Galore International Journal of Health Sciences and Research
Vol.4; Issue: 3; July-Sept. 2019
Website: www.gijhsr.com
Original Research Article *P-ISSN: 2456-9321*

Mifepristone for Cervical Ripening and Induction of Labour in Patients with Lower Segment Caesarean Section - A Prospective Case Control Study

Dr Gagan Lata[1], Dr Sukhbir Pal Kaur[1], Dr Susmita Sharma[2]

[1]Assistant Professor, [2]Professor & Head,
Dept. of Obstetrics and Gynecology, Adesh Medical College & Hospital, Mohri, Shahbad, Haryana.

Corresponding Author: Dr Sukhbir Pal Kaur

ABSTRACT

Introduction- Induction of labour in previous caesarean section (CS) poses a significant challenge for obstetricians. Whenever there is a need of termination of pregnancy for obstetric indication, trend is shifting towards elective repeat caesarean section and the rates of IOL in women with previous CS are decreasing globally. Vaginal birth is associated with less complications as compared to repeat CS. Thus, there is a need for an agent with better outcomes in terms of vaginal birth.

Methods- This was a prospective randomized case-control study carried out at a tertiary care centre in North India on fifty-two term pregnant females with previous one caesarean section admitted for IOL for various indications. They were divided into two study groups of twenty-six each. Group A females received tablet Mifepristone and group B females received placebo. The study was aimed to evaluate the efficacy of Mifepristone for cervical ripening and induction of labour.

Results- There was statistically significant difference in induction to onset of labour with Mifepristone as compared to control group. Time interval between induction to onset of labour was 24 hrs 7 min and 37 hrs 3 min in mifepristone group and control group respectively. Mean induction delivery interval was 33 hrs 1 min and 46 hrs 9 min in cases and control group. Twenty-one patients (80.7%) delivered vaginally in the mifepristone group as compared to 15(57.6%) in the control group.

Conclusions: Mifepristone is simple and effective method for induction of labour in term women with previous LSCS with a favourable outcome.

Keywords: Lower segment caesarean section, Mifepristone, IOL

INTRODUCTION

Induction of labour is an intervention which is designed to initiate the uterine contractions artificially leading to progressive dilation and effacement of cervix and birth of the baby. Induction of labour is indicated only when mother or foetus seems to get benefit from higher probability of a healthy outcome than if birth is delayed. [1] Induction of labour in previous caesarean section (CS) poses a significant challenge for the obstetrician due to paucity of available options as well as limited evidence in favour of any methods. Globally rates of induction of labour in women with previous CS are decreasing. Whenever there is a need of termination of pregnancy for obstetric indication trend is shifting towards elective repeat caesarean section. Vaginal birth is associated with less complications as compared to repeat CS more so in population like ours where multiparity is more common.

The status of cervix is a major contributor for successful labour which can be assessed by Bishop pelvic scoring system. Bishop score of less than 6 usually requires cervical ripening agent. [2] Common approaches for induction of labour range from frequent walking, vaginal intercourse, heavy exercise, consumption of laxatives, spicy foods, nipple stimulation and administration of enema [3] to physical stimulation mainly achieved by dilators,

Trans cervical Foley's catheter, extra amniotic saline infusion, [4] cervical stretching and amniotomy. Pharmacological methods include oxytocin, prostaglandins and antiprogestins like mifepristone. [5] Mifepristone is a 19 nor-steroid derivative and it antagonizes progesterone hence increases sensitivity of the uterus to prostaglandins and initiates the labour. [6] It is not a very old drug for research on cervical ripening and labour induction in viable pregnancies. It has not been studied so widely as oxytocin and PGs in induction of labour in previous lower segment caesarean section (LSCS)cases. Also, in previous CS, there are limited cervical ripening agents which can be used. Women with previous caesarean birth have an increased risk of uterine scar rupture after induction of labour. [7] But the incidence is quite low in well monitored labour. Some serious complications which are seen with oxytocin and prostaglandins, lead to adverse outcomes for mother and child, such as hysterectomy, genitourinary tract injury, and postpartum blood transfusions and neurological impairment or even death for the child. [8] Thus, an agent which is not only a good uterotonic but also a good cervical ripening agent is desirable. Hence, this study was planned with the aim to know the efficacy of Mifepristone as cervical ripening and induction agent in term pregnancy with previous caesarean section.

METHODS

This was a prospective case control study done at a tertiary care centre of North India. Total of fifty-two cases of singleton, term pregnancy with previous one LSCS planned for induction for various indications with Bishop's score of less than 6 were included for the study. In all women demographic details, detailed history, examination including per vaginal examination and investigations were noted.

Twenty-six women were given tablet Mifepristone 400mg orally (Group A-Cases) and twenty-six received placebo in form of vitamin C (Group B, Control group) randomly. Indication of induction of labour was also noted. Before the medication was given, Bishop's score was assigned. Number of women who successfully went into spontaneous labour within 48 hours of administration of the drug was documented and results were assessed. If the labour did not start within 48 hours, vaginal examination was repeated and Bishop's score was re-calculated. If Bishop's score still remained unfavorable (< 6) women were then induced with Foley's catheter. Subjects were assessed 12 hours later and if the bishop score still remained unfavorable, caesarean section was performed for failed induction. If at any stage Bishop's score was 6 or more amniotomy was done and oxytocin infusion was started. Time interval between induction to onset of labour and induction to delivery was noted. Active stage of labour was monitored with partogram. Mode of delivery and Apgar score was recorded. Efficacy of the drug was assessed by the number of women who went into spontaneous labour within 48 hours of Mifepristone administration or by Bishop's score of 6 or more at 48 hours. The statistical difference between two groups was evaluated by using student t test and Chi square test. The p value of < 0.05 was considered as statistically significant. The study complied with the guiding principles for human research per the declaration of Helsinki and was approved by the institutional ethics committee. Written informed consent was obtained from all patients.

RESULTS

Women in group A and group B were compared for age, period of gestation and Bishop score as shown in Table 1.

Table 1. Characteristics of the subjects

Characteristic	Mifepristone group	Control group
Age (mean in years)	25	25
POG	39weeks 6 days	39 weeks 5 days
Median Bishop Score	3.6	4
Indication of induction		
Post term	21	19
IUGR	2	4
PIH	3	3

Age, period of gestation and median bishop score before induction was comparable in both groups and it was not statistically significant. Indications of induction in both groups were post term pregnancy, IUGR and PIH. Time interval between induction to onset of labour and induction delivery interval was less in Mifepristone group as compared to control group as shown in Table 2.

In group A, after the initial dose of 400mg of mifepristone (two tablets of 200mg mifepristone orally), 21 (80.7%) women out of 26 went into labour within 48 hrs. and had Bishop score of≥8. In these women, amniotomy was performed and augmentation with oxytocin infusion was given as per study protocol if needed. Five females who did not had onset of labour within 48 hours, were again induced with Foley's catheter and reassessed after 12 hours. Out of these five, two delivered vaginally and three underwent LSCS.

In group B, out of 26 women 15(57.6%) had spontaneous onset of labour within 48 hours. Foleys was put in 11 cases. Eight patients underwent LSCS for various indications three delivered vaginally. Indications are mentioned in Table 2. Neonatal weight, Apgar score and neonatal complications were comparable in both groups.

Table 2. Labour characteristics and delivery data of patients with previous LSCS

Characteristic	Mifepristone group	Control group	P value
Time interval between induction to onset of labour	24 hrs 7min	37hrs 3 min	0.025*
Induction delivery interval	33 hrs 1 min	46 hrs 9 min	0.067
LSCS	3	8	
Fetal distress	1	2	
Failed Induction	2	4	
Non progress of labour		2	
VBAC	23	17	
Instrumental delivery		1(Fetal distress)	
Adverse effects of the drug			
Nausea/vomiting	2	1	
Headache	1		
Labour complications			
Hypertonus		1	
Tachysystole	3	1	
MSL		2	
PPH			
Neonatal Weight(kg)			
<2.5	3	4	
2.5-3	20	20	
>3	3	2	
Neonatal outcome			
Apgar score <7 at 5 min	10	10	
Neonatal hyperbilirubinemia	1		

