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Original Research Article

Role of mifepristone in preinduction cervical ripening and induction of labour at term: an observational study

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ABSTRACT

Background: Induction implies stimulation of uterine contractions before spontaneous onset of labour. It is indicated when the benefits to either mother or fetus outweigh those of pregnancy continuation. Of the various medical methods of induction, prostaglandins and oxytocin remain the most popular and acceptable methods in obstetric practice. Mifepristone is a steroid compound, with anti-progesterone activity. It increases uterine activity and causes cervical dilatation and effacement. We intend to study the role of oral mifepristone in preinduction cervical ripening and induction of labour in term pregnancies.
Methods: In a prospective observational study carried out from Jan 2023 to June 2023 at a zonal hospital, 100 antenatal women at term with Bishop score less than 6 participated. Tablet mifepristone 200 mg single dose was given orally for induction. All patients were assessed after 24 hours for cervical ripening, need for augmentation, mode of delivery, maternal and neonatal outcome.
Results: It was observed that there was a significant improvement in Bishop score 24 hours after giving mifepristone. Out of 100 women in the study, 82% delivered vaginally, 15% had caesarean section and 3% had instrumental delivery. 21% needed no second method of labour induction. 76% patients delivered within 48 hrs of ingestion of mifepristone. The majority of patients had good maternal and neonatal outcome.
Conclusions: Mifepristone is an effective and safe method for preinduction cervical ripening and induction of labour in term pregnancies.

Keywords: Bishop score, Induction of labour, Mifepristone

INTRODUCTION

Induction implies stimulation of contractions before spontaneous onset of labour, with or without ruptured membranes. When the cervix is closed and uneffaced, labour induction often commences with cervical ripening, a process that generally employs prostaglandins to soften and open the cervix. Induction is indicated when the benefits to either mother or fetus outweigh those of pregnancy continuation.

In an ideal world all pregnancies would go to term and labour would begin spontaneously. The progress of Medicine in general and of Obstetrics has allowed the termination of pregnancy at term or close to term for high risk pregnancies with maternal or fetal indication.[1] The status of cervix is assessed by Bishop scoring system at the start of labour induction. Bishop score less than 6 usually requires cervical ripening agent.[2]

Membrane stripping and amniotomy for those females keen to avoid as much intervention as possible has been

shown to result in established labour. Mechanical methods like balloon catheter and hygroscopic dilators have shown to trigger release of endogenous prostaglandins or extract water from cervical tissue and cause cervical expansion. Prostaglandins like Cerviprime gel (PGE2) and tablet Misoprostol (PGE1) have gained wide popularity for labour induction in obstetric practice.

Recently, the most fascinating synthetic mifepristone (RU-486) has been the focus of attention in the arena of various labour inducing agents. Mifepristone is a steroidal compound that has antiglucocorticoid and antiprogesterone properties. It has an established role in termination of pregnancy during the early first and second trimesters.[3] Mifepristone increases uterine activity and causes cervical dilatation and effacement. It has rapid absorption and a long half-life of 25 to 30 hours. Hapangama and Neilson in Cochrane collaboration published in 2009 are of the opinion that there is insufficient evidence to support a particular dose, but single dose of 200 mg mifepristone appears to be the lowest effective dose for cervical ripening.[4]

METHODS

This was single blind prospective observational study. The study was conducted in a zonal hospital of the Armed Forces over a period of six months. After written informed consent, 100 women with a Bishop score <6 were recruited for the study. On admission, a detailed history and complete general and obstetric examination was carried out. Gestational age was calculated by Naegle's rule and corroborated with first trimester ultrasonography. Non stress test (NST) was done and found to be reactive. Pervaginal examination was done under strict aseptic precaution and Bishop score less than 6 was found.

All patients were given tablet mifepristone 200 mg single dose orally for preinduction cervical ripening and labour induction. Repeat Bishop score was checked after 24 hours. If it was less than 6, labour was induced with cerviprime gel 0.5 mg instilled intracervically and repeated after 6 hours till patient went into active labour. If Bishop score was more than 6 at the end of 24 hours, artificial rupture of membranes was done and augmentation with Oxytocin if need be. Throughout labour, patients were monitored by cardiotocographic machine and labour was monitored by partogram. Patients with smooth progress of labour and normal fetal heart rate delivered vaginally. Those patients who had fetal distress or labour dystocias ended up in cesarean section.

Inclusion criteria

Patient with singleton live gestation, cephalic presentation, POG > 37 weeks, age 20 to 35 years, patient not in labour and membranes intact, unfavourable cervix with Bishop score less than 6, maternal or fetal indication for labour induction were included in this study.

