

Outcome of Mifepristone and Misoprostol Verses Misoprostol for Induction of Labour in third Trimester Intra Uterine Foetal Death in Tertiary Care Center in P.B.M Hospital, Bikaner

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Abstract

Background: Due to limited study was conducted in our hospital. The present study is undertaken to compare the effectiveness and safety of combination regime of mifepristone and misoprostol with misoprostol alone in 28 week of IUD.

Methods: Hospital based prospective study conducted on 100 women. Group A (50 pregnant women with IUFD receiving combination of mifepristone and misoprostol) and Group B (50 pregnant women with IUFD receiving misoprostol alone group).

Results: The general characteristics of both groups comparable. Mean Bishop score in group A and group B was 1.56 and 2.41 respectively. The mean induction delivery interval was more in group B than group A (25.98 hour versus 18.74 hour). In group A number of cases delivered within 24 hours of induction were more than group B. Mean number of 50µg misoprostol required in group A was 2.40±1.37 while in group B it was 2.54±1.30. Need of supplementation with oxytocin was more in group B as compared to group A. Mean birth weight in group A was 2.46±0.89 kg and in group II was 2.65±0.89kg. The induction was successful in 100.00% cases in group-A while in group-B was in 96.00%. In group-A, 94.00% cases had not found any complication, fever was found in 4.00% cases, retained placenta was found 2.00% cases. In group B, 78.00% cases were no found any complication, fever and nausea /vomiting, retained placenta was found in 6.00% cases each, uterine tachystole & PPH was found in 4.00% cases each.

Conclusion: We concluded that both the regimen was equally safe, easy to administer and affordable but the Combination Regimen had a slight edge over misoprostol alone regimen in terms of tolerance, fewer side effects and efficacy with regard to early onset of labour, shorter Induction to Delivery Interval and relatively less dose of misoprostol than misoprostol alone regimen.

Keywords: Misoprostol, Mifepristone, Labour, IUD

Introduction

Intrauterine fetal death (IUFD) is one of the most devastating obstetric complications. A clinically accepted definition of IUFD is the death of fetus at or after 20 weeks of pregnancy¹, but for

international comparison WHO has now recommended IUFD as a baby born with no sign of life at or after 28 weeks of gestation².

Mifepristone has potential as a method of inducing labour in late pregnancy through its actions in antagonising progesterone, thus increasing uterine contractility and the sensitivity of the uterus to the actions of prostaglandins. Mifepristone has been shown to induce labour in rats, through opposition to progesterone-induced suppression of oxytocin receptors, and enhanced synthesis of prostaglandins. Mifepristone has also been shown to induce preterm birth in mice, associated with a rise in prostaglandins and cytokines³.

In women, mifepristone combined with subsequent prostaglandins is also being commonly used for labour induction after fetal death in later pregnancy. The data from women undergoing termination of early pregnancy have shown that mifepristone is more effective in nulliparous women⁴.

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.

Material and Method

Study design: Hospital based prospective comparative study.

Study period: From 1st Feb 2021 to 31st January 2022 (1-year study).

Sample size: Total 100 Pregnant women-

Group A- 50 pregnant women with intrauterine foetal death receiving combination of mifepristone and misoprostol

Group B- 50 pregnant women with intrauterine foetal death receiving misoprostol only

Inclusion criteria:

1. Women above the age of 18.
2. Women who presented with death of singleton fetus greater than gestational age 28weeks.
3. Women who will not in labor.
4. Women who consented to participate in study.

Exclusion criteria:

1. Pregnant women with multiple gestation.

2. Women with history of placenta previa, asthma, coagulopathy, epilepsy, renal and hepatic diseases, cardio vascular diseases.

3. Women with known allergy/contraindication to the use of mifepristone and misoprostol.

4. Women with previous cesarean section, myomectomy.

5. Women with grand multi-parity (parity > four).

6. Not willing to participate in study.

7. Patient in spontaneous labour.

8. Malpresentation.

9. Severe local lesion, active genital herpes.

10. Adrenal insufficiency.

Sampling methods: Random sampling

Data collection: After proper counselling and informed consent from pregnant women selected in the study population, detailed history-taking, physical and obstetrical examinations was performed and all routine base line investigations were include according to our hospital protocol in IUFD cases, the participants were allocated in two groups.

Group A (50 pregnant women with IUFD receiving combination of mifepristone and misoprostol) Women of group A received a single oral dose of 200 mg of mifepristone, and after 24 hours, 50 mcg of oral misoprostol administered followed by 50 mcg of orally misoprostol at 6 hours interval for a maximum of 5 doses if required.

Group B (50 pregnant women with IUFD receiving misoprostol alone group) received only misoprostol in the dose of 50 mcg orally 6 hours for a maximum of 5 doses (5x50 mcg=250 mcg). Primary outcome were measure by the rate of successful delivery in 24 hours and induction delivery interval from first dose of misoprostol to complete delivery of fetus and placenta.

Data Analysis: All data collected were entered into Microsoft Excel and was analyzed with the help of appropriate software and test of significance considering level of significance as $p < 0.05$

Ethical Approval: The goal and methodology of the study was described to all patient relatives

after approval of hospital ethics committee. Both verbal and written consents was taken from the patient and her close relatives. The potential benefits and inconvenience of all aspects of the

study was clearly stated to the patient and her close relatives.

Observation

Table 1: Study outcome

Variable		Group-A(n=50)	Group-B (n=50)	P-value
Demographic profile	Age in yrs	24.16±3.61	25.08±4.44	0.258
	Booked : unbooked	34:16	31:19	0.675
Bishop score		1.56±0.98	2.41±1.01	0.02
Mode of delivery (Vaginal : LSCS)		50:0	48:2	0.53
Induction to delivery interval (hrs)		18.74±6.82	25.98±8.95	0.01
Delivered with in 24 hours		41(82.00%)	33(66.00%)	0.231
Number of dose 50µg misoprostol required		1.90±0.70	3.50±0.81	0.01
Oxytocin augmentation required		0(0.00%)	6(12.00%)	0.01
Successful of induction		50(100.00%)	48(96.00%)	0.01
Birth weight in kg		2.46±0.89	2.65±0.89	0.256
Maternal complication	Fever	2(4.00%)	3(6.00%)	
	Nausea / Vomiting	0(0.00%)	3(6.00%)	
	PPH	0(0.00%)	1(2.00%)	
	Retained placenta	1(2.00%)	3(6.00%)	
	Uterine tachysystole	0(0.00%)	1(2.00%)	

Mean age in group A was 24.16±1.13years while in group B it was 25.08±4.44 years. On comparing the two groups with respect to age they were found to be statistically non significant ($p>0.05$). In group A, 68.00% cases were registered whereas in group B, 62.00% cases were registered. 32.00% and 38.00% cases were unregistered in group A and B, respectively. Mean Bishop score in group A and group B was 1.56 and 2.41 respectively. Both groups are comparable with respect to Bishop score at the time of induction and p value is significant (p -value=0.02). In group-A 100.00% cases were delivered vaginally whereas in group-B 96.00% had vaginal delivery and 4.00% cases underwent LSCS. The mean duration of induction to delivery interval in group A was 18.74 hour and

in group B was 25.98 hour. The results were compared statistically and p value found to be significant ($p=0.001$). In group A, 82.00% cases were delivered within 24 hours of induction whereas in group B, 66.00% cases delivered within 24 hours of induction. This difference was found statistically non significant ($p=0.212$). Mean number of dose 50µg misoprostol required in group A was 1.90±0.70 while in group B it was 3.50±0.81. In group A, whereas 12.00% cases in group B required augmentation with oxytocin. In group-A induction was 100.00% successful whereas in group-B 96.00% had successful induction while 4.00% cases induction failed induction. In group A mean birth weight was 2.46 kg and in group B mean birth weight was 2.65 kg. In group-A, 94.00% cases had not any

complication, Fever was found in 4.00% cases, retained placenta was in 2.00% cases. Whereas in group B, 78.00% cases did not develop any complication, fever, nausea /vomiting, retained placenta was found in 6.00% cases each, uterine tachystole and PPH was found in 4.00% cases in Group A and B respectively.

Discussion

Present prospective study is an attempt to compare outcome. In our study 100 cases were randomly selected and divided in group A & group B of 50 cases. Majority of patients geastation age was belonged between 28 to 36 weeks in both groups. In group A, 40.00% cases were of 28-32 weeks gestational age, 38.00% of between 33 to 36 weeks and 22.00% of between 37 to 40 weeks. In group B, 36.00% cases were of between 28 to 32 weeks gestational age, 48.00% of between 33 to 36 weeks and 16.00% of between 37 to 40 weeks. The two groups was statistically comparable in terms of gestational age and p value was non significant ($p=0.302$). In comparison to study conducted by Arjunan Y et al (2017)⁶, Abbasi S et al (2017)⁷ they found that maximum cases were of 33-36 weeks gestational age. Sharma D et al (2011)⁸ was found that 40.00% of cases were belong to <34 weeks gestation age in both groups.

