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Critical analysis of misoprostol versus mifepristone with misoprostol in medical termination of pregnancy

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ABSTRACT

Background: Termination of pregnancy by any method before the viable period is called abortion. Medical methods can avoid complications of surgical method of abortion which has many disadvantages like perforation of uterus, hemorrhage, sepsis and increased morbidity. The WHO has approved mifepristone and misoprostol combination for medical abortion.

Aims and Objectives: 1. To compare the efficacy of Misoprostol versus combination of mifepristone with Misoprostol. 2. To assess the side effects of Misoprostol and combination of Mifepristone and Misoprostol.

Materials and Methods: It is prospective observational study consisting of two groups with each 61 subjects of MTP patients. Group A (Misoprostol alone): Receive tablet misoprostol 600 microgram start placed per vaginally followed by 400 microgram misoprostol tablet placed per vaginally every 4th hourly up to maximum five doses. In case of first trimester cases 800 microgram tablet misoprostol placed per vaginally followed by 400 microgram misoprostol tablet placed per vaginally every 4th hourly up to maximum four doses. Group B (Mifepristone and Misoprostol): Receive tablet mifepristone 200mg orally on empty stomach. After 24 hours will receive tablet misoprostol as mentioned in group A.

Results: Misoprostol alone has success rate of 78.69% whereas combination with Mifepristone success was 93.44%. The mean Induction - abortion interval in misoprostol alone group was 11.803 hours and with mifepristone combination it was 5.623 hours.

Conclusion: Medical termination of pregnancy by sequential administration of mifepristone with misoprostol has less induction abortion interval compared to using misoprostol alone. This combination has more success rate and also has lesser side effects.

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1. Introduction

Termination of pregnancy by any method before the viable period is called abortion. Though medical and surgical methods are methods of abortion, nowadays medical abortion is gaining popularity. Because of its effectiveness as well as technical related benefits.

Unplanned pregnancies are one of the major problems with which patient present to hospital. Most of the patients

present in the first trimester and they are managed by the medical method of abortion. But few patients require to undergo second trimester abortion for indications such as foetal anomalies, missed abortion, unwanted pregnancy which was missed in the first trimester, victim of rape. On other side newer diagnostic modalities like ultrasonography, amniocentesis and cordocentesis are detecting more and more anomalies or defects in the growing fetuses. Hence, there is increase in number of medical termination of cases too.

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Around 56 million abortions occurring every year worldwide. In eastern part of Asia itself contributing nearly 13 million.¹ As per reports there are 10 mortalities occurring in India in everyday due to unsafe abortions.²

In India medical termination of pregnancy can be done up to twenty weeks of pregnancy, now it is increased to 24 weeks as per new amendment of MTP act 2021 under certain specified indications like risk to the life of the pregnant woman or of grave injury of physical or mental health, anomalous foetus, rape or failure of contraception.

Second trimester abortions have more morbidity than first trimester abortions. Incomplete abortion and method failure are the main problems associated with late termination.

Surgical abortion has many disadvantages like perforation of uterus, haemorrhage, sepsis and increased morbidity. The advantages of medical abortions are improvement in abortion access with safety. It also needs less infrastructure.^{3–6}

The WHO has approved combination of mifepristone with misoprostol for abortion up to 9 weeks of gestation.⁷ Misoprostol alone has been used for second trimester medical termination of pregnancy with success rate of 97.2% and the mean induction to abortion interval found to be 19.6 hours.⁸

Many researchers had quoted that combination of mifepristone and misoprostol will give better results than misoprostol alone. But with varying results and study done in first and second trimesters separately.

2. Aims and Objectives

1. To compare the efficacy of Misoprostol versus combination of mifepristone with Misoprostol in Medical Termination of Pregnancy.
2. To assess the side effects of Misoprostol and combination of Mifepristone and Misoprostol

3. Material and Methods

The study was undertaken in Obstetrics and Gynaecology department of Gadag Institute of Medical Sciences, Gadag, and Karnataka, India. It is interventional, comparative study conducted from January 2021 to June 2022.

