Original Research Article

Effect of Mifepristone on induction of labour and perinatal outcome in post-dated pregnancy

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Abstract

Background: Induction of labour is most common obstetric intervention. Mifepristone is a progesterone antagonist, is known to cause softening and dilation of the human pregnant cervix and an increase in uterine activity. It is used for induction of labour. **Aim and objective:** To study the effect of Mifepristone on induction of labour and it's perinatal outcome in post dated pregnancy **Methodology:** Present study was a prospective study carried out in 110 post dated pregnant females. Tab mifepristone 200mg single dose was given for induction. Bishop's score was assessed before induction and the end of 24 hours. The effectiveness of Mifepristone was assessed on the basis of improvement in bishop score, and duration of induction to active phase of labour. Safety of Mifepristone was assessed in terms of effect of the drug on maternal and prenatal outcome. **Results:** Pre induction BISHOP's score was 3.24 ± 0.9 and Post induction score was 8.35± 1.8. Out of total 110 patients, (70) 63.64% of women delivered without the need of any other methods of induction within 48 hours of admission. IDI in muligravidae patients was significantly lower than primigravidae patients (P<0.001). No perinatal deaths and no significant perinatal morbidity and mortality was observed.

Key Word: Mifepristone.

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INTRODUCTION

The ability to induce labour has been of interest to many societies from the primitive to the ancient to the modern. For the majority of women, labour starts spontaneously and results in vaginal delivery at or near term. Labour inductions are among the most common obstetrical interventions today. Labour inductions are considered to be any method used to artificially start woman's labour. [1] According to ACOG 2009 Goal of IOL (Induction of labour) is to achieve vaginal delivery by stimulating uterine contractions before the spontaneous onset of labour. The method for labour inductions has also changed over time. Both mechanical and chemical methods are used to ripen a women's cervix to help initiate labour. [2] Induction of labour is indicated in medical, obstetric and fetal conditions when prolongation of pregnancy would affect the maternal and fetal well being provided there are no contraindications for the use of prostaglandins and oxytocin. [3] ACOG guidelines Indications for induction of labour as per ACOG guidelines 2009 includes Abruptio placentae, Chorioamnionitis, Fetal demise, Gestational hypertension, Preeclampsia, eclampsia, Premature rupture of membranes, Post term pregnancy, Maternal medical conditions (eg, diabetes mellitus, renal disease, chronic pulmonary disease, chronic hypertension, antiphospholipid syndrome) and Fetal compromise (eg. severe fetal growth restriction, isoimmunisation, oligohydramnios).[4] Mifepristone is used for early pregnancy and Second trimester pregnancy termination, treatment of Uterine fibroids (25 to 50mg/day, treatment of Endometriosis(50mg/day) and as an Emergency postcoital contraception.

Mifepristone (RU 486) is a 19-norsteroid which has specific high affinity binding to the progesterone receptor

and thus to compete with progesterone at the level of their respective binding site.[5] Also this compound exerts some antiglucocorticoid property. Mifepristone is absorbed rapidly after oral administration, reaching maximum serum levels within 2 hours and has a half-life of about 25 h. [6] As a result of the withdrawal of the inhibitory effect of progesterone there is an increase in the synthesis of prostaglandins and inhibition of prostaglandin dehydrogenase action. [7,8] Sensitivity of the myometrium to the contraction inducing activity of prostaglandins markedly increased after mifepristone administration64 and labour often starts without addition inductors. Mifepristone exposure at 41 weeks of gestation associated with significant increase of estradiol, estriol, progesterone and cortisol in saliva and plasma without alterations of corticotropin-releasing hormone and adrenocorticotropic hormone levels. [9,10] These properties of mifepristone determined its use for the cervical ripening and preparation for the pregnancy termination. Mifepristone is recognized as a component of safe abortion and is included to the WHO Model Lists of Essential Medicines. [11] Present study was conducted to see the effects of Mifepristone on induction of labour and it's perinatal outcome in post dated pregnancy.

Aim and objective: To study the effect of Mifepristone on induction of labour and it's perinatal outcome in post dated pregnancy

MATERIAL AND METHODS

Present study was a prospective study carried out in post dated pregnant females. This study was restricted to the patients who were admitted to the Chigateri hospital, Women and Children hospital, and Bapuji hospital, Davangere.

Study was carried out during the period of November 2016 –October 2018.

Inclusion Criteria:

1. Maternal age >18 years
2. Gestational age 41-42 weeks
3. Singleton pregnancy
4. Cephalic presentation
5. Reactive FHR pattern in live fetus
6. Intact membranes
7. Bishop's score <6

Exclusion Criteria:

1. 1.Estimated fetal weight >4.5kg or <2kg(IUGR)
2. Antepartam haemorrhage
3. Hypertensive disorders of pregnancy
4. Chorioamnionitis
5. Parity<4
6. Severe oiligohydramnios
7. Any medical complications of mother
8. Contraindications to vaginal birth.

Study was approved by ethical committee of the institute. A valid written consent was taken from the patients after explaining study to them.

Sample size is calculated using the formula :

$$n = \frac{\{Z1-\alpha/2\}^2 \times S^2}{d2}$$

According to the formula sample size was 108. We studied 110 patients.

After enrolment of the patients, data was collected with pre tested questionnaire. Clinical history of the patients was noted. clinical examination included general examination, per abdominal examination and pelvic examination. BISHOP"s score was noted. After the examination Tab mifepristone 200mg single dose was given. Bishop"s score was again assessed at the end of 24 hours. If the score was less than 6 then other inducing agents were used. These inducing agents were tablet misoprostol 25 micrograms every 4 hourly or cerviprime gel instillation till the score is more than 6. If the score is more than 6 at the end of 24 hours , artificial rupture of membrane was done. Oxytocin was started if required. Patients were monitored for progress of labour. If induction failed or other indication for casaerean section then patients were shifted for casaerean section.

The effectiveness of Mifepristone was assessed on the basis of improvement in bishop score, and duration of induction to active phase of labour. Safety of Mifepristone was assessed in terms of effect of the drug on maternal and prenatal outcome.

Failed induction was considered when women failed to enter into active labour at the end of 48 hours of administration of tab Mifepristone. For hyperstimulation syndrome terbutaline 250µgms subcutaneous injection was given. Episodes of uterine tachysystole defined as >5 contractions in 10 minutes or a single contraction lasting more than 2 minutes and FHR abnormalities (variable decelerations and bradycardia) were sought. The frequency was assessed by counting the number of contractions occurring was measured in seconds. Hypertonus is defined as a single sustained uterine contraction lasting for >2 minutes. Hyperstimulation syndrome is defined as presence of tachysystole or hypertonus accompanied by fetal heart rate abnormality. (Deceleration or tachycardia)

Data was analysed with appropriate statistical tests.

RESULTS

In our study 65 women (59.1%) were primigravidae, 28 women (25.5%) multigravidae, and 17 women (15.5%) were with previous 1 LSCS. Out of total 110, 95 (86.4%)women involved in the study were with gestational age 41 weeks and beyond and 15 women (13.6%) of women were with gestational age less than 40 weeks.

Table 1 shows Mean BISHOP"S score in patients at pre induction and 24 hours after mifepristone administration. Pre induction score was 3.24 ± 0.9 with a range of 2-5. Post induction score was 8.35± 1.8 with range of 4-12. Thus we can say that mifepristone causes significant change in BISHOP"S score in patients (p<0.001). Out of total 110 patients, (70) 63.64% of women delivered without the need of any other methods of induction within 48 hours of admission. (10)9.1% of women delivered with 1 dose of 25microg oral misoprostol and 10% women were induced with 1 dose cerviprime gel. (11)10% women underwent caesarean section. Out of 11 patients posted for casaerean section, 8 patients were of failed induction and 3 patients were having other indications for casaerean section. Mean induction delivery interval in primigravidae was 47.77 hours and in multigravidae was 37.56 hours. IDI in muligravidae patients was significantly lower than primigravidae patients (P<0.001). (fig 1) Table 11, Perinatal outcome was assessed and comparison was made between healthy baby and Babies with adverse outcome (perinatal death / NICU admission) . Only one baby was admitted to NICU in view of low APGAR score. No perinatal deaths and no significant perinatal morbidity and mortality.3 babies were admitted to NICU in view of meconium and discharged successfully. (table 4) There were no major adverse effects like uterine hyperstimulation , or abnormal fetal heart rate pattern.

