Original Research Article

A comparative study of medical termination of pregnancy between 8-12 weeks with misoprostol versus mifepristone along with misoprostol at tertiary care hospital

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Abstract

Introduction: Medical method of abortion has advantages over surgical methods as it is non-invasive. Hence, no complications of anesthesia and administration of drugs is easy in medical methods. There is a need for evolving a safe and effective method for safe and effective method for terminating pregnancy in the first trimester.

Aim: We have taken up the present study to know the efficacy of combination of mifepristone and misoprostol versus single drug misoprostol alone for 1st trimester abortion.

Materials and methods: It was a Cross-Sectional Study carried on pregnant women coming for MTP under family planning op at CKM hospital for 2 years. The study included two groups Group-A and Group-B. Group-A consisted of 50 randomly selected cases received Vaginal Misoprostol 600 micrograms stat dose followed every 4th hourly by 400 micrograms for 24 hours, for a maximum of 4 doses. Group-B has 50 cases received Oral Mifepristone 200 mg and simultaneously 600 micrograms of vaginal Misoprostol stat dose followed every 4th hourly with 400 micrograms vaginal Misoprostol for a period of 24 hours maximum 4 doses. Depending on response USG was done within 24-48 hours in both studies and rescan after 2 weeks.

Results: Among Group B subjects 86% had expulsion within 5-10 hrs and remaining 14% had expulsion within 10-15 hours. Among Group A subjects 76% required >24 hrs for expulsion, 10% required 20-24 hrs, 6% required 15-20 hrs and 8% needed 10-15 hrs for expulsion. The difference between grouping and induction to abortion interval was found to be statistically significant. In Group A, 15 subjects (30%) had complete expulsion of products. 35 subjects (70%) required D&C. In Group B, 43 subjects (86%) had complete expulsion, 7 subjects (14%) required D&C. The difference between grouping and final outcome was found to be statistically significant. Majority of study subjects who require D&C were present in Group A compared to Group B. The difference between grouping and D&C was found to be statistically significant.

Conclusion: Thus combination of Mifepristone and vaginal Misoprostol is more efficacious than vaginal Misoprostol alone.

Key words

Mifepristone, Vaginal Misoprostol, Medical Method of Abortion.

Introduction

Unplanned and unwanted pregnancy is a proxy indicator for the unmet need for contraception. Termination of pregnancy with RU-486 is considered extremely safe under supervision with appropriate counseling. Use of RU-486 followed by Misoprostol is an established and safe method for terminating early pregnancy. The subject of pregnancy termination or induced abortion has evolved all over the world along with changes in the socio-cultural, political and economical issues. Advances in the medical and pharmaceutical technology has influenced in a big way for this evolution.

Prostaglandins soften the cervix, cause uterine contractions and are used orally or vaginally for ripening of the cervix before surgical or for medical termination of pregnancy. The most commonly used prostaglandins are Gemeprost given vaginally and Misoprostol, oral or vaginal [1]. Misoprostol is inexpensive can be stored at room temperature and is available in many countries for the treatment and prevention of peptic ulcers caused by NSAIDs. In contrast, Gemeprost, which is available only as a vaginal pessary, is expensive, thermolabile and requires refrigeration [2].

Antiprogestogen blocks the receptors for progesterones and glucocorticoids. It increases the sensitivity of the uterus to prostaglandins [12]. The conventional timing of Misoprostol administration after for medical abortion is two days, but more flexible intervals, which may make the regimen more convenient, have not been studied [3]. In September 2000, the United States Food and Drug Administration approved the use of the oral 600 mg followed by oral Misoprostol 400mcg, limited to the first 49 days of amenorrhea [4, 5]. The Drug Controller of India licensed medical abortion in April 2002, following the same protocol (same dosage and gestational duration of use) as that of the United States Food and Drug Administration. However, The National Consortium's guidelines recommended the use of 200mg of orally followed 48 hours later by 400 microgram of oral Misoprostol for the first 56 days pregnancy [6]. Nonetheless, the clinical safety, efficacy and acceptability of 200 mg with Misoprostol beyond 49 days gestation in the Indian context has been well studied and documented. Moreover, the World Health Organization has approved this combination for medical abortion up to 63 days amenorrhea. Medical abortion has a lower rate of success than surgical abortion. The most severe side effects of combined with Misoprostol is excessive vaginal bleeding. Commonly reported adverse effects are abdominal pain, nausea, vomiting and uterine cramps. The need for analgesic drugs is more with medical abortion. These shortcomings of medical abortion are not withstanding, has the advantage of a high rate of

