Original Research Article

Indian Journal of Obstetrics and Gynecology
Volume 8 Number 4, October–December 2020
DOI: http://dx.doi.org/10.21088/ijog.2321.1636.8420.7

Low Dose Vaginal Misoprostol in the Mangement of Intrauterine Fetal Death: Two Years Retrospective Study at Navodaya Medical College, Raichur

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How to cite this article:
Rita D, V Himaja. Low Dose Vaginal Misoprostol in the Mangement of Intrauterine Fetal Death: Two Years Retrospective Study at Navodaya Medical College, Raichur. Indian J Obstet Gynecol. 2020;8(4):237–241.

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Abstract

Introduction: Management of intrauterine fetal death (IUFD) poses dilemma for obstetrician.[1] Options for health care are either to await for spontaneous labour or to induce labour.[2] Medical consequences of postponing delivery can be significant in view of complications like disseminated intravascular coagulopathy or haemorrhage and even maternal death.

Aims and Objectives: To evaluate effectiveness and side effects of repeated vaginal administration of small doses of misoprostol in termination of second and third trimester pregnancies.[1]

Methods: This study carried out on 100 women with IUFD in second and third trimester pregnancies collected from NMC Medical college, RAICHUR, from October 2017 to October 2019. Patients history taken, physical examination, Bishop scoring assessed. 25µg of misoprostol in the posterior fornix of vagina was placed every 4th hourly over 24 hours. The progress, and outcomes were assessed.

Results: The success rate was 92.76% and 64.52% in women with third and second trimesters respectively. The mean induction-delivery interval was 15.67+9.64 and 24.94+8.23. The induction delivery interval correlated negatively with the duration of gestation age. The mean value x of total required dose of misoprostol was 192.42 +128.99 and 361.29 + 139.92 for 2nd trimester and 3rd trimester women.

Conclusion: Low dose Misoprostol appears safe, effective, practical and inexpensive method for termination of third trimester pregnancies compared to second trimester pregnancies complicated with intrauterine fetal death and its effects increases with duration of gestation.

Keywords: DIC; Haemorrhage; Intrauterine fetal death; Induction of labour; Misoprostol.

Introduction

The management of intrauterine fetal death (IUFD) poses a dilemma for obstetrician confronted.[1] The frequency of IUFD with a retained fetus varies but is estimated to occur in 1% of all pregnancies.[2] Significant number of these patients will spontaneously go into labour with in several weeks, many do not.[1] The options for health care are either to await onset of spontaneous labour or to induce labour.[2] In cases of intrauterine fetal death with a retained fetus, the choice to induce labour in a patient with ripe cervix is straightforward and procedure often uncomplicated. But the complexity in medical management increases significantly when the cervix is unripe or unfavorable (Bishop Score< 6). Inducing labour in a pregnant woman with an unripe cervix is associated with failed induction of labour and a higher risk of caesarean delivery.[2]

The medical consequences of postponing delivery can be significant[1] in view of complications like disseminated intravascular coagulopathy (DIC), haemorrhage,[3] maternal death and amniotic embolism.

Misoprostol, a synthetic analogue of prostaglandin E[14,5,] is effective and inexpensive, stable at room temperature, easy to administer and bring about cervical changes and uterine contractions[4] for labour induction. The vaginal route is advantageous because peak levels are reached slowly and sustained for long and associated with fewer side effects. Hence vaginal route is more effective than the oral route.[1]

Aims and Objectives

To evaluate the effectiveness and side effects of repeated vaginal administration of small doses of misoprostol in termination of second and third trimester pregnancies complicated with IUFD.

Different Routes of Administration

Route of administration start of effect (min) Maximum effect (min)

Oral	7.8±3.0	25.5±5.0
Vaginal	20.9±5.3	46.3±20.7

Materials and Methods

Source

The study population consists of 100 pregnant women with IUFD admitted in NMC Medical College, RAICHUR from Oct 2017 to Oct 2019 during which the data was collected and subjected to statistical analysis.

Method of Collection

Before collection of data, ethical committee clearance and Counseling the patient and obtaining written consent.

All cases would be subjected to

- History taking, general, clinical examination, and ultrasound examination.
- The induction regimen includes application of misoprostol 25 ug tablet in the posterior fornix of the vagina every 4 hours (upto 6 doses) after determination of Bishop score.
- If the first dose does not lead to effective contractions the subsequent dose could be doubled to 50 ug to 100 ug after 4 hours.
- If no efficient regular uterine contractions occurred after 6 doses, augmentation of uterine contractions to be done by with oxytocin drip, 4 hours after last misoprostol dose.[1]
- Recording the total dose of misoprostol received and the need for surgical interference to remove the dead fetus or the retained placenta or both.
- The induction trial was considered successful when induction delivery interval was less than 24 hours.
- Failure of delivery within 24 hours is considered "failed trial' but its not the indication to stop the trial i.e. the trial will be completed till termination.
- Observation of patients for 24 hours after delivery.
- Any complication during induction and 24 hours after delivery were reported.

