

A COMPARATIVE STUDY OF MIFEPRISTONE AND MISOPROSTOL VERSUS MISOPROSTOL ALONE IN MID TRIMESTER TERMINATION OF PREGNANCY

Surendra Nath Soren¹, Pravin Kumar Dash²

¹Associate Professor, Department of Obstetrics and Gynaecology, M.K.C.G. Medical College, Berhampur, Odisha.

²Third Year Postgraduate Student, Department of Obstetrics and Gynaecology, M.K.C.G. Medical College, Berhampur, Odisha.

ABSTRACT

BACKGROUND

Termination of pregnancy in second trimester continues to be a challenge in developing countries especially in rural areas. There is an exponential rise in complications of abortion along with advancing gestational age. The search is on for an ideal method of abortion, which is reliable, safe and cheap. This study was conducted in M.K.C.G. Medical College and Hospital, Berhampur, from November 2015 to October 2017 with the aim of finding an effective method to induce second trimester abortion within reasonable time with fewer complications.

MATERIALS AND METHODS

A total of 80 patients were studied to compare combination of mifepristone and misoprostol (30 patients) with single drug misoprostol alone (50 patients) for second trimester abortion. The Induction Abortion Interval (IAI), success rate, misoprostol dose requirement and side effects with demographic characteristics were compared between the two groups.

RESULTS

There was a significant difference in the IAI in both the groups. The mean IAI was 562.218 minutes in study group, whereas in control group, IAI was 922.698 minutes. The success rate (complete abortion) was 92.5% in study group and 68.4% in control group, and this was statistically significant. Misoprostol dose requirement (average) in study group was 1081.48 µg and in control group was 1675.67 µg. More side effects were observed in the control group.

CONCLUSION

Mifepristone followed by misoprostol was more effective than misoprostol alone as it had a shorter IAI, better success rate, less requirement of misoprostol and fewer side effects.

KEYWORDS

Mifepristone, Misoprostol, Second Trimester, Medical Abortion.

HOW TO CITE THIS ARTICLE: Soren SN, Dash PK. A comparative study of mifepristone and misoprostol versus misoprostol alone in mid trimester termination of pregnancy. J. Evid. Based Med. Healthc. 2018; 5(3), 255-259. DOI: 10.18410/jebmh/2018/52

BACKGROUND

As stated by Margaret Sanger "no woman can call herself free until she can choose consciously whether she will or will not become pregnant" (Ankelessaria 1999).¹

But, MTP is one of the oldest and commonest form of fertility control. No human community has ever shown a marked fall in birth rate without a significant recourse to induced abortion and it is unlikely in foreseeable future that contraception methods alone will be sufficient means of population control especially in developing countries (Potts, 1970).² Globally-induced abortion- safe or unsafe, legal or illegal- is a reproductive health service that is part of the lives of women, couples and communities in both developed

and developing countries. When faced with unintended pregnancies, especially in contexts in which women lack access to effective family planning, induced abortion is an important part of women's reproductive healthcare. In India, the second most populous country in the world, abortion has been legal on a broad range of grounds since 1971.^{3,4}

Worldwide, 10-15% of induced abortions occur in the second trimester of pregnancy. Contributing factors include, among others, late diagnosis of pregnancy or foetal anomalies, logistic and financial barriers to abortion services, ambivalence or fear of disclosure or of the procedure (Drey 2006).⁵

Surgical and medical methods of second trimester abortion have both evolved in the past 30 years. Dilatation and Evacuation (D and E) introduced in 1970s has become the preferred surgical technique over dilatation and curettage and hysterectomy because of its relative safety. Intra-amniotic instillation of hypertonic saline and prostaglandins have largely been replaced by oral or vaginal prostaglandin analogues with or without the antiprogestin and mifepristone.

With the introduction of prostaglandin E and F analogues, the efficacy of induction abortion improved and

Financial or Other, Competing Interest: None.

