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Original Article

Outcome of Mifepristone in Induction of Labor in Pregnancy with Intrauterine Death

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Abstract:

Induction of labor in delivery of intrauterine death cases is associated with higher incidences of prolonged initiation of labor. Mifepristone is thought to be the safest and cost effective modalities for induction of labor in pregnancy after intrauterine death. The aim of this study was to assess the outcome of induction of labor in intrauterine death with mifepristone. This prospective observational study was conducted at the Department of Obstetrics & Gynaecology in Faridpur Medical College & Hospital, Faridpur during July 2023 to June 2024. Total 95 pregnant women with intrauterine death at/after 28 weeks were interviewed after taking written informed consent. Participants were given mifepristone (200mg) orally 8 hourly for 48 hours. Bishop's score was assessed before induction and after 24 and 48 hours of doses. Collected data was analyzed by the SPSS 25.0. The mean age of patients was 28.12±5.51 years. Maximum women were nulliparous (53.68%) and had gestation for >36 weeks (64.21%). The mean value of bishop's score significantly increased after 24 hours of induction, compared to on-administration value (4.87±1.55 vs 7.46±1.65, p<0.001). Overall, majority respondents (77.89%) had successful induction and had vaginal delivery. Nausea/vomiting (68.42%), dizziness (46.32%), abdominal crumps (10.53%) and fever (6.32%) were the common complications. The most prevalent complication was nausea and vomiting (68.42%).

Key words: Intrauterine death, Mifepristone.

Introduction:

Intrauterine fetal death (IUFD) is an unpleasant pregnancy outcome and prompt delivery of the dead fetus is usually desired by mothers[1]. IUFD is a devastating pregnancy outcome and brings with it enormous distress and grief[2]. It is the birth of a fetus with no signs of life at or after 28 weeks of gestation[3]. It is also an indicator of maternal and perinatal health of a given population[4]. When a fetus dies in utero, the vast majority (over 90%) of women will go into labor spontaneously and deliver within 3 weeks of IUFD[5]. Prolonged pregnancy is known to be associated with significantly increased risks of perinatal and maternal complications[6,7]. Different methods of labor induction in full-term pregnancy are widely practiced to try and prevent the problems mentioned above[8,9].

Mifepristone (RU 486) is a 19-norsteroid which has a specific high affinity binding to the progesterone receptor and thus to compete with progesterone at the level of their respective binding site[10]. Also this compound exerts some anti-glucocorticoid activity. Mifepristone is absorbed rapidly after oral administration, reaching maximum serum levels within 2 hours and has a half-life of about 25 hours[11]. Mifepristone is anti-progesterone

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available in a tablet form that is stable at room temperature and not expensive.

It is formulated for oral use but is also effective by buccal or sub-lingual administration for the purpose of delivery[12]. Mifepristone is anti-progesterone that blocks the receptors for progesterone and glucocorticoids. It increases the sensitivity of the cervix and facilitates labor[13]. So, there is very less chances of scar dehiscence and rupture uterus in IUFD with previous caesarean section[14]. In women with previous caesarean section and IUFD, mifepristone initiate the labor as naturally, causes cervical ripening, promote uterine contractions by forming gap junctions and increasing influx of calcium. It also increases the prostaglandins release without acting as a direct uterotonics[14,15].

Mifepristone is highly effective, safe drug for induction of labor and acceptable to women in low- and middle-income countries, making it a feasible option for reducing maternal morbidity and mortality worldwide[16]. This study result will generate evidence for the physicians which will eventually aid the patients to receive a proper treatment. The findings will help the health policy makers to develop national policy to reduce the burden of this issue.

Materials and Methods:

