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Original Research Article

Comparative study of mifepristone and misoprostol versus misoprostol alone in induction of labour in late intrauterine fetal death

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ABSTRACT

Background: Intrauterine fetal death is most undesirable consequence of pregnancy and stressful condition for women and family and for health professional. Naturally, majority of women (over 90%) go in for spontaneous labour and deliver within 3 weeks of intrauterine death. Prolonged retention of dead fetus in utero has complications like DIC, psychological stress and infection. Various methods are available to induce labor in intrauterine fetal death. One such regimen is medical management using a combination of Mifepristone and Misoprostol. The objective of this study was to compare efficacy and safety of combination of mifepristone and misoprostol versus misoprostol only in induction of labour in late intrauterine fetal death.

Methods: A prospective study was carried out in KIMS, Hubli between Jan 2014 to Dec 2015. Data from 100 women with intrauterine fetal death between gestational age of 24-42 weeks were analysed. They were divided into 2 groups of 50 each. Group I received single oral dose of 200mg mifepristone followed 24 hours later with oral misoprostol (100µg-50µg) every 4 hourly. Group II received only misoprostol. Outcomes were measured in terms of induction to delivery interval and number of misoprostol doses required.

Results: Mean induction to delivery interval in Group I was 8.3 hours versus 13.4 hours in Group II. Induction delivery interval was shorter in combined regimen. Total dose of misoprostol was also less in Group I.

Conclusions: Both regimens are safe for induction of labour in late intrauterine fetal death. However, the induction delivery interval and dose of misoprostol required was decreased in combination regimen.

Keywords: Late intrauterine fetal death, Induction of labour, Mifepristone, Misoprostol

INTRODUCTION

The importance of obstetrics is attested to by the use of maternal and neonatal outcome as an index of quality of health and life in human society.¹ The antepartum death occurring beyond 28 weeks is termed as intrauterine death. Cause for IUD is not known in 25-35% of cases. Maternal, paternal and fetal conditions are known to result in fetal demise

In 80% of women with IUD, spontaneous expulsion occurs by 3 weeks. Retention of death fetus in utero can lead to complications like intrauterine infection, DIC,

psychological stress and increased risk of consumptive coagulopathy.²

Many methods of induction of labour in intrauterine fetal death have been used. Prostaglandins have changed the scenario in modern obstetrics.

Prostaglandins have been used extensively for induction of labour in intrauterine fetal death.^{3,4} They can be used by various modes like oral, vaginal, sublingual, rectal, IM or IV. Side effects are dependent on route of administration and type of prostaglandins used. Misoprostol, a synthetic analogue is cost effective, stable

at room temperature and easy to administer.⁵ Hence it has been used extensively. Nausea, vomiting and shivering are the major side effects of misoprostol.

Mifepristone, 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.⁶⁻⁸

Mifepristone if 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. This present study is undertaken to compare the effectiveness and safety of combination regime of mifepristone and misoprostol with misoprostol alone.

METHODS

This prospective observational study of 2 years from January 2014 to December 2015 was undertaken at KIMS, Hubli. 100 pregnant women with IUD after 24 weeks of gestation were studied. The assessment of gestational age was based on LMP and confirmed by ultrasound measurements. All women with intrauterine fetal death were counselled regarding IUD and risk and consequences of the same.

Inclusion criteria

- Women with intrauterine fetal death confirmed by USG.
- Women not in labour.
- Women gave informed written consent for induction.

Exclusion criteria

- Women In labour.
- Multiple pregnancy with one intrauterine fetal death.
- Major degree CPD.
- Previous 1 LSCS.
- Patients with glaucoma, epilepsy, asthma, heart diseases.
- Women with abnormal coagulation profile.
- Women who did not give consent.
- Grand multipara.

The patients had a detailed clinical examination and USG confirmation of IUD. Consent for induction was taken. 100 pregnant women with intrauterine fetal death were divided randomly, alternatively into with two groups of 50 each.

Group I (combination regimen) women received 200mg mifepristone orally. After 24 hours oral misoprostol was given. The dose of misoprostol was 100µg for 24-26 weeks and 50µg for gestational age >26 weeks, every 6 hourly for a maximum of 4 doses.