Inclusion Criteria

- Patient with IUFD with gestational age from 13 weeks to term, absent spontaneous labour pain and bishop cervical score < 9.
- Patients with IUFD with gestational age from 13 weeks to term in spontaneous labour with Bishop cervical score > 6.
- Group-I: Pregnancies from gestational age 13 weeks to 26 weeks (2nd trimester) complicated with IUFD as documented by USG examination.
- Group-II: Pregnancies beyond 26 weeks of gestational age (3rd trimester) complicated with IUFD as documented by USG examination.

Exclusion Criteria

1. Contraindications to misoprostol induction: Allergy to prostaglandins.
2. Contraindications to vaginal delivery such as: Placentaprevia, Transverse Lie, CPD
3. IUFD with complications like DIC, amniotic embolism, shock.
4. Previous LSCS or any other uterine surgeries like hysterotomy.

Modified Bishop score

Score	0	1	2	3
Dilatation of cervix (cms)	Closed	1-2	3–4	>4
Length of cervix (cms)	4	2–4	1–2	<1
Position of cervix	Posterior	Mid	Anterior	–
Consistency of cervix	Firm	Average	Soft	–
Station of presenting part	–3	–2	–	–1/0+1/+2

Total score: 13, Favorable score: 6–13, Unfavourable score: 0–5.

Duration of Study- 2 Yrs

Sample Size- 100 Cases

Prior to each dose modified bishop score was assessed. The dosage was repeated every 4th hourly until adequate contraction pattern sets in (establishment of 3 uterine contractions in a period of 10 minutes) or once the cervical dilatation reaches 4 cm, maximum upto 5 doses. After induction, the patients were monitored for signs of labour, when labour ensued, they were closely monitored for maternal vital signs and progress of labour.

Maximum allowable doses were 6. If labour did not ensue even after 4 hours following last dose, induction was stopped and an alternative method of induction used.

The following parameters were noted like number of doses, escalation of doses and in the interval between induction to onset of uterine contraction, induction delivery interval, mode of delivery, maternal complications and adverse effect of medication like fever, diarrhoea, nausea and others.

Tachysystole was defined as more than 5 uterine contractions per 10 minutes.

Results

Table 1: Associated Conditions.

Associated Conditions	Gestational age	
	T2 n(%)	T3 n(%)
Antepartum eclampsia	2 (6.50)	5 (7.20)
Severe PE	4 (12.90)	13 (18.80)
Mild PE	0 (0.00)	1 (1.40)
Gestational hypertension	0 (0.00)	3 (4.30)
Oligohydromnios	0 (0.00)	2 (2.90)
PROM	0 (0.00)	1 (1.40)
Others (abruptio placenta, severe anemia, RH Negative, Anamolous baby	25(80.6)	45(65.2)
Total	31(100%)	69(100%)

There were 29 cases of hypertensive disorders of pregnancy of which 10 cases of abruption placenta. (Table 1)

Table 2: Response to dosage of drug.

No. of doses	Gestational age	
	T2 n(%)	T3 n(%)
1	0(0)	13(18.8)
2	1(3.2)	15(21.7)
3	2(6.5)	13(21.7)
4	10(32.3)	12(17.4)
5	7(22.6)	7(10.1)
6	11(35.5)	9(13.0)
Total	31(100.)	69(100.0)
Mean±SD	4.80±1.10	3.17±1.65

T value=1.14; P value=0.012 (<0.05)(HS).

This table shows the distribution of cases according to the required number of doses of Misoprostol for induction by vaginal route. Majority of the cases in T2 group needed 6 doses whereas majority in T3 group needed 1–3 doses, with a mean of 4.80+1.10 and 3.17+1.65 respectively which is highly significant with a p value of 0.01. (Table 2)

Table 3: Induction delivery interval (IDI) in relation to parity.

IDI (hrs)	Primi n(%)	Multi n(%)
1–10	20	9
	40.0	18.0
11–20	17	18
	34.0	36.0
21–30	9	15
	18.0	30.0
31–40	1	7
	2.0	14.0
>40	3	1
	6.0	2.0
Total Mean±SD	50	50
	100.0	100.0
	16.70±10.38	20.38±9.65

Chi square=11.201; P value=0.024(<0.05)(S).

The induction delivery interval in primigravida was lesser compared to multigravida with a mean of 16.70±10.38 and 20.38±9.65 respectively. (Table 3)

The p value is 0.024 which is significant.

Table 4: Success rate and Failed Induction.

Gestational age	Failed induction n(%)	Success rate n(%)
T2	11	20
	35.48	64.52
T3	5	64
	7.24	92.76
Total	16	84

The failed induction in second trimester is 35.48% whereas in Third trimester it is 7.24%. Hence the success rate in 2nd trimester is 64.52% whereas in 3rd trimester, it is 92.76%. (Table 4)

In these failure cases, alternative methods of induction were used.

- Out of 100 cases, 31 patients belong to 2nd trimester and 69 belonged to 3rd trimester. Of this majority within 21 to 25 years with range of 18–35 years.
- Majority of the cases belonged to 3rd trimester in both primi and multigravida.
- 70% of the cases in T2 needed increased dosage upto 100 µgm, whereas in T3 group only few cases needed increase in dosage upto 50 µgm. Majority didnot need any escalation of dosage and delivered with 25 µgm alone.
- Induction delivery interval (IDI) in relation to gestational age is insignificant but with parity it is significant(p , 0.05) (Table 4).
- All women delivered vaginally.
- Failed induction in second trimester is 35.48% whereas in Third trimester it is 7.24%. The success rate in 2nd trimester is 64.52% whereas in 3rd trimester, it is 92.76%. In failure cases, alternative methods were used.
- Side effects like fever are seen in 15 cases (26.9%), Nausea, Vomiting in 11 cases (23.04%), diarrhoea in 2 cases (2.8%). Maternal complications like Tachysystole occurred in 5 12.4%. adverse effects are more in 3rd trimester than 2nd trimester group.

Discussion

The mean induction to vaginal delivery interval was 24.94+8.23 in T2 group as compared to 15.67+9.64 in T3 group which is statistically significant. This is consistent with the above mentioned studies. The inverse relationship between gestational age and induction delivery interval has been confirmed in this study. Significant negative correlation between gestational age and induction pain interval, induction delivery interval and total required dose of Misoprostol is well established in this study which correlates with studies of El-Gharib et al, Nakintu et al, Shetty et al etc.

Studies have demonstrated that, the optimal intravaginal dose of Misoprostol is 25 µg taken every 4–6 hours. Higher doses or Shorter dosing intervals are associated with a higher incidence of side effects and complications like Tachysystole/ Hyperstimulation syndrome.

The current investigation was conducted to assess the effectiveness of vaginal Misoprostol in termination of second and third trimester pregnancies complicated with IUFD. The mean and total dose of Misoprostol used in T3 group is lesser compared to T2 group.

Induction pain interval in relation to parity in primi (9.68±7.20) is lesser than multi (14.8±8.82).

Inverse relation between gestational age and induction pain interval is well Established which is comparable with EL-Gharib et al and carlan et al7 (T2 – 9.6±7.20), (T3–14.58±8.82).

Induction delivery interval in primigravida (16.70±10.38) is lesser than multigravida (20.38±9.65) which correlates with the study of Pak Chung Ho et al.[6]

Inverse relationship between gestational age and induction delivery interval (Table 5).

The success rate was 92.76 % in T3 group compared to 64.52% in T2 group which is

Table 5: Induction delivery interval (IDI) in relation to gestational age

Student and year	T2			T3		
	No. of cases (n)	Total dosage (µg)	IDI (hrs)	No. of cases (n)	Total dosage (µg)	IDI (hrs)
E1-Gharib et al (2001)	160	150–275	30±8.25	164	100–175	21.05±3.63
Nakintu N et al (2001)	60	200–750	23.3	60	100–200	12.4
Shetty et al (2001)	–	–	–	95	100–250	10.68±8.10
Nyende et al (2004)	–	–	–	20	200–400	13.5±8.3
Ezechi OC et al (2004)	–	–	–	37	100–400	14.18±5.30
Eray Caliskan et al (2005)	51	741±413 (mean)	10.68±6.34	–	–	–
Present study	31	150–450	24.94±8.23	69	25–250	15.67±9.64

statistically significant. This proves that as the gestational age advances there is shorter induction delivery interval. This result agrees with that of El – Gharib and Bugalho et al.[8]

The oxytocin augmentation in 3rd trimester (23.18%) is significantly higher than 2nd trimester (3.22%) group in this study. This is contradictory to the study of El Gharib and others.

Incidence of adverse effects is more in 3rd trimester (30.24%) group than in 2nd trimester (22.5%) group. Upto 80 % of these cases in both T2 and T3 groups had an induction delivery interval of >20 hours and the total dose of Misoprostol administration was more than 300 µg. The study of El–Gharib et al says that all side effects occurred after an induction delivery interval of ≥ 34 hours. The study of Caliskan et al says that side effects occurred after a total dose of 400 µg of Misoprostol which correlates with the present study.

Tachysystole was observed in 2.8% of cases in T3 group whereas 9.6% cases in T2 group. The total dose required for T3 and T2 groups were 25–150 µg and 150–450 µg of Misoprostol respectively. This shows that tachysystole occurred when total dose of Misoprostol is increased.

All patients in this study delivered vaginally. For all failed induction cases, alternate method of induction mostly oxytocin was used.

The success rate was lesser in T2 group as compared to T3 group which is statistically significant. This indicates that as the gestational age advances, prompt response to low dose Misoprostol is seen.

Placenta in all the cases expelled completely.

Conclusion

The present study concludes that low dose Misoprostol is a safe, effective, practical and inexpensive method for termination of 3rd trimester pregnancies compared to 2nd trimester pregnancies complicated with intrauterine fetal death. The effect of Misoprostol increases with duration of gestation.

Abbreviations

IUFD-Intrauterine fetal death,

T2-Second trimester,

T3-Third Trimester.

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