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Comparative Study of "Mifepristone with Vaginal Misoprostol" and "Vaginal Misoprostol Alone" in Second Trimester Medical Termination of Pregnancy

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Abstract

Objective: *The present study was conducted with the aim to assess and comparatively evaluate the safety and efficacy of misoprostol alone and mifepristone with misoprostol for second trimester termination of pregnancy.*
Methods and Materials: *The study was conducted in 100 selected cases, divided in two groups of 50 cases each. In the group A mifepristone 200 mg was given 48 hrs after which vaginal intravaginal insertion of 400ug of misoprostol upto a maximum of 5 doses or until the abortion occurs, whichever occurs early. In the group B only misoprostol was inserted in the same dose regimen. The results were analysed.*
Results: *The success rate is greater in mifepristone with misoprostol group with 98% than misoprostol group with 90% Mean induction abortion interval from the insertion of the first misoprostol tablet is significantly shorter in the mifepristone pretreated group 12.93+4.19 hr as compared to 19.18+3.97 hr in the misoprostol alone group (p<0.001). The mean dose of the misoprostol required is significantly less in the mifepristone group as against misoprostol group (p=0.008). The side effects and complications observed in both the groups are mainly nausea vomiting, fever, abdominal cramps, bleeding, rigor, dizziness, retained products of consumption and these side effects are more in misoprostol group.*
Conclusion: *Pretreatment with mifepristone 48 hrs before intravaginal misoprostol significantly improves the induction abortion interval with lesser side effects & complication.*

Keywords: *Second trimester termination of pregnancy, mifepristone, Misoprostol.*

Introduction

Abortion is defined as the termination of pregnancy after implantation of the blastocyst in the endometrium but before fetus has attained the period of viability , before 20 weeks of gestation or weight less than 500 grams.(WHO)[1]. Approximately 1/3 rd of all abortion are performed under unsafe conditions. Unsafe abortion is the cause of serious complications and disability. About 85% of the induced abortions are in the first trimester and 15% in the second trimester. Ideally if the first trimester termination is done, prognosis is better. Morbidity and mortality rates in second trimester are 3-4 times higher than that of the first trimester terminating. The reasons for delay in seeking abortion are lack of information on the availability of abortion facilities, Ignorance and or psychological denial of pregnancy, ambivalence regarding the desirability of abortion Late identification of Medical disorders contraindicating the continuation of pregnancy, Late discovery of fetal malformation , Lack of financial resources to reach the hospitals. Among the various methods, surgical methods have the following disadvantages: Uterine hemorrhage, Pelvic infection, Cervical injury, Uterine perforation, Retained products, Continuation of pregnancy especially in vacuum aspiration cases and Maternal morbidity and mortality may be increased. Medical abortion is an approach to pregnancy termination which is non invasive with minimal side effects. There is a search for better, safer, quickest, cost effective, convenient and feasible method for termination in second trimester.

Misoprostol, synthetic prostaglandin analogue, originally approved by FDA for treatment of gastric ulcer has been found to have good uterotonic potential. Till date, it is not a approved drug by FDA for pregnancy termination in second trimester. Misoprostol is being (off label) used for termination of pregnancy in different doses and by different routes, in between 13 and 20 weeks with satisfactory results[3] So in this study, medical method of termination of second trimester pregnancy with mifepristone and misoprostol is compared with misoprostol alone.

Aim of the study

1) To compare the outcome of tablet mifepristone and vaginal misoprostol versus vaginal misoprostol alone

for second trimester medical termination of pregnancy.
2) To evaluate induction abortion interval
3) To study and evaluate failure rate, complications, and side effects.

Material and methods

This is an Interventional Prospective Comparative clinical study for the period of 1 year with 100 cases of eligible women. The study to be conducted in women admitted in GRH for second trimester termination of pregnancy.

Inclusion criteria

1) Pregnant women who need MTP from 13 – 20 weeks in family planning OPD
2) Pregnant women with anomalous baby from 13-20 weeks of gestation.
3) Pregnant women with obstetric & medical indications for 2nd trimester termination from 13-20 weeks

Exclusion criteria

1) Previous allergic reaction to one of the drugs
2) Known / suspected ectopic pregnancy
3) Pregnancy with previous LSCS scar
4) Multiple pregnancy
5) Preexisting heart disease
6) Women on long term corticosteroid therapy
7) Known case of asthma
8) Inherited porphyria

A detailed history of the case regarding menstrual, obstetric, personal, medical with special reference to cardiovascular, respiratory, GIT, endocrinal disorder and coagulopathy was obtained. General and systemic examination of the cases was done. Investigations were done. Proper counseling and written consent were obtained They were grouped into two GROUP A-mifepristone &misoprostol and GROUPB-misoprostol alone

Group A

T. mifepristone 200mg orally given. 48 hrs later, under strict aseptic precaution, misoprostol 400µg is kept in the posterior fornix. The dose is repeated after 8hrs, 6hours, 4hours, 4hours to the maximum of 5 doses.

Group B

Under strict aseptic precaution 400µg misoprostol is kept in the posterior fornix. The dose is repeated after 8hrs, 6hours, 4hours, 4hours to the maximum of 5 doses.