Group II (misoprostol only) women received oral misoprostol, the dose being 100µg for gestational age of 24-26 weeks and 50µg for gestational age >26 weeks, every 6 hourly for a maximum of four doses.

Number of doses of misoprostol used and induction delivery interval was noted. Statistical analysis was performed by using Chi-square test. P value >0.05 was taken as significant.

Successful treatment was defined as delivery within 72 hours of first misoprostol dose. Side effects of the treatment were constantly monitored. Serious complications like uterine tachysystole and hypertonicity were monitored. Pervaginal examination was kept to minimum to prevent infections.

RESULTS

Obstetric parameters of both groups were comparable with no significant differences Table 1 shows the same.

Table 1: Age, parity and period of gestation of subjects studied.

Group	Age in years (mean±SD)	Parity (mean ±SD)	Period of gestation in weeks (mean±SD)
Group I	23±3.8	1.74±1.04	33.72±4.45
Group II	24±4.1	2.04±1.32	35.34±4.27
P value	NS	NS	NS

Efficacy of combined regimen was compared by following parameter. The induction to delivery interval reflects the time interval between first dose of misoprostol to expulsion of fetus. Dose of misoprostol required were compared between two groups.

Table 2: Comparison of efficacy of both groups.

Study group	IDI (mean±SD) in hours	No. of dose of misoprostol (Mean ±SD)
Group I	8.3±3.48	1.52±1.14
Group II	13.34±4.82	2.76±1.05
P value	<0.001	<0.001

Mean induction delivery interval in group I and group II were 8.3 hours and 13.3 hours respectively which was statistically significant. The number of doses of misoprostol required in Group I was significantly less compared to group II.

Induction delivery interval was ranging from 4-22 hrs in group I and 6-29 hours in group II Side effects of both the groups were compared. Group I had mild gastrointestinal side effects like nausea and diarrhoea whereas Group II has more shivering and fever. No cases of uterine

tachysystole, hypertonicity, haemorrhage, rupture uterus or coagulopathy was recorded in any group.

Table 3: Side effects comparison of both groups.

Side effects	Group I (%)	Group II (%)	P value	
Nausea	12 (24%)	5 (10%)	0.06	NS
vomiting	-	-		
Abdominal cramps	-	-		
Diarrhoea	3 (6%)	2 (4%)	0.06	NS
Shivering	10 (20%)	18 (36%)	0.075	NS
Fever	11 (22%)	16 (32%)	0.26	NS
Headache	4 (8%)	3 (6%)	0.69	NS

DISCUSSION

A variety of routes of administration of prostaglandins analogues including PGE2 and PGF2 α have been used with success. A preliminary trial by Cabrol et al reported successful induction of labour and further using a prospective double-blind trial confirmed that mifepristone can be useful in management of intrauterine death.⁹

Wagaarachchi et al performed an observational study on 96 women with late intrauterine fetal death and reported a mean induction delivery interval of 8.5 hours and 98.9% of women delivered within 72 hours.¹⁰ He concluded that combined method was safe and effective method to induce labour in IUD and has shorter induction delivery interval than using misoprostol alone. Fairley et al had a same observation.¹¹

In this study, induction delivery interval was less in Group I. Present study is in agreement with study of Vavyrynen et al and Sharma et al.^{12,13}

In current study, the induction delivery interval was 8.3 hours in combination regimen whereas in misoprostol alone it was 13.34 hours which is statistically significant. Dosage of misoprostol required was significantly higher in misoprostol group which can be explained on the basis of pharmacokinetics of mifepristone.

Our regimen carried mild gastrointestinal side effects like nausea and diarrhoea in combination regimen whereas in misoprostol alone group shivering and fever was more frequent. The complication like uterine rupture was not seen in the present study. No cases in the study group had severe PPH or coagulopathy.

Use of prostaglandins and their analogues are limited by dose related side effects which can be minimised by vaginal administration or giving relative low doses at frequent intervals. In present study we had used misoprostol orally to achieve patient acceptability and to reduce the risk of introducing infection by repeated per vaginal examination.

CONCLUSION

The combination of mifepristone and misoprostol for induction of labour in intrauterine fetal death has shorter induction to delivery interval and lesser amount of misoprostol dosage when compared to only misoprostol alone.

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Ethical approval: The study was approved by the Institutional Ethics Committee

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