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Evaluation of Efficacy of Mifepristone for Cervical Ripening and Induction of Labour at a Tertiary Care Centre

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ABSTRACT

Background: One of the most common indications for labour induction is prolonged pregnancy. Mifepristone now has an established role in termination of pregnancy (in combination with prostaglandins) during the early first, and the second trimesters. Hence; under the light of above mentioned data, the present study was undertaken for assessing the efficacy Mifepristone for cervical ripening and induction of labour.

Materials and Methods: A total of 50 patients were enrolled in the present study. Women with prolonged pregnancy and with maternal age of more than 18 years were included in the present study. Blood samples were taken and hematological and biochemical analysis was carried out. All the patients were broadly divided into two study groups as follows: Study group: Patients who were given Mifepristone tablets, Control group: Patients who were given Placebo. Calculation of Bishop's score was done at various time intervals. Successful induction was referred to as patients who entered active labor within 24 h of administration of mifepristone or placebo.

Results: Mean Bishop's score at the end of 24 hours was higher among the subjects of the study group in comparison to the control group. Mean induction to active stage interval among the subjects of the control group was 1802.44 minutes and was found to be significantly higher than that of subjects of the study group (1642.28 minutes). Mean induction delivery interval among the subjects of the control group was 2108.50 minutes and was found to be significantly higher than that of subjects of the study group (1845.18 minutes).

Conclusion: For cervical ripening and induction of labour, Mifepristone is an effective agent.

Keywords: Labour, Mifepristone, Ripening.

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INTRODUCTION

One of the most common indications for labour induction is prolonged pregnancy as it is associated with the increased risk to the fetus, including increased perinatal mortality rate, low 5-min Apgar scores, dysmaturity syndrome, and increased risk of death within the first year of life. A ripe or favorable cervix is a prerequisite for successful vaginal birth. So, cervical ripening should be assessed before any regimen is selected.[1,2]

Mifepristone /RU-(486), a new class of pharmacological agents (antiprogestins) have been developed to antagonize the action of progesterone. Of these, mifepristone (also called RU 486) is best known. It is a 19 nor-steroid which has greater affinity for progesterone receptors than does progesterone itself. It blocks the action of progesterone at the cellular level. Mifepristone now has an established role in termination of pregnancy (in combination with prostaglandins) during the early first, and the second trimesters. Mifepristone is also being investigated as a possible contraceptive agent (both for planned and emergency contraception).[3-6] Cervical softening and uterine contractions have been reported in humans treated with mifepristone. These ripening properties are used for cervical preparation before first-trimester curettage, and in combination with prostaglandin analogues, for elective abortion and medical termination. After intrauterine death, mifepristone 600 mg/d for 2 days leads to fetal expulsion in two thirds of cases within 72 hours, or reduces prostaglandin requirements.[7-10] Hence; under the light of above mentioned data, the present study was undertaken for assessing the efficacy Mifepristone for cervical ripening and induction of labour.

MATERIALS AND METHODS

The present study was conducted in the Department of Obstetrics and Gynaecology, Rajshree Medical Research Institute & Hospital, Bareilly, Uttar Pradesh (India) and it included assessment of efficacy Mifepristone for cervical ripening and

induction of labour. A total of 50 patients were enrolled in the present study. Ethical approval was obtained from institutional ethical committee and written consent was obtained after explaining in detail the entire research protocol. Women with prolonged pregnancy and with maternal age of more than 18 years were included in the present study. Only those patients were included in which bishop's score was less than 6. Complete demographic and clinical profile of all the patients was obtained. Blood samples were taken and hematological and biochemical analysis was carried out.

All the patients were broadly divided into two study groups as follows:

Study group: Patients who were given Mifepristone tablets

Control group: Patients who were given Placebo

Calculation of Bishop's score was done at various time intervals. Successful induction was referred to as patients who entered active labor within 24 h of administration of mifepristone OR placebo. All the results were recorded in Microsoft excel sheet and were analyzer by SPSS software. Mann-Whitey U test and chi-square test were used for assessment of level of significance.

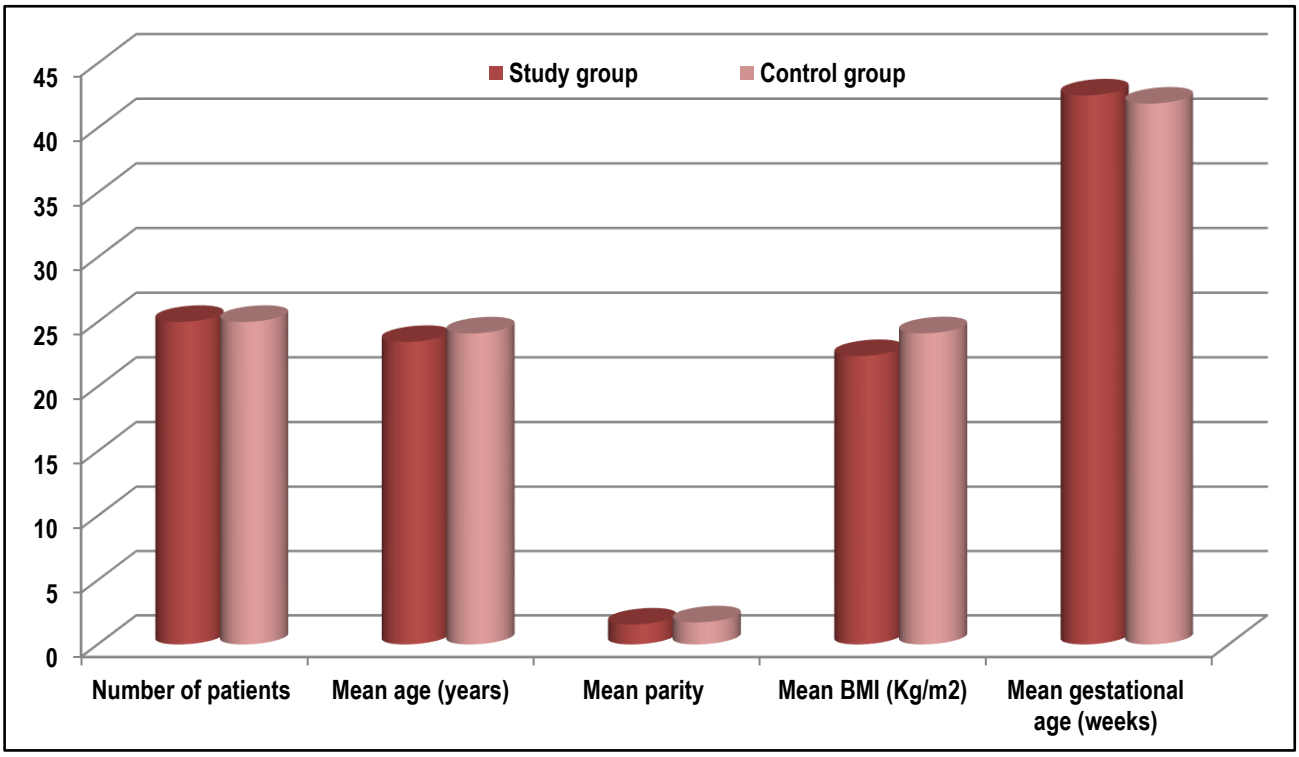
Table 1: Comparison of Mean Bishop's score and mean duration of induction to active stage

Mean Bishop's score	Study group	Control group	p- value
At 0 hour	2.08	2.21	0.18
At the end of 24 hour	6.02	4.11	0.00 (Significant)
Mean induction to active stage interval (minutes)	1642.28	1802.44	0.01 (Significant)

Table 2: Comparison of Maternal outcome

Parameter		Study group	Control group	p- value
Mean induction delivery interval (minutes)		1845.18	2108.50	0.00 (Significant)
Outcome	**Success (n)**	23	24	0.81
	Failure (n)	2	1	

Graph 1: Comparison of demographic and clinical data



RESULTS

In the present study, a total of 50 subjects were analyzed. Mean age of the subjects of the study group was 23.45 years and mean age of the patients of the control group was 24.11 years. Mean BMI of the patients of the study group and the control group was 22.36 and 24.12 Kg/m^2 respectively. Mean gestational age of the subjects of the study group and the control group was 42.51 weeks and 41.88 weeks respectively.

Mean Bishop's score at 0 hours among study group and control group patients was 2.08 and 2.21 respectively. Mean Bishop's score at the end of 24 hours among study group and control group patients was 6.02 and 4.11 respectively. Mean Bishop's score at the end of 24 hours was higher among the subjects of the study group in comparison to the control group. Mean induction to active stage interval among the subjects of the control group was

1802.44 minutes and was found to be significantly higher than that of subjects of the study group (1642.28 minutes). Mean induction delivery interval among the subjects of the control group was 2108.50 minutes and was found to be significantly higher than that of subjects of the study group (1845.18 minutes).

In the study group, the success rate was found to be 92 percent, while in the control group, the success rate was found to be 96 percent.

DISCUSSION

Mifepristone has potential also as a method of inducing labour in late pregnancy through its actions in antagonising progesterone, thus increasing uterine contractility and by increasing the sensitivity of the uterus to the actions of prostaglandins. Mifepristone has been shown to induce labour in rats, through opposition to progesterone-induced suppression of oxytocin receptors, and enhanced synthesis of prostaglandins. Mifepristone has also been shown to induce preterm birth in mice, associated with a rise in prostaglandins and cytokines.[3- 6]

In the present study, a total of 50 subjects were analyzed. Mean age of the subjects of the study group was 23.45 years and mean age of the patients of the control group was 24.11 years. Mean BMI of the patients of the study group and the control group was 22.36 and 24.12 Kg/m^2 respectively. Mean gestational age of the subjects of the study group and the control group was 42.51 weeks and 41.88 weeks respectively.

Mean Bishop's score at 0 hours among study group and control group patients was 2.08 and 2.21 respectively. Mean Bishop's score at the end of 24 hours among study group and control group patients was 6.02 and 4.11 respectively. Mean Bishop's score at the end of 24 hours was higher among the subjects of the study group in comparison to the control group. Yelikar K et al assessed the efficacy of oral mifepristone in pre-induction cervical ripening and induction of labour in prolonged pregnancy. This was a single blind randomized control trial. 100 women with prolonged pregnancy beyond 40 weeks and Bishop score <6 were recruited, and randomly allocated into two groups. Women who received Tab. Mifepristone 200 mg orally were assigned in Study Group (n = 50) and who received placebo orally were assigned in Control Group (n = 50). There was no statistically significant difference in perinatal outcomes between two groups. Mifepristone had a modest effect on cervical ripening when given 24 h prior to labour induction and appearing to reduce need for misoprostol compared with placebo.[10] Wing DA et al compared the effect of mifepristone with placebo on cervical ripening before labor induction in prolonged pregnancies. One hundred eighty women with pregnancies beyond 41 weeks and undilated, uneffaced cervices were assigned randomly to receive mifepristone 200 mg or placebo and observed for 24 hours. Among 180 subjects, 97 received mifepristone and 83 received placebo. The mean interval (+/- standard deviation [SD]) from start of induction to delivery was 2209 +/- 698 minutes for mifepristone-treated subjects and 2671 +/- 884 minutes for placebo-treated subjects (P <.001, log-transformed data). There were nine cesareans in the mifepristone group and 18 in the placebo group (P =.02). More nonreassuring fetal heart rate patterns and uterine contractile abnormalities occurred in mifepristone-treated subjects. There were no statistically significant differences in neonatal outcomes between groups. Mifepristone had a modest effect on cervical ripening when given 24 hours before labor induction, appearing to reduce the need for misoprostol and oxytocin compared with placebo.[11]

In the present study, mean induction to active stage interval among the subjects of the control group was 1802.44 minutes and was found to be significantly higher than that of subjects of the study group (1642.28 minutes). Mean induction delivery interval among the subjects of the control group was 2108.50 minutes and was found to be significantly higher than that of subjects of the study group (1845.18 minutes). In the study group, the success rate was found to be 92 percent, while in the control group, the success rate was found to be 96 percent. Prevention of progestogenic effect by mifepristone promotes cervical ripening owing to the action of estrogens, such as increase in cervical collagenase and prostaglandin synthetize activity; enhance expression of the extracellular matrix degrading protease stromelysin-1 (MMP-3). 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. Efficacy and safety of medical abortion has been confirmed based on use of mifepristone for over two decades. The most commonly used approved indications for mifepristone in obstetrics include: termination of early pregnancy, cervical dilatation prior to surgical abortion, labour induction in case of fetal death in utero. Fewer studies have been conducted on the effect of mifepristone on cervical ripening and induction of labour in term pregnancy with a live fetus.[12]

P.-L. Giacalone et al. reported more uterine tachysystole and hypertonia in women treated with mifepristone for induction of labour. There were no cases of such complications in our trial, might be due differences of oxytocin infusion protocols. Since mifepristone crosses the placenta the fetus is exposed to maternal mifepristone intake. Maximum fetal plasma concentrations of mifepristone occur 4 h after treatment with a subsequent decrease to 24 and 48 h. The mifepristone concentration in umbilical cord blood varies within 11%–35% of maternal.[13, 14]

CONCLUSION

From the above results, it can be concluded that for cervical ripening and induction of labour, Mifepristone is an effective agent. However; further studies are recommended.

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