*statistically significant

DISCUSSION

It has been seen globally that rates of induction of labour in women with previous CS are decreasing. Whenever there is a need of termination of pregnancy for obstetric indication trend is shifting towards elective repeat caesarean section. Around 20-30% women require induction of labour (IOL) for some maternal or fetal indication. [7] IOL in patients with previous LSCS has decreased successful outcome as compared to spontaneous onset of labour and also associated with scar dehiscence, rupture of uterus and increased rate of fetal and maternal mortality and morbidity. [8] According to Cochrane database review, there is no ideal method of IOL with previous CS. [9] Studies on various pharmacological and non-pharmacological methods of induction of labour are encouraging. [5]

Mifepristone which is an antiprogesterone agent has been used orally for IOL. The advantage of Mifepristone is that it is not an oxytocic so it is not associated with hyper stimulation of uterus, hence decreasing the incidence of rupture uterus. [6] Mifepristone causes cervical

ripening by stimulating the release of nitric oxide [10,11] and promotes uterine contractions by increasing myometrial cell excitability, establishing gap junctions between cells and influx of calcium [12] and increases the release of prostaglandins by decidual cells [13,14] without acting as a direct uterotonic. Because of these benefits, it may be a safer agent for IOL in females at term with previous caesarean section.

In our study, we observed that mifepristone was associated with favourable outcome after IOL in most of the women with previous CS. There was also very less need of oxytocin requirement for augmentation of labour which is a risk factor for scar dehiscence and rupture uterus. A prospective double-blind placebo-controlled trial by Le Laider et al also had similar results with mifepristone as induction agent in previous LSCS cases. [15]

In our study, we observed that twenty-one (80.76%) women had labour onset and cervical ripening within 48 hours of administration of mifepristone. The observations of various studies in existing literature show a success rate of labour onset of 66–93%. [16-19] Gia-calone et al have shown a success rate after IOL of (68.3%) [20] Stenlund et al. (79%) and Frydmann et al. (54.5%) [21] respectively while using mifepristone as compared to placebo in women without previous CS. The associated risk of serious complications like scar rupture and others in various studies was reported to be0.4-0.7%. [22,23,24] However, most of these studies were in patients without caesarean section. In our study we did not observe significant fetal or maternal side effects of Mifepristone. According to a hypothesis by Cochrane systematic review using mifepristone for IOL in previous CS is a safe option as mifepristone is not a uterotonic, chances of scar dehiscence or rupture uterus might not be increased in these women. [6] The incidence and caesarean section for intrapartum fetal distress was not statistically significant in both groups. In Cochrane meta-analysis, it has been stated that abnormal fetal heart rate patterns are common with mifepristone. However, there are no statistically significant differences in Apgar score <7 at 5 minutes of birth or an increased rate of caesarean section for fetal distress. [6]

One of the major limitations of our study is that the number of patients is less. Further evaluation regarding the optimum dose of mifepristone for cervical ripening, antenatal and perinatal complications and the safety of drug in relation to other procedures is also needed.

CONCLUSION

The present study shows that treatment with mifepristone is a simple and effective method of inducing labour in women with term pregnancy and unripe cervix. Mifepristone stimulates labour as naturally as possible and thus is a safer option. The use of mifepristone provides an interesting new alternative to classic uterotonic agents as induction agent. From this study it is evident that mifepristone is a good alternative option for IOL in women with previous CS. However, further research is needed with large randomised controlled trials for evaluating the efficacy of mifepristone alone as a safe agent for IOL in previous caesarean section.

REFERENCES

1. Managing complication in pregnancy and childbirth: a guide for midwives and doctors. Geneva: World Health Organization; 2000. (available at: http://www.who.int/reproductivehealth /publications/maternal_perinatal_health /9241545879/en/index.html)
2. Tenore JL. Methods for cervical ripening and induction of labour. AmFam Physician 2003; 67:2123-28.
3. Schaffir J. Survey of folk beliefs about induction of labour. Birth 2002;29:47-51.
4. Karjane NW, Brock EL, Walsh SW. Induction of labour using a Foley balloon, with and without extra-amniotic saline infusion. ObstetGynecol 2006; 107:234-9.
5. MacKenzie IZ. Induction of labour at the start of the new millennium. Reproduction 2006;131:989-98.

6. Hapangama Dharani, Neilson JP. Mifepristone for induction of labour. Cochrane Database of Systematic Reviews 2009, Issue 3. Art. No:CD002865. DOI: 10.1002/14651858.CD002865.pub2.
7. Arulkumaran S.Caesarean section rates are increasing worldwide. Preface. BestPract Res ClinObstetGynaecol. 2013; 27:151–2.
8. ACOG Practice bulletin no. 115. Vaginal birth after previous caesarean delivery. American College of Obstetricians and Gynaecologist. Obstet Gynecol. 2010; 116:450-63
9. Jozwiak M, Dodd JM. Methods of term labour induction for women with a previous Caesarean section. Cochrane Database Syst Rev. 2013.
10. Brogden RN, Goa KL, Faulds D. Mifepristone. A review of its pharmacodynamicand pharmacokinetic properties, and therapeuticpotential. Drugs. 1993; 45:384–409.
11. Chwalisz K, Garfield RE. New molecular challenges in theinduction on cervical ripening. Hum Reprod. 1998; 13:245–52.
12. Garfield RE, Blennerhassett MG, Miller SM. Control of myometrial contractility: role and regulation of gap junctions. Oxf Rev Reprod Biol. 1988;10:436–90.
13. Cheng L, Kelly RW, Thong KJ et al. The effects of mifepristone (RU486) on prostaglandin dehydrogenase in decidual and chorionic tissue in early pregnancy. Hum Reprod. 1993; 8:705–9.
14. Cheng L, Kelly RW, Thong KJ et al. The effect of mifepristone (RU486) on the immunohistochemical distribution of prostaglandin E and its metabolite in decidual and chorionic tissue in early pregnancy. J Clin Endocrinol Metab. 1993; 77:873–7.
15. Lelaidier C, Baton C, Benifla JL et al. Mifepristone for labour induction after previous caesarean section. Br J ObstetGynaecol.1994;101:501–3.
16. McGill J, Shetty A. Mifepristone and misoprostol in the induction of labour at term. Int JGynaecol Obstet. 2007; 96:80–4.
17. Stenlund PM, Ekman G, Aedo AR et al. Induction of labour with mifepristone- a randomized, double-blind study versus placebo. ActaObstetGynecol Scand.1999; 78:793–8.
18. Li L, Gao W, Chen S. Labour induction in women at term with mifepristone and misoprostol. Zhonghua Fu Chan KeZaZhi. 1996; 31:681–4.
19. Edwards MS. Mifepristone: cervical ripening and induction of labour.ClinObstetGynecol.1996; 39:469–73.
20. Giacalone PL, Targosz V, Laffargue F, Boog G, Faure JM. Cervical ripening with mifepristone before labour induction: a randomized study. ObstetGynecol1998; 92:487–492
21. Frydman R, Lelaidier C, Baton C, Fernandez H, Vial M, Bouget P. Labour induction in women at term with mifepristone (RU-486); a double blind, randomized, placebo-controlled study. ObstetGynecol1992; 80:972–975.
22. Zwart JJ, Richters JM, Ory F, de Vries JI,Bloemenkamp KW, van Roosmalen J. Uterine rupture in The Netherlands: a nation-wide population-based cohort study. BJOG.2009; 116:1069-78.
23. Landon MB, Hauth JC, LevenoKJ, et al. Maternal and perinatal outcomes associated with a trial of labour after prior cesarean delivery. NEngl J Med.2004; 351:2581-9.
24. Mozurkewich EL, Hutton EK. Elective repeat cesarean delivery versus trial of labour: a meta-analysis of the literature from 1989 to 1999. Am J Obstet Gynecol. 2000; 183:1187-97.

How to cite this article: Lata G, Kaur SP, Sharma S. Mifepristone for cervical ripening and induction of labour in patients with lower segment caesarean section - a prospective case control study. Galore International Journal of Health Sciences & Research. 2019; 4(3): 165-169.

******