Submission 27-12-2017, Peer Review 05-01-2018,

Acceptance 11-01-2018, Published 13-01-2018.

Corresponding Author:

Dr. Pravin Kumar Dash,

PG Hostel-2, Room No. 83,

M.K.C.G. Medical College and Hospital, Berhampur, Odisha.

E-mail: kmpravin1989@gmail.com

DOI: 10.18410/jebmh/2018/52



side effects were reduced. The most frequently employed prostaglandin analogue is misoprostol (Goldberg 2001),⁶ which is used alone or in combination with mifepristone. So, under this background, the present study was proposed to compare a time tested and popularly used drug, i.e. misoprostol with misoprostol-mifepristone combination for conducting mid trimester MTPs. The purpose of the study is to search for a standard method for second trimester MTPs, which would be more effective, safer, easily available, relatively economical and minimal side effects and complication rates. The present study aims at increasing the efficacy and reducing the mortality associated with second trimester abortions.

MATERIALS AND METHODS

This is a prospective comparative randomised clinical trial undertaken in Department of Obstetrics and Gynaecology at M.K.C.G Medical College and Hospital, Berhampur, Odisha, over a period of 2 years from October 2015 to October 2017. A total of 80 patients fulfilling the inclusion criteria were enrolled in the study.

Group 1- The group 1 comprised of patients to whom tablet mifepristone 200 mg given orally, and after 24 hours, Tab. Misoprostol 400 micrograms given vaginally, then 400 micrograms misoprostol was given orally 4 hourly for maximum 5 doses.

Group 2- The group 2 comprised of patients to whom Tab. Misoprostol 400 micrograms was given vaginally, followed by 400 micrograms misoprostol was given orally 4 hourly for maximum 5 doses.

Inclusion Criteria- 12-20 weeks of pregnancies that fulfilled indications of MTP as per guidelines of MTP Act, 1971.

Exclusion Criteria- (1) Scarred uterus. (2) Grand multipara. (3) Contraindications to misoprostol and mifepristone like ectopic pregnancy or undiagnosed adnexal mass, haemorrhagic disorders or concurrent anticoagulant therapy, inherited porphyria, bronchial asthma, cardiac disease, placenta previa and unexplained vaginal bleeding.

Success- Defined as complete expulsion of product of conception within 24 hours of 1st dose of misoprostol.

Failure- Defined as incomplete or no expulsion of product of conception within 24 hours of 1st dose of misoprostol.

Induction Abortion Interval- Time period between 1st dose of misoprostol to complete expulsion of product of conception.

RESULTS

Maximum number of patients (70%) from both groups were from age group of 21-30 years. Mean age in Group 1 and Group 2 were 25.77 ± 4.62 years and 26.10 ± 4.34 years, respectively (Table 1).

Most of the females (86.25%) in both the groups were married and living in rural areas (61.25%). Majority of females (86.25%) belonged to socioeconomic class III and below. The education level of majority of patients (70%) were from primary school up to high school level. Large number of females (55%) were para 2 and 3 in both the groups. Mean parity of Group 1 and 2 was 2.13 ± 1.34 and 2.02 ± 1.22, respectively (Table 2). Majority of females, i.e. 47.50% in both the groups were carrying 12-14 weeks of pregnancy. The mean gestational age in Group 1 was 15.50 ± 2.85 weeks and in Group 2, it was 15.72 ± 2.75 (Table 3). Failure of contraception was the most common indication (65%) in both the groups (Table 4). The success rate of Group 1 (90%) was significantly higher than that of Group 2, which was 76% (P value <0.001) (Table 5). The successful abortion rate did not depend on the gestational age in Group 1, but in Group 2, in 12-16 weeks pregnancy, success rate was higher than 17-20 weeks gestation (P value <0.001) (Table 6). Rate of incomplete abortion was significantly lower in Group 1 (7.5%) than that of Group 2 (31.6%) and P value <0.002 (Table 7). Average induction abortion interval was 9.3703 hours in Group 1. It was significantly lower than that of Group 2, i.e. 15.3783 hours. (P value <0.01) (Table 8, 9). The mean dose requirement of misoprostol in Group 1 was 1081.48 µg and in Group 2 was 1675.67 µg (P value <0.001) (Table 10). Side effects of both the groups were minimal and there were no serious complications, which confirmed the safety of both the methods.