efficacy in women with early pregnancies. It does not require anesthesia and has been found safe and acceptable to women. Medical abortion offers great potential for improving abortion access and safety, as it requires a less extensive infrastructure than surgical abortion.

One way of reducing the mortality and morbidity associated with unsafe abortions is the early decision by the woman for termination of the pregnancy by the use of Medical Method of Abortion (MMA) for termination of early pregnancy. In India many studies have not been done regarding the use of combination of and Misoprostol for 1st trimester abortion. Hence, an attempt is made to study the efficacy of combination of and Misoprostol versus single drug Misoprostol alone for 1st trimester abortion.

Materials and methods

Cross-Sectional Study was carried on pregnant women coming for MTP under family planning op at CKM hospital for 2 years i.e. (September 2015 to 2017) in the department of Obstetrics and Gynecology for 24 Months from September 2015 to September 2017. The study included two groups Group-A and Group-B.

Group-A:
Fifty randomly selected cases received Vaginal Misoprostol 600 micrograms stat dose followed every 4th hourly by 400 micrograms for 24 hours, maximum 4 doses.

Group-B:
Fifty randomly selected cases received Oral Mifepristone 200 mg and simultaneously 600 micrograms of vaginal Misoprostol stat dose followed every 4th hourly with 400 micrograms vaginal Misoprostol for a period of 24 hours maximum 4 doses.

Depending on response USG was done within 24-48 hours in both studies and rescan after 2 weeks.

At the end of the procedure, we look for following outcomes:

Primary outcome: Induction abortion interval and Complete abortion/ RPOC

Secondary outcome: Side effects, Complications and Incomplete abortion requiring surgical intervention.

Inclusion criteria

- Pregnant women between 8 - 12 weeks gestation those who need MTP.
- Pregnant women between 8-12 weeks willing for MTP including one previous LSCS.
- Pregnant women with medical, socio-economic, therapeutic, eugenic reasons, pregnancy caused by rape.
- Pregnancy caused by sterilization failure.

Exclusion criteria

- Pregnant women after 12 weeks of gestation.
- Previous allergic reactions to one of the drugs involved.
- Pregnancy with more than one previous LSCS.
- Known or suspected ectopic pregnancy.
- Hematological disorders in pregnancy.
- Systemic diseases in pregnancy.
- Pregnancy with placenta covering internal os.

Statistical analysis

Data entry and statistical analysis was performed with the help of epi-info software, Microsoft excel 2007 and SPSS version 17.0, while categorical variables are presented as number and percentages. Chi square test was used to compare differences in categorical variables. The statistical significance level was fixed at $p<0.05$.

Results

Majority of the patients came with indication of MTP and B/L Tubectomy for unwanted pregnancies (66%). 34% of the patients came with indication of missed abortion (**Table – 1**).

Table - 1: Distribution of study subjects according to their indication for MTP.

Indication for MTP	Frequency	Percent
Missed abortion	34	34.0
MTP & B/L Tubectomy for unwanted pregnancies	66	66.0
Total	100	100.0

Table - 2: Distribution of study subjects showing association between Grouping and age category.

