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Research Article

Second trimester abortion- mifepristone and misoprostol or misoprostol alone?

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ABSTRACT

Background: From historical times termination of pregnancy was practiced with or without legal and social sanctions. Over the last few years, induced abortions have gained more popularity because of safe techniques and medications available. Induced abortion means willful termination of pregnancy before the period of viability. Medical abortion in the second trimester with misoprostol alone has been shown to be affective, although in comparison with the combination of mifepristone and misoprostol, misoprostol-only protocols have required higher doses, side effects are more common and the time to complete the abortion is longer.
Methods: Total of 50 eligible women were enrolled for this study and were divided in two groups of 25 each of the case group and control group. This study was conducted in the Dhiraj General Hospital, Piparia, Waghodia. Women in the case group were given Tablet Mifepristone (200 mg) orally followed by Tablet Misoprostol (200 mcg) vaginally after 24 hours which may be repeated every 6 hrs till 5 doses. Women in control group were given Tablet Misoprostol (200 mcg) vaginally which may be repeated every 6 hrs till 5 doses.
Results: The combination of mifepristone and misoprostol is now an established and highly effective and safe method for medical method second trimester abortion. The combination of mifepristone with misoprostol significantly reduces the abortion to induction interval and also have fewer side effects and complications and also reduces the dose of misoprostol. Where mifepristone is not available or affordable, misoprostol alone has also been shown to be effective, although a higher total dose is needed and efficacy is lower than for the combined regimen. Therefore, whenever possible, the combined regimen should be used.
Conclusions: Mifepristone followed by misoprostol was more effective and has a shorter IAI and fewer side effects.

Keywords: Abortion, Mifepristone, Misoprostol, Second trimester

INTRODUCTION

The Indian Penal Code of 1860, draws heavily from the British offences against the Person Act of 1861, which criminalised causing a miscarriage unless it was done to save the woman's life. In contrast to the trend in the western world, where legislative reform of abortion laws took place in the 1960s and 70s. In fact, it was demographers who justified legalising abortion to help curb population growth, while the medical profession advocated liberalising the law in order to reduce the high morbidity and mortality from unsafe abortions.

During 20th century, abortion has become legal in many Western countries, but it is regularly subjected to legal challenges and restrictions by profile groups.[1]

There is a need for evolving a safe and effective method of terminating pregnancy in the second trimester, most recently due to the increase in the use of antenatal diagnostic procedures like amniocentesis, USG and cordocentesis.

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.

From historical times termination of pregnancy was practiced with or without legal and social sanctions. Over the last few years, induced abortions have gained more popularity because of safe techniques and medications available. Induced abortion means willful termination of pregnancy before the period of viability.[2]

Second trimester abortions constitute 10-15% of all induced abortions worldwide but are responsible for two-thirds of major abortion-related complications. In India, 6 million abortions takes place every year, of which 4 million are induced and 2 million are spontaneous.[3] Although abortions was legalized in India is 1972, illegal abortion is still (urban) five (rural) times more common than legal abortion.[4]

Medical abortion in the second trimester with misoprostol alone has been shown to be affective, although in comparison with the combination of mifepristone and misoprostol, misoprostol-only protocols have required higher doses, side effects are more common and the time to complete the abortion is longer.[5]Higher doses (600 and 800μg) have shown comparable successful abortion rates but are associated with higher rates of side effects. The 3-hour interval is more effective than 6 hours interval.[6]

Unsafe abortion (2002) remains one of the leading causes of maternal death in most of developing countries. Infection rate associated with misoprostol was significantly lower than that with alternative traditional methods. If given in sufficient frequency, alone can abort a high proportion of pregnancies. Regimen of mifepristone and misoprostol has been found safe and effective in both developed and developing countries for 2nd trimester termination of pregnancy. Best appears to be combination of mifepristone followed by misoprostol. Popular regimens includes oral dose of mifepristone 200 mg followed by 1-3 doses later with vaginal misoprostol upto 800μg.[7]

Aims and Objectives

1. To evaluate the efficacy of tablet Mifepristone in combination with tablet Misoprostol in management of second trimester abortion and compare it with Misoprostol alone.
2. To observe the course and outcome of abortion in this combined regimen.
3. To study the possible side effects of these drugs.
4. To study the effective cost of both the regimens.

METHODS

Case Selection

- The present study is a prospective non-randomized comparative study done at Department of Obstetrics and Gynecology, Dhiraj General Hospital
- Total of 50 eligible women were enrolled for this study and were divided in two groups of 25 each.

