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A comparative study between misoprostol and combination of mifepristone and misoprostol for termination of pregnancy with late intrauterine fetal death

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Abstract
Background: The antepartum death occurring beyond 28 weeks is termed as intrauterine death. In 80% of women with IUD, spontaneous expulsion occurs by 3 weeks. Oral misoprostol administration for labor induction with IUD was first used in 1987 for obstetrical purposes. Mifepristone administered before Misoprostol sensitizes the uterus to the action of prostaglandins and ripens the cervix.
Aims and Objective: To compare the combination of mifepristone and misoprostol regimen with misoprostol only for induction of labor in late intrauterine fetal death.
Material and Methods: This was a retrospective observational study included 116 women with IUD after 24 weeks of gestation. They were divided into two groups of 58 each. Group 1 women received 10 µg of misoprostol inserted in posterior fornix every four hour. Subsequently, group 2 women received a single dose of 200 mg mifepristone orally, following which a 24-hour-interval was recommended before administration of misoprostol. After 24 hour, 100µg of misoprostol was inserted into the posterior vaginal fornix.
Results: Mean parity was 2 and 2.5 for combination and misoprostol only group respectively and the mean period of gestation was 34 weeks 2 days for combination group and 35 weeks 2 days for misoprostol only group. Mean induction delivery interval in combination group was 8 hours 30 minutes while for misoprostol only it was 14 hours. The mean repeating of 100 micrograms misoprostol in combined group was 1.74 time and 3.6 times in misoprostol only group.
Conclusion: Combination therapy of mifepristone and misoprostol is more effective regimen to cut short the labor pain than conventional regimen of misoprostol alone for induction of labor in women with intrauterine fetal death.

Keywords: Induction of labor, Intrauterine fetal death, mifepristone, misoprostol

Introduction

Intrauterine fetal death is when an unborn baby (fetus) dies inside the womb before birth. This is described as 'late' when it happens in a woman who is 24 weeks pregnant or more, and is estimated to occur in 1% of all pregnancies. In the pregnancies where this happens, if the women were left to go into labor naturally, more than 90% would do so within 3 weeks [1].

Intrauterine death can lead to various complications like psychological upset and intrauterine infections. If dead fetus is retained in uterus for more than 4 weeks, it can lead to consumptive coagulopathy and disseminated intravascular coagulation[2]. Intrauterine fetal death is devastating event for parents and waits and watchful in such circumstance for spontaneous labor pain is frustrating event for parents.

Oral misoprostol administration for labor induction with IUFD was first used in 1987. Since that time use of misoprostol for obstetrical purposes has grown widely [3, 4]. Mifepristone is a steroid compound that antagonises progesterone and glucocorticoid action at receptor level. This compound is widely used for first and second trimester termination of pregnancy [5-7]. Mifepristone administered before Misoprostol sensitizes the uterus to the action of prostaglandins and ripens the cervix. Due to this effect of Mifepristone on the cervix, lower doses of Misoprostol are required to induce expulsion of fetus[8]. So we decided to compare the combination of mifepristone and misoprostol regimen with misoprostol only for induction of labor in late intrauterine fetal death.

Material and Methods

Study Population

This was a retrospective observational study conducted in the Department of Obstetrics and Gynecology, Mathura Das Mathur Hospital under Dr. S N Medical College, Jodhpur, Rajasthan over a period of one years from June 2018 to May 2019. There were 116 women with IUFD after 24 weeks of gestation were enrolled. The assessment of gestational age was based on LMP and confirmed by ultrasound measurements. All women with intrauterine foetal death were counselled regarding IUD and risk and consequences of the same. The study was approved by the Institute Ethics Committee.

Inclusion criteria

i). Gravid up to fourth
ii). without previous lower segment cesarean section (LSCS)
iii). Not in labor (no regular contractions or unfavorable cervix)
iv). willing for medical management

Exclusion criteria

i). Gestational age < 24 weeks
ii). Previous LSCS and associated significant co morbid conditions.

Methodology

A total of 116 pregnant women were randomly allocated into two groups. Group 1 (misoprostol only)) i.e 58 women received 10 µg of misoprostol inserted in posterior fornix every four hourly (maximum 600 µg in 24 hours). Subsequently, group 2 (combination regimen) another 58 women taken was managed using following regimen. The women received a single dose of 200mg mifepristone orally, following which a 24-hour-interval was recommended before administration of misoprostol. After 24 hour, 100µg of misoprostol was inserted into the posterior vaginal fornix. Following administration of the first dose, a further four doses of misoprostol 100µg were given per vaginum every four hourly if required. Subsequent to misoprostol administration, uterine contractions, pulse, blood pressure, temperature and systemic symptoms were monitored hourly. Oxytocin was used for augmentation of labor in active labor if required.

Results

Obstetric parameters of both groups were comparable with no significant difference in terms of age, parity, gestation age. The mean age of females for combination group is 26.9 years and 25.6 years for misoprostol group. Mean parity was 2 and 2.5 for combination and misoprostol only group respectively and the mean period of gestation was 34 weeks 2 days for combination group and 35 weeks 2 days for misoprostol only group. Mean induction delivery interval in combination group was 8 hours 30 minutes while for misoprostol only it was 14 hours which was statistically significant. The mean repeating of 100 micrograms misoprostol in combined group was 1.74 time and 3.6 times in misoprostol only group. Augmentation with oxytocin required in 6 cases in misoprostol only group with one female had PPH in misoprostol group.

