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ROLE OF MIFEPRISTONE AND ITS EFFICACY IN INDUCTION OF LABOUR AFTER TWENTY WEEKS IN PREVOIUS ONE AND TWO LOWER SEGMENT CAESAREAN SECTION WITH INTRAUTERINE FETAL DEMISE

Obstetrics & Gynaecology

Dr Monica Chauhan Assistant Professor

Dr Neetu Kochhar Associate Professor

Dr Himani Palariya Postgraduate Resident

ABSTRACT

Background and objective: Induction of labour is a commonly performed procedure in obstetrics. Women with previous caesarean delivery have increased risk of uterine rupture particularly if labour is induced. Performing repeat caesarean in women with previous cesarean section with intrauterine fetal demise is not a good idea, effort should be made to deliver vaginally. But it is unclear that which inducing agent is preferred in previously scarred uterus. So with this background, current study was done to evaluate the efficacy of mifepristone for cervical ripening and induction of labour in previous 1 and 2 cesarean sections with intrauterine fetal demise after 20 weeks of gestation. **Material and method:** Total 41 women who had previous 1 or 2 lower segment cesarean section at term with intrauterine fetal demise in current pregnancy after 20 weeks were taken for the study. Patients who meet inclusion criteria received tablet mifepristone 200mg orally and repeated 24 hours after first dose. Reassessment of bishop score was done 24 hour and then 48 hours after first dose. Patients were allowed to go into spontaneous Labour. labour was augmented with oxytocin in patients whom it was required. **Result:** In our study mean pre and post induction bishop score was 2.48 and 10.48(after 24 hour) and 7.19(after 48 hour) respectively. 13 (31.7%) patients went into spontaneous labour and 21 (51.2%) patients required augmentation of labour, 7(17.07%) patients required foley's induction as additional method of induction. In our study all 41 patients delivered vaginally. No case of scar dehiscence or scar rupture was found. **Conclusion:** Mifepristone is safe and efficient agent for cervical ripening.

KEYWORDS

mifepristone, Bishop score, labour induction, scar rupture, Intra Uterine Fetal Demise

INTRODUCTION

Intrauterine fetal demise at any gestational is a mental trauma both for the patient and obstetrician. IUFD is defined as fetal death (FD) after 20weeks of gestation [2] which can either early or late IUFD. If FD occurs <24 weeks, it is called early IUFD. If FD occurs >24 weeks, it is called late IUFD. According to the Indian census of 2006, the rate of IUFD is 6.4 per 1000 live births in India. The lowest rates of IUFD are seen in Finland and Singapore, where it is as low as 2 per 1000 births, while the highest rates are found in Pakistan, where it is 47 per 1000, and Nigeria, where it is 42 [3]. In last one year, number of IUDs delivered at Government Doon Medical College were 158 which is 2.4% of total deliveries (6452).

Induction of labour in previous cesarean section poses significant challenge for the obstetrician due to limited favourable available options [4]. There is also increased chances of uterine rupture after induction of labour in previously scarred uterus in comparison to unscarred uterus. Vaginal delivery is always better and is associated with less complications as compared to caesarean section. The probability of vaginal delivery depends upon the status of cervix. Condition of cervix best assessed by scoring called Bishop Score. Score of less than 6 require induction of labour. There are various pharmacological agents which are available and can be used for labour induction such as oxytocin, prostaglandins and antiprogesterone (mifepristone).

Nowadays Mifepristone is also being used for induction of labour. Mifepristone is a 19 nor-steroid derivative and it is progesterone antagonist hence increases sensitivity of the uterus to prostaglandins. Mifepristone is rapidly absorbed when given orally and attains maximum serum level in 2 hours and half-life is 25 hours[5]. So the inhibitory action of progesterone is withdrawn, also prostaglandin dehydrogenase action is inhibited and there is increased synthesis of prostaglandins[6,7]. 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)[8,9]. These properties of Mifepristone makes it a useful drug for cervical ripening and hence termination of pregnancy. We have performed this study to evaluate the role of mifepristone in previous one and two LSCS with intrauterine fetal demise.