			Age category				Total
			<20 years	21-25 years	26-30 years	>31 years	
Grouping	Group A	Frequency	4	24	16	6	50
		Percent	40.0%	54.5%	44.4%	60.0%	50.0%
	Group B	Frequency	6	20	20	4	50
		Percent	60.0%	45.5%	55.6%	40.0%	50.0%
Total		Frequency	10	44	36	10	100
		Percent	100.0%	100.0%	100.0%	100.0%	100.0%

Chi-square= 1.608, df= 3, P value= 0.658, Statistically not significant

Table - 3: Distribution of study subjects showing association between Grouping and gravida.

			Gravida					Total
			Primi	G2	G3	G4	G5	
Grouping	Group A	Frequency	4	2	32	8	4	50
		percent	50%	25%	48.50%	57.10%	100%	50%
	Group B	Frequency	4	6	34	6	0	50
		percent	50%	75%	51.50%	42.90%	0%	50%
Total		Frequency	8	8	66	14	4	100
		percent	100%	100%	100%	100%	100%	100%

Chi-square= 6.346, df= 4, P value= 0.175, Statistically not significant

Table - 4: Distribution of study subjects showing association between Grouping and parity.

			Parity				Total
			Zero	One	Two	Three	
Grouping	Group A	Frequency	4	8	30	8	50
		percent	50%	44.40%	50%	57.10%	50%
	Group B	Frequency	4	10	30	6	50
		percent	50%	55.60%	50%	42.90%	50%
Total		Frequency	8	18	60	14	100
		percent	100%	100%	100%	100%	100%

Chi-square= 0.508,df= 3, P value= 0.917, Statistically not significant

Out of 50 patients in group A, majority (24) belongs to age group of 21-25 years. Out of 50 patients in group B, majority (20) belongs to age group of 21-25 years. The difference between age category and grouping was found to be statistically not significant (**Table – 2**).

More number of patients from both the groups belongs to gravida 3. When comparing between the groups, group A had 48.5% of patients and group B had 51.5% of patients.The difference between the grouping and gravida was found to be statistically not significant (**Table – 3**).

Table – 5: Distribution of study subjects showing association between Grouping and previous abortions.

			Abortions				Total
			Zero	**One**	**Two**	**Three**	
Grouping	**Group A**	Frequency	40	6	2	2	50
		Percent	45.50%	75%	100%	100%	50%
	Group B	Frequency	48	2	0	0	50
		Percent	54.50%	25%	0%	0%	50%
Total		Frequency	88	8	2	2	100
		Percent	100%	100%	100%	100%	100%

Chi-square= 6.727, df= 3, P value= 0.081, Statistically not significant

Table - 6: Distribution of study subjects showing association between Grouping and gestational age.

			Gestational age in weeks		Total
			8-10 weeks	**11-12 weeks**	
Grouping	Group A	Frequency	46	4	50
		percent	53.5%	28.6%	50.0%
	Group B	Frequency	40	10	50
		percent	46.50%	71.40%	50.0%
Total		Frequency	86	14	100
		percent	100.0%	100.0%	100.0%

Chi-square= 2.990, df= 1, P value= 0.074, Statistically not significant

Table - 7: Distribution of study subjects showing association between Grouping and final outcome.

			Final outcome				Total
			Complete expulsion of products. No RPOC	Expulsion of products with minimal RPOC (<14 mm)	Incomplete expulsion of products. RPOC (14mm-30mm)	Incomplete expulsion of products. RPOC >30 mm requiring D&C	
Grouping	**Group A**	**Frequency**	15	5	18	12	50
		Percent	30.0%	10.0%	36.0%	24.0%	100%
	Group B	**Frequency**	43	7	0	0	50
		Percent	86.0%	14.0%	0	0	100%

Chi-square= 43.85,df= 3, P value= 0.0001, Statistically significant

Table - 8: Distribution of study subjects based on missed abortion and unwanted pregnancy

			Missed abortion by USG		Total
			Unwanted Pregnancy	Missed Abortion	
Grouping	Group A	Frequency	32	18	50
		percent	64%	36%	100.0%
	Group B	Frequency	34	16	50
		percent	68%	32%	100.0%

Chi-square= 0.04,df= 1, P value= 0.8415, Statistically not significant

Majority of the patients belongs to parity two in both group A and group B. The difference between the grouping and parity was found to be statistically not significant (**Table – 4**).