Table 1: Age, parity and period of gestation of subject studied

	Age in years	Parity Mean SD	POG in weeks
Combination group	26.9 ± 4.4	2 ± 1.3	34.2 ±0.8 weeks
Misoprostol group	25.6 ± 5.6	2.5 ± 1.5	35.2 ±0.7 weeks
P value	Not significant	Not significant	Not significant

Table 2: Comparison of efficacy of both regimens

Study group	Induction delivery (Mean ± SD)	No. of dose of misoprostol (Mean ± SD)
Combination group	8.36 ± 3.12	1.74±. 67
Misoprostol group	14± 2.14	3.6 ±1. 22
P value	< 0.001	< 0.001

Table 3: Safety and tolerance of both regimens were compared in following parameter

Parameter	Combined Regimen	Misoprostol group
No cases	25 (43%)	37 (63.8%)
Required	11 (18.96%)	Oral
Oxytocin required	P	6 (12.34%)
Adverse effect	4 (6.9%)	4(6.9%)
PPH	0	1 (1.7%)
Retained placenta	2(3.45%)	5 (8.6%)

Discussion

Misoprostol doses regimen varied in different studies, we used dose regimen given by World Health Organization (WHO) for induction of IUFD cases after 26 weeks of gestation. In this study the mean age of females for combination group is 26.9 years and 25.6 years for misoprostol group.

Induction delivery interval depends on parity and period of gestation, but confounding effect of these can be ruled out as both groups were comparable in these parameters.

In this study we found that mifepristone and misoprostol combination had shorter induction delivery interval i.e. 8 hours 30 minutes while for misoprostol only it was 14 hours. Our results are concordant with study done by Wagaarachchi *et al.* [9] and Varynen *et al.* [3] who also reported similar results.

In this study we found that dose of misoprostol required was significantly higher in misoprostol alone group and more number of per vaginal examination in misoprostol only group lead to more chances of local infections and more frustrating and annoying for patients. Our results are in agreement with the findings of Gupta *et al.* [10] and Agarwal *et al.* [11] who also reported the similar findings. Dosage of misoprostol required was significantly higher in misoprostol Group which can be explained on the basis of pharmacokinetics of mifepristone.

In this study augmentation with oxytocin required in misoprostol only group lead to more systemic side effects in misoprostol only group. The incident rate of retained placenta was 8.6% in misoprostol group as compared to 3.45% in combination group. Our findings are in agreement with earlier study done by De Heus R *et al* who also reported the similar results [4].

Use of prostaglandins and their analogues are limited by dose related side effects which can be minimized by vaginal administration or giving relative low doses at frequent intervals or combining them with mifepristone. In present time when double dose of mifepristone is recommended for induction of labor in IUFD we need to give more emphasis on add on drugs to prostaglandin to limit the side effects of such drugs and more acceptance for induction of labor in such situations.

Conclusion

Combination therapy of mifepristone and misoprostol is more effective regimen to cut short the labor pain. It is equally safe, easily, tolerable, and more efficacious than conventional regimen of misoprostol alone alone for induction of labor in women with intrauterine fetal death.

References

1. Induction of labour in late intrauterine fetal death: vaginal misoprostol (after oral mifepristone) Evidence summary [ESUOM11]: April 2013.
2. Pritchard JA. Fetal death in utero. Obstet Gynecol 1959; 14:573 e 80.
3. Vayrynen W, Heikinheimo O, Nuutila M. Misoprostol only versus mifepristone plus misoprostol in induction of labor following intrauterine fetal death. Acta Obstet Gynecol Scand. 2007; 86:701-5.
4. De Heus R, Graziosi GC, Christiaens GC, Bruinse HW, Mol BW. Medical management for termination of second and third trimester pregnancies: A comparison of strategies. Eur J Obstet Gynecol Reprod Biol. 2004; 116:16-21.
5. Newhall EP, Winikof B. Abortion with mifepristone and misoprostol: regimen efficacy, acceptability and future directions Am J Obstet Gynaecol. 2000; 182:44-53.
6. El- Refacy H, Rajashekhar. D, Abdalla M, Calder T, Templeton A. Induction of abortion with mifepristone (RU486) and oral or vaginal misoprostol N Engl J M. 1995; 332:983-7.
7. Ashok PW, Flett GM, Templeton A. An effective regimen for early medical abortion: a report of 2000 consecutive cases. Human Reprod. 1998; 13(100):2962-5.
8. Role of Combination OF Mifepristone and Misoprostol Verses Misoprostol alone in Induction of Labour in Late Intrauterine Fetal Death: A Prospective Study; Subrat panda *et al*.; J Family Reprod Health. 2013; 7(4):177-9
9. Wagaarachchi PT, Ashok PW, Narvekar NN, Smith NC, Templeton A. Medical management of late intrauterine death using a combination of mifepristone and misoprostol. BJOG: Int J Obstet Gynaecol. 2002; 109(4):443-7.
10. Gupta S, Kagathra B, Desai A. Mifepristone and misoprostol versus misoprostol alone in the management of intrauterine death. Tai J Obstet Gynecol. Int J Reprod Contracept Obstet Gynecol. 2016; 5:2935-8.
11. Agarwal A, Basnet P, Thakur A, Rizal P, Rai R. Induction of labor using misoprostol with or without mifepristone in intrauterine death. J Nepal Med Assoc. 2014; 52(194):785-90.