Primary outcome measures

Induction abortion interval,

Complete abortion occurred

Secondary outcome

Side effects, complications

Incomplete abortion/failure requiring any surgical interventions

Induction abortion interval

Time period between first dose of misoprostol to the expulsion of products of conception.

Completeness of abortion

The procedure is said to be complete when no products of conception are seen in the uterine cavity when USG done after 24hrs of abortion. The procedure is incomplete when there is part or whole of the placenta is retained in the uterus and if there is retained products of conception in USG done after 24 hours of abortion. These cases underwent check curettage.

Success

The procedure is considered success if expulsion of products of conception occur within 30hrs of first dose of misoprostol.

Failure

The procedure is considered to be failed when the products of conception did not expel within 30hrs since the insertion of first dose of misoprostol. The failed cases are reassured and further treated with other methods of MTP.

Results and Discussion

Table 1

Factors	Mifepristone + misoprostol group	Misoprostol alone group
Age in years (mean)	26.36	26.84
Parity Primi Multi	 44% 56%	 48% 62%
Gestational Age in weeks (Mean)	16	16

In our study, majority of the patients in both groups are between 25-30 years. The mean age is 26.36 in mifepristone and misoprostol group and 26.84 in misoprostol group and is not a statistically significant difference. (p=0.621) (Table – 1)

In the present study, most of the patients are multigravida 56% in mifepristone & misoprostol group

and 62% in misoprostol group. The difference in parity of two groups is not statistically significant. (p=0.904) (Table – 1)

The range of gestational age of both the group is 13 weeks to 20 weeks. There is no statistically significant (p value=0.478) difference in both group with regard to gestational age. (Table – 1)

Table 2

Induction abortion interval	Mifepristone & misoprostol		Misoprostol	
	No	%	No	%
Up to 8 hrs	8	16	0	0
8.1 – 16 hrs	34	68	7	14
16.1 – 24 hrs	6	12	32	64
> 24 hrs	1	2	6	12
Failed induction	1	2	5	10
Total	50	100	50	100
Range	6 – 25.5		12.2 – 26.5	
Mean	12.93		19.18	
S. D	4.19		3.97	
P Value	<0.001 Significant			

In the present study, the mean interval between start of induction and vaginal delivery is shorter in mifepristone and misoprostol group 12.93 hrs than misoprostol group 19.18 hrs .This difference is statistically significant. P value is <0.001 **(Table – 2)**

Table 3

No. of doses of misoprostol 400ug	**Mifepristone &misoprostol**		**Misoprostol**	
	No	**%**	**No**	**%**
1	8	16	0	0
2	26	52	7	14
3	12	24	19	38
4	1	2	16	32
5	3	6	8	16
Total	50	100	50	100
< 2 doses	**34**	**68**	**7**	**14**
> 2 doses	**16**	**32**	**43**	**86**
P value	0.008 Significant			

The number of doses of misoprostol used in mifepristone and misoprostol group is less than in misoprostol alone group and is statistically significant. (p=0.008) (Table – 3).

Table 4

Oxytocin augmentation	**Mifepristone& misoprostol**		**Misoprostol**	
	No.	**%**	**No.**	**%**
Required	2	4	5	10
Not required	48	96	45	90
Total	50	100	50	100
p value	0.481 Not Sig			

Requirement of oxytocin augmentation is less in patients receiving mifepristone and misoprostol group as compared to those receiving misoprostol alone but it is not statistically significant. (p= 0.481) (Table – 4)

Table 5

Type of abortion		Mifepristone& misoprostol		Misoprostol	
		No.	%	No.	%
Success	Complete	45	90	30	60
	Incomplete	4	8	15	30
Failure		1	2	5	10
Total		50	50	50	50
p value		0.027 Significant			

In the present study, the success rate is 98% in tab. Mifepristone and tab. misoprostol group and 92% in misoprostol alone group. There is statistically significant difference in success rate. (P=0.027) The success rate is higher in mifepristone and misoprostol group than misoprostol group. (Table-5)

Failure rate is 2% in mifepristone and misoprostol group and 10% in misoprostol group. Those patients who were not started abortion after 30hrs were reassured and further treated with one of the following measures.

Interventions needed in failure cases	Mifepristone & misoprostol	Misoprostol
Second course of misoprostol	---	---
Course of mifepristone and misoprostol	---	2
Bougie insertion	1	3
Hysterotomy	---	---
TOTAL CASES	1	5

Table 6

Side effects	Mifepristone & misoprostol		Misoprostol	
	No.	%	No.	%
Abdominal pain	3	6	6	12
Diarrhea	1	2	3	6
Dizziness	1	2	2	4
Fever	1	2	3	6
Nausea, vomiting	2	4	8	16
Rigor	1	2	2	4
Bleeding	0	0	2	4
Infection	0	0	0	0
Rupture	0	0	0	0
With complications	**9**	**18**	**26**	**52**
Nil complications	41	82	24	48
Total	50	100	50	100
P value	0.012 Significant			

The incidence of side effects and complications are more in misoprostol group (52%) than mifepristone and misoprostol group (18%) and is statistically significant. (p=0.012) Table – 6.