This observational study was conducted in the Department of Obstetrics & Gynaecology, Faridpur Medical College Hospital. Total 95 pregnant women with IUFD after 28 weeks of gestation admitted in above mentioned department were selected. Patient with singleton pregnancy, with gestational age more than twenty-eight weeks and who are not in labor with ultrasonographic confirmation of IUFD were included in this study and patients with myoma/uterine anomaly, parity greater than 3, severe hypertension/preeclampsia, diabetes, impaired renal, adrenal, or hepatic function, fetal malformations, breech presentation were excluded. In this study effectiveness and outcome of using mifepristone among the participants were assessed. The objective of the study was addressed in detail with the patients or their attendants before their decision to enroll themselves into the study and a written consent was taken. All women were subjected to detailed history, clinical examination and investigations like complete blood count, renal function test and coagulation profile study before starting the treatment. All benefits and risk associated with induction of labor, delivery and complications were explained to patients and relatives along with advantages and concerns regarding the use of mifepristone. Patients were prescribed Tab. Mifepristone (200mg), 1 tablet orally 8 hourly for 48 hours (Total of six doses of mifepristone ie; 1200 mg). Initiation of labor and Bishop's score were assessed before giving each dose. Pulse, blood pressure and temperature were recorded 4 hourly. Uterine contraction was monitored and next dose of drug was omitted if the women progressed into labor. Then the total number of required doses to complete the procedure was recorded in the data collection sheet. Induction delivery time, number of deliveries within 48 hours, mode of delivery and side-effects were recorded. Patients, who did not deliver within forty-eight hours of the last dose of drug, were regarded as failures and managed by other protocol of induction. Effectiveness of mifepristone in induction of labor was measured as i) cervix unfavorable/ unchanged after 24 to 48 hours; ii) need of other uterotonics, iii) Duration of onset of labor. Outcome was measured as i) Vaginal delivery, ii) LSCS, iii) Laparotomy, iv) Rupture uterus, v) Blood transfusion, vi) Post-partum hemorrhage, vii) Retained placenta. All the information was collected in a preformed questionnaire and analyzed to assess the outcome of mifepristone in induction of labor in IUFD cases. Data entry and analysis was done using SPSS for windows version 25.0. A 'p' value less than 0.05 was considered significant.

Results:

Table-I shows obstetrical variables of the study patients. It was observed that 53.68% respondents were nulliparous, 46.32% were multiparous. Among multiparous respondents 31 (70.45%) had history of previous vaginal delivery and 13 (29.55%) had previous 1 cesarean section (CS). Most of the respondent's gestational week was more than 36 weeks (64.21%).

Table I: Distribution of patients according to obstetric history (n=95)

Maternal findings	Frequency (%)
Parity	
Nulliparous	51 (53.68)
Multiparous	44 (46.32)
Previous history of delivery	
Previous VD	31 (70.45)
Previous CS	13 (29.55%)
Gestational week	
<36 weeks	34 (35.79)
>36weeks	61 (64.21)

The mean value of Bishop's score after 24 hours of application of Mifepristone was found to increase from 4.87 ± 1.55 to 7.46 ± 1.65. (Table II)

Table II: Evaluation of Bishop's score on admission and after 24 hours of induction (n=95)

Bishop's score	Mean (±SD)	P-value
On admission	4.87 (1.55)	<0.001
After 24 hours	7.46 (1.65)	

Total 74 (77.89%) of the total responders had vaginal delivery (VD) with effective mifepristone induction, while the remaining 21 (22.11%) required misoprostol induction after mifepristone induction failed. Total 9 (42.86%) of the 21 patients who had unsuccessful mifepristone induction had a vaginal delivery using misoprostol; 7 (33.33%) required oxytocin augmentation. The remaining 5 (23.81%) respondents required LUCS for delivery after failing misoprostol induction (Table III).

Table III: Distribution of patients according to need of uterotonics- oxytocin/misoprostol (n=95)

Vaginal delivery with mifepristone	Number of patients (%)
Successful induction	74 (77.89%)
Need uterotonics	21 (22.11%)
Only misoprostol vaginal delivery	9 (42.86%)
Misoprostol with oxytocin augmentation VD	7 (33.33%)
Failed misoprostol (LUCS)	5 (23.81%)

Nulliparous respondents needed more time for onset of labor and delivery of the fetus. The mean value of number of mifepristone dose needed among all respondents was 4.18±1.08 (SD). Mean dose was higher in nulliparous respondents than multiparous (Table IV).

Table IV: Distribution of patients according to time duration of induction to onset of labor, mifepristone dose and delivery among respondents (n=95)

Duration	Mean (±SD)	p-value
Induction to onset of labor		0.040
Nulliparous	38.04 (±10.24)	
Multiparous	31.47 (±11.68)	
Induction to delivery		0.005
Nulliparous	49.29 (±9.96)	
Multiparous	40.22 (±11.73)	
Number mifepristone		
Nulliparous	4.18 (±1.08)	<0.001
Multiparous	3.47 (±1.68)	

There were very few complications of mifepristone induction presented including vomiting (68.42%), dizziness (46.32%), abdominal crams (10.53%), fever (6.32%) and postpartum hemorrhage (PPH) (4.21%) (Table V).

