Role of Misoprostol in Induction of Labor: Sublingual versus Vaginal in Tikrit City

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Received 12/2/2012 Accepted 23/5/2012

Abstract

A successful induction of labor leads to vaginal delivery of a healthy baby, in an acceptable time frame with minimum maternal discomfort or side effects. To compare the efficacy and safety of sublingual and per vaginal 25µg misoprostol for labor induction. Primary outcome measures were the number of cases delivering vaginally, Secondary requirement, the incidence of meconium-stained liquor, number of cesarean deliveries, the incidence of hyperstimulation/tachysystole, maternal adverse effects and neonatal outcomes. A prospective study was conducted in Tikrit Teaching Hospital. Indications were reviewed; 416 women randomly received misoprostol 25 µg vaginally and sublingually every three hourly for maximum three doses. Outcomes were analyzed accordingly. The number of the cases who successfully delivered vaginally was greater in the sublingual group. The induction to vaginal delivery interval was significantly shorter in sublingual group. The incidence of tachysystole and meconium-stained liquor were more in the vaginal than in the sublingual group. The mean doses, mode of delivery, oxytocin augmentation and maternal outcomes were significantly favorable in sublingual group. No significant difference is seen in neonatal outcome. Sublingual misoprostol 25 µg administered three hourly for labor induction has better effficacy as compared to 25 µg of vaginal misoprostol.

Key words: Misoprostol, tachysystol, meconium stained liquor, cervical ripening

Introduction

In the modern era of day-care obstetrics, a smooth timely delivery and return to the routine activity is desired by everyone with the wide acceptance of active management of labor. The concern over the problem of labor induction has justifiably grown over the year. Induction of labor near term is required in 10-20% of women. Medications that ripen the cervix within a short period of time play an important role in modern obstetrics. A successful induction of labor leads to vaginal delivery of a healthy baby, in an acceptable time frame with minimum maternal discomfort or side effects.[1] A timely induction is advantageous both to the obstetrician as well as the patient. Induction of labor means initiation of uterine contraction (after the period of viability) by any method medical, surgical or combined for the purpose of achieving vaginal delivery. It is done with aim of achieving vaginal delivery whenever, the continuation of pregnancy presents a threat to the life or well-being of the mother and her unborn child. Before induction one must ensure the gestational age as well as the pulmonary maturity of the fetus. Rarely, preterm induction may have to be done. Modern obstetrics techniques have greatly increased the safety and reliability of induction of labor so that it can be performed with greater confidence of success. The transition from pregnancy to labor is a gradual process marked by prelabor changes such as increased uterine contractility and cervical ripening. A ripe soft cervix requires a lower quantum of uterine work compared to an unripe hard and rigid one.[2] The drugs commonly available for the purpose of induction of labor are oxytocin, dinoprostone gel and recently misoprostol. Misoprostol, the most fascinating synthetic prostaglandin E_1 analog has recently been the focus of attention amongst various labor inducing agents. Misoprostol was originally made for the healing of gastric ulcers induced by nonsteroidal anti-inflammatory drugs (NSAIDs).[3,4] They also potentiate the action of oxytocin on the myometrium. Prostaglandins act as the ultimate uterine stimulant. Unlike spontaneous labor, induction of labor carries the possibility of uterine hyperstimulation, rupture and fetal distress.[5] Labor induction with misoprostol has become an intensely investigated subject. The present study aims to evaluate, the comparison between sublingual tablets 25 µg of misoprostol versus vaginal 25 µg of misoprostol in cervical ripening and induction of labor.

Subjects and Methods

The present study was carried out in Tikrit Teaching Hospital from September 2009 to August 2010 on 416 pregnant women having indication for induction of labor. They were selected randomly for preinduction cervical ripening and induction of labor either with 25µg of sublingual versus vaginal 25 µg of misoprostol.

Women enrolled in the study fulfilled the following inclusion criteria:

- Singleton pregnancy at gestational age 37 weeks or more
- Obstetrics indication for induction
- Vertex presentation
- Unfavorable cervix (Bishop's score < 6)
- No cephalopelvic disproportion
- No history of bronchial asthma, glaucoma, serious cardiovascular disorders, renal diseases, metabolic or endocrinal disorders or allergy to misoprostol
- Nulliparous and multiparous women (parity < 5)
- Reassuring fetal heart tracing (since admission)
- Intrauterine death

The patients with the following clinical history or findings were excluded from the study:

- Transverse lie or presentation other than cephalic
- Previous operation on uterus
- Known hypersensitivity to prostaglandins
- Placenta previa, abruption or unexplained vaginal bleeding
- Patient with known hemoglobinopathy
- Grand multiparity
- Significant fetal or maternal conditions that make induction necessary under continuous monitoring (e.g., sever pre-eclampsia, sever IUGR), renal or hepatic dysfunction.