In our study mean Bishop score in group A and group B was 1.56 and 2.41 respectively. Both groups are comparable with respect to Bishop score at the time of induction and p value is significant ($p\text{-value}=0.02$). Similar result by Arjunan Y et al (2017)⁶ was found that most patients (76.00%) had bishop score 0 to 3 in both groups. Sharma D et al (2011)⁸ was found that most patients (80%) had bishop score 0 to 3 in both groups. Abassi S et (2017)⁷ mean Bishop score in group A and group B was 2.36 and 2.49 respectively. Both groups are comparable with respect to Bishop score at the time of induction and p value is Insignificant. Arjunan Y et al (2017)⁶ was found that most patients (76.00%) had bishop score 0 to 3 in both groups.

In group A, 12.00% cases were delivered within <12 hours and 4.00% within <12 hours in group-B. Modak R et al (2018)⁹ was found that delivery within 12 hours of misoprostol administration occurred significantly in higher proportion of women receiving the mifepristone pre-treatment on comparison to misoprostol alone (55.56% vs.10.53%, $p=0.001$). Comparable results were reported by various studies (choudhary P et al. and Sharma D et al.)^{10,8} but the mean interval varies in all these studies.

In our study, 70.00% cases between 12-24 hours and 18.00% cases in >24 hours after induction whereas in group B, 62.00% cases between 12-24 hours and 34.00% cases in >24 hours after induction. The mean induction delivery time in group A was 18.74 hour and in group B was 25.98 hour. The results were compared statistically and p value found to be significant ($p=0.001$). Our result similar to Maheshwari S et al (2017)¹¹ was found that Mean Induction to Delivery Interval was 17.43 ± 5.58 hours in Group A which was very less compared to 25.56 ± 10.78 hours in Group B and was statistically found to be extremely significant.

In our study, overall 74.00% cases delivered within 24 hours. In group A, 82.00% cases and in group B 66.00% cases delivered within 24 hours. ($p=0.212$). In our study, average number of $50\mu\text{g}$ misoprostol required in group A was 1.90 ± 0.70 whereas in group B, it was 3.50 ± 0.81 . Mifepristone administered before misoprostol increases the sensitivity of the uterus to prostaglandins and ripens the cervix allowing lower doses of misoprostol to induce expulsion of fetus. Our results correspond with the findings Sharma D et al⁸ and Abrassi et al⁷.

In present study the requirement of oxytocin for supplementation in group B is significantly higher ($p=0.001$). No cases in group A required oxytocin as compared to 12.00% in group B. Comparable result observed by Sharma D et al⁸ with no cases in the combination group and

11.3% cases in the Misoprostol alone group requiring oxytocin induction

In our study in group-A induction was 100.00% successful whereas group-B was 96.00% successful and 4.00% cases were failed. Comparable result observed by Maheshwari et al (2017)¹¹, Arjunan Y et al (2017)⁶, Abbasi S et al(2017)⁷, Choudhary P et al (2015)¹⁰, they found that the in group –A maximum cases induction was successful as compare to group-B.

In our study, the postpartum complications were very less in group-A, 94.00% cases had not found any complication, fever was found in 4.00% cases, retained placenta was found 2.00% cases. In group B, 78.00% cases were no found any complication, fever and nausea /vomiting, retained placenta was found in 6.00% cases each, uterine tachystole &PPH was found in 4.00% cases each. Sharma D et al (2011) ⁸ was found that misoprostol, the side effects like nausea, vomiting, headache, diarrhea, and fever were experienced by 10.75%, 25%, 14.29%, 7.15%, and 17.86% of women, respectively whereas in combination group 2 cases experienced nausea/ vomiting.

Conclusion

It was observed in the study that both the regimen was equally safe, easy to administer and affordable but the Combination Regimen had a slight edge over misoprostol alone regimen in terms of tolerance, fewer side effects and efficacy with regard to early onset of labour, shorter Induction to Delivery Interval and relatively less dose of misoprostol than misoprostol alone regimen. Further studies are necessary on a larger population to define the ideal treatment option and optimum dosage for a better management of IUFD

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