Case: Women who received Mifepristone and Misoprostol.

Control: Women who received Misoprostol alone.

Inclusion Criteria

1. Gestational age more than 16 weeks but less than 20 weeks.
2. Singleton pregnancy
3. No regular uterine contractions
4. Upto para 4.

Exclusion Criteria

1. Grand multipara
2. Scarred uterus
3. Multiple pregnancy
4. Heart disease or known contraindication to the use of study drugs

Study Design

- All the eligible patients were explained about the procedure and their written informed consent was taken.
- Women in the case group were given Tablet Mifepristone (200 mg) orally followed by Tablet Misoprostol (200 mcg) vaginally after 24 hours which may be repeated every 6 hrs till 5 doses.
- Women in control group were given Tablet Misoprostol (200 mcg) vaginally which may be repeated every 6 hrs till 5 doses.

Data Analysis

- All the data were collected with the above mentioned methods and entered in to epi info version 3.5.3 and Chi- Square test was applied.

RESULTS

There were total 13 Nulliparous and 12 parous women taken in the Control group for the study. There was no woman in either nulliparous or parous group who required just 1 misoprostol tablet (1 misoprostol tablet= 200 µg) for abortion. 2 women from nulliparous group and 4 women from parous group required 2 misoprostol tablets for abortion. There were 5 nulliparous and just 1 woman from parous group who required 3 misoprostol tablets for abortion. 5 women from nulliparous group and 8 women from parous group who required 4 misoprostol tablets for abortion. There was no woman in either group who required 5 misoprostol tablets for abortion.

Table 1: Dosage of misoprostol required in control group.

No. of Misoprostol Tablets Required (200µg)	Nulliparous N=13		Parous N=12	
	No.	%	No.	%
1	00	0	00	0
2	02	16.66	04	30.77
3	05	41.67	01	7.69
4	05	41.67	08	61.54
5	00	0	00	0

Table 2: Dosage of misoprostol required in case group.

No. of Misoprostol Tablets Required (200µg)	Nulliparous N=13		Parous N=12	
	No.	%	No.	%
0	07	53.84	07	58.33
1	03	23.07	03	25
2	03	23.07	02	16.66
3	00	00	00	00

Same number of women in both nulliparous and parous groups were taken for as case group as like in control group, that was 13 women in nulliparous group and 12 women in parous group.

In case group, there were 7 nulliparous women and also 7 parous women who required 0 misoprostol tablet for abortion. There were 3 nulliparous women and also 3 parous women who required 1 misoprostol tablet for abortion. 3 nulliparous and 2 parous women required 2 misoprostol tablets for abortion. There was not a single woman of either group who needed 3 misoprostol tablets for abortion.

Table 3: Average dosage of misoprostol required in both groups.

	Mifepristone + Misoprostol N=25	Misoprostol Alone N=25
Average Dosage of Misoprostol Required	122 µg	696 µg

In the case group the average dosage of Misoprostol required for abortion was 122 µg. The dosage of Misoprostol required for abortion in control group was 696 µgm.

The mean induction abortion interval in women who were given mifepristone and misoprostol both was 18.94±9.30 hours and in the women who were given misoprostol alone was 24.29±11.53 hours.

Requirement of Oxytocin augmentation was much less in patients receiving Mifepristone+Misoprostol as compared to those receiving Misoprostol alone.

The incidence of adverse effects was higher in patients receiving only Misoprostol than those receiving Mifepristone and Misoprostol.

Table 4: Induction abortion interval (IAI).

IAI in Hours	Mifepristone + Misoprostol N=25				Misoprostol Alone N=25			
	Nulliparous N=13		Parous N=12		Nulliparous N=13		Parous N=12	
	No.	%	No.	%	No.	%	No.	%
0-6	01	7.69	02	16.66	00	0	00	0
>6-12	04	30.76	03	25	01	8.33	00	0
>12-18	03	23.07	00	0	02	16.66	04	30.76
>18-24	00	0	02	16.66	05	41.66	03	23.07
>24-30	02	15.38	02	16.66	04	33.33	03	23.07
>30-36	03	23.07	03	25	00	0	01	7.69
>36	00	0	00	0	00	0	02	15.38

Table 5: Mean induction abortion interval.