Table 1: Pre and post induction Mean BISHOP"S score in patients

BISHOP"S score	Minimum	Maximum	Mean	SD
PRE induction	2	5	3.24	.918
POST induction	4	12	8.35	1.810
IDI	24	72	43.59	11.890

Table 2: Distribution of patients according to other methods of induction

Other Methods of Induction	No. of patients	Percent
1 CP GEL	11	10.0
1 MISO	10	9.09
2 CP GEL	8	7.27
NO	70	63.64
Casaerean section	11	10
Total	**110**	**100.0**

Table 3: Distribution of patients according to indication for caesarean section

Indication	No. Of patients	Percent
Failed Induction	8	7.27
Other causes	3	2.73

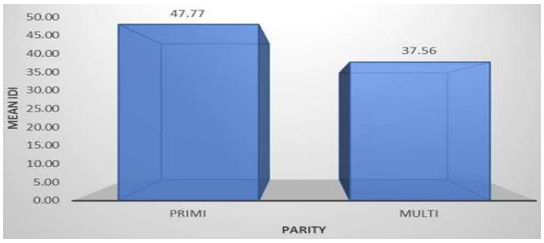

Figure 1: Comparison of Induction Delivery Interval in primigravidae and multigravidae patients

Table 4: Distribution of patients according to Neonatal outcome

Neonatal outcome	No. Of patients	Percent
MECONIUM	3	2.7
NICU ADMISSION	1	0.9
HEALTHY	106	96.4
Total	**110**	**100.0**

DISCUSSION

The present study to evaluate the efficacy of Mifepristone in preinduction cervical ripening and induction of labour at term was carried out on 110 women with prolonged pregnancy. Research continues to invent and modify doses of different drugs for induction of labour. The female sex hormone, progesterone stops the uterus contracting during pregnancy. Drugs such as mifepristone have been used to stop the action of this hormone, either to induce labour or to allow the pregnancy to be terminated. In the present study tab Mifepristone 200mg single dose was given after assessing Bishop's score on admission. There was significant change in the mean Bishop's score at the end of 24, 48 hours after the administration of tab Mifepristone single dose (p<0.001). In our study, Out of total 110 patients, (70) 63.64 % of women delivered without the need of any other methods of induction within 48 hours of admission. (10)9.1% of women delivered with 1 dose of 25microg oral misoprostol and 10% women were induced with 1 dose cerviprime gel. (11)10% women underwent caesarean section. Hapangama D, Neilson JP (May 2009), in their study of "Mifepristone for induction of labour" compared to placebo (108 women) , mifepristone treated women were more likely to have a favourable cervix at 48 hours [risk ratio (RR) 2.41, 95% confidence intervals (CI) 1.70 to 3.42]. Less likely to undergo caesarean section or failure of induction. [12]

Acharya R *et al.* [13] conducted a study on Mifepristone as a cervical ripening agent for labour induction with previous one caesarean section" and concluded that Mifepristone (RU-486) is a safe, efficient and suitable agent for cervical ripening and for initiation of labour when given 48 hr before labour induction. In previously scarred uterus, when other methods of induction of labour are Similar study done by Lelaidier C *et al.* , in 1994, also reported its safety and efficacy as a labour induction method in women at term in previous caesarean section. [14]

Study conducted by Khanan yelikar A single blind randomized control trial, 68% women delivered vaginally within 24-48 hours after single dose mifepristone administration , 12% caesarean section rate and there was reduced need of prostaglandin or oxytocin augmentation following use of mifepristone. [15] In our study total – cases with previous 1 LSCS willing for trial of labour were given a single dose of tab mifepristone at 39 weeks . Total 17 patients were involved in the study, and all delivered vaginaly with proper maternal and fetal monitoring throughout. Hence it is found to be safe as an inductive agent as a cervical ripening agent in a patient with previous 1 LSCS willing for normal vaginal delivery. Chanderdeep sharma *et al.* [16] conducted a study on "Role of Mifepristone for induction of labour in women with previous caesarean section" . It was retrospective study all women with prior section received mifepristone for induction of labour were compared with women who had spontaneous onset of labour pains and concluded that mifepristone may be considered as an alternative agent for induction of labour. Oleg R.Baev *et al.* conducted randomized controlled trial of 149 women were randomized, 74 for cervical ripening and induction with mifepristone and 75 with expectant management. They found that After 48 h from enrollment mean gain in Bishop score was 2.58 -1.33 in the induction group and 1.15- 0.97 in the expectant group (<0.001). [17] In the present study no patients were reported to have tachysystole, hyperstimulation of the uterus or postpartum hemorrhage. No significant maternal mortality and morbidity. In this study 96.7% neonates were healthy, with 0.9% rate of NICU admission with no perinatal deaths . No significant perinatal mortality and morbidity was observed. Hapangama and Neilson reported abnormal fetal heart rate pattern, common after mifepristone treatment (RR 1.85,95% CI 1.17–2.93), but there was no difference in other neonatal outcome. [12]

CONCLUSION

Mifepristone is an effective and safe inductive agent for induction of labour in post dated pregnancy.

