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**Research Article**

# Evaluation of mid trimester abortion (13-20 weeks) using newer regimen of mifepristone with misoprostol versus misoprostol alone

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## ABSTRACT

**Background:** Termination of pregnancy in second trimester continues to be a challenge in developing countries especially in rural areas. There is an exponential rise in complications of abortion along with advancing gestational age. The search is on for an ideal method of abortion which is reliable, safe and cheap. This study was conducted in Tata main hospital, Jamshedpur from 15th November 2012 to 14th November 2014, with the aim of finding an effective method to induce second trimester abortion within reasonable time with fewer complications.
**Methods:** A total of 80 patients were studied to compare combination of mifepristone and misoprostol, with single drug misoprostol alone for second trimester abortion. The induction abortion interval (IAI), success rate and side effects were compared between the two groups. .
**Results:** There was a significant difference in the IAI in both the groups. The mean IAI was 196.28 minutes in study group whereas in control group IAI was 318.92 minutes. The success rate (complete abortion) was 97.5% in study group and 92.5% in control group, but this was not statistically significant. More side effects were observed in the control group.
**Conclusions:** Mifepristone followed by misoprostol was more effective than misoprostol alone as it had a shorter IAI and fewer side effects.

**Keywords:** Second trimester abortion, Mifepristone, Misoprostol

## INTRODUCTION

Majority of abortions are performed in the first trimester. The indications of second trimester abortion could be a delay in diagnosis of fetal anomalies, logistic and financial difficulties in obtaining abortion services and failure to recognise an undesired pregnancy in the first trimester, which all contribute to the continuing need for late abortions.[1,2] Second trimester abortion comprises only 10-15% of the total 42 million abortions that occur worldwide each year.[3] Second trimester abortions are responsible for two-thirds of major abortion-related complication. Among the methods listed as outdated by WHO, but still commonly used in several developing countries (e.g. India, China and until recently Mongolia) is intra or extra amniotic administration of ethacryidine lactate, especially to terminate late second trimester pregnancies.[4] The drawbacks of older methods include long duration of labour, hospitalization for several days and the need for curettage. There is a need for evolving a safe and effective method for terminating pregnancy in the second trimester. The introduction of prostaglandins and later prostaglandin analogues has improved the efficacy of medical abortion and reduced the risk of complications and side effects. The outcome of medically induced abortion has further improved after mifepristone became available in the 1990s.[5-9]

The primary aim of this study was to evaluate the efficacy of tablet mifepristone in combination with tablet

misoprostol in management of second trimester abortion and compare it with misoprostol alone and also to observe the course and outcome of abortion in this combined regimen. The secondary aim was to study the possible side effects of these drugs.

## METHODS

This is a prospective, comparative clinical study undertaken in the department of obstetrics and gynecology at Tata main hospital, Jamshedpur, India over a period of two years from 15th November 2012 to 14th November 2014. A total of 80 women fulfilling the inclusion criteria were enrolled for this study. They were randomly distributed as case (A group) and control (B group) (40 women in each group).

Inclusion criteria were gestational age more than 13 weeks but less than 20 weeks, women fulfilling indications of MTP Act of India, singleton pregnancy with no regular uterine contractions.

Grand multipara, multiple pregnancy and those with scarred uterus, heart disease or known contraindication to mifepristone or misoprostol were excluded from the study. After proper counseling, written consents were taken. Women in the case group received mifepristone 200 mg orally, followed 36-48 hours later by misoprostol 800 micrograms vaginally and thereafter by repeated doses of 400 micrograms misoprostol vaginally, every 3 hours, to a maximum of 4 doses. Whereas women in control group received vaginal misoprostol 800 micrograms, followed by 400 mcg every 3 hours, to a maximum of 4 vaginal doses. Maternal side effects of drugs were observed and treated accordingly. Both groups received injection tetanus toxoid. If patient was Rh negative, injection Anti D 300 microgram was given intramuscularly after abortion.

## RESULTS

The distribution of patients in Group A and B were similar and maximum patients were in the range of 20-25 years (Table 1). In group A, mean age is 25.08, SD 4.78, whereas in group B, mean age is 24.88, SD 4.57. Most of the cases were primigravida in both the groups (study group 70% (n=28), control group 72.5% (n=29)) (Table 2). The mean gestational age was 16.55±2.36 weeks in study group and 16.75±2.28 weeks in control group (Table 3). The induction abortion interval (IAI) was defined as time from administration of first dose of misoprostol (800 mcg) to abortion of foetus (Table 4). One case from study group and 3 cases from control group were excluded due to incomplete abortion). It was observed that the mean induction abortion interval in both primigravida and multigravida were lesser in case group compared to control group. Though it is statistically significant only in case of multigravida ($p < 0.05$) (Table 5). With increasing gestational age, the time taken for completeness of the process was as shown in Table 6. Time taken for early mid trimester abortion (13-16 weeks) was less when compared to late mid trimester abortion (16.1-20 weeks).