METHODS:

This prospective study was conducted at department of Obstetrics and Gynaecology, Government Doon Medical college, Doon Female Hospital, Dehradun, Uttarakhand after Ethical approval. All pregnant women with previous one and two LSCS with IUD in 2nd and 3rd trimester were included in the study.

Sample size is calculated by using the formula:

$$N = \frac{(z_\alpha)^2 \cdot (s)^2}{(d)^2}$$

In our study we took a sample size of 41 to achieve a power of 80% and a level of significance of 5% (two sided), for detecting a mean of the differences of 9 between pairs, assuming the standard deviation of the differences to be 20 using the online software statulator.

A written and informed consent was taken from the patients after explaining them the study.

Inclusion Criteria were 18-45 years, Singleton IUD pregnancy, Cephalic presentation, previous one and two LSCS, bishops <6 and Exclusion criteria were interconception period less than 18 months, estimated fetal weight more than 4kg, PROM, PPROM, chorioamnionitis and other contraindications of vaginal delivery.

Detailed history was taken. Examination included general, systemic and local. Per abdomen and per vaginal examination was done, condition of the cervix was assessed by modified Bishop Score. All relevant investigation Complete Blood Count, Blood group, Urine Routine Microscopy, Oral Glucose Challenge Test, Viral markers, Serum Creatinine, SGPT/SGOT, PT/INR were done. Women who met the inclusion criteria received Tab Mifepristone 200mg OD for 2 days. Reassessment of bishops score was done after 24 hours of mifepristone. If it was less than 6 then second dose of mifepristone was given and Bishop was seen after 24 hours of second dose. If Bishop score was less than 6 after 2 doses of mifepristone then further induction was done with foley's catheter. Number of patients requiring augmentation of labour was noted.

The parameters noted were Pre and post induction bishop score, induction to delivery interval, mode and route of delivery, outcome of labour and maternal complications.

Statistical Analysis-

All data were entered in to Ms Excel then analyzed using SPSS V 22.0 . Categorical data were presented in the form of Frequency and

percentage. Continous data were presented in the form of mean and SD. Comparison of three group was done using ANOVA. All p values <0.05 is considered to be significant.

RESULTS:

Total 41 patients were included in our study. Age distribution was found to be as in table 1. Majority (54.8%) patients were in age group 21-30 year. Figure 1 depicts, Out of 41 patients 34 patients(83.3%) had previous one LSCS and 7 patients(16.6) had previous two LSCS. Table 2 presents that 23 patients (56%) were in third trimester. maximum patients (24) delivered between 31-40 hours. Table 2 shows the comparison of Bishop Score at 24 hour and 48 hours. By using analysis of variance significant difference was observed overall. In age group less than 20 and in 31-40 age groups the difference is significant. In third trimester the mean difference also observed to be significant. According to mean induction delivery interval the mean difference was also found to be significant. All patients delivered vaginally. None of the patients had any major complications.

Table 1: Age Distribution of respondents

Age in years	N	%
< 20	5	12.2
21-30	22	53.6
31-40	14	34.1

Table 2- Trimester Distribution

Trimester	N	%
Second(20-28 weeks)	18	43.9
Third(29-40 weeks)	23	56

Table 3- Distribution of maternal Outcome

Maternal outcome	N	%
Vaginal delivery	41	100
Required mechanical dilatation (foley's induction)	7	17

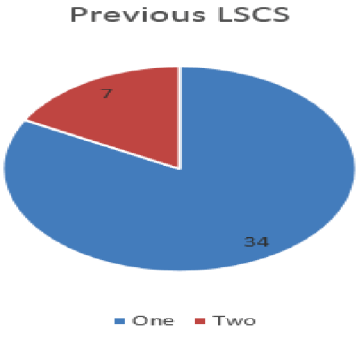

Figure 1

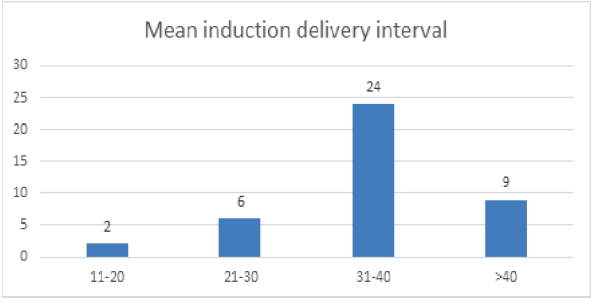

Figure 2

Table 2 – Comparsion of Bishop Score

Variables	Mean±SD Bishop score(Pre)	Mean±SD Bishop score(At 24 Hour)	Mean±SD Bishop score(At 48 hour)	F value	P value
Total	2.88±1.27	5.81±1.92	7.85±1.99	3.247	0.010
Age in years					
< 20	2.00±0.53	5.13±0.99	9.00±1.41	1.547	0.012
21-30	3.20±1.32	6.38±2.46	6.33±2.31	2.458	0.417
31-40	3.00±1.33	5.69±1.74	7.83±1.94	3.145	0.011
Previous LSCS					
One	2.73±1.25	5.88±2.02	7.86±2.03	4.251	0.147
Two	3.12±1.31	5.69±1.79	7.83±2.13	4.287	0.239
Trimester					
Second	2.67±1.19	5.70±1.55	8.50±1.51	9.464	0.156
Third	2.77±1.16	5.75±2.26	6.80±2.38	8.263	0.021
Mean induction delivery interval					
11-20	3.10±1.28	5.71±1.38	9.00±1.00	6.250	0.007
21-30	2.77±1.48	5.38±1.59	7.33±2.08	7.197	0.024
31-40	2.80±1.22	6.33±2.59	8.50±2.12	4.167	0.017
>40	2.84±1.28	5.77±1.96	7.20±2.49	6.764	0.144
Additional inducing agent					
Required mechanical dilatation	2.54±1.12	5.55±1.75	8.29±1.70	6.547	0.037

DISCUSSION:

Intrauterine fetal demise is a tragic event for parents. Despite of advancement in medical sciences and availability of various diagnostic modalities, pregnancy loss still occurs. Many methods are available for induction of labour but in previous LSCS with IUFD we have very less options. Study on use of labour inducing agent in second and third trimester in intrauterine fetal demise was first conducted by Cabrol et al[10] in 1985. He conducted study on 11 women with IUFD at mean gestational age of more than 18 weeks, using mifepristone at dose of 200 mg twice a day for two days and reported successful induction of labor in 81% of women with mean induction to delivery interval of 39±12.5 hours. No side effects were reported[11]. Later in 1990, he did a double blind placebo controlled multicentric study involving 94 women with IUFD to demonstrate the efficacy of mifepristone. He used mifepristone in the dose of 200mg TDS for 2 days. He found that labour ocurred in 63% patients in the mife group as compared to only 17% in placebo group($p<0.001$). It has now been seen that mifepristone has an established role in termination of pregnancy during early first trimester and second trimester. Frydman used 200mg mife for IOL at term on day 1 and 2 and found that patients who received mifepristone required very low dose of oxytocin for labour augmentation[12]. Since then various studies have been conducted to evaluate efficacy of mife as an inducing agent in women with live pregnancy and IUFD.

In Cochrane Systematic review study (2009) " Mife for IOL", Hepangama et al found that women who were induced with mife had more favourable cervix at 48 hours compared to placebo group. No serious complications were noticed in our study group, whereas complications such scar rupture was noticed in 0.4-0.7% in various other studies[13,14,15]

In our study we observed that Bishop Score was dramatically improved in most of the patients after mifepristone. Dose and duration of oxytocin requirement was also less. In 24(58.5%) women out of 41 mean induction delivery interval was 31-40 hours after 2 doses of mifepristone. No serious complication such as scar dehiscence or uterine rupture was seen in our study. None of our patients required blood transfusion. However complication such as scar rupture was reported in 0.4-0.7% in various other studies[16,17,18].

One of the main limitation in our study was number of patients were less. Further studies are needed for optimal dosing and duration of mifepristone and associated complications with this drug.

CONCLUSION:

Mifepristone is safe, efficient and suitable agent for induction of labour. In a previously scarred uterus when other methods of induction of labour are contraindicated, mifepristone is a wonder drug to be used as an inducing agent. But proper dose has not been fixed so further clinical trials are required.

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