Group A had more number of one to three abortions. Group B had more number of one to three abortions. The difference between grouping and abortions was found to be statistically not significant (**Table – 5**).

Patients with 8-10 gestational weeks were more in Group A and Patients with 11-12 gestational weeks were more in Group B. The difference between grouping and gestational age was found to be statistically not significant (**Table – 6**).

In Group A, 15 subjects (30%) had complete expulsion of products. 35 subjects (70%) required D&C. In Group B, 43 subjects (86%) had complete expulsion, 7 subjects (14%) required D&C. The difference between grouping and final outcome was found to be statistically significant (**Table – 7**).

Missed abortions were more in Group A patients than group B. The difference between grouping and missed abortions was found to be statistically not significant (**Table – 8**).

Among Group B, subjects 86% had expulsion within 5-10 hours and remaining 14% had expulsion within 10-15 hours. Among Group A subjects, 76% required >24 hours for expulsion, 10% required 20-24 hours, 6% required 15-20 hours and 8% needed 10-15 hours for expulsion. The difference between grouping and induction to abortion interval was found to be statistically significant (**Table – 9**).

Majority of study subjects who require D & C were present in Group A compared to Group B. The difference between grouping and D&C was found to be statistically significant (**Table – 10**).

Gastrointestinal side effects were more among group B subjects compared to group A. Excessive bleeding (>100 ml) was more in group A compared to group B (**Table – 11**).

Table - 9: Distribution of study subjects showing association between Grouping and induction to abortion interval.

Induction to abortion Interval	Group A		Group B	
	Frequency	Percent	Frequency	Percent
5-10 hrs	0	0%	43	86%
10-15 hrs	4	8%	7	14%
15-20 hrs	5	10%	0	0%
20-24 hrs	3	6%	0	0%
>24 hrs	38	76%	0	0%
Total	50	100%	50	100%

Chi-square= 89.82,df= 4, P value= 0.0001, Statistically significant

Table - 10: Distribution of study subjects based on grouping and D&C.

D & C	Group A		Group B	
	Frequency	Percent	Frequency	Percent
Yes	35	70%	7	14%
No	15	30%	43	86%
Total	50	100%	50	100%

Chi-square= 29.93,df = 1, P value= 0.0001, Statistically significant.

Discussion

Abortion is not accepted as a sole method of family planning but its place is great as a backup method and as a recruiting method for acceptance of contraception.

Mifepristone, a progesterone receptor antagonist is effective in shortening the induction to

abortion interval when used in combination with prostaglandins. Amongst the prostaglandins Misoprostol, a prostaglandin E1 analogue has been extensively used for induction of abortions in first and second trimester. There are many advantages in using Misoprostol instead of other prostaglandins such as its low cost and easy storage facilities. The drug can be used orally, vaginally, sublingually or in combination in different dosages. A wide variety of dosage regimens are being used to effect late first trimester pregnancy termination.

Table - 11: Distribution of study subjects based on grouping and side effects.

Side effects	Group-A		Group-B	
	Frequency	Percentage	Frequency	Percentage
No	37	74%	40	80%
Nausea & Vomiting	2	4%	4	8%
Abdominal pain	3	6%	4	8%
Excess Bleeding	8	16%	2	4%
Total	50	100%	50	100%

Table – 12: Mean induction to abortion interval in hours.

Mean- induction – to abortion interval (in hours)	References
23.1	Nuutila M, et al. [14]
14	Jain JK, et al. [15]
18.2	Dickinson JE, et al. [16]
8.7	Ho PC, et al. [17]
6.1	Bartley J, et al. [18]
14.1	Wong KS, et al. [19]
15.2	Wong KS, et al. [20]

The present study was a cross sectional study conducted to evaluate the use of Misoprostol alone and Misoprostol along with Mifepristone for termination of pregnancy between 8-12 weeks.