Age Group in Years	Group 1 (Mifepristone + Misoprostol)		Group 2 (Misoprostol)		Total	
	No.	%	No.	%	No.	%
18-20	6	19.99	8	16.00	14	17.50
21-25	10	33.33	18	36.00	28	35.00
26-30	11	36.67	17	34.00	28	35.00
31-35	3	9.99	7	14.00	10	12.50
Total	30	100	50	100	80	100
Mean Age	25.77 ± 4.62		26.10 ± 4.34			
SE	6					
Z Value	0.055					
P Value	>0.5					

Table 1. Age Distribution

Parity	Group 1 (Mifepristone + Misoprostol)		Group 2 (Misoprostol)		Total	
	No.	%	No.	%	No.	%
Nullipara	5	16.69	7	14	12	15.00
Para 1	4	13.33	10	20	14	17.50
Para 2	8	26.66	14	28	22	27.50
Para 3	9	29.99	13	26	22	27.50
Para 4 and above	4	13.33	6	12	10	12.50
Total	30	100	50	100	80	100
Mean Parity	2.13 ± 1.34		2.02 ± 1.22			
SE (d)	0.03					
P Value	>0.05					

Table 2. Parity Wise Distribution

Gestational Age (Weeks)	Group 1 (Mifepristone + Misoprostol)		Group 2 (Misoprostol)		Total	
	No	%	No	%	No	%
12-14	14	46.66	24	48.00	38	47.50
15-17	6	20.00	8	16.00	14	17.50
18-20	10	33.33	18	36.00	28	35.00
Total	30	100	50	100	80	100
Mean	15.50 ± 2.85		15.72 ± 2.75			

Table 3. Gestational Age Wise

Indications	Group 1 (Mifepristone + Misoprostol)		Group 2 (Misoprostol)		Total	
	No.	%	No.	%	No.	%
Failure of contraception	18	60.00	34	68.00	52	65.00
Congenital anomalies of foetus	5	16.67	10	20.00	15	18.75
Unmarried/rape (social grounds)	5	16.67	6	12.00	11	13.75
Medical grounds of mother	2	6.66	-	-	2	2.50

Table 4. Indications of MTP

Successful/Fail	Group 1 (Mifepristone + Misoprostol)		Group 2 (Misoprostol)		Total	
	No.	%	No.	%	No.	%
Successful	27	90.00	38	76.00	65	81.2
Failed	3	10.00	12	24.00	15	18.8
Total	30	100	50	100	80	100
Df	1					
P Value	<0.001					

Table 5. Success Rate Wise

Successful/Fail	Group 1 (Mifepristone + Misoprostol)		Group 2 (Misoprostol)		Total	
	12-16 Weeks	17-20 Weeks	12-16 Weeks	17-20 Weeks	12-16 Weeks	17-20 Weeks
Successful	16 (88.8 %)	11 (91.6%)	28 (87.5%)	10 (55.5%)	44 (88%)	21 (70%)
Failed	2 (11.2 %)	1 (8.4%)	4 (12.5%)	8 (44.5%)	6 (12%)	9 (30%)
Total	18 (100%)	12 (100%)	32 (100%)	18 (100%)	50 (100%)	30 (100%)
Df	1					
P Value	0.3127		<0.001			

Table 6. Gestational Wise Success Rate

Nature of Abortion	Group 1 (Mifepristone + Misoprostol)		Group 2 (Misoprostol)		Total	
	No.	%	No.	%	No.	%
Complete	25	92.5	26	68.4	51	78.4
Incomplete	2	7.5	12	31.6	14	21.6
Total	27	100	38	100	65	100
Df	1					
P Value	<0.002					