Exclusion criteria

Patient with malpresentation, multiple gestation, previous caesarean section, premature rupture of membranes, contraindication to vaginal delivery, significant cardiac, renal or hepatic maternal complication, and non-reassuring fetal heart rate pattern were excluded from this study.

Complete blood count (CBC), blood group, viral markers, non-stress test (NST) were investigated.

Effectiveness of Mifepristone was assessed by following criteria: 1) Favourability of Bishop score at 24 hours, 2) Need for induction with Cerviprime gel, 3) Need for Oxytocin augmentation, 4) Drug administration to delivery interval, 5) Mode of delivery, 6) Cesarean section rate, 7) Maternal complications, and 8) Fetal outcome.

Successful induction was considered when patients went into active labour within 24 to 48 hours after administration of oral mifepristone. Failed induction was considered when patients failed to go into active labour at end of 48 hours of medicine intake.

Statistical analysis

Statistical analysis was done using SPSS version 20. P value of less than 0.05 was considered significant.

RESULTS

In our study group, the patients belonged to age group 20 to 35 years, the mean age being 26.95±3.66 years. In our study, 31% patients belonged to age group 20-24 yrs, 45% patients were 25-29 yrs and 24 % patients were greater than 30 yrs (Figure 1).

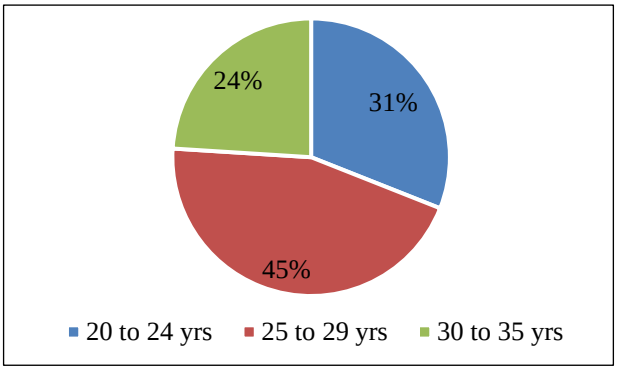

Figure 1: Distribution of patients as per age group.

In our study population, 59% were primigravida and 41% were multigravida. The mean period of gestation at induction was 274.01±5.65 days (39 weeks). Antenatal comorbidity profile of our patients is depicted in Table 1.

Out of 100 cases who received mifepristone, 49% were applied cerviprime gel, 30% required augmentation with

oxytocin and 21% did not need any other method of labour augmentation as shown in Figure 2.

Table 1: Comorbidity profile of patients.

Comorbidity profile	Total % (n = 100)
No comorbidity	64
Rh negative pregnancy	3
Gestational diabetes mellitus	8
Pregnancy induced hypertension	4
Intrauterine growth restriction	4
Intrahepatic cholestasis	5
Recurrent pregnancy loss	4
Hypothyroidism	6
Post IVF/post IUI pregnancy	2

Table 2: Bishop score - pre and post induction.

Bishop score	Mean	SD	t value	p value
Pre induction	3.1	0.85		
Post induction	6.09	2.00	- 18.557	0.000

SD=Standard deviation

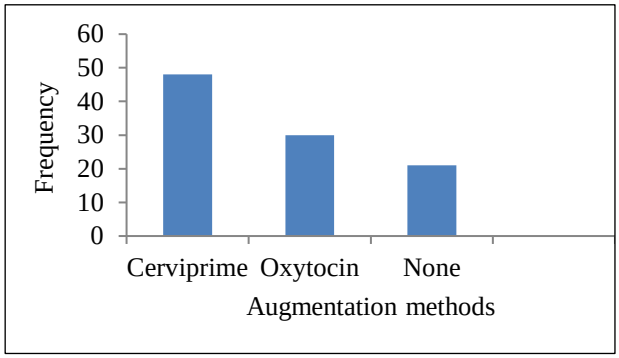

Figure 2: Augmentation methods.

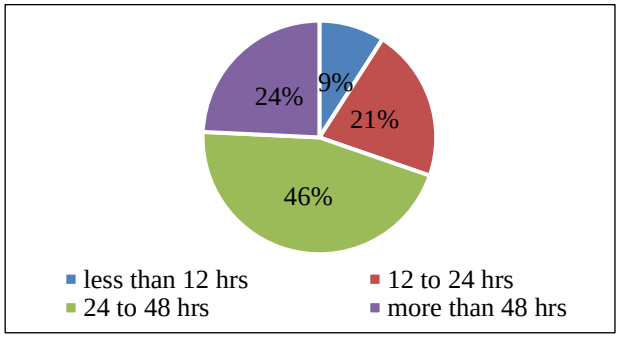

Figure 3: Distribution of patients according to Induction to delivery interval.

