

Combination of Mifepristone and Misoprostol Compared with Misoprostol alone in the Termination of Pregnancy in Late Intra-Uterine Fetal Death.

Lalrinfela¹, Vanremmawii¹, C.Lalsangzuala²

¹Specialist, Department of Obs and Gyne, State Referral Hospital, Falkawn, Mizoram.

²Managing Director, Alpha Hospital, Kulikawn, Aizawl, Mizoram.

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ABSTRACT

Background: This study aims to assess the effectiveness of Misoprostol alone and combination of Misoprostol and Mifepristone in termination of pregnancy in intra-uterine fetal death. **Methods:** This randomized prospective study was conducted in the antenatal ward of State Referral Hospital, Falkawn Mizoram. 54 women with Intra-uterine death after 24 weeks of gestation were divided into 2 groups, Group A and Group B. Group A, comprised of 25 patient who were given Misoprostol alone; and 29 patients of Group B receives a combination of Misoprostol and Mifepristone as per the doses recommendation of International Federation of Gynecology and Obstetrics (FIGO). **Result:** There were no significant differences between the groups as regards to age, parity, gestational age and bishops score, The mean induction delivery interval was shorter with the use of combination regime (9.6±2.4 hrs) than misoprostol alone group (17.1±3.7 hrs). The number of dosage of misoprostol required for both the groups was compared and was found significantly less in women receiving mifepristone prior to misoprostol. There were no statistically significant differences in the observed side effects like chills, nausea and diarrhoea in both the groups. **Conclusion:** Medical induction of labour in late intrauterine death is more effective with misoprostol if the uterus is primed with mifepristone earlier.

Keywords: Misoprostol, Mifepristone, Intra Uterine Death, Induction of labor.

INTRODUCTION

Intra-uterine fetal death denotes death of fetus in utero beyond period of viability ie. 28 weeks (24 weeks in developed countries) of gestation. It is still a common obstetric problem in developing countries due to low socio-economic status, ignorance and poor infrastructure of maternal health care system.

When fetal death occurs after 24 weeks of gestation, there may be delay in spontaneous onset of labor and expulsion may take several hours, days and even weeks. Such retention of dead fetus in uterus can be associated with emotional distress to mother and family members, intra-uterine infections if membrane ruptures and time related risk of consumptive coagulopathy. As a result, expulsion within optimum time interval is vital and essential in order to avoid such related risk. Consequently, medical induction to expel dead fetus is recommended, provided it can be undertaken safely. Prostaglandins have been use for induction of labor

in case of intra-uterine fetal death. The therapeutic effect is dose related and is limited by its side effects. The side effects are also dependent on the type of prostaglandin and route of administration. Misoprostol, a prostaglandin E1 analogue, is probably the most preferred because of its low cost, stability in room temperature and ease of administration.

Mifepristone, a 19-norethisterone derivative, antiprogesterone which block progesterone at the receptor level, is widely used for first and second trimester termination of pregnancy. Mifepristone causes vascular damage, decidual necrosis, cervical softening and increased uterine sensitivity to prostaglandins, with a maximum action at 36 to 48 hours, thereby allowing lower doses of Misoprostol to induce expulsion of fetus.

MATERIALS AND METHODS

The present study was conducted in Department of Obstetrics & Gynecology, State Referral Hospital, Falkawn, Mizoram, India during a period of March 2016 to April 2018, a consecutive series of 54 women with Intra-uterine death after 24 weeks of gestation were studied. The assessment of gestational age was based on menstrual history confirmed by ultrasound.

Name & Address of Corresponding Author

Dr. Vanremmawii
Specialist, Department of Obs and Gyne,
State Referral Hospital,
Falkawn,
Mizoram.

A detailed history with physical and obstetrical examination and all routine examination were done. Assessment of cervix was based on Bishop's Score. The diagnosis of intra-uterine death was confirmed on ultrasound by absence of fetal heart pulsation, and only women who were not in labor were included in the study. Treatment was considered successful if delivery occurred within 24 hours of first dose of Misoprostol.

Patients with the previous caesarean section or any other scar on the uterus, grand multipara, history of allergy to mifepristone and misoprostol, or who are already in labor and any patient with obstetrical or medical indication for immediate delivery were excluded in the study.

The Patients were randomly divided into 2 groups, Group A and Group B. Group A, comprised of 25 patient who were given Misoprostol alone; and 29 patients of Group B receives a combination of Misoprostol and Mifepristone.

