Section: Obstetrics & Gynaecology

Research

A COMPARATIVE STUDY OF MISOPROSTOL ALONE VERSUS (VS) MIFEPRISTONE AND MISOPROSTOL FOR INDUCTION OF LABOR IN INTRAUTERINE FETAL DEATH (IUFD)

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Abstract

Background: The management of IUFD poses a dilemma as to which regimen to follow for effective delivery of dead fetus. Routine use of prostaglandins is recommended for medical induction of labor for IUFD, therefore, aim of study is to show the efficacy & safety of management of IUFD using misoprostol alone vs mifepristone and misoprostol combination. **Materials and Methods:** The present prospective study was carried out in 40 pregnant women admitted with intrauterine death after 28 weeks of gestation in labor ward of department of Obstetrics & Gynecology at MATA GUJRI MEMORIAL MEDICAL COLLEGE & LSK Hospital, after ethical clearance. The women were divided randomly, Group 1(combination group) -it included 20 women, who were induced with mifepristone and misoprostol combination. Group 2(Misoprostol group)-It included 20 women who received oral misoprostol till she went into active labor for a maximum of four doses. Every alternate patient was assigned the respective group. **Result:** Both the groups were comparable in terms of age, parity, gestation age, and bishop score. There were 60% primigravida and 40% multigravida in the Group 2 and 50% primigravida and 50% multigravida in the Group 1. Most patients (70%) had bishop score 0-3 in the two groups. Success of induction with mifepristone was not related to age, parity, and bishop score (Table 2, $p > 0.05$). In the Group 1, there were four patients who had bishop score>3 and all of these patients delivered with mifepristone, whereas 16 patients had bishop score 0-3 of which only 8 patients (50%) delivered after giving mifepristone. The rest of the 8 patients, who did not deliver with mifepristone, had bishop score 0 before the start of treatment and 4 hours after 36 hours of treatment. The change is highly significant ($p < 0.01$). On correlating the success of induction in the Group 1 (12 patients), with parity, gestation, and bishop score, there was no significant difference. **Conclusion:** It was observed that a lesser number of misoprostol doses and shorter duration of IDI in combination therapy of mifepristone and misoprostol was more effective and safer approach to induce labor than misoprostol alone in IUFD.

INTRODUCTION

The antepartum death occurring beyond 20 weeks is termed as intrauterine death for all practical purposes. A number of maternal, placental, and fetal conditions can result in fetal demise, but in about 25%-35% of cases, the cause remains unknown. 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.

When the fetal death occurs, spontaneous expulsion will usually occur in most cases i.e. in about 80% of cases, within 2 weeks of death. But, it can be evacuated earlier at the request of women to relieve emotional distress. Various methods have been tried in the management of intrauterine death.

After such an evacuation or extraction, the foetus shows no indications of life, including breathing, heart rate, umbilical cord pulsation, or voluntary

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muscle movement, all of which are indicative of intrauterine death (IUFD). It's important to identify the foetal heartbeat from fleeting cardiac contractions and breathing from brief gasps.[1,2]

There have been many attempts to induce labour in cases of intrauterine foetal death. Misoprostol is a prostaglandin E1 analogue that is preferred because to its inexpensive cost, stability at room temperature, and ease of administration. Mifepristone is a steroid used to stop pregnancies in the first and second trimesters because it blocks progesterone's receptors.[3-5]

Taking mifepristone prior to ovulation makes the uterus more receptive to prostaglandin action and prepares the cervix for an abortion. As a result of mifepristone's mechanism of action on the cervix, lower doses of misoprostol are required to induce labour.

Misoprostol often causes unwanted side effects include fever, nausea, vomiting, dizziness, diarrhoea, and headache. Abnormal uterine action, such as uterine hyperstimulation, is the most concerning risk associated with misoprostol since it might cause uterine tachysystole and rupture.[6]

Several therapeutic approaches have been offered for terminating a pregnancy due to intrauterine death, however the optimal method for inducing labour has not yet been established. Therefore, the purpose of this study is to evaluate the relative efficacy of misoprostol and mifepristone for inducing labour in IUFD.

MATERIALS AND METHODS

The present prospective study was carried out in 40 pregnant women admitted with intrauterine death after 28 weeks of gestation in labor ward of department of Obstetrics & Gynecology at MATA GUJRI MEMORIAL MEDICAL COLLEGE & LSKH after ethical clearance. The women were divided randomly, alternatively, into two groups of 20 each, the patient came first was assigned Group A, the next patient Group B, then Group A, and so on. Total number of patients was decided by power analysis.

