055–8.
19. Ngoc NT, Blum J, Raghavan S, Nga NT, Dabash R, Diop A, Winikoff B. Comparing two early medical abortion regimens: mifepristone+misoprostol vs. misoprostol alone. Contraception. 2011;83(5):410–7.
20. Chong E, Tsereteli T, Nguyen NN, Winikoff B. A randomized controlled trial of different buccal misoprostol doses in mifepristone medical abortion. Contraception. 2012;86(3): 251–6.
21. von Hertzen H, Huong NT, Piaggio G, Bayalag M, Cabezas E, Fang AH, Gemzell-Danielsson K, Hinh ND, Mittal S, Ng EH, Chaturachinda K, Pinter B, Puscasiu L, Savardekar L, Shenoy S, Khomassuridge A, Tuyet HT, Velasco A, Peregoudov A. Misoprostol dose and route after mifepristone for early medical abortion: a randomised controlled noninferiority trial. BJOG. 2010; 117(10):1186–96.
22. Tan YL, Singh K, Tan KH, Gosavi A, Koh D, Abbas D, Winikoff B. Acceptability and feasibility of outpatient medical abortion with mifepristone and misoprostol up to 70 days gestation in Singapore. European Journal of Obstetrics & Gynecology and Reproductive Biology. 2018 Oct 1; 229:144-7.