INDUCTION OF LABOUR WITH VAGINAL MISOPROSTOL IN INTRAUTERINE FOETAL DEATHNeeta Sarma¹¹Assistant Professor, Department of Obstetrics and Gynaecology, Silchar Medical College and Hospital.**ABSTRACT****BACKGROUND**

Intrauterine foetal death is an unfortunate event met in obstetric practice. Misoprostol has emerged as an efficient and relatively safe drug to deliver the baby in this condition. The objective of this study is to evaluate the safety and efficacy of vaginal misoprostol tablets for the induction of labour in intrauterine foetal death.

MATERIALS AND METHODS

This uncontrolled clinical trial was performed on 100 women with intrauterine foetal death from January 2016 to December 2016 at Silchar Medical College and Hospital. All women were properly evaluated. Informed consent was taken and vaginal misoprostol tablets at a dose of 50 mcg 4 hourly was used to induce labour. The results were assessed.

RESULTS

In a study of 100 women, mean natural age was 26.21 ± 4.98 years, mean gestational age was 38.81 ± 4.26 weeks, 61% women were primigravida and the rest were multigravida; 80% were booked cases, 72% belonged to rural areas and 76% were illiterates. The mean initial Bishop's score was 2.23 ± 1.82 (range 0 to 6), while following induction with misoprostol the mean Bishop's score was 6.98 ± 2.1 , the mean difference was 4.75. P value was statistically significant. The mean induction-labour onset interval was 10 ± 6.65 hours and the mean induction-delivery interval was 13.60 hours with 46.46% women delivering within 12 hours. The mean misoprostol dose required was 152.5 ± 88.5 mcg. Induction was successful in all women, but laparotomy was needed in 1 woman because of uterine rupture. The side effects noted were nausea (7%), vomiting (2%), diarrhoea (4%), fever (5%), uterine hyperstimulation (4%), ruptured uterus (1%), retained placenta (3%) and atonic post-partum haemorrhage (3%).

CONCLUSION

Misoprostol is an effective, economic and safe drug that can be used for cervical ripening and labour induction in intrauterine foetal death. Clinical significance- the response to misoprostol is influenced by the gestational age, Bishop's score and parity of the women.

KEYWORDS

Vaginal Misoprostol, Intrauterine Foetal Death, Labour, Induction, Non-Randomised Interventional Prospective Study.

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BACKGROUND

Intrauterine foetal death is a nightmare for a pregnant lady as well as her obstetrician. Left undisturbed the women usually go into spontaneous labour, but if a dead foetus is retained in the uterus for too long there is risk of developing sepsis and coagulation disorders coupled with mental trauma to the lady. Hence, induction of labour is often required. However, unlike in normal term pregnancy in patients with intrauterine foetal death the uterus is less sensitive to oxytocics, the cervix is usually not ripe and surgical methods of induction carries the risk of infection. Intravenous oxytocin has been used since ages but often large doses over prolonged duration are needed, particularly if the cervix is unfavourable leading to water intoxication. Condition of the cervix prior to induction is an important predictor of success of induction.

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Therefore, medications that will reliably ripen the cervix in a short period of time play an important role in modern day obstetrics. Prostaglandins - PGE2 gel (intracervical) and PGE1 analogue misoprostol have been used for cervical priming and labour induction with high success rate. Misoprostol, a methylester of PGE1, is a potent uterotonic that can be administered by oral, vaginal, rectal and buccal routes. Vaginal administration has been found to be more effective than oral.^{1,2,3} In contrast to other prostaglandins, misoprostol is selective for the uterus and has no significant effect on the bronchi or blood vessel. Side effects like nausea, diarrhoea and fever are infrequent and dose related. Its safety, cost effectiveness, long shelf-life and ease of administration makes it ideal for low-resource settings.⁴ In recent years, there has been a considerable interest in the use of misoprostol^{5,6,7} for cervical ripening and labour induction. With this background information, the current trial was designed to evaluate the safety and efficacy of misoprostol tablet when used vaginally for induction of labour in intrauterine foetal death with special emphasis on the induction delivery interval, the mode of delivery, the success rate of the drug in labour induction and the incidence of side effects and complications.