**Table 1: Age distribution among the patients.**

| Age (year ) | Group - A | | Group - B | | Total | |
|---|---|---|---|---|---|---|
| | No. | % | No. | % | No. | % |
| 18-20 | 6 | 15 | 6 | 15 | 12 | 15 |
| 20-25 | 18 | 45 | 17 | 42.5 | 35 | 43.75 |
| 26-30 | 10 | 25 | 12 | 30 | 22 | 27.5 |
| >30 | 6 | 15 | 5 | 12.5 | 11 | 13.75 |

**Table 2: Comparison of gravida distribution.**

| Gravida | Group A (n=40) | | Group B (n=40) | | Total | |
|---|---|---|---|---|---|---|
| | No. of patients | Percentage | No. of patients | Percentage | No. | Percentage |
| Primi | 28 | 70% | 29 | 72.5% | 57 | 71.25% |
| Multi | 12 | 30% | 11 | 27.5% | 23 | 28.75% |

**Table 3: Comparison of gestational age in weeks between two groups.**

| G.A (weeks) | Group A | | Group B | | Total | |
|---|---|---|---|---|---|---|
| | No. | Percentage | No. | Percentage | No. | Percentage |
| 12-14 | 11 | 27.5% | 9 | 22.5% | 20 | 25% |
| 15-16 | 9 | 22.5% | 12 | 30% | 21 | 26.25% |
| 17-18 | 9 | 22.5% | 7 | 17.5% | 16 | 20% |
| 19-20 | 11 | 27.5% | 12 | 30% | 23 | 28.75% |
| Total | 40 | 100% | 40 | 100% | 80 | 100% |
| Mean±S.D | 16.55±2.36 | | 16.75±2.28 | | | |

Though on comparing between the two groups the p value was not significant in early mid trimester abortion (13-16 weeks), but a statistically significant p value was seen in late mid trimester (16.1-20 weeks) abortion. Completeness of abortion was defined as expulsion of both placenta and fetus without operative assistance. Completeness of abortion was 97.5% in study group and 92.5% in control group (p-value=0.6080). The side effects commonly observed were nausea (47.5%and 75%, p-value=0.021), vomiting (20%and 32.5%, p-value =0.309) , diarrhoea(10% and 10%, p-value=1), fever(7% and 17.5%, p-value=0.311), pain (5% and 15%, p-value=0.263) and shivering (10% and 7.5%, p-value=1) in the study and control groups respectively. Most of the side effects were more in group B compared to group A, but they were not statistically significant except nausea.

**Table 4: Comparison of IAI (in minutes) between two groups.**

| IAI (minute) | Group A (n=39) | Group B (n=37) |
|---|---|---|
| Range | 60 to 550 | 90 to 600 |
| Mean±S.D. | 196.28±112.86 | 318.92±158.32 |
| 95% of C.I. | 60.05 to 185.23 | |

**Table 5: Comparison of IAI (in minutes) according to gravidity.**

| Gravidity | Group A (n=39) Mean±s.d. | Group B (n=37) Mean±s.d. | $\lvert t \rvert_{cal}$ | D.F. | P-value |
|---|---|---|---|---|---|
| Primi | 222.22±122.83 (n=27) | 285.71±120.60 (n=28) | 1.934 | 53 | 0.0584 |
| Multi | 137.92±54.50 (n=12 ) | 422.22±218.73 (n=9) | 4.360 | 19 | 0.03 |

**Table 6: Comparison of IAI (in min) according to G.A. (in weeks).**

| G.A. | Group A (n=39) Mean±s.d. | Group B (n=37) Mean±s.d. | I t $I_{cal}$ | D.F. | p-value |
|---|---|---|---|---|---|
| 13-16 weeks | 228.42±120.07 (n=19) | 290.53±164.43 (n=19) | 1.33 | 36 | 0.1920 |
| 16.1-20 weeks | 165.75±88.99 (n=20) | 348.89±150.33 (n=18) | 4.626 | 36 | P <0.0001 |

## DISCUSSION

This study compared combination of mifepristone and misoprostol with single drug misoprostol alone for second trimester abortion (13-20 weeks). In our study mean age of patient was 25.08±4.78 years in study group and 24.88±4.65years which was similar as seen in other studies.