Out of 100 patients, 9% patients delivered within 12 hrs of taking mifepristone, 67% within 12 to 48 hrs and 24% delivered after 48 hours (Figure 3).

In our study, 82% delivered vaginally, 3% had vacuum delivery and 15% underwent caesarean section. The indications for cesarean delivery were fetal distress, non progress of labour, failure of induction. Two patients had thick meconium stained liquor and unfavourable cervix. One patient with polyhydramnios had cord prolapse and underwent emergency cesarean section (Table 3).

Table 3: Indications for cesarean section.

Indication	Total % (n = 100)
Fetal distress	6
Non progress of labour	4
Failed induction	2
Meconium stained liquor	2
Cord prolapse	1

The mean birth weight of babies was 2.96±0.42 kg. In our study, 13% babies were low birth weight (<2.5 kg). 56% were male babies and 44% were females. 9% newborns were admitted to NICU but later discharged in good health. There was no still birth. 3% patients had postpartum hemorrhage which was effectively managed. Overall, there was no adverse maternal or neonatal outcome.

DISCUSSION

The process of labour initiation remains a mystery. It is well known, however, that progesterone is integral in the maintenance of pregnancy. It is hypothesized that anti progestin exposure in pregnancy will enhance the initiation of parturition. Mifepristone (RU-486) was discovered by Roussel Uclaf of France in 1980 while they were studying glucocorticoid receptor antagonists.[5] Mifepristone is established for termination of first and second trimester pregnancy.[3] Studies have suggested that the drug increases uterine activity and causes cervical dilatation and effacement.

In our study, 31% patients belonged to age group 20-24 yrs, 45% were 25-29 yrs and 24% were more than 30 yrs age. Mean age being 26.95±3.66 yrs. Yelikar et al in their study observed mean age of 22.98 yrs.[6] 59% patients were primigravida and 41% were multigravida in our study. Mean POG at induction was 274.01±5.65 days (39 weeks) and was 41.1 weeks in study by Yelikar et al.[6] Mean Bishop score at induction was 3.01±0.85 and 6.09±2.00 after 24 hrs. Shetty et al observed that mean preinduction Bishop score was 3.236 and was 8.355 after 24 hrs.[6] Bishop score improved with use of oral mifepristone as also suggested by Athawale et al, Vellanki et al and Fathima et al.[8-10]

In our study, 9% patients delivered within 12 hrs, 21% within 12-24 hrs, 46% within 24-48 hrs and 24% delivered after 48 hrs of mifepristone ingestion. Hapangama and Neilson in their study in 2009 reported that mifepristone treated women were likely to be in labour or to have favourable cervix at 48 hrs [risk ratio(RR) 2.41, 95% confidence intervals (CI)1.70 to 3.42].[4] Similar results were reported by Wing et al where 54% of mifepristone

treated women went into labour compared to only 18.2% who were given a placebo.[11] In our study, 82% patients had normal vaginal delivery, 3% were applied vacuum and 15% had cesarean section. Similar results were observed in study by Vellanki et al where rate of vaginal delivery was 79% and cesarean rate of 21%.[9] A similar comparison was found in study by Zhonghua et al from Beijing where vaginal delivery rate was 80.8%. A study by Mcgill et al from United Kingdom depicted lower rate of cesarean section for women induced with oral mifepristone.

In our study, meconium passage in utero was seen in 5% of patients, 2% of them had caesarean section and 3% delivered vaginally. In a study by Wing et al meconium passage was 9.1% in mifepristone treated group.[11] In study by Jain et al, meconium passage was 4.34%.[12] Abnormal fetal heart rate (FHR) pattern was observed in 6% patients in our study. But a Cochrane review 2009 stated that the rate of abnormal FHR pattern was higher in the mifepristone treated group.[4] However, a study by Karl et al stated no difference in rate of fetal distress. Clamart et al from France states that mifepristone appears safe and useful with no adverse effects on fetus or mother.

In our study, 9% babies were admitted to NICU and all were discharged healthy indicating good perinatal outcome. Vellanki et al depicted in their study a 13% NICU admission rate.[9] Yelikar et al also mentioned a minimum NICU admission rate.[6] In our study, 3% patients had postpartum hemorrhage (PPH) and managed effectively by uterotonics. There were no major maternal complications; and such results were also found by Athawale et al and Jain et al.[8,12]

CONCLUSION

Mifepristone is an effective agent for preinduction cervical ripening and induction of labour at term. With the drug usage, there is reduction in induction to delivery interval, reduced need for further augmentation, less caesarean rate and no increase in adverse events on mother or fetus.

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

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