Among 416 women enrolled, 208 women received sublingual tablet and 208 women received vaginal misoprostol.

Pre-treatment Data

Cases were randomized into two groups: Group I (sublingual) and Group II (vaginal). The following procedure was adopted:

- A written consent of patient
- A thorough physical examination
- Complete obstetrical examination which included:
  - Per abdomen examination
  - Fetal heart rate was auscultated every hour throughout the 1st stage of labor and every five minutes during the 2nd stage of labor.
  - Uterine contraction was monitored every 30 minutes.

Hemoglobin, blood group, urine analysis were done in the all patients. Subsequent doses were given after every three hours till the patient developed adequate uterine contractions, the cervical dilatation reached ≥4 cm and spontaneous rupture of membranes or up to maximum of three doses. Vaginal examination was done every three hours Oxytocin augmentation was commenced six hours after the last dose of misoprostol if the patient was not yet in established labor after artificial rupture of membranes[ARM], using an standard oxytocin regime of 1, 2, 8. 16 U in 500 ml of 5% dextrose at 15, 30, 60 drops per minute (2, 4, 8, 6 and 32 mU 64 m% per minute, respectively) increments at 20-minute intervals.Adverse effects (like nausea, vomiting, etc.) if present were noted and treated accordingly. All events of labor were graphically recorded in the form of Partogram. Failed induction was considered when no progress following three doses misoprostol, ARM and oxytocin drip acceleration. If labor in active phase did not end within 12 hours spontaneously it was considered as failure to progress and other methods of termination of pregnancy were looked for. Fetal outcome in terms of live or stillbirth, weight, Apgar scoring at one minutes and five minutes, etc. were recorded. Both mother and the baby were observed for at least 48 hours. The results were represented as statistically modified ' t ' test.

Results and Discussion

In the present study, 170 (81.74%) patients in the sublingual group and 162 (77.89%) patients in vaginal group level were in the age group 20-25 years. Also, 112 patients in the sublingual group and 107 patients in the vaginal group were primigravida; 96 patients in sublingual group and 101 patients in the vaginal group were multigravida. Our results show that in equivalent doses, the sublingual route of administration of misoprostol resulted in shorter induction to labor interval (Table 1). Labor was established within six hours in 78.85% of patients in sublingual group and 63.47% patients in vaginal group. Sublingual misoprostol was more effective than vaginal

misoprostol in inducing labor. This clinical observation is strengthened by the study of Zieman et al who found a maximum plasma concentration at 34 minutes after oral dosing and 80 minutes after vaginal administration by misoprostol.[6]

Medication-delivery Interval

In the present study, 62.5% patient in the vaginal group and 75% in the sublingual group delivered within 12 hours. It was statistically significant (Table 2). The mean induction to delivery interval was less in the sublingual group compared to vaginal group. The mean induction to delivery interval was less in sublingual than vaginal group in study by Bennett.[7]

Doses

Majority of cases (134) in sublingual misoprostol group delivered with one dose of misoprostol compared to 102 of cases in vaginal group, which is statistically significant. This may be because of the systemic bioavailability of sublingual administrated misoprostol, which avoids first-pass metabolism. Vaginal secretions also decrease the local effect of vaginal route.

Mode of delivery

In the present study, there is significant difference in mode of delivery in either group; 19.71% of sublingual group and 34.62% of vaginal group required abdominal delivery and 80.28% in sublingual group and 65.38% in vaginal group delivered vaginally (Table 3). In one study, 152 women were analyzed. Eighteen out of 73 patients in sublingual group versus 28 out of 79 patients in vaginal group had cesarean deliveries. The sublingual route was associated with slightly fewer cesarean section.[8] Mode of cesareans in vaginal group were due to fetal distress (19%) compared to 12% in sublingual group. Higher incidence of fetal distress in vaginal group was due to higher rate of hyperstimulation, which requires a more cautious approach in the vaginal administration of misoprostol group.***Pre-induction Bishop Score:*** In the present study, it was comparable in both groups.

Tachysytole and Hyperstimulation

In the present study, tachysystole and hyperstimulation developed in 32 (15.4%) patients in the sublingual group and 76 (36.54%) in the vaginal group. Sublingual misoprostol mimics the efficacy of the vaginal route by having a similar pharmacokinetic profile, while causing less hyperstimulation by avoiding the cervical effects.[9] In the study done by Shetty et al, there were five tachysystoles and 14 hyperstimulations in the vaginal group and two tachysystoles and 8 hyperstimulations in the sublingual group.[10]

Meconium-stained Liquor

There were 38.46% cases of meconium-stained liquor in the vaginal group compared to 21.15% in the sublingual group which may be due to the higher incidence of hyperstimulation and tachysystole in the vaginal group (Fig. 1).

Oxytocin-augmentation Requirement

In the present study, oxytocin was required more commonly in the sublingual group (n=62; 29.8%) than in the vaginal group (n= 104; 50%) (Fig. 1).