REFERENCES

1. Akinsipe DC, Villalobos LE, Ridley RT. A systematic review of implementing an elective labor induction policy. Journal of obstetric, gynaecology and Neonatal Nursing. 2012;14(1):5-16.
2. Jarvelin MR, Harlikainem-Sorri AL, Rantakallio P. Labor induction policy in hospitals of different levels of specialisation. British Journal of Obstet Gynae 1993;100(4):310-15.
3. Xenakis MJ, Piper JM, Conway DL, Langer O. Induction of labour in the nineties Conquering the unfavourable cervix. Obstet Gynaecol.1997;90:235-9.
4. American College of Obstetrician and Gynecologists. Induction of Labour ACOG Practice Bulletin. 107, 2009 Aug;114(1):386-97
5. Papp C, Schatz F, Krikun G, Hausknecht V, Lockwood CJ. Biological mechanisms underlying the clinical effects of mifepristone (RU 486) on the endometrium. Early Pregnancy 2000;4(4):230-9.
6. Heikinheimo O. Clinical pharmacokinetics of mifepristone. Clin Pharmacokinet 1997;33(1):7-17.
7. Smith SK, Kelly RW. The effect of the antiprogestins RU 486 and ZK 98734 on the synthesis and metabolism of prostaglandins F2 and E2 in separated cells from early human decidua. J Clin Endocrinol Metab 1987;65(3):527-34.
8. Cheng L, Kelly RW, Thong KJ, Hume R, Baird DT. The effects of mifepristone (RU486) on prostaglandin dehydrogenase in decidual and chorionic tissue in early pregnancy. Hum Reprod 1993;8(5):705-9.
9. Byrne JD, Wing DA, Fraser M, Fassett MJ, Goodwin TM, Challis JR. Mifepristone: effect on plasma corticotropin-releasing hormone, adrenocorticotropic hormone, and cortisol in term pregnancy. J Perinatol 2004;24(7):416-20.
10. Fassett MJ, Lachelin GC, McGarrigle HH, Wing DA. Alterations in saliva steroid hormone levels after oral mifepristone administration in women with pregnancies of greater than 41 weeks' gestation. Reprod Sci 2008;15(4):394-9.
11. WHO Model Lists of Essential Medicines 19th List (April 2015) http://www.who.int/medicines/publications/essentialmedicines/en/.
12. Dharani H, James PN. Mifepristone for induction of labour (review) . Chochrane Database Syst Rev. 2009;3:CD002865.
13. Acharya R, Chaudhari P, Choudhary A, Sharma A, Jain S. Mifepristone as cervical ripening agent for Labour induction in women with Previous one Caesarean Section. Int J Med Res Rev 2016;4(4):624-9.
14. Lelaidier C, Baton C, Benifla JL, Fernandez H, Bourget P, Frydman R. Mifepristone for labour induction after previous caesarean section.Br J Obstet Gynaecol. Jun 1994;101(6):501-3.
15. Kanan Y, Deshapande S, Deshapande R, Lone D. Safety and Efficacy of Oral Mifepristone in Pre-induction Cervical Ripening and Induction of Labor in Prolonged Pregnancy.The Journal of Obstetrics and Gynecology of India. July-August 2015;65(4):221-5.
16. Chanderdeep Sharma, Anjali Soni, Pawan K. A Retrospective Case-Control Study Evaluating the Role of Mifepristone for Induction of Labor in Women with Previous Cesarean Section. The Journal of Obstetrics and Gynecology of India. 2016;66(S1):S30-S37.
17. Baev OR, Rumyantseva VP, Tysyachnyu OV, Kozlova OA, Sukhikh GT. Outcomes of mifepristone usage for cervical ripening and induction of labour in full term pregnancy . Randomized controlled trial. Eur J Obstet Gynecol Reprod Biol. Oct 2017;217:144-9.

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