Table 7. Types of Successful Abortion

Induction Abortion Interval (Hours)	Group 1 (Mifepristone + Misoprostol)		Group 2 (Misoprostol)	
	No.	%	No.	%
<8	4	14.8	2	5
8-12	20	74.00	5	13.0
13-18	3	11.2	22	58.00
>18	0	0	9	24.00

Table 8. Induction to Abortion Interval

	Group 1	Group 2	P value
Induction abortion range	7-13 hours	7-20 hours	<0.01
Average	9.3703 hours	15.3783 hours	

Table 9. Mean Induction Abortion Interval

Dose (μg)	Group 1 (Mifepristone + Misoprostol)		Group 2 (Misoprostol)	
	No.	%	No.	%
400	0	0	0	0
800	9	33	2	5.2
1200	17	63	5	13.1
1600	1	4	17	45.00
2000	0	0	12	31.5
2400	0	0	2	5.2
Average	1081.4814 μg		1675.67 μg	
P value	<0.001			

Table 10. Dose Requirement of Misoprostol

DISCUSSION

Our study compared mifepristone and misoprostol combination with misoprostol alone in second trimester abortion (12-20 weeks). In our study, mean age of patients in group 1 was 25.77 ± 4.62 years, which was similar to other studies.^{7,8,9}

Mean parity of group 1 was 2.13 ± 1.34 , which corresponds to that of study by Neha Agarwal et al in 2014.¹⁰ In our study, mean gestational age was 15.5 ± 2.85 and 15.72 ± 2.75 in group 1 and group 2, respectively. This is comparable to study by Carbonella et al¹¹ in which they found 15.7 ± 2.4 for combined regimen and 15.1 ± 2.0 for misoprostol alone regimen. Demographic parameters were comparable as there is no statistically significant difference in both the groups.

Mean Induction Abortion Interval (IAI) in group 1 was 562 minutes (9.37 hours) compared to 390 minutes in the study by Webster et al in 1996.¹² Mean IAI in group 2 was 922 minutes (15.3 hours) as compared to 846 minutes in the study by Wong et al in 1998.¹³ In our study, it was seen that a statistically significant P value (<0.01) was achieved by comparing the two groups. Patel et al¹⁴ found IAI of 18.94 ± 9.3 hours in combined regimen group and 24.2 ± 11.53 hours in misoprostol alone group. This difference in time interval was due to different doses of misoprostol (200 μg) compared to our study (400 μg).

Kapp N et al¹⁵ in 2007 also found higher efficacy (97% versus 72% with misoprostol alone) and shorter IAI (10.0 hours versus 18.0 hours with misoprostol alone).

Success rate in group 1 was 92.5% compared to Webster et al (94.3%). Different studies have shown success rates varying from 73-97% with combination of mifepristone and misoprostol.^{16,17,18}

The mean doses of misoprostol required in group 1 was 1081.48 μg . Other studies found dosage requirements varying from nil to 2200 μg .¹⁹

CONCLUSION

In the last few years, medical methods of second trimester induced abortion have considerably improved. In most of the cases, surgical evacuation and its complications can be avoided by using medical methods of pregnancy termination. Today, safe and efficient medical abortion services can be offered by healthcare facilities. Second trimester terminations should take place in a hospital where blood transfusion and emergency surgery (including laparotomy) are available because of the potential for heavy

vaginal bleeding and serious complications.

The combined regimen of mifepristone and misoprostol is an effective and safe method for second trimester abortion. This regimen significantly reduces the dose of misoprostol. Misoprostol alone has also been shown to be effective, although a higher dose is needed and efficacy is lower than for the combined regimen. Hence, whenever possible, the combined regimen of mifepristone and misoprostol should be used.