MATERIALS AND METHODS

This uncontrolled clinical trial was carried out in the Department of Obstetrics and Gynaecology, Silchar Medical College and Hospital (SMCH) over a period of one year from

January 2016 to December 2016 and was approved by the local Institute of Ethical Committee. 100 women aged 18 - 40 years including primigravida and multigravida (upto gravida 3) with gestational age beyond 28 weeks having single dead foetus in cephalic presentation with membranes intact or ruptured were included in the trial. Women excluded from the study included those with hypersensitivity to prostaglandins, those with history of liver disease, glaucoma, convulsive disorder, those with scarred uterus due to previous caesarean section or myomectomy and those with placenta praevia. Each woman was properly evaluated by detailed history taking and thorough clinical examination and diagnosis was confirmed by ultrasonography. The purpose and procedure of induction, the advantages and the possible risks were well explained to the woman and her attendant and a written and informed consent was taken. All patients were investigated and the Bishop's score was assessed. Tablet misoprostol 50 mcg vaginally in posterior fornix was used four hourly till the patient went into active labour or upto a maximum dose of 400 mcg. Active labour was diagnosed when the cervix was 3 cm dilated or uterine contractions were 3 in 10 minutes, each lasting at least 40 seconds. The induction was categorised as having failed if the woman did not go into labour even after 4 hours of the eighth dose. The patient was thereafter augmented with oxytocin by escalation method or considered for caesarean section as required. Progress of labour was assessed by noting the frequency, duration and strength of painful uterine contractions half hourly, the rate of cervical dilatation and head descent three hourly and complications were dealt with symptomatically. Uterine hyperstimulation was said to occur if uterine contractions were ≥ 5 in 10 minutes, each lasting ≥ 90 seconds and was managed by removal of tablet from the vagina if possible or administration of uterine relaxants like nifedipine 10 mg sublingual or injection terbutaline 250 mcg subcutaneously. During the course, injection tramadol 100 mg intramuscular or injection promethazine 25 mg intramuscular was used in the early stages of labour for analgesia if felt necessary. After delivery, the woman was observed throughout the hospital stay for any complications.

The main measure of efficacy was success rate of induction. Other measures were total dose of misoprostol required, induction - labour onset interval, rate of cervical dilatation, duration of labour, induction - delivery interval, need for oxytocin augmentation and analgesia, mode of delivery, any operative procedure required, side effects and complications. Baseline characteristics noted were maternal age, pregnancy duration, parity, socioeconomic status and pre-induction cervical score.

Statistical Analysis

Appropriate statistical analysis was done with the help of SPSS version 20. Data analysis was done by unpaired student's 't' test and P value < 0.05 was considered significant.

RESULTS

The observations that were noted from the study have been tabulated. A total of 100 women with intrauterine foetal death admitted in the Obstetrics and Gynaecology Department, SMCH, were taken up for the study.

As seen in Table 1, majority of the cases (60%) were in the age range of 18 to 25 years. 61% of them were nulliparous. The cases were mostly unbooked (80%), hailing from rural areas (72%) and illiterates (76%). 46% were of term pregnancy, the mean gestational age being 38.81 ± 4.26 weeks. Baseline Bishop's score ranged from 0 to 6, maximum (61%) had a score of 0 to 2.

There was significant change in the Bishop's score (Table 2) following labour induction.

Table 3 shows the total dose of misoprostol required ranged from 50 mcg to 350 mcg. The mean total dose required was 152.5 ± 88.5 mcg. The induction - labour onset interval ranged from 2 hours to 25 hours, the mean being 10 ± 6.65 hours. The induction delivery interval ranged from 3 hours 40 minutes to 38 hours 30 minutes, the mean being 13.66 hours.

The mean total dose requirement, the mean induction - labour onset interval and the mean induction - delivery interval was found to decrease with increase in pregnancy duration, parity and increasing Bishop's score. The duration of first stage of labour was inversely and the cervical dilatation rate was directly related to the gestational age, Bishop's score and parity.

Induction was successful (Table 4) in all cases. But vaginal delivery occurred in 99% cases and in 1 % case laparotomy was needed due to uterine rupture.

Side effects (Table 5) like nausea, fever and diarrhoea were related to higher doses of misoprostol. Retained placenta was seen in 3% cases and were related to multiparity and lower gestational age. Atonic PPH was seen in 3% cases and all the cases were multiparous.

Variables	Mean $\pm$ S.D	Frequency
Age (years) ^a	26.21 ± 4.98	Multi 39% Primi 61%
Gestational age (week) ^a	38.81 ± 4.26	
Parity ^a		
Socio-economic status ^a		Booked 20% Unbooked 80% Urban 28% Rural 72% Literate 24% Illiterate 76%
Initial Bishop's Score ^a	2.23 ± 1.82 (0-6)	

Table 1. Demographic Characteristics of All Cases

^aStudent's 't' test- Data represented as mean $\pm$ S.D or %

Mean Bishop's before Induction	Mean Bishop's after Induction	Mean Difference	P Value
2.23 ± 1.82	6.98 ± 2.1	4.75	0.0001

Table 2. Change in Bishop's Score

P value is significant. Student's 't' test, data represented as mean $\pm$ S.D.

Outcome	Range/ Frequency
Induction-labour onset interval (hours)	10 ± 6.65 (2-25)
Induction-delivery interval (hours)	13.60 (3.66 – 38.50)
< 12 hours (%)	46.46
12 - 24 hours (%)	42.43
> 24 hours (%)	10.11
Dose of misoprostol (mcg)	152.5 ± 88.5 (50 – 350)
50 mcg (%)	19
100 mcg (%)	29
150 mcg (%)	22
≥ 200 mcg (%)	30
Need for oxytocin augmentation (%)	35
Analgesia requirement (%)	34
Duration of labour	
First stage (hours)	3.3 ± 1.8 (1.25 – 12.56)
Second stage (minutes)	39.29 ± 19.56 (10 – 100)
Third stage (minutes)	6.89
Rate of cervical dilatation (cm/ hour)	2.12 ± 0.93 (0.54 -5.60)

Table 3. Intrapartum Variables

Student's 't' test- data represented as mean ± S.D or %

Outcome	Number of Cases	%
Successful induction	100	100
Mode of delivery		
Vaginal	99	99
Abdominal (laparotomy)	1	1

Table 4. Success of Induction and Delivery Method

Variables	Percentage of Cases
Nausea	7
Vomiting	2
Diarrhoea	4
Fever	5
Uterine hyperstimulation	4
Ruptured uterus	1
Retained placenta	3
Atonic PPH	3

Table 5. Side Effects and Maternal Complications

DISCUSSION

In our study 60% women were in the age group of 18 - 25 years, 61% were primigravida, while the rest were gravida 2 or 3; 46% were of term pregnancy. The initial Bishop's score ranged from 0 to 6 with 61% having a score of 0 to 2.

In the study by Easmin S et al,⁸ 46% belonged to the age group 18 - 25 years, 80% had gestational age of 28 - 37 weeks, 64% had the initial Bishop's score of 0 to 3 and the rest 4 to 6. In the study by Sharma D et al,⁹ 50% were of term pregnancy.

In our study, 50 mcg misoprostol was used vaginally four hourly till the onset of active labour or a maximum dose of 400 mcg and the mean total dose used was 152.5 ± 88.5 mcg. The optimal dosage regimen of misoprostol and the frequency of administration has not yet been determined.