Maternal complications

In the present study, maternal side effects were more in the vaginal group; 29.94% in the vaginal group and 14.57% in the sublingual group had adverse effects of misoprostol (Fig. 1). According to Carlan 2002,[8] maternal complications were significantly more in vaginal group.

Neonatal Outcomes

In the present study, there were no significant differences in the Apgar score at 1- or 5-minute and passage of meconium in either group, Neonatal admissions were more in the vaginal group (24%) as compared to sublingual group (19%). Hyperbilirubinemia was observed in nine neonates in vaginal group and seven in sublingual group. Septicemia was seen in eight neonates in vaginal group and 6 neonates in sublingual group. Apgar score was <7 at 1-minute in 4 patients in sublingual group and in six neonates in vaginal group. Apgar score was <7 at 5-minute in six neonates in sublingual group and 8 neonates in vaginal group. Meconium aspiration syndrome was observed in 16 neonates in sublingual group and 18 neonates in vaginal group. In the study by Carlan-2002,[8] 11 cases in the sublingual and 10 in pervaginal group had neonatal complications (p=0.67). Recent studies have found that sublingual administration of misoprostol is very effective for induction of labor.[11-17]

Table (1):- Distribution of Patients According to Medication to Pain Interval (In Minutes).

Duration	Sublingual group(n=208)	Vaginal group(n=208)
Total Interval	1,597.96±813.16	1,954.14±924.7

Table (2):- Distribution of Numbers of Patients Treated According to Medication to Delivery Interval.

Delivery Interval (hours)	Sublingual group(n=208)		Vaginal group(n=208)	
	No.	%	No.	%
<12	156	75	130	62.50
12-24	28	13.46	36	17.31
>24	24	11.54	42	20.19
Total	208	100	208	100

Table (3):- Distribution of Patients According to Mode of Delivery.

Mode of Delivery	Sublingual group(n=208)		Vaginal group(n=208)	
	No.	%	No.	%
Vaginal	167	80.28	136	65.38
Abdominal	41	19.71	72	34.62
Total	208	100	208	100

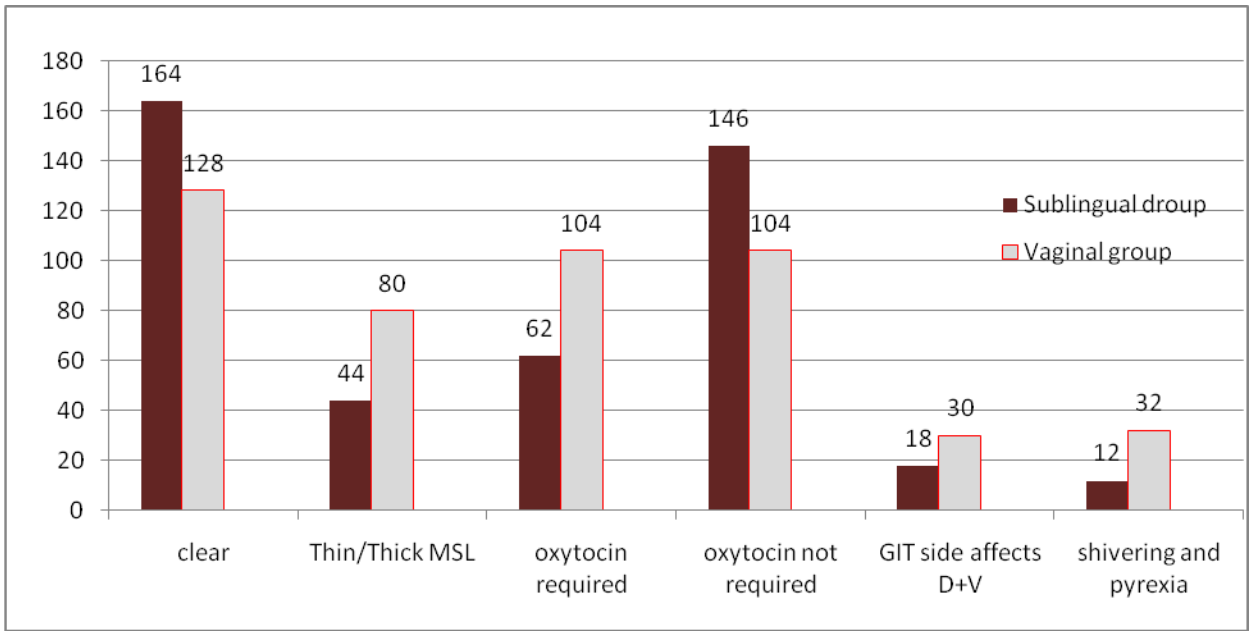

Figure (1): Number of patients according to color of liquor, oxytocin requirement and mental adverse effects in sublingual and vