Original Research Paper

Volume - 11 | Issue - 01 | January - 2021 | PRINT ISSN No. 2249 - 555X | DOI : 10.36106/ijar

Obstetrics & Gynecology

STUDY OF THE EFFICACY AND SUCCESS RATE OF MIFEPRISTONE AND MISOPROSTOL V/S MISOPROSTOL ALONE IN MID-TRIMESTER ABORTION

Karuna Kanta Das* — Associate Professor, Obstetrics and Gynaecology department, Gauhati medical college and Hospital, Guwahati, Assam, India. *Corresponding Author

Bijoy Kumar Dutta — Associate Professor, Obstetrics and Gynaecology department, Gauhati medical college and Hospital, Guwahati, Assam, India.

Chintumoni Gogoi — Post Graduate Trainee, Obstetrics and Gynaecology department, Gauhati medical college and Hospital, Guwahati, Assam, India.

ABSTRACT

Objective- To compare the relative efficacy and success rate of combination of mifepristone and misoprostol with misoprostol alone in mid-trimester abortion by correlating induction abortion interval (IAI) between two study groups.

Methods- A comparative study was carried out by dividing 100 women seeking for abortion into two groups (50 each). GroupA received 200mg mifepristone orally followed by 600mcg misoprostol vaginally (24 hours later) which was repeated 4 hourly by 400mcg sublingual misoprostol upto a maximum of 5 doses. GroupB received 600mcg misoprostol vaginally and dose was repeated 4 hourly by 400mcg of misoprostol sublingually.

Result- The success rate in GroupA was 100%, whereas in Group B was 94%. The mean IAI in GroupA was lesser (10.8 hours) as compared to GroupB (13.5 hours) p value 0.01. The mean dose of misoprostol in GroupA was 1400mcg compared to GroupB 1760mcg (p value 0.0001).

Conclusion- Pre-treatment with mifepristone significantly shortens the IAI and increase the successful abortion rate.

KEYWORDS : Misoprostol, Mifepristone, MTP, Abortion

INTRODUCTION

The word abortion derives from the Latin word *aboriri*—which means miscarry or disappear.

Between the years 2015-2019, on average 73.3 million induced abortions occurred worldwide each year[1]. Although the majority of abortions are performed in the first trimester, there is still a gradual increase in second-trimester abortion because of delayed diagnosis of fetal anomalies, failure to recognize an undesired pregnancy in the first trimester and widescale introduction of prenatal diagnostic tests.

A significant yet prevalent cause of maternal mortality in India is unsafe abortion. Based on data from the year 2010-2014, approximately 45% of all abortions worldwide were unsafe[1]. Unsafe abortions are a frequent cause of severe short term and long term sequelae. The most common complications are haemorrhage, pelvic infection, uterine perforation, cervical injury and shock. The late sequelae include infertility, chronic pelvic pain and ectopic pregnancy. Almost every abortion related women's disability and death could be prevented through education, use of effective contraception, provision of safe, legal induced abortion, and timely care for complications.[2]

The Indian abortion laws fall under the Medical Termination of Pregnancy (MTP) Act. The MTP act was introduced in India in 1971, and legalized from 1972 as a maternal health measure and not a birth control measure [3]. The MTP Act came into effect from 1 April 1972 and was amended in the years 1975 and 2002.

The methods that are available for second trimester pregnancy termination are dilatation and evacuation, intrauterine (either intra-amniotic or extraovular space) instillation of abortifacients and administration of systemic abortifacients. Medical methods are comparatively safer and have superseded the surgical methods because of risks involved in surgical methods.

The various drugs used for bringing about termination of pregnancy have undergone tremendous change. The most effective regimen relies on antiprogestin – mifepristone, along with misoprostol. Mifepristone binds to Progesterone receptors resulting in necrosis and detachment of placenta. It also softens the cervix and causes mild uterine contractions. It sensitizes the uterus to the action of prostaglandin which is given 1-2 days later. Synthetic prostaglandin E_1 analogue – misoprostol, which binds to myometrial cells causing strong myometrial contraction and causes cervical softening and dilatation. This leads to expulsion of fetus from the uterus. The present study was undertaken to evaluate the efficacy and safety of combination of Mifepristone and misoprostol with misoprostol alone in the termination of second trimester pregnancy.

OBJECTIVES OF THE STUDY

To compare the relative efficacy and success rate of mifepristone and misoprostol combination versus misoprostol alone in mid-trimester abortion by correlating the IAI between two study groups.

MATERIALS AND METHODS

A prospective non randomized comparative study was conducted in the Department of Obstetrics and Gynaecology, Gauhati Medical College and Hospital, Guwahati from 1st June, 2019 to 31st May, 2020 over a period of 12 months. The study was conducted among the patients requesting for mid-trimester termination of pregnancy after detailed history, clinical examination, ultrasonography (USG) and routine blood investigations. This study included 100 subjects, where 50 were allocated in GroupA: mifepristone- misoprostol combination group and another 50 in GroupB: misoprostol alone group.

Documentation as per MTP Act (Form1, Form2, Form3, Form C) were completed after opinion for MTP was reached by 2 Registered Medical Practitioner.

Inclusion Criteria:

- 14 – 20 weeks gestation
- Women fulfilling indications for MTP according to MTP act
- Singleton pregnancy
- Willing to follow the study protocol and provide informed consent
- Willing to undergo required follow-up and surgical management when indicated.

Exclusion Criteria:

- Missed abortion
- Multiple pregnancy
- Allergy to misoprostol or other prostaglandins
- History of previous uterine surgery (myomectomy or Caesarean section)
- Bleeding disorders
- Hepatic disorders

GroupA (n=50) received 200mg mifepristone orally, 24 hours later followed by 600mcg misoprostol vaginally which was repeated 4 hourly by 400mcg sublingual misoprostol upto a maximum of 5 doses in 24 hours.

GroupB (n=50) received 600mcg misoprostol directly and dose was repeated 4 hourly by 400mcg of misoprostol upto a maximum of 5 doses in 24 hours.

The maternal side effects were recorded. The blood pressure, pulse and frequency of uterine contraction were monitored. After expulsion, the

products of conception (fetus and placenta) were examined to see whether the abortion was complete. If the placenta is not expelled within 15-20 minutes of fetal expulsion, 20 units of oxytocin in 500 ml of Ringer solution at 125 ml/h for 2 hours.

In patients who failed to expel both fetus and placenta after maximum of 5 repeat doses of misoprostol in 24 hours were given rest for next 12 hours. If expulsion fails to occur in span of total 36 hours, counted from the administration of starting dose of misoprostol, it is then considered failed induction. Next, Tab. Mifepristone 200 mg is given to these patients and misoprostol was repeated in doses and route of administration as before. In some, unit policy was followed in case of failed abortion. A repeat USG done after expulsion to exclude retained products. The additional measure adopted in patients with incomplete abortion was instrumental evacuation wihin 24 hours of expulsion. $Rh_o(D)$ immunoglobulin was given to Rh negative mothers.

Outcome: COMPLETE abortion- when both placenta and fetus were expelled without operative intervention. INCOMPLETE abortion- when placenta or placental bits were retained. FAILED abortion- when both fetus and placenta were not expelled in 36 hours (calculated since the time of administration of the first dose of misoprostol).

Statistical Analysis

In this study, Chi square or Fishers exact test is used to evaluate difference between categorical variables. Independent t- test is used depending on fulfilment of normality assumption for mean difference and Anova was used to compare between more than two groups for continuous data. All data were analyzed using SPSS version 21. A p value less than 0.05 is considered as statistically significant at 5% level of significance.

Ethical Consideration

The study was conducted after it was approved by the institutional ethics committee.