Table 7

Group	Mifepristone& misoprostol	Misoprostol
Retained products of conception requiring curettage	4	15
Percentage	8	30
p value	0.038 Significant	

Incomplete abortion requiring curettage is more with misoprostol group (15/50) 30 %than mifepristone with misoprostol group (4/50) 8% and is statistically significant (p=0.038) Table – 7.

Table 8

Induction outcome vs Age	Mifepristone &misoprostol	Miso prostol
Success (Mean +SD)	**26.06 ± 5.07**	**26.65 ± 4.73**
Failure (Mean +SD)	**28.5 ± 5.6**	**27.25 ± 4.12**
p value	0.282	0.664

There is no statistical significance of age in relation to induction outcome in both the groups (Table : 8)

Table 9

Induction outcome vs Parity	Success		Failure	
	Mifepristone with misoprostol	Misoprostol	Mifepristone with misoprostol	Mistoprostol
Primi	30	26	0	4
Multi	68	64	2	6
Total	98	90	2	10
p value	0.932 / 0.879 Not significant			

The success rate is 31.8% in primi, 68.2% in multigravida. There is no statistical significance of parity in relation to induction outcome in both the groups. (Table – 9)

Table 10

Induction outcome vs GA	Mifepristone &misoprostol		Misoprostol	
	Success	Failure	Success	Failure
13	10		14	2
14	18		18	2
15	10		8	
16	12		14	
17	10		8	
18	14	2	10	4
19	6		4	2
20	18		14	
Total	98	2	90	10
P value	P=0.381		P=0.161	

There is no statistically significance of gestational age in relation to induction outcome in both the groups (Table – 10)

Discussion

- Misoprostol has proven its efficacy as an effective abortifacient for the second trimester termination of pregnancy. It is being successfully used through all the routes. ie. sublingual, oral and vaginal and in different regimens with the induction abortion interval varying from 12 hrs to as high as 33 hrs. Misoprostol is a sympathetic PGE1 analog induces cervical ripening and strong uterine contraction leading to expulsion. The receptors are present throughout the pregnancy. Hence effective for termination of pregnancy of at all gestational age. Misoprostol is a proven induction agent in the second trimester for termination of pregnancy or fetal death. One regimen is 400 µg vaginally every 6 hours up to 48 hours[2].
- Combination of mifepristone with misoprostol is now widely used method for pregnancy termination. Priming of the uterus with mifepristone makes it more sensitive to prostaglandins. It binds with the progesterone on prostaglandin synthesis and metabolism resulting in increase in production and decreased deactivation of prostaglandins. It also induces cervical softening thus, enhancing the efficacy of the prostaglandins as an abortifacient.
- In this study, the induction abortion interval is much lesser in mifepristone with misoprostol group (12.93+4.19) than misoprostol group (19.18+3.17). Number of doses of misoprostol is lesser in mifepristone with misoprostol group than in misoprostol group. Although the requirement of oxytocin augmentation is lesser in mifepristone with misoprostol group it is not statistically significant. The success rate is higher in mifepristone with misoprostol group (98%) than misoprostol group (90%). Among the success group the incomplete abortion requiring surgical evacuation is lesser in mifepristone with misoprostol group (8%) than in misoprostol group (30%) The side effects and complications are lesser in mifepristone with misoprostol group (18%) than in misoprostol group (52%) The complications are abdominal pain, diarrhea, dizziness, fever, nausea vomiting, rigor and bleeding.
- This method can be used in an outpatient clinic or primary health centre where facilities for surgical evacuation are not available. In case of any problem, like retained products, suspected abortion failure, heavy bleeding per vaginum, the patient can be referred to health facilities where surgical evacuation are available. Hence the morbidity and mortality due to illegal abortions can be markedly reduced.

Conclusion

The combination of mifepristone and misoprostol is now an established and highly effective, safe method for second trimester medical termination of pregnancy. The combination of mifepristone and misoprostol significantly reduces the induction abortion interval. Mifepristone followed by misoprostol reduces the number of doses of misoprostol and hence the incidence of side effects and complications are reduced. Where mifepristone is not available or affordable, misoprostol alone has also been used and is shown to be effective, although higher total

dosage is needed and the efficacy is lower than for the combined regimen.

Therefore, whenever possible, combined regimen should be used. Future studies should focus on improving the pain management, treatment of women with failed medical abortion after 24 hrs and the safety of medical abortions regimens in women with a previous caesarean section or uterine scar.

References

[1]. Medical methods of termination of pregnancy WHO technical report series 871, WHO Geneva, 1997

[2]. Wong KS, Ngai CS, Yeo EL, *et al*. A comparison of two regimen of intravaginal misoprostol for termination of second trimester pregnancy: a randomized trial. Hum Reprod. 2000;15: 709–712.

[3]. Herbutya Y, Chanarchakul B, Punyavachira P. Vaginal misoprostol in the termination of second trimester pregnancy. J Obstet Gynaecol Res. 2000;26:121–125. 4.