The total number of subjects were 122 of which divided into two groups with 61 study subjects in each. It is calculated by standard formula of proportion using previous study of Meetal Mukund et al. With 95% percent confidence interval, 5% level of significance with 4% desired precision and also applying 10% rule. We use Purposive sampling technique.

3.1. Data collection method

Women coming to hospital seeking abortion upto 20 weeks will be admitted in the hospital. Detailed history and

detailed examination was done in all the subjects. Written informed consent was taken. Clinical profile of the patient will be taken. Investigations will be done as per department protocol in all subjects. Gestational age will be estimated by last menstrual period date, clinical examination and confirmed by ultrasonography.

3.2. Inclusion criteria

All cases those will fulfil indication of Medical Termination of Pregnancy, as per guidelines of MTP Act of 1971.

3.3. Exclusion criteria

1. Previous LSCS
2. Ectopic pregnancy
3. Grand multiparous women
4. Any contraindications to misoprostol as well as mifepristone

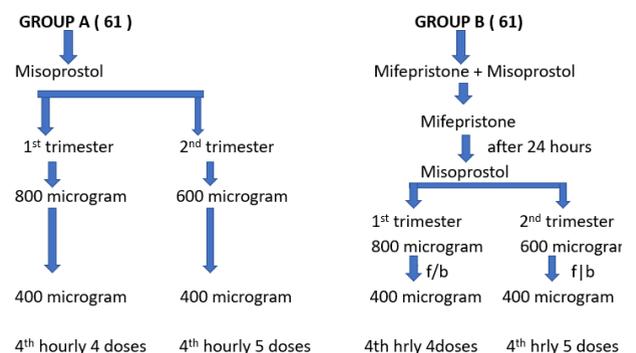
3.4. Methods of administration of drugs

3.4.1. Group A (Misoprostol alone)

Sixty one purposive selected cases will receive tablet misoprostol 600 microgram start placed per vaginally followed by 400 microgram misoprostol tablet placed per vaginally every 4th hourly up to maximum five doses including the first dose in second trimester cases. In case of first trimester cases 800 microgram tablet misoprostol placed per vaginally followed by 400 microgram misoprostol tablet placed per vaginally every 4th hourly up to maximum four doses including first dose.

3.4.2. Group B (Mifepristone and Misoprostol)

Sixty one purposive selected cases will receive tablet mifepristone 200mg orally on empty stomach. After 24 hours will receive tablet misoprostol as mentioned in group A.



The side effects of due drugs was observed and if necessary treatment was given. All the patients received injection Tetanus Toxoid intramuscularly, If not

taken after confirmation of pregnancy. If the patient is Rh negative injection anti D 300microgram will be given intramuscularly after abortion. The associated complications like fever, nausea and vomiting was recorded. The patients were monitored with respect to frequency of uterine contractions, pulse rate and blood pressure. Completeness abortion was confirmed by thorough examination of products of conception. If incomplete further steps were taken.

The mean induction abortion interval was considered from administration time of first dose of misoprostol to till complete abortion. The doses analgesics used recorded. The volume of blood loss was measured clinically. The total doses of misoprostol used was calculated. If incomplete abortion cases check curettage was done.

Success: was defined as complete abortion within 24 hours of starting time of misoprostol.

Failure: was defined as incomplete abortion within 24 hours of starting time of misoprostol.

In the events of failure, pre-consent will be taken that termination of pregnancy would be done by surgical method or other medical methods like oxytocin acceleration and managed accordingly.

3.5. Statistical method

Data was statistically described in terms of mean (\pm SD), frequencies and percentages. For Comparison of quantitative variables between the two groups was done using Student T test for independent samples. Chi square test was used for comparing categorical data. P value less than 0.05 was considered as statistical significance. Data analysed by using SPSS software version 22 and t test.

4. Results

It is a prospective cross-sectional study conducted on 122 subjects of which divided into 2 groups that is group A and group B, each consisting of 61 subjects respectively. In our study Group –A subject's age ranged from 18 years to 30 years. The majority 27 (44.26%) of them were in the age group of 21 - 25 years and mean age was 25.85 years. In Group –B subjects age ranged from 18 years to 30 years with majority 33 (54.10%) of them were in the age group of 21 -25 years and mean age was 25.05 years. There is no significant age difference between the both groups ($p=0.659$).

