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Comparision of Mifepristone and Misoprostol in the Induction of Labor At Term

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ABSTRACT

Aim: To assess the ability of mifepristone and misoprostol individually in priming the cervix.
When mifepristone alone is insufficient, to determine if vaginal misoprostol used sequentially, is effective in inducing labor.
Methods: prospective randomized comparative study conducted in LadyGoschen Hospital, Mangalore.
Inclusion criteria: singleton term pregnancy and Bishop's score <6.
Exclusion criteria:Parity >5, scarred uterus, cephalopelvic disproportion, antepartum hemorrhage, oligohydramnios.
Statistical analysis:was performed using the χ^2 test, p-value of <0.05 was considered significant.
Results: The study demonstrated significant efficacy of mifepristone for cervical ripening and induction of spontaneous labor after drug administration. In the present study 66% of women entered labor spontaneously or had a sufficiently ripened cervix within 48hrs of intake of mifepristone, but there was no difference in time between misoprostol administration and delivery interval between the groups. There were less number of LSCS in the mifepristone group but the difference was not statistically significant. Maternal and neonatal outcomes were comparable in both groups.

KEYWORDS Misoprostol , Induction, Mifepristone

INTRODUCTION:

Induction of labor is one of the important tools in an obstetrician's armamentarium as he/she can intervene and induce labor as a life saving procedure for mother or fetus or both, when the physiological process of labor becomes unnatural. In the current obstetric practice, induction is performed for obstetric or medical indications or at times for patient's convenience. The availability of new oxytocics and induction techniques which are more effective as well as more predictable have significantly modified our traditionally conservative attitude towards induction of labor, which was once regarded as 'meddlesome midwifery'[1]. The search for newer and safer agents is still ongoing.

As a fall in the level of progesterone is considered one of the important events in the onset of spontaneous labor, the antiprogesterone agent mifepristone was used in several trials to induce labor at term. Mifepristone (RU 486) is a 19-nor steroid that binds strongly to progesterone receptor and inhibits the activity of progesterone at cellular level with potent antiprogestogenic, antiglucocorticoid and a weak antiandrogenic actions, has minimal effects on uterine contractility as it ripens the cervix, making it an option for use in induction and enhance the rates of spontaneous labour, with no apparent maternal or neonatal side effects [2]. In late pregnancy, the uterus is sensitized by mifepristone to prostaglandins and promotes cervical dilatation which induces labor. Various studies conducted on induction of labor in live term pregnancies with mifepristone in doses of 200-400 mg has shown to improve cervical ripening and rates of spontaneous labor with no apparent maternal or fetal side effects [3]. The sequential use of mifepristone and a prostaglandin has been extensively researched for termination of pregnancy in all trimesters and in inducing labor in cases of intrauterine deaths [4]. Considering all the above, the present study is an attempt to evaluate the role of mifepristone followed by sequential use of misoprostol [5] if required in induction of labor in live term pregnancies.

MATERIALS AND METHODS:

Study Design : Prospective randomized comparative study

Study Place : LadyGoschen Hospital, Mangalore

Study Period : Sep 2012 to Aug 2013

Number of Patients : 100 pregnant women at term gestation (37-42 wks) scheduled for induction of labor, 50 women in the mifepristone group and 50 in the misoprostol group.

Inclusion Criteria:

- Women with ultrasonographically confirmed singleton pregnancy of 37-42 wks duration, with cephalic presentation and no contraindication for vaginal delivery are included if,
- Labor induction is indicated.
- Induction could be postponed for 48 hrs.
- The cervical bishop score is <6 prior to induction.

Exclusion Criteria:

- Parity >5.
- Previously scarred uterus
- Known hypersensitivity to prostaglandins or mifepristone.
- Major cephalopelvic disproportion
- Medical problems like, impaired renal hepatic or adrenal

function.
- Others including non reactive NST, antepartum hemorrhage, severe oligohydramnios.

Statistical Analysis:
- Association done by Chi square test.
- A p-value of <0.05 was considered significant.

Method of Study:
After getting an informed consent, women who met the inclusion criteria are given 2 tablets of 200mg of mifepristone orally and are asked to report to labor room if labor started or are reassessed after 24 hours if labor did not start. If the bishop score is 8 or greater, they are transferred to the labor ward and ARM is performed and oxytocin started.

- Even after 48 hours, if Bishop's score is ≤6, 25µg of misoprostol is administered vaginally every 8th hourly to a maximum of 3 doses.
- When the Bishop's score is 8 or greater, ARM is done and oxytocin started.
- Even after 3 doses of misoprostol, if the Bishop's score has not changed, the induction attempt is categorized as failed.
- The women in misoprostol only group are selected based on the same inclusion and exclusion criteria and each in this group are induced with 25ug of misoprostol in the posterior fornix, which is repeated upto 3 times at 6 hours interval. If Bishop's score is >8 ARM is performed and oxytocin started.
- If cervix remains unfavourable even after 3 attempts, induction is categorized as failed.
- APGAR scores at 1 and 5 minutes are recorded.
- Neonatal blood glucose estimations are done 24 hours post delivery, using basal metabolic sticks following a heel prick (<2.6 mmol are managed as hypoglycemia.)