Group I(combination group) -it included 20 women, who were induced with mifepristone and misoprostol combination. The women received 200 mg of mifepristone; and after 36 hours, misoprostol was administered orally (100ug if pregnancy< 34 weeks) (50ug if pregnancy>34 weeks)for every 4 hours, till they went into active labor for a maximum of four doses.

Group II(Misoprostol group)-It included 20 women who received oral misoprostol (100ug if pregnancy <34 weeks) (50ug if pregnancy >34 weeks)4 hourly, till she went into active labor for a maximum of four doses. Every alternate patient was assigned the respective group.

Inclusion Criteria

healthy women aged between 21 and 35 years with singleton intrauterine pregnancy >28 weeks of gestation admitted for termination of pregnancy.

Exclusion Criteria

Women with previously scarred uterus, multiple gestation, glaucoma, asthma, heart disease, and grand multipara, placenta previa, hemorrhagic disease, known cases of renal and liver diseases were excluded.

Primary outcome measures were achievement of successful induction and induction delivery interval. Success of induction was defined as vaginal delivery occurring within 36 hours of administration of mifepristone and within 24 hours of administration of first dose of misoprostol.

Women who did not deliver after four doses of misoprostol were considered as failure of regimen. In all the women details of the demographic profile, bishop score before the start of mifepristone and misoprostol, induction delivery interval, and adverse effect of the drug were noted. The induction delivery interval and success of induction was also correlated with bishop score [<3 (very poor bishop) and 0.3] at the start of the treatment in the two groups. Data were analyzed by using Student t test and Chi-square test.

RESULTS

[Table 1] reveals that the age (mean SD) of women in groups I and II was 24.64±3.28 and 25.21±5.49 years, respectively. In group I and group II, the parity and gestational age were 2.11±0.96, 2.24±1.24, 32.42±5.41, and 32.31±4.66 weeks, respectively. The mean BMI for Group I was 29.45±3.22 kg/m2 and for Group II it was 28.45±2.45 The difference in demographic and obstetric factors between the two groups was not statistically significant ($p > 0.05$). However, the mean and standard deviation for the number of Misoprostol doses in Group 1 was 0.98±1.42 and in Group II it was 2.41±1.68, indicating a statistically significant difference between the two groups ($p = 0.002$).

Table 1: Distribution of various parameters in two groups

Parameters	Group:I (n=20)	Group: II (n=20)	p value
Age	24.64±3.28	25.21±3.49	0.475
Parity	2.11±0.96	2.24±1.26	0.741
Gestation	32.42±5.41	32.31±4.66	0.234
BMI	29.45±3.22	28.45±2.45	0.128
Initial Bishop Score	2.71±1.09	2.77±1.32	0.423
No of Misoprostol Doses	0.98±1.42	2.41±1.68	0.002

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Table 2: Bishops' score of women was modified based on time intervals.

Groups	Bishops' score	Preinduction, at the time of admission)	Preinduction (after mifepristone in group I)	After 12 hours of induction
Group-I (n=20)	0-3	15(75.0%)	7(35.0%)	1(5.0%)
	4-6	5(25.0%)	13(65.0%)	7(35.0%)
	>6	0(0.0%)	0(0.0%)	12(60.0%)
Group-II(n=20)	0-3	13(65.0%)	12(60.0%)	5(25.0%)
	4-6	7(35.0%)	8(40.0%)	13(65.0%)
	>6	0(0.0%)	0(0.0%)	2(10.0%)

At the time of admission, a maximum number of women in both groups had Bishops scores in the range of 0 to 3. 13 (65.0%) of the women in group I had a preinduction Bishops score in the range of 4–6 whereas 12 (60.0%) of the women in group II had a preinduction Bishops score in the range of 0–3. At 12 hours, the Modified Bishops score was >6 in 12.0 (60%) of the women in group I, compared to 2 (10%) of the women in group II, and the difference was statistically significant.