Our study shows uniform distribution between two groups with relation to gravidity ($p=0.529$). Majority were multigravida consisting of 77 subjects (63.11%). In our study in both groups majority of them were first trimester cases accounting to 74 (60.66%) whereas 48 (39.34%) were second trimester cases.

The mean gestational age in Group A was 9.3 weeks with minimum and maximum was 6.2 weeks and 18.4 weeks

respectively. On the other side Group B mean gestational age was 12 weeks with minimum and maximum gestational age was 5.3 weeks and 20 weeks respectively.

In our study missed abortion was major indication for MTP in both groups that is group A 43 (70.49%) and group B 38 (62.29%) accounting for 81(66.39%) out of 122 subjects followed by anomalous foetus 25 cases (20.49%) and contraception failure 16 cases (13.12%).

In our study Group A (misoprostol alone) complete abortion was achieved in 48 patients (78.69%) where as in Group B (mifepristone +misoprostol) 57 patients (93.44%) with statically significant value ($p=0.001$) Table 1. Hence, success is more in mifepristone and misoprostol combination.

In our study the mean induction to abortion interval (IAI) in Group A was 11.803 hours with shortest of 2.5 hours and longest was 22.00 hours. In Group B mean IAI was 5.623 hours with shortest of 2.00 hours and longest was 10.00 hours (Tables 2 and 3).

In our study misoprostol alone group had 34 (55%) patients had side effects, frequent side effect was excessive vaginal bleeding 48%(24) followed by pain abdomen,⁶ vomiting,³ fever² and diarrhoea. In misoprostol and mifepristone group 34 (55%) patients had side effects, the most frequent side effect was excessive vaginal bleeding followed by vomiting, pain abdomen and fever. In both the groups 44.26% of the patients have no side effects. Overall the most frequent side effect in both the groups was excessive vaginal bleeding.

The mean doses of misoprostol used in misoprostol alone group was 3.5 whereas mifepristone combination group was 1.8. Which was statistically significant with p value <0.0001 .

Surgical intervention was required in 21.31% misoprostol group whereas only 6.55% in mifepristone combination group. The surgical method used was dilatation and curettage.

5. Discussion

When Mifepristone is used in abortion it will shorten the induction abortion interval if combined with prostaglandins because it is a progesterone receptor antagonist. The present study aimed to evaluate the combination effects of Misoprostol and Mifepristone in medical method of abortion.

In our study both groups were comparable with respect to patient's age, period of gestation and parity. The mean age of misoprostol and mifepristone with misoprostol combination group were 25.85 years and 25.05 years respectively. The study conducted by Kapp, Nathalie MD, MPH¹⁶ mifepristone + misoprostol group mean age was 25.7 years and that in misoprostol was 25.5 years. In another study conducted by Justin J Chu et al¹⁷ in 2020, the mean age in misoprostol alone is 32.7 years and in mifepristone +

Table 1: Shows distribution of study subjects of final outcome

Out come	Misoprostol group		Mifepristone +misoprostol group		Total	
	Number	Percentage	Number	Percentage	Number	Percentage
Success	48	78.69	57	93.44	105	86.07
Failure	13	21.31	4	6.56	17	13.93
Total	61	100	61	100	122	100
Inferences	Failure are more in misoprostol group 13 (21.31%) when compared to mifepristone +mifepristone group 4 (6.56%) with statistically significance. (p=0.001)					

Table 2: Shows distribution of study subjects according to induction abortion interval (IAI)

IAI in hours	Group A		Group B		Total	
	Number	Percentage	Number	Percentage	Number	Percentage
<12	29	50.82	61	93.44	88	72.13
12-18	21	36.07	0	6.56	26	23.31
18-24	6	13.11	0	0	8	6.56
Total	61	100	61	100	122	100
Mean ± SD	11.803±4.62		5.623±2.833		8.713±4.868	

Table 3: Shows a mean induction to abortion interval

Group	Mean time of induction to abortion interval (in hours)	Median	Standard deviation	Minimum	Maximum	T value	p value
Group A misoprostol alone	11.803	8.5	4.512	2.50	22.00	9.059	<0.001
Group B Mifepristone +Misoprostol	5.623	6.0	2.833	2.00	10.00		

Table 4: Comparison of induction abortion interval of various studies

Studies	Misoprostol group	Mifepristone + Misoprostol group
Meetali Mukund Khairnar and Abhijeet Madhukar Patil ⁹ (2018)	10.82 ± 2hours	6.22± 2 hours±
Prasanna Lekha Akkenapally ¹⁰ (2016)	10.67±3.96 hours	6.19±2.70 hours
Nagaria Tripti, Sirmor Namrata ¹¹ (2011)	12.29± 3.14hours	6.72±2.26 hours
Priyanka Gupta, Subhaschandra R. Mudanur. Neelamma Patil, et al ¹² (2017)	NA	9.3 ±hours
Present study	11.80±4.62 hours	5.62± 2.83 hours

Table 5: Abortion success rate of previous studies

Authors	Misoprostol alone	Mifepristone + misoprostol
Sarita Sonalkar et al ¹³ (2020)	NA	90%
Patil N et al ¹² (2017)	-	100%
Meetali Mukund et al ⁹ (2018)	84.7%	98.6%
Schreiber et al (2018) ¹⁴	67.1%	83.8%
Parul S. Jani et al ¹⁵ (2018)		91.2%
Prasanna Lekha Akkenapally ¹⁰ (2016)	89%	96%
Nagaria T et al ¹¹ (2011)	90%	95%
Present study	78.69%	93.44%

misoprostol is 32.8 years and Jan E Dickinson¹⁸ the mean age was 32 years in both groups.

Around 60.66% of misoprostol and 65.57% of mifepristone and misoprostol group of our study had one prior delivery which comparable which is comparable to study of Jan E Dickinson¹⁸ where misoprostol group had 60.3% and mifepristone with misoprostol group had 57.8% prior one delivery.

In our study the mean period of gestation in misoprostol group was 10.5 weeks whereas in mifepristone + misoprostol group was 12.0 weeks. In a study of Justin J Chu et al¹⁷ in 2020, the mean period of gestation in misoprostol alone group was 13.8 weeks and in mifepristone + misoprostol group was 13.1 weeks.

The mean induction to abortion interval in misoprostol group is 11.803±4.62 hours and in mifepristone +misoprostol group is 5.623±2.833 hours with statistically significant difference with p<0.001 which is comparable with below mentioned previous studies summarized in Table 4.

RCOG Best practice in comprehensive abortion care¹⁹ 2016 suggests Mifepristone 200 mg orally followed 12-48 hours later by misoprostol 800µgm vaginal then 400µgm every 3 hours till she aborts. As per ACOG recommendation mifepristone 200 mg orally given. After 24-48 hours later misoprostol 800µgm vaginally given. Followed by 400µgm every 3 hours maximum of 5 doses. Whereas WHO suggestion is 200 mg mifepristone given orally. After 36 to 48 hours later misoprostol can be given. FOGSI also suggests 36-48 hours gap after giving mifepristone. But our study results appears that misoprostol can be started after 24 hours later of mifepristone administration which can also give similar results with no serious complications or side effects.

In the present study complete abortion rate was 78.69% in misoprostol alone group where as it was 93.44% in Mifepristone combination group with statically significant value (p<0.001). The same has been compared in Table 5.

In our study the most frequent side effect in both groups was excessive vaginal bleeding 48-55% where as it is 84.2% in study of Paul S Jani et al.

6. Conclusion

Medical termination of pregnancy by combination of mifepristone with misoprostol has less induction abortion interval compared to using misoprostol alone. This combination has more success rate and also has lesser side effects. Hence, unnecessary surgical interventions and its associated complications can be avoided.

7. Source of Funding

None.

8. Conflict of Interest

None.

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