In present study, primigravida were 70% and 72.5% whereas multigravida were 30% and 27.5% in study and control group respectively implying that more primigravida were there in the study group compared to multigravida. Similar findings were also seen in study of Premila et al.[13] 50% cases were in early second trimester (13-16 weeks) and 50% were in late gestational age (16-20 weeks). Mean gestational age was 16.55%±2.36 and 16.75±2.28 in study and control group respectively. This is almost comparable to the study done by Carbonella et al who found the mean gestation age 15.1±2 for misoprostol alone regimen and 15.7±2.4 for combination regimen.[14] Hence in present study, demographic parameters were comparable in both study and control group.

Mean induction abortion interval (IAI) in study group was 196.28±minutes (95% CI 60.05 to 185.23 in minutes) compared to 390 minutes in the study by Webster et al 1996.[15] Mean IAI in control group is 318.92±158.32 minutes as compared to 846 minutes in the study by Wong et al 1998.[16] The difference in the time was due to different doses and routes and regimen of misoprostol used in different studies.

**Table 7: Mean age of patient in various studies.**

| Author | Year | Title | Mean age (year) |
|---|---|---|---|
| Mendileioglu M, Simsek PE, Seker O, Erbay CG, Zorlu B[10] | 2002 | Misoprostol in second and early third trimester for termination of pregnancies with fetal anomalies | 26.4 |
| Julia Bartley, David T. Baird[11] | 2002 | Misoprostol and Gemeprost in combination with mifepristone for induction of abortion in the second trimester of pregnancy | 25 |
| Goh SE, Thong KJ[12] | 2006 | Induction of second trimester abortion(12-20weeks) with mifepristone and misoprostol | 25.5 |

But considering our study it was seen that a statistically significant p value (0.0002) was achieved on comparing

both the groups. Statistically significant results were comparable to the study of Patel U et al.[17] The mean induction abortion interval in women who were given mifepristone and misoprostol both was 18.94±9.30 hours and the women who were given misoprostol alone was 24.2±11.53 hours. This difference in time was due to different doses of misoprostol (200 mcg).

On comparing IAI with respect to gestational age, it was seen that statistically significant results were obtained in the patients with late trimester (16-20 weeks) abortion. 35% aborted within 180 minutes in study group compared to 16.21% in controls. 46.15% aborted in 180-360 minutes interval compared to 16.21% in the control group. These results were statistically significant. Hence pre-treatment with oral mifepristone reduces IAI. These findings were comparable to the study of Kapp N et al who found that use of mifepristone in addition to misoprostol for medical termination of pregnancy results in higher efficacy (97% vs 72% with misoprostol alone) and a shorter induction to abortion interval (10.0 h vs 18.0 h with misoprostol alone).[18]

Although it is well known that the sensitivity of the uterus increases to prostaglandins with increasing gestation, our findings suggest a statistically significant difference in the number of doses of prostaglandins required to induce abortion and a shorter median induction- to -abortion interval at increased gestation. Primigravida in study group took 222.22±122.83 minutes whereas in control group 285.71±120.60 minutes for complete expulsion. Similarly multigravida in study group took 137.92±54.50 minutes and in control group took 422.22+/-218.73mins implying that with increasing parity the IAI was reduced in study group but not so in control. These results showed that IAI time was statistically significant according to the parity between both groups.

Success rate in study group was 97.5% in our study compared to 94.3% in the study done by Webster et al.[15] Similarly, success rate in control group was 92.5% compared to 80% in the study done by Wong et al.[16] These results are not statistically significant.

After receiving 800 mcg of misoprostol by both the groups, further misoprostol dose requirement in study group was 34 whereas in control group it was 64. More number of tablets (2 or 3) were used in control group. These results were statistically significant.

The regimen described in this study is a cost effective method for second trimester termination of pregnancy, with particular relevance to the developing world. Unsafe abortion in many of these countries is a consequence, not of illegality, but of lack of access to medical resources.

## CONCLUSION

In the last decade, medical methods for second trimester induced abortion have 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. It is advisable that second trimester terminations take place in a health care facility where blood transfusion and emergency surgery (including laparotomy) are available because of the potential for heavy vaginal bleeding and serious complications.

The combination of mifepristone and misoprostol is an effective and safe method for second trimester abortion. The combined regimen significantly reduces the dose of misoprostol. Where mifepristone is not available or affordable, misoprostol alone has also been shown to be effective, although a higher dose is needed and efficacy is lower than for the combined regimen. Therefore, whenever possible, the combined regimen should be used.

Among the two methods, mifepristone followed by misoprostol is more effective and has a shorter induction abortion interval (IAI) and fewer side effects. However, both are feasible as far as end results are concerned.

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