RESULTS AND OBSERVATIONS

Age and gravida distribution was similar in both groups 73% of women in this study were multigravidae. Mean age is 27.02±5.8 years in groupA. Whereas, its 27.22±6.1 years in groupB. Distribution of patients in both groups was comparable in view of gestational age. Most of the pregnancies were terminated in 14 to 16 weeks of gestation in both groups. Mean gestational age in groupA is 16.14±2.18 weeks and in groupB is 16.2±2.08 weeks. Social reasons (83%) account for most of the reasons for MTP. Social ground constitutes contraceptive failure, completed family, socio-economic condition and unmarried status. Congenital anomalies accounted for 13% of total indications.

Table 1: Demographic Details Of Study Population

	Mifepristone + Misoprostol	Misoprostol alone
Mean Age (years)	27.06	27.22
Nulliparous	26%	28%
Gestational age(weeks)	16.14	16.20
Most common Indication of MTP	Social cause (83%)	
	Congenital malformation (13%)	

The mean IAI in groupA was 10.82±4.17 hours and in groupB was 13.5±6.03 hours. The difference between them was found to be statistically significant (p value 0.011). It is observed that (Fig.1) as parity increases Induction to abortion interval decreases, which is statistically significant (p Value <0.0001). According to gestational age, IAI is shorter in gestational age 14-16 weeks (Fig.2) (p value 0.01).

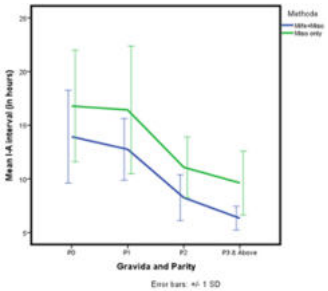

Fig.1: Line Graph Showing The Mean IAI And Their Standard Deviation Comparing Two Study Groups In Relation To Parity

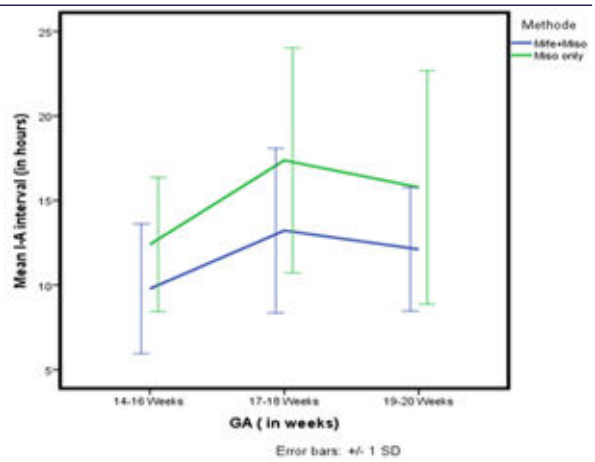

Fig.2: Line Graph Showing The Mean IAI And Their Standard Deviation Comparing Two Study Groups In Relation To Gestational Age.

The mean dose of misoprostol required in groupA was 1400 µg and in groupB was 1760 µg, the difference is statistically significant (p value <0.0001). In our study the repeat dosage required in groupA was lesser while that in the groupB was comparatively more. The percentage of complete abortion in groupA was 76% while that in groupB was 28%. The difference between the two groups was statistically significant (p value 0.0001). The percentage of incomplete abortion was 24% in groupA and 66% in groupB which was statistically significant. 6% failed to undergo expulsion in 36 hours in misoprostol only group (p value <0.0001). Out of 3 cases of failed induction, all 3 received Mifepristone-Misoprostol combination, of them 2 had expulsion; while 1 patient, who was multipara did not expel even after receiving combination drug and underwent hysterotomy with tubal sterilisation. The percentage of successful abortions was 100% in groupA and 94 % in groupB. 56% of patients in groupA expelled within 12 hours as opposed to 34% in groupB. With groupA, 100% of the women had expelled in 24 hours as opposed to 88% in misoprostol only group. 94% of groupB expelled in 36 hours. Failure rate in misoprostol alone group is 6%. It is statistically significant (p value 0.047).

