International Journal of Current Advanced Research
ISSN: O: 2319-6475, ISSN: P: 2319 – 6505, Impact Factor: SJIF: 5.995
Available Online at www.journalijcar.org
Volume 6; Issue 7; July 2017; Page No. 4472-4475
DOI: http://dx.doi.org/10.24327/ijcar.2017.4475.0521

Research Article

MIFEPRISTONE PLUS MISOPROSTOL VERSUS MISOPROSTOL FOR SECOND TRIMESTER TERMINATION OF PREGNANCY

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A R T I C L E I N F O

Article History:

Received 11th April, 2017
Received in revised form 10th May, 2017
Accepted 4th June, 2017
Published online 28th July, 2017

Key words:

Second trimester termination of pregnancy, Mifepristone and Misoprostol

A B S T R A C T

Objective: The present study was conducted with the aim to assess and comparatively evaluate the safety and efficacy of mifepristone plus misoprostol versus only misoprostol in second trimester termination of pregnancy

Materials and Methods: The present study was conducted in Rajindra Hospital, Government medical college, Patiala. Group A received Tab Mifepristone 200mg orally. After 48 hours 400 µg of Tab Misoprostol was placed vaginally. Then every 4th hourly 400 µg of misoprostol tab was placed vaginally upto maximum of five doses including the first dose or till expulsion of foetus. Group B received tablet misoprostol as mentioned in group A without prior mifepristone .After 24 weeks of gestation 200 µg of misoprostol was used. The subjects were closely monitored for any side effects. Induction abortion interval is the time period between insertion of first intravaginal misoprostol tablet to expulsion of products of expulsion. The process was considered failure if abortion failed to occur even after 12 hours of last dose of misoprostol.

Results : Mean time for onset of contractions was 4.53 hours in group A and 7.43 hours in group B. Mean time of onset of bleeding was 4.54 hours in group A and 7.39 hours in group B(P value <0.001). Induction abortion interval when calculated in both groups came out to be 8.12 hours in group A and 13.41 hours in group B which was statistically significant. Mean dose of misoprostol was 769.89 µg in group A and 1043.2 µg in group B Side effect profile was similar in both groups. Shivering was the most common side effect in both groups followed by diarrhoea followed by nausea and vomiting. Side effects were not related to number of doses of misoprostol given and occurred in most of the subjects quite early after 2nd or 3rd dose. The number of subjects who needed check curettage were almost similar in both groups. Success rate was 97% in group A and 87% in group B. The subjects who were unsuccessful either had drug failure or had to discontinue misoprostol due to severity of side effects.

Conclusion: Mifepristone and misoprostol combination is better than misoprostol alone for second trimester termination of pregnancy. The time of onset of contractions, the time of onset of bleeding, Induction abortion interval, mean doses of misoprostol are reduced with the combination regimen. Success rate of combination regimen is more as compared to misoprostol only regimen.

INTRODUCTION

Although the majority of abortions are performed in first trimester, there is still a need for second trimester abortions because of wide scale introduction of prenatal screening programmes detecting woman whose pregnancies are complicated with fetal anomalies such as craniovertebral, cardiovascular and skeletal malformations. Research to identify an ideal (safe, effective) method for termination of second trimester pregnancy is still ongoing. A number of medical and surgical methods have been tried in the past.

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Surgical Methods

- Dilatation and Evacuation
- Hysterotomy

Medical Methods

- Extra Amniotic instillation of Drugs
- Intra Amniotic Instillation of Hypertonic Saline
- Intra muscular injections of Prostaglandin $F_2\alpha$
- Mifepristone Plus Misoprostol

The discovery of antiprogestin, mifepristone, in 1980, made it possible to develop effective nonsurgical methods for termination of pregnancy.

Mifepristone alone is not sufficient, and the most effective and safest regimen requires the use of prostaglandin analogue such as misoprostol following administration of mifepristone. It acts by blocking progesterone receptors results in vascular damage, decidual necrosis and bleeding, which leads to cervical softening.. It is orally active (200mg) with good bioavailability.

Misoprostol: Synthetic PGE-1 analogue having half life of 90 mins. The receptors are present throughout the pregnancy; hence, PGs and PG analogues are effective for termination of pregnancy irrespective of gestation .It causes myometrial contractions by interacting with specific receptors on myometrial cells .This interaction results in a change in calcium concentrations thereby initiating muscle contractions. By interacting with prostaglandin receptor, Misoprostol causes the cervix to soften and uterus to contract thereby causing expulsion of uterine contents. Maximal priming effect on the myometrium is achieved 36-48 hours after pre-treatment with mifepristone. A shorter interval of 24 hours resulted in a slightly longer induction-to-abortion interval, a higher total dose of misoprostol used and a higher rate of uterine curettage.