Table V: Distribution of patients according to complication of induction (n=95).

Complications	Frequency (%)
Fever	6 (6.32)
Abdominal Cramp	10 (10.53)
Nausea/vomiting	65 (68.42)
Dizziness	44 (46.32)
PPH	4 (4.21)

Discussion:

Labor following IUFD often requires to be induced by medical method[17]. Spontaneous labor and delivery may not occur for several weeks and therefore a clear management plan is necessary to reduce the time-related risk of psychological distress and sepsis (if the membranes are ruptured)[18]. Mifepristone administration increases the sensitivity of the uterus to prostaglandins and ripens the cervix, thereby also reduce the need for other augmentations to induce expulsion of the fetus[19]. This cross sectional observational study was conducted in total 95 admitted pregnant women with IFUD after 28 weeks of gestation. The purpose of the study was to assess the outcome of induction of labor in IUD with mifepristone.

The current study demonstrated a strong relationship between bishop's score on administration of mifepristone and after 24 hours, which were 4.87±1.55 and 7.46±1.65, respectively. Amin et al.[20] also found similar observation with our study, they showed significant association was found with bishop's score on administration of mifepristone and after 24 hours were 4.86±1.55 and 7.36±1.65 respectively. Anandi et al.[21] and Sharma et al.[22] also support our findings.

About 74 (77.89%) of the total responders had vaginal delivery (VD) with effective mifepristone induction, while the remaining 21 (22.11%) required misoprostol induction after mifepristone induction failed, 9 (42.86%) of the 21 patients who had unsuccessful mifepristone induction had a vaginal delivery using misoprostol; 7 (33.33%) required oxytocin augmentation. The remaining 5 (23.81%) respondents required LUCS for delivery after failing misoprostol induction. In the study of Deora et al.[23] total 100 pregnant women with IUFD with term and near term gestation received two doses of mifepristone orally, out of which 97 women's delivered vaginally within 72 hours of first dose without any need of augmentation and 1 woman delivered vaginally after oxytocin augmentation and 1 woman required CS because of failed trial[23]. In the study of Arora et al.[24] spontaneous labor occurred in 74.3% (29/39) women while operative (cesarean/ hysterotomy) delivery occurred in 17.9% (07/39)[24]. In the study of Athawale et al. only 26% patients required augmentation after mifepristone induction for cervical ripening[25].

Nulliparous respondents needed more time for onset of labor and delivery of the fetus. The mean value of number of mifepristone dose needed among all respondents was 4.18±1.08. In Anandi et al.[21] induction delivery interval in mutigravidae patients was significantly lower than primigravidae patients (P<0.001) and the mean induction delivery interval in primigravidae was 47.77 hours and in mutigravidae was 37.56 hours[21]. Present study showed that there were very few complications of mifepristone induction presented including vomiting (68.42%), dizziness (46.32%), abdominal cramps (10.53%), fever (6.32%) and postpartum hemorrhage (PPH) (4.21%). When the side effects of both the inducing agents were compared in Maheshwari et al. the tolerance to Group A (combined regimen of mifepristone and misoprostol) was better than Group B (Misoprostol alone regimen)[26].

Conclusion:

Induction of labor is associated with higher odds of extended labor in cases of IUFD during delivery. After an IUFD, mifepristone is regarded as one of the safest and most cost-effective means of inducing labor in pregnancies. This study evaluated the efficacy of mifepristone in inducing labor during IUFD delivery. This study discovered that the mean value of the bishop's score grew considerably after 24 hours and majority of respondents experienced a successful induction and vaginal delivery though nulliparous women required longer time for the commencement of labor and delivery of the fetus than multiparous women. However, the most prevalent problem was nausea/ vomiting (68%). Overall, this study revealed that induction of labor in IUFD delivery with mifepristone has good outcome with successful induction and vaginal delivery in most cases. However, further larger multicenter studies are recommended to corroborate my research findings.

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