Comparing the two methods, mifepristone followed by misoprostol is more effective and has a shorter Induction Abortion Interval (IAI). However, both are feasible as far as end results are concerned. Further well designed and randomised studies with more sample size maybe justified.

Acknowledgement

This study was approved by the Institutional Ethics Committee (314/Chairman IEC, M.K.C.G Medical College).

REFERENCES

- [1] Anklesaria BS, Savaliya MV. Psychosocial Aspects of MTP. Manual on Medical Termination of Pregnancy 1999;3:33-36.
- [2] Potts DM. Termination of pregnancy. Br Med Bull 1970;26(1):65-71.
- [3] Department of social affairs, population division, United Nations: World population prospects. The 2012 revision. Vol II. Demographic profiles. New York, UN 2012.
- [4] Govt. of India. The medical termination of pregnancy act. Act No- 34, 1971.
- [5] Drey EA, Foster DG, Jackson RA, et al. Risk factors associated with presenting for abortions in second trimester. Obstet Gynaecol 2006;107(1):128-135.
- [6] Goldberg AB, Greenberg MB, Darney PD. Misoprostol and pregnancy. N Eng J Med 2001;344(1):38-47.
- [7] Mendilcioglu M, Simsek PE, Seker PE, et al. Misoprostol in second and early third trimester for termination of pregnancies with fetal anomalies. Int J Gynae Obst 2002;79(2):131-135.
- [8] Bartley J, Baird DT. A randomized study of misoprostol and gemeprost in combination with mifepristone for induction of abortion in the second trimester of pregnancy. BJOG 2002;109(11):1290-1294.
- [9] Goh SE, Thong KJ. Induction of second trimester abortion (12-20 weeks) with mifepristone and misoprostol: a review of 386 consecutive cases. Contraception 2006;73(5):516-519.

- [10] Agarwal N, Gandhi G, Batra S, et al. Evaluation of mifepristone and misoprostol for medical termination of pregnancy between 13-20 weeks of gestation. *Indian Journal of Clinical Practice* 2014;24(9):859-862.
- [11] Carbonell JL, Gallego FG, Llorente MP, et al. Vaginal vs. sublingual misoprostol with for cervical priming in second-trimester abortion by dilation and evacuation: a randomized clinical trial. *Contraception* 2007;75(3):230-237.
- [12] Webster D, Penney GC, Templeton A. A comparison of 600 and 200 mg mifepristone prior to 2nd trimester abortion with the prostaglandin misoprostol. *Br J Obstet Gynaecol* 1996;103(7):706-770.
- [13] Wong KS, Ngai CS, Wong AY, et al. Vaginal misoprostol compared with vaginal gemeprost in termination of second trimester pregnancy: a randomized trial. *Contraception* 1998;58(4):207-210.
- [14] Patel U, Chauhan K, Singhi S, et al. Second trimester abortion- mifepristone and misoprostol or misoprostol alone? *Int J Reprod Contracept Obstet Gynecol* 2013;2(3):315-319.
- [15] Kapp N, Borgatta L, Stubblefield P. Mifepristone in second-trimester medical abortion: a randomized controlled trial. *Obstet Gynecol* 2007;110(6):1304-1010.
- [16] Lalitkumar S, Bygdeman M, Gemzell-Danielsson K. Mid-trimester induced abortion: a review. *Hum Reprod Update* 2007;13(1):37-52.
- [17] Hammond C. Recent advances in second-trimester abortion: an evidence-based review. *Am J Obstet Gynecol* 2009;200(4):347-356.
- [18] Ho PC, Nagi SW, Liu KL, et al. Vaginal misoprostol compared with oral misoprostol in termination of second-trimester pregnancy. *Obstet Gynecol* 1997;90(5):735-738.
- [19] El-Refaey H, Templeton A. Induction of abortion in the second trimester by a combination of misoprostol and mifepristone: a randomized comparison between two Misoprostol regimens. *Hum Reprod* 1995;10(2):475-478.