Aims and Objectives

- To evaluate the efficacy of Mifepristone in combination with Misoprostol in management of second trimester termination of pregnancy
- To evaluate the efficacy of Misoprostol alone in second trimester termination of pregnancy
- To compare both the regimens in terms of efficacy, course and outcome.
- To study the possible side effects of drugs.

MATERIAL AND METHODS

The present study was conducted in Department of Obstetrics and Gynecology in Government Medical College and Rajindra Hospital, Patiala. 200 pregnant women in second trimester of their pregnancy were taken up for study after proper counseling and taking written consent. The subjects were divided into two groups (Group A and Group B) of 100 each.

Inclusion Criteria

- Pregnant women with intra uterine fetal death (IUFD) in second trimester.
- Pregnant women with anomalous baby (not compatible with life) in second trimester.
- Pregnant women needing termination due to any medical/obstetric complication in second trimester.

Exclusion Criteria

- Inherited Porphyria
- Allergy to drugs
- Severe uncontrolled asthma
- Pre-existing cardiac disease
- Acute and chronic renal failure
- Pregnancy with placenta previa
- Current use of system corticosteroids

METHODOLOGY

All the eligible candidate were divided into two groups :-

Group A - Mifepristone plus Misoprostol
Group B - Misoprostol alone

Group A - Subjects were given tablet mifepristone 200mg on Day 1. Subjects were called up again approximately after 48 hours (Day 3) for 1st dose of misoprostol. 400µg of misoprostol (2 tablets) was kept high up in posterior vaginal fornix. Subjects were observed for onset of uterine contraction and bleeding per vaginum. Dose of misoprostol will be repeated every four hourly till expulsion of fetus or upto a maximum of 5 doses (2000µg). If the subject was having good uterine activity then the dose of misoprostol (400µg) was omitted. Further dose interval was adjusted according to uterine contractions. In case of incomplete abortion surgical evacuation was done.

Group B - subjects were given 400µg of tablet misoprostol intravaginally which was kept high up in posterior vaginal fornix. Dose of misoprostol was repeated every 4 hourly till expulsion of fetus or upto maximum of 5 doses. If the subject was having good uterine activity then the dose of misoprostol (400µg) was omitted. Further dose interval was adjusted according to uterine contractions. In case of incomplete abortion surgical evacuation was done.

In case the pregnancy is beyond 24 weeks then a lower dose of misoprostol was used. Instead of 400µg of misoprostol, 200µg of misoprostol was used in both regimens.Induction abortion interval was taken from the dose of first misoprostol given. The data was entered in a predesigned proforma and analyzed in the end.

OBSERVATIONS

Maximum number of subjects were in the age group of 26-30 years in both study groups. The mean age in group A was 25.58 years and in group B was 25.77 years.

There were 43% primigravidas and 57% multigravidas in group A as compared to 32% prmigravidas and 68% multigravidas in group B. Majority of subjects were multigravida in both groups. Minimum gestation in both groups was 12 weeks. Maximum Gestation in both groups was 28 weeks. Intrauterine death or missed abortion was the most common indication for termination in both groups that is 61% in group A and 65% in group B. The second most common indication was congenitally malformed foetus accounting for 39% in group A and 29% in group B. The medical condition for termination comprised of only 6% subjects in group B and the associated condition was antepartum eclampsia in all the cases. The mean time of onset of contractions came out to be 4.53 hours in group A and 7.43 hours in group B which was statistically significant Similarly the mean time of onset of bleeding came out to be 4.54 hours in group A and 7.39 hours in group B .The mean induction abortion interval came out to be 8.12 hours in group A and 13.41 hours in group B. The mean dose of misoprostol came out to be 769.89 µg in group A and 1043.2 µg in group B. Shivering was the side effect in maximum number of subjects followed by diarrhoea followed by nausea and vomiting. Most of the side effects occurred after 2nd or 3rd dose.

None of the subjects in group A had any side effect with mifepristone. Rest of the Side effect profile was almost similar in both groups.

In group A out of 97 successful subjects seven subjects had incomplete removal of placenta .So check curettage was done. As compared to group A, in group B out of 87 successful subjects nine required check curettage.

In group A 97% of subjects had success with mifepristone and misoprostol combination regimen. Three subjects had to discontinue misoprostol due to severe side effects. Among remaining 97 subjects 5 subjects expelled with mifepristone only.

In group B success rate is 87%. Out of thirteen unsuccessful subjects seven subjects had to discontinue misoprostol due to severe side effects in form of shivering or diarrhoea and six subjects had drug failure.