Table 2: Success Rates In Both Groups

	GroupA		GroupB		p value
HOURS	**N**	**%**	**N**	**%**	
0-<12	28	56.0%	17	34.0%	
12-24	22	44.0%	27	54.0%	**0.047**
24-36	0	0.0%	3	6.0%	
Failure	0	0.0%	3	6.0%	

Majority of the patients did not have any side effects in either groups. There were no side effects that differ significantly statistically between the two study groups. The Side effects were treated symptomatically and no major complications were found in either group. Maximum patients had complaints of fever and rigor in our study.

DISCUSSION

INDUCTION ABORTION INTERVAL (IAI):

In the present study the mean induction abortion interval was 10.82±4.17 hours for groupA and 13.5±6.03 hours for groupB which was statistically significant (p value 0.01). It is comparable to study of Rasha et al.[4], they reported mean IAI of 10.4 ±6.8 hours in mifepristone group and 20.6±9.7 hours in misoprostol only group. Reduction in induction to abortion interval is likely to improve the acceptability of women.

It is accepted that multiparous women aborted faster and required lesser total misoprostol dose than nulliparous in our study, with p value <0.001 in groupA, and p value of 0.002 in groupB. Similar result is seen in various other studies, Heini et al.[5] found that induction of labour is easily accomplished in multiparous compared with primiparous. In their study, majority (94%) of women who were multiparous completed medical termination faster (<8 hrs).

In our study, women with gestational age <17 weeks aborted faster with shorter induction-abortion interval 9.78 hours in groupA, and 12.4 hours in groupB; and required lesser misoprostol dose than

women with >17 weeks of gestation. It is statistically significant in both groups A and B, with p value 0.017 and 0.01 respectively. It is comparable to other studies. In the study by Maninder et al.[6], with mean IAI 8.23 hours in <17 weeks of gestation, and 14.26 hours in > 17 weeks of gestation. Mentula et al.[7] in their study reported the median Induction-Abortion Interval was 8.5 hours (in 1 day group). The median Induction-Abortion Interval was 3 hours longer in nulliparous and in women with gestational age >16 weeks.

DOSE OF MIFEPRISTONE AND MISOPROSTOL:

In most recent studies, pre-treatment with mifepristone is done at dosage of 200 mg, unlike many previous studies where upto 600 mg Mifepristone were used. From various studies, it is shown that the outcome with 200 mg mifepristone is similar when 600 mg of mifepristone is used[8,9]. In our study, mean dose of misoprostol is 1400 mcg and mean IAI is 10.82 hours in groupA which is comparable to the study of Akkenapally[10] which is 1046mcg and IAI of 6.18 hours. In our study, the mean dose of misoprostol required in misoprostol only group was 1760 µg. In an another study by Khairnar et al.[11], a loading dose of 400 µg misoprostol was given followed by 200 µg misoprostol 4 hourly, with mean total dose of misoprostol 1591.66 µg and mean IAI 10.8 hours. However, the route of administration varies. In Khairnar et al.[11] study, vaginal route was used.

Success Rates:

The success rate in Mifepristone followed by Misoprostol group is 100% in present study. In almost all the studies, maximum patients had abortion before 24 hours. Abbas et al.[12] showed that misoprostol when given at 24 hour interval of administration of mifepristone, success rate at 24 hours is 94.4% and in the end of 48 hours is 96.8%. In the study by Akkenapally[10], success rate was 96% in the end of 24 hours. The success rate at less than 12 hours was 34% within groupB which is similar to the study of Khairnar et al.[11] But the final success rate at 24 hours and 36 hours in the present study was 88% and 94% respectively in Misoprostol alone groups. It is comparable to other studies. In the study by Akkenapally[10], success rate at 24 hours was 87% and Bilolikar's[13] study 88% in the end of 24 hours. Like other studies, surgical intervention for incomplete abortions was needed more in groupB as compared to groupA, which is statistically significant with p value 0.002.