RESULTS:
Both the groups were comparable regarding maternal age, gestational age, parity and indication for induction. The mean induction to delivery interval was 18.172 hours in the misoprostol alone group and 32 hours in mifepristone alone group, whereas the mean induction to delivery interval was 65.25 hours in the 17 women of mifepristone group who required misoprostol for induction of labor (16.38 hours after the administration of misoprostol). There was not much difference in both the groups in the time from prostaglandin administration to vaginal delivery between the sub group of women who required misoprostol following priming with mifepristone and the misoprostol group. 'Table 1 and 2 about here'

Spontaneous vaginal deliveries were more and the incidence of caesarean sections was less in the mifepristone group when compared to the misoprostol group but the difference was not statistically significant.

Non reassuring fetal heart status (NRFHS) were seen in two cases in misoprostol group and one case in mifepristone group (p > 0.05 NS). There was no cases of hyperstimulation in both the groups. There were 4 failed inductions in the misoprostol group where as only 2 in the mifepristone group. Indication for LSCS was similar in both groups. There were 10 caesarean sections in the mifepristone group and 14 caesarean sections in the misoprostol group. 'Table 3 about here'. More neonates in the misoprostol alone group had APGAR <7 at 1 minute and 5 minutes. But the difference is not statistically significant (p > 0.05) . 'Table 4 about here'. Three neonates in the misoprostol alone group required NICU admission when compared to only one in the mifepristone group. But difference was not statistically significant. Three cases of meconium stained amniotic fluid (MSAF) were seen in the mifepristone group and four cases in the misoprostol group.

DISCUSSION:
The earliest studies on the use of mifepristone for induction of labor was done by Frydman and colleagues in 1990's [6]. Also it was reported that mifepristone is better than a placebo in ripening the cervix and there is evidence of a possible reduction in the incidence of cesarean section rates following mifepristone treatment. In the present study indications for induction and patient characteristics were comparable in both the groups. The study demonstrated significant efficacy of mifepristone for cervical ripening and induction of spontaneous labor after drug administration as more women had favorable Bishop's score at the end of 48 hours. The need for augmentation was also less in the mifepristone group, as very few women required oxytocin or ARM for augmentation when compared with the misoprostol alone group. In the present study 66% of women entered labor spontaneously or had a sufficiently ripened cervix within 48 hours of intake of mifepristone, but there was no difference in time between prostaglandin administration and delivery interval. There were less number of caesarean sections in the mifepristone group but the difference was not statistically significant (p=0.228). Maternal complications and neonatal out comes were comparable in both the groups. Even though, there is a theoretical risk of hypoglycemia in the newborn, the present study showed no difference among the 2 groups.

CONCLUSION:
Mifepristone is a safe, efficient and suitable agent for cervical ripening and for initiation of labor when given 48 hours before labor induction. It appears to reduce the need for augmentation with misoprostol or oxytocin after cervical priming. Although there were no adverse effects with sequential use of misoprostol, it was more difficult to induce labor in women who did not respond to mifepristone alone. Even though the misoprostol alone group had significantly less induction to delivery interval, there was no significant difference in time between prostaglandin administration and delivery interval between the groups. The potential advantage of mifepristone over prostaglandins and oxytocin, mainly in situations where they are contraindicated (for example scarred uterus) has been proved, but requires more studies. Even though mifepristone is expensive, as it can be administered on out patient basis and significantly less need for hospital admission, it may be speculated that, there might be overall savings in this group. Hence mifepristone provides an interesting new alternative to classic uterotonic agents used for induction of labor at term and can be considered by the obstetricians as a simple and safe method of labor induction.

Table 1 Change in Bishop Score

Bishop's score	Mifepristone group (n=50)	Misoprostol alone group (n=50)
Mean pre induction score	2.32 ± 0.76	2.56 ± 0.64
Mean post induction score at 48 hours	7.25 ± 1.75	7.58 ± 1.95
	p <0.001	p <0.001

Table 2 Induction to Delivery Interval

	Mifepristone group	Misoprostol alone group	p value
IDI (in hours)	32	18.17	0.001

Table 3 Comparison of Complications

Complications	Mifepristone group (n=50)	Misoprostol alone group (n=50)
MSAF	3	4
NRFHS	1	2
APGAR<7	1	8
Failed Induction	2	4

Table 4 APGAR<7 At Birth

APGAR (in mins)	Mifepristone alone	Mifepristone + misoprostol	Misoprostol alone group (n=50)
1	1	-	5
5	-	-	3

REFERENCES

[1] Silvestre L, Dubois C, Renault M, Rezvani Y, Baulieu E-E & Ulmann A. N. Engl. J. Med. 1990, 322, 645-8. | [2] Newhall E. P & Winikof B. Am. J. Obstet. Gynecol. 2000, 182, 44-53. | [3] Clark K, Ji H, Feltovich H, Janowski J, Carroll C & Chien E. K. Am. J. Obstet. Gynecol. 2006, 194, 1391-8. | [4] Praveena G, Shameem V. P. A, Rao A & Rao B. Int. J. Pharm. Biomed. Res. 2013, 4, 108-110. | [5] Raksha M, Rao A, Kamath Anagha & Shameem V.P.A. Int. J. Pharm. Biomed. Res. 2013, 4(4), 202-205. | [6] Kulsum S. U, Khatun S &Tabib S. M. S. B. Medicine Today 2010, 22, 94. | [7] Frydman R, Lelaider C,Baton C.S.M, Fernandez H, Vial M & Bouget P. Obstet. Gynecol. 1992, 80, 972-5. |