Parameter	Group A(N=100)	Group B(N=100)	P Value
Mean time of onset of contraction	4.53±2.29hours	7.43±3.20hours	<0.001
Mean time of onset of bleeding	4.54±2.32hours	7.39±3.20hours	<0.001
Induction abortion interval	8.12±3.97hours	13.41±5.46hours	<0.001

Mean Dose of Misoprostol in Both Groups

Mean dose ±S.D (in µg)	Group A(N=100)	Group B(N=100)	P value
	769.89±364.69	1043.2±502.36	<0.001

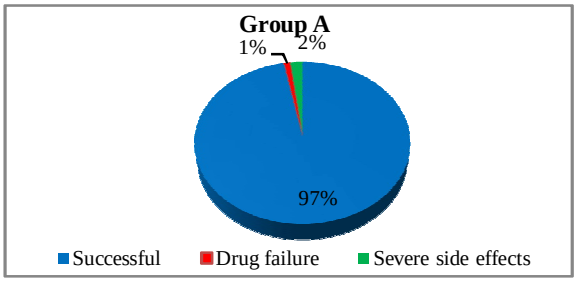
Side Effects of Drugs

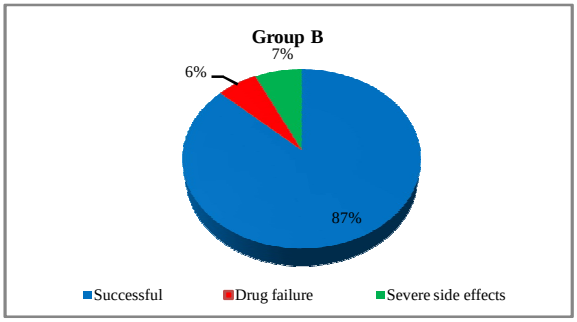
Side Effects	Group A		Group B	
	No	%age	No	%age
Shivering	6	6	6	6
Nausea	2	2	3	3
Vomiting	1	1	3	3
Diarrhea	3	3	4	4
Fever	1	1	2	2
Headache	0	0	0	0
Rupture	0	0	0	0

Surgical Intervention Needed or Not

Check curettage done	Group A		Group B	
	No	%age	No	%age
	7	**7.22**	**9**	**10.34**
Not Needed	90	92.78	78	89.66

Final Outcome





DISCUSSION

Second trimester pregnancy termination is still a complicated procedure in developing countries especially in rural areas. There is a constant research going on for an ideal method which is 100% reliable, safe, cheap and efficacious.

The combination of oral mifepristone followed by vaginal misoprostol provides a non invasive effective regimen for medical termination of pregnancy and significantly reduces the induction to abortion interval with lesser side effects and good patient compliance. Misoprostol alone can also be used for termination of pregnancy.[2]

In the present study the mean time of onset of contractions in group A was 4.53 hours and 7.43 hours in group B which was comparable to study conducted by Tripti and Namrata *et al* (2007). Our study was consistent with the study of Tripti and Namrata *et al*[8] in comparing the mean time of onset of bleeding. In the present study, the mean induction abortion interval in group A came out to be 8.12 hours while in group B it was 13.41 hours which is consistent with studies done by Tripti and Namrata (2007), Gandhi *et al* (2013), Mukhopadhayay *et al* (2011), Patil and Biliangady(2014), Patel *et al* (2013) and Shah et a] (2015)

In the present study mean doses of misoprostol was 769.89 µg in group A and 1043.2 µg in group B which was comparable to study of Mukhopadhayay *et al* (2011) and Tripti and Namrata (2007). Our study is comparable to other studies done by Tripti and Namrata (2007), Mukhopadhyay *et al* (2012), Shah *et al* (2015) and Patil and Biliangady (2014) who also showed increased need for check curettage in subjects not given pretreatment with mifepristone. In the present study the success rate was 97% in group A and 87% in group B which is comparable to the studies done by Tripti and Namrata (2007), Mukhopadhyay *et al* (2011), Shah *et al* (2015) who also found better success rate in subjects who were given both mifepristone and misoprostol as compared to subjects who were given only misoprostol. Our success rate with misoprostol only group was lower as compared to studies done by Tripti and Namrata[8], Mukhopadhyay *et al*[27] and Shah *et al*[34] as our study excluded subjects who had to discontinue misoprostol due to severe side effects.

CONCLUSION

Mifepristone and misoprostol combination is better than misoprostol alone for second trimester termination of pregnancy. The time of onset of contractions, the time of onset of bleeding, Induction abortion interval, mean doses of misoprostol are reduced with the combination regimen. Success rate of combination regimen is more as compared to misoprostol only regimen.