Table 3: Outcome

Parameters	Group:I (n=20)	Group: II (n=20)	p value
Induction labor interval (hours)	2.54±1.99	7.24±6.42	<0.0001
Induction delivery interval (hours)	9.22±8.45	15.47±11.47	<0.0001
Oxytocin augmentation needed	2(10%)	8(40%)	0.033
Birth weight (mean ± SD)	1547.32±874.32	1652.42±865.56	0.067

Mean induction labor interval was 2.54±1.99 hours in group I as compared to 7.24±6.42 hours in group II; and mean induction to the delivery interval was 9.22±8.45 and 15.47±11.47 hours in group I and group II, respectively, and the difference was found to be statistically significant. Mean birth weight in group I was 1547.32±874.32 gm and in group II was 1652.42±865.56 gm, and the difference was found to be statistically non-significant (p -0.067)

Table4: Adverse effect

Parameters	Group:I (n=20)	Group: II (n=20)	p value
Vomiting	3(15.0%)	5(25.0%)	0.346
Loose stools	1(5.0%)	4(20.0%)	0.169
Hyperthermia	2(10.0%)	6(30.0%)	0.117

Mild adverse effect found in both groups, The difference of adverse effect was not statistically significant p value was>0.05.

DISCUSSION

In our study, the ages of both groups were equivalent, and there was no statistically significant difference between them in terms of mean age. 8–12 Both groups had a mean gestational age that was older than the current study, but the difference was not statistically significant.[7]

In accordance with previous research, the mean number of misoprostol doses delivered to women in the present study was lower in the combination group than in the misoprostol group.[8] They concluded that pretreatment with mifepristone reduced the number of misoprostol doses required to induce labour in women. We found a significant decrease in the need for misoprostol with prior use of mifepristone, which is consistent with the literature showing a decreased need for prostaglandin in cases where mifepristone was administered and also due to the effective cervical ripening caused by mifepristone administration.

In group II, the average induction labour interval was longer than in group I. It was determined that the difference was statistically significant. Multiple studies reported comparable outcomes.[9] However, the mean period from induction to delivery differs across research. The likely cause is a discrepancy in the dosage and administration schedule of misoprostol according to distinct study protocols. Women who were primed with mifepristone before receiving misoprostol had a considerably shorter induction-delivery interval (IDI) than those who received misoprostol alone.

The induction to delivery interval represents the time between the first dose of misoprostol and foetal ejection. In the present study, the mean period from induction to delivery was shorter in group I than in group II, and the difference was statistically significant. Mifepristone is an antiprogestational steroid that causes cervical ripening and increases uterine activity, hence resulting in foetal evacuation.[10] Similar results were demonstrated by many writers.[11] Most current guidelines[12] advocate a time gap of 36 to 48 hours between mifepristone and misoprostol administration. Following such an interval, uterine muscle is most sensitive to prostaglandins and their analogues, which explains this mechanism. This difference was found to be statistically significant by Sindhuri et al.,[13] Hemalatha et al,[14] and Trivedi et al.,.[15] They discovered that the combined regimen had shorter induction delivery intervals compared to the misoprostol-only regimen.

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Although group II had a slightly higher mean birth weight, the difference was judged to be inconsequential from a statistical standpoint. Modak et al.[16] observed comparable outcomes, although Arjunan et al.[17] found a slightly higher mean birth weight in the combination group, which was contrary to our findings but not statistically significant.

Fever and shivering were more prevalent in the misoprostol group than in the combined therapy group.[13,14] According to Panda et al.[7], there was no significant difference between the two groups in terms of labour and delivery difficulties.

Compared to group I, the majority of women in group II have maternal factors of IUFD, and the difference is statistically significant. Abruption (22.5%) was the most prevalent cause in group II, whereas anaemia (16.4%) and preeclampsia (16.4%) were the most prevalent causes in group I.

CONCLUSION

It was observed that a lesser number of misoprostol doses and shorter duration of IDI in combination therapy of mifepristone and misoprostol was more effective and safer approach to induce labor than misoprostol alone in IUFD

So, both mifepristone in combination with misoprostol and misoprostol alone achieved successful induction in women with intrauterine fetal death. Mifepristone led to significant improvement in bishop score in patients who were not delivered by this drug. The combination therapy led to short induction delivery interval than that of misoprostol alone. In addition, the number of doses of misoprostol required was less in patients who were pretreated with mifepristone. To conclude, combination therapy of mifepristone and misoprostol is more effective than the misoprostol alone for induction of labor in women with intrauterine fetal death.

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