Dosage and administration (Misoprostol alone): For 24-26 weeks gestation, 100 mcg of Misoprostol was kept vaginally in the posterior fornix, 6 hourly upto a maximum of 4 doses. Period of gestation more than 26 weeks were given 50 mcg of misoprostol 4 hourly upto a maximum of 6 doses which is as per the recommendation of International Federation of Gynecology and Obstetrics (FIGO).^[1]

Dosage and administration (Combination of Misoprostol and Mifepristone): Mifepristone 200 mg was given followed by Misoprostol dosage as above (Misoprostol alone) after 36 hours of administration of Mifepristone.

All the patients were admitted in the hospital. And vital signs and progress of labour was recorded in partographs. Any complication like post-partum haemorrhage, retained placenta were noted. The rate of successful delivery and induction delivery interval (1st dose of misoprostol to delivery of fetus and placenta) was the primary outcome. Secondary outcome measures include the dose of misoprostol required, complication and side effect related to drugs. Successful induction was defined as delivery within 24 hours of first dose of misoprostol. The analyses of the quantifiable results like Mean and SD, Chi Square etc. were done with IBM SPSS 21.0 version.

RESULTS

Table 1: Demographic profile and obstetric parameters.

Parameters	Group A (n=25)	Group B (N=29)	P Value
Age (Years)	26.9±4.8	27.6±4.6	NS
Primigravida (%)	50	50	NS
Gestational age (weeks)	32.5±6.6	30.1±5.8	NS
Bishop Score	2.5±1.6	3.2±1.7	NS

Fifty four patients with IUD were included in this study .As regards to age, parity ,gestational age and

bishops score, the patients in group A and B were comparable with no significant differences.

[Table 2] shows the primary outcome. Successful deliveries within 24 hours of administration of misoprostol occur in 76% of women who received misoprostol alone and 93% of women who received combination of mifepristone with misoprostol. The difference was statistically significant (P<0.05)

The mean induction delivery interval was shorter with the use of combination regime (9.6±2.4 hrs) than misoprostol alone group (17.1±3.7 hrs)

The number of dosage of misoprostol required for both the groups was compared and was found significantly less in women receiving mifepristone prior to misoprostol.

Table 2: Comparison of efficacy of the drugs.

Parameters	Group A (n=25)	Group B (N=29)	P Value
Induction to Delivery Interval(Hours)	17.1±3.7	9.6±2.4	< .01*
Successful delivery	19 (76%)	27 (93%)	< .05**
Total dose of Misoprostol administered	8.9±2.1	6.1±1.1	< .05**

Table 3: Outcome after induction

Parameters	Group A (n=25)	Group B (N=29)	Chi square	P Value
Retained Placenta	1	1	0.4295	.8067 Not significant at P<.05
Oxytocin required	4	3		
Side effects	7	6		

There was retained placenta in one case each in group A and B, the side effects like chills, nausea diarrhoea were recorded in both the groups and the difference was not statistically significant. Augmentation with oxytocin was required in 4 (16%) cases of group A and 3 (10.3%) cases in group B.

DISCUSSION

We observed significant increase in successful delivery and shorter induction delivery in women who were primed with mifepristone prior to misoprostol compared with misoprostol alone. And the total amount of misoprostol was also lower in the group receiving combined regime.

The rate of successful delivery with the combined regime in our study (93%) was comparable with the results of Stibbe et al,^[5] (86%), Wagaarachchi et al,^[2] (87.5%). And Chaudhuri P et al,^[10] (92.5%).

The induction delivery interval in our study was 9.4±2.4 hrs in the combination regime which is comparable to the findings of Wagaarachchi et al,^[2] (8.6 hrs), Gupta S et al,^[9] (9.6±3.03), and Chaudhuri P et al,^[10] (9.8±4.4).

Whereas, Varynen et al,^[4] in a retrospective trial and Gandhi et al in a prospective study fail to show any significant difference in IDI among the groups receiving combined regime and misoprostol alone.

Our study show significant reduction in the mean dose of misoprostol with the use of mifepristone pretreatment, which is similar to other studies.^[3,6,8]

There was no serious complication in our study, but one study reported a higher incidence of retained placenta in patients receiving misoprostol alone (11.5%) in comparison to mifepristone pretreated group (3.8%).^[8]

CONCLUSION

In conclusion, medical induction of labour in late intrauterine death is more effective with misoprostol if the uterus is primed with mifepristone earlier, which is shown by higher successful delivery with shorter induction delivery interval. However, further research may be conducted to optimize the dose of drugs and the frequency of administration.

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