CONCLUSION

From the present study, it can be concluded that misoprostol is an effective agent for termination of second trimester pregnancy. Using the combined regimen of mifepristone and misoprostol seems to have the highest efficacy and shortest induction to abortion interval. When mifepristone is not available, misoprostol alone can be a good alternative. The complete abortion rate and abortion rate at 24 hours was increased in Mifepristone – Misoprostol combination group as compared to misoprostol alone group, thereby reducing the chances of incomplete abortion and related complications. The side effects were comparable in both groups. The dose of Misoprostol required is much lesser in Mifepristone- Misoprostol combination, thus increases the patient compliance. Multigravidae and women with early gestation aborted faster; however, further studies are needed in this aspect so that gestational and parity wise more refined regimen can be developed for second trimester terminations.Misoprostol alone group doesn't have the 24 hours of anxiety or unease from the time of mifepristone administration. More studies are further needed in view of finding appropriate dose of misoprostol and interval between mifepristone and misoprostol administration.

REFERENCES

1. Bearak J,Popinchalk A, Ganatra B, Moller A-B, Beavin C. Unintended pregnancy and abortion by income, region, and the legal status of abortion: estimates from a comprehensive model for 1990-2019. Lancet Glob Health 2020;8(9):e1152-e1161
2. Haddad L. Unsafe Abortion: Unnecessary Maternal Mortality. Rev Obstet Gynecol 2009 Spring;292):122-26.
3. Manual for First Trimester MTP. Technical Operations Division, Ministry of Health and Family Welfare, Govt. of India, Nirman Bhawan, New Delhi. p 11.
4. Dabash R, Chelli H, Hajri S, et al. A double blind randomized controlled trial of mifepristone or placebo before buccal misoprostol for abortion at 14–21 weeks of pregnancy. Int J Gynaecol Obstet. 2015;130(1):40–4.
5. Heini JM, Paula K, Anne TM. Clinical efficacy of mifepristone and misoprostol in second trimester pregnancy termination. Acta Obstet Gynaecol. 2010; 89(12):1552–6.
6. Kaur M, Kaur H, Sharma S, et al. editors. Mifepristone followed by Misoprostol for Mid trimester Abortion-A Prospective Study. J Obstet Gynaecol India.2015;2(4): 227-31.
7. Heikinheimo O, Mentula M, Suhonen S, Haukkamaa M. One- and two day mifepristone-misoprostol intervals are both effective in medical termination of second-trimester pregnancy-a randomized trial. Hum Reprod 2011;26(10):2690-7.
8. Webster D, Penney GC, Templeton A. A comparison of 600 and 200 mg mifepristone prior to second trimester abortion with the prostaglandin misoprostol. Br J Obstet Gynaecol 1996;103:706-9.
9. World Health Organization TaskForce on Post-ovulatory Methods of Fertility Regulation. Termination of pregnancy with reduced doses of mifepristone. BMJ 1993; 307:532-7.
10. Akkenapally PL . A Comparartive Study of Misoprostol Only and Mifepristone Plus Misoprostol in Second Trimester Termination of Pregnancy. J Obstet Gynaecol India 2016 Oct; 66(suppl 1):251-57.
11. Khairnar MM, Patil AM. Study of efficacy and success rate of single dose oral mifepristone and vaginal misoprostol versus vaginal misoprostol alone for second trimester termination of pregnancy. MVP J Med Sci 2019;4:216-221.
12. Abbas DF, Blum J, Ngoc NTN, et al. editors. A Randomized Controlled Trial of Simultaneous Administration Compared With a 24-Hour Mifepristone–Misoprostol Interval in Second-Trimester Abortion. Obstet Gynecol 2016;128:1077–83.
13. Bilolikar M. A Comparartive Study of Second Trimester Termination of Pregnancy with Mifepristone and Misoprostol Vs Misoprostol Alone. Sch J App Med Sci 2018; 6(10):3927-3930.