Duration (In Hours)	Mifepristone + Misoprostol N=25	Misoprostol Alone N=25
	18.94±9.30	24.29±11.53

Table 6: Distribution of patients who required oxytocin augmentation.

Oxytocin Augmentation	Mifepristone +Misoprostol N=25		Misoprostol Alone N=25	
Required	04	16	10	40
Not Required	21	84	15	60
	P=0.0272			

Table 7: Adverse effects of drugs.

Side Effects	Mifepristone +Misoprostol N=25		Misoprostol Alone N=25	
	No.	%	No.	%
Nausea	00	-	01	04
Vomiting	01	04	03	12
Diarrhoea	00	-	01	04
Fever	00	-	02	08
Headache	00	-	00	00
Rigor	00	-	04	16
Hypertonicity	00	-	03	12

Table 8: Comparison of hospital stay in both groups.

No. of Days	Mifepristone +Misoprostol N=25		Misoprostol Alone N=25	
	No.	%	No.	%
≤3	12	48	13	52
4-6	11	44	10	40
>6	02	08	02	08

Comparative hospital stay in patients receiving Mifepristone +Misoprostol was more or less similar to patients receiving Misoprostol alone.

Table 9: Mean cost of drugs used in the study.

Drugs Used	Mifepristone +Misoprostol	Misoprostol Alone
Mifepristone	Rs.395	Rs.0
Misoprostol	Rs.12.05	Rs.68.73
Oxytocin	Rs.96.8	Rs.242
Total Cost	Rs.503.85	Rs.310.73

The mean cost of the drugs in case group was Rs 503.85 and in control group was Rs.310.73.

Table 10: Type of abortion occurring by both the groups.

Type of Abortion	Mifepristone +Misoprostol N=25	Misoprostol Alone N=25
Complete	25	21
Incomplete	00	04

It was observed that complete abortion occurred in 25 patients receiving mifepristone and misoprostol both and in 21 patients receiving misoprostol alone. There was no patient who had incomplete abortion after receiving mifepristone and misoprostol and 4 patients receiving misoprostol alone.

DISCUSSION

Second trimester pregnancy termination is still a complicated procedure in developing countries especially in rural areas.

There is constant search going on for an ideal method which is 100% reliable, safe and cheap.

The IAI, success rate, hospital stay duration, side effects, and costs are compared between the two groups.

- There was significant difference in the IAI in both the groups, the mean IAI of 18.94 hours for Group A, whereas in Group B IAI is 24.29 hours.
- There was also difference in the success rate and hospital stay duration. The hospital stay was longer in Group B than Group A.
- Side effects were also seen more in Group B than Group A.

The combination of oral mifepristone 200 mg pre-treatment, followed by vaginally misoprostol, provides a non-invasive effective regimen for medical second trimester termination of pregnancy and significantly reduces the induction to abortion interval and lesser side effects and good patient compliance. The side effects observed were actually directly associated with the dosage of misoprostol.

This method can be used in an outpatient clinic or primary health centre where facilities for surgical evacuation are not available. The doctors with back up facility who are not trained in MTP's can perform this procedure. In case of any problem like retained products, suspected abortion failure, heavy bleeding per vaginum the patient can be referred to health facilities for surgical evacuation are available. With this procedure morbidity

and mortality due to illegal abortions can be markedly reduced.

CONCLUSION

During the last decade, medical methods for second trimester induced abortion have been considerably improved and become safe and more accessible. Today, in most cases, safe and efficient medical abortion services can be offered or improved by minor changes in existing health care facilities.

Because of the potential for heavy vaginal bleeding and serious complications, it is advisable that second trimester terminations take place in a health care facility where blood transfusion and emergency surgery (including laparotomy) are available. The combination of mifepristone and misoprostol is now an established and highly effective and safe method for medical method second trimester abortion. The combination of mifepristone with misoprostol significantly reduces the abortion to induction interval and also have fewer side effects and complications and also reduces the dose of misoprostol. Where mifepristone is not available or affordable, misoprostol alone has also been shown to be effective, although a higher total dose is needed and efficacy is lower than for the combined regimen. Therefore, whenever possible, the combined regimen should be used. Efforts should be made to reduce unnecessary surgical evacuation of the uterus after expulsion of the fetus.

So among the two methods, mifepristone followed by misoprostol was more effective and has a shorter IAI and fewer side effects. But in fact, both are feasible as far as end results are concerned.

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Conflict of interest: None declared
Ethical approval: The study was approved by the Institutional Ethics Committee

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