References

1. Lalitkumar S, Bygdeman M, Gemzell-Danielsson K. Mid-trimester induced abortion: a review. *Hum Reprod Update*. 2007; 13(1):37-52.
2. Patel U, Chauhan K, Singhi S, Kanani M. Second trimester abortion- mifepristone and misoprostol or misoprostol alone? *Int J Reprod Contracept Obstet Gynecol*. 2013; 2(3): 315-319.
3. Padubidri VG and Daftary SN. Birth Control and Medical Termination of Pregnancy. In: Howkins &

Bourne Shaw's Textbook of Gynaecology 14th edn. Elsevir 2008; 18S: 220-24.
4. Gupta N and Mittal S. Is Mifepristone Needed for Second Trimester Termination of Pregnancy? *J Turkish-German Gynecol Asso.* 2007; 8(1):58-62.
5. Shah PK. Non-Medical Methods of Second Trimester Abortion. Comprehensive Abortion Care & Post abortion Contraception. *The Federation of Obstetric and Gynaecological Societies of India* 2012; 34-36. .
6. Tripti N and Namrata S. Misoprostol Vs Mifepristone and Misoprostol in Second Trimester Termination of Pregnancy. *The Journal of Obstetrics and Gynecology of India* 2011; 61(6):659-62.
7. Tang OS, Gemzell-Danielsson K, Ho PC. Misoprostol: pharmacokinetic profiles, effects on the uterus and side-effects. *Int J Gynaecol Obstet*. 2007; 99 Suppl 2:S160-7.
8. World Health Organization. WHO Essential Medicines Library Website. Available from http://www.who.int/ medicines/publications/essential medicines/en/.
9. Fiala C and Danielsson G.K. Review of medical abortion using mifepristone in combination with a prostaglandin analogue Contraception.2006; 74:66-86.
10. Brunton LL, Chabner BA, Knollmann BC. Goodman and Gilman Pharmacological basis of therapeutics. (12th edn.) McGraw-Hill
11. Danielsson KG and Laltikumar S. Second trimester medical abortion with mifepristone -misoprostol and misoprostol alone: a review of methods and management. *Reproductive health matters.* 2008; 16(3 1):162-72.
12. Faundes A. The combination of mifepristone and misoprostol for the termination of pregnancy. *International Journal of Gynecology and Obstetrics* 2011; 115:1-4.
13. Practice Bulletin. Clinical Management Guidelines for Obstetrician - Gynaecologists: Second-Trimester Abortion. *Obstetrics and Gynecology* 2013; 121(6):1394-1406.
14. Brece JS. Novak's Gynecology (13th edn.) Lippincott Williams and Williams Publication 2002; 279-281.
15. Ngoc NT, Shochet T, Raghavan S, Blum J, Nga NT, Minh NT *et al*. Mifepristone and misoprostol compared with misoprostol alone for second-trimester abortion: a randomized controlled trial. *Obstet Gynecol.* 2011; 118(3):601-8.
16. Wildschut H, Both MI, Medema S, Thomee E, Wildhagen MF, Kapp N. Medical methods for mid-trimester termination of pregnancy. *Cochrane Database of Systematic Reviews* 2011; 1:CD005216.
17. Stibbe J.K, Weerd S. Induction of delivery by mifepristone and misoprostol in termination of pregnancy and intrauterine fetal death: 2nd and 3rd trimester termination of pregnancy. *Arch gynaecol obster.* 2012;286:795-796
18. Mukhopadhyay P, Bag TS, Kyal A, Bhuniya A, Saha TK. Second Trimester Abortion with Vaginal Misoprostol: Is There Any Advantage with Prior Mifepristone Priming? A Comparative Study. *Journal of South Asian Federation of Obstetrics and Gynaecology* 2012;4(1):25-27
19. Gandhi P, Shameen VPA, Rao A, Rao B. Mifepristone plus misoprostol versus only-misoprostol in induction of labour in intra uterine fetal death. *Int J Pharm Biomed Res* 2013; 4(2):108-110.
20. Aggarwal A, Bisnet P, Thakur A, Rizal P, Rai R. Induction of labour using misoprostol with or withour mifepristone in intrauterine death, *Journal Of Nepal Medical Association.*2014;52(194):781-86.

How to cite this article:

Aayushi Kaushal *et al* (2017) ' Mifepristone Plus Misoprostol Versus Misoprostol For Secondtrimester Termination Of Pregnancy', *International Journal of Current Advanced Research,* 06(07), pp. 4472-4475.
DOI: http://dx.doi.org/10.24327/ijcar.2017.4475.0521

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