Age distribution

- In the present study, Majority (44%) of the study subjects belonged to 21-25 Years followed by 26-30 years (36%). Study subjects belonging to < 20 years and > 31 years constitute 10% each. The overall mean age was 25.62 ranging from 19 years to 37 years.
- In a study conducted by Kailash T, et al. [6], Out of total pregnant women studied, maximum number of 28 (32.9%) women belonged to the age group of 25- 29, followed by 21 (24.7%) of age group of 30-34 years.
- In a study conducted by Jain M, et al. [7], Majority of cases 76.7% are in the age group of 20-29 years.

Gravida

In the present study, Majority (66%) of the study subjects belongs to G3 followed by G4 (14%). Study subjects belonging to Primi gravida and G2 constitutes 8% each followed by G5 in 4% of study subjects.

Gestational age

- In the present study, Majority of study subjects belongs to 8-10 weeks of gestational age (86%) followed by 11-12 weeks.
- In a study conducted by Kailash T, et al. [7], There were 59 (69.7%) women with fetal gestational age of 40-49 days followed by 21 (24.7%) women with 30-39 days. Mean gestational age was 41.5 days.
- In a study conducted by Jain M, et al. [6], 55% cases had 6-7 weeks of gestation.

Parity

- In the present study, Majority of study subjects belongs to second parity (60%). Remaining study subjects constituted 40%.
- In a study conducted by Jain M, et al. [6], Majority of women 61.7% are of second parity.

Live births

In the present study, Majority of study subjects had two live births (64%) followed by one live births (18%), three live births (10%) and zero live births (8%).

Abortions

In the present study, Majority of study subjects had zero abortions (88%) followed by one abortion (8%). 4% constitutes two and three abortions.

Final outcome

- In present study, in Group A, 15 subjects (30%) had complete expulsion of products. 35 subjects (70%) required D&C. In Group B, 43 subjects (86%) had complete expulsion, 7 subjects (14%) required D&C.
- Complete abortion success rate findings with other studies as follows: Das V, et al. (96.67%), Kumar S, et al. (95.65%), Grossman D, et al. (93.8%) [8, 9, 10].
- In a study conducted by Jain M, et al. [6], out of 60 cases 57 had complete abortion.
- In the study done by Parchasilpchai N, et al. [11] success rate at 48 hours was 89.4% (84 of 94) and 10 (10.6%) women who did not abort within 48 hours.
- In the study done by Goh SE, et al. [12], Induction of second trimester abortion (12–20 weeks) with Mifepristone and Misoprostol: a review of 386 consecutive cases success rate after 24 hours was (97.9%) and low incidence of surgical evacuation (3.2%) for women between 12 and 20 weeks.
- In the study done by Kapp N, et al. [13], Mifepristone in second trimester medical abortion the success rate in Misoprostol alone compared to combination group of Misoprostol with Mifepristone group it's 97%.

Missed abortions

34% of the study subjects were diagnosed with missed abortion with USG. 66% of the study subjects had no missed abortions.

Induction time for abortions

For 43% of study subjects, induction to abortion interval was within 5–10 hours. For 11% of study subjects, induction to abortion interval was within 10–15 hours. For 3% of study subjects, induction to abortion interval was within 15–20 hours. For 5% of study subjects, induction to abortion interval was within 20–24 hours. For 38% of study subjects, induction to abortion interval was >24 hours. Mean induction to abortion interval in hours in other studies were as per **Table – 12**.

Conclusion

Medical abortion is acceptable and effective in the late first trimester and offers women an acceptable alternative to surgical abortion. When combined with Mifepristone, Gemeprost (analogue of PG1) and vaginal Misoprostol are equally effective for termination of first trimester abortion, but may be associated with varying intensity of side effects. Combination of Mifepristone and Misoprostol had more rates of complete expulsion, lower rates of surgical intervention, less number of doses required, low induction abortion interval, faster expulsion, less hospital stay, low failure rates, less side effects. Thus combination of Mifepristone and Misoprostol is more efficacious than Misoprostol alone.

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