El Gharib et al¹⁰ have used 25 mcg four hourly over 24 hours with a mean total dose of 120 ± 28.79 mcg. Panda S et al¹¹ have used 100 mcg four hourly, the maximum dosage being 600 mcg in 24 hours; Sharma et al⁹ have used 100 mcg

and 50 mcg misoprostol every 3 hourly in pregnancies less than 37 weeks and beyond 37 weeks respectively till the beginning of active labour or a maximum of 4 doses, whereas Easmin S et al⁸ have used 50 mcg every 4 hourly upto effective contractions or a maximum of 6 doses.

Our study has showed a 100% success rate of induction. El Gharib et al¹⁰ has recorded 90% and 45% success rate in the third and second trimester foetal deaths respectively. Chaudhari P et al¹² have achieved 92.5% and 71.2% success rates in their study which compared use of misoprostol with or without mifepristone respectively. P value being 0.001, which was significant. A 98% success rate of induction was shown by Easmin S et al,⁸ whereas Dodd et al¹³ have noted comparable rates of vaginal delivery within 24 hours with a similar induction to birth interval in their assessment comparing vaginal misoprostol with other prostaglandin preparations.

The mean induction - delivery interval noted in our study was 13.66 hours and it was found to correlate negatively with pregnancy duration, parity and initial Bishop's score. El Gharib et al¹⁰ had shown induction delivery interval of 8.95 ± 2.63 hours, which decreased with increasing duration of gestation.

Chaudhari P et al¹² in their study had found induction delivery interval of 9.8 ± 4.4 hours and 16.3 ± 5.7 hours with or without the use of mifepristone along with misoprostol respectively. P value being < 0.001, which was significant. Easmin S et al⁸ has obtained a mean induction delivery interval of 11.8 hours (6 to 23 hours), whereas Sharma D et al⁹ have shown it to be 11.81 ± 6.33 hours and 6.72 ± 3.34 hours without or with the combined use of mifepristone with misoprostol respectively. Parity, gestational age and Bishop's score did not affect the induction- delivery interval in the study by Sharma D et al.⁹

In our study 35% required oxygen augmentation, whereas El Gharib et al¹⁰ has shown oxygen requirement in 55% women undergoing induction in third trimester foetal death. Agrawal A et al¹⁴ and Panda et al¹¹ in their studies have shown oxytocin requirement in those women where misoprostol alone was used as compared to those where mifepristone was used as well.

Analgesic requirement was noted in 34% of the study population, which was comparable to the studies by Nyende et al³ which was 35.5% and De Heus et al¹⁵ which was 32.8%.

The side effects and complications of using vaginal misoprostol in the present study and in other studies like Chittacharoen et al,¹⁶ Nyende et al,³ De Hues et al,¹⁵ Ezechi et al,¹⁴ Dodd et al¹³ and Easmin et al⁸ included nausea, diarrhoea, vomiting, pyrexia, retained placenta, postpartum haemorrhage and hyperstimulation syndrome. Diarrhoea and elevated temperature were found to increase with increasing dose of misoprostol in the present study and the study by Dodd et al.¹³

CONCLUSION

Intrauterine foetal death is a rather unwanted, yet invariably encountered situation. Misoprostol is a very effective drug for induction of labour, as it has the dual property of cervical ripening and initiating uterine contractions and can be used at all gestational ages. Although the optimal dosing has not yet been determined, use of higher doses at frequent intervals for cases with lesser gestational age, poorer cervical score or

lesser parity and vice versa should usually serve the purpose of bringing about successful induction and also avoiding unwanted complications. Given the possible complications inherent in the induction of labour, a specific signed informed consent should be mandatory and there should be institution-specific practice guidelines and protocols to guide dosing and dose scheduling and careful chart documentation of all relevant outcomes whenever misoprostol is administered.

Compliance with ethical requirements and conflicts of interest- The study is in compliance with ethical standards. Permissions have been sought and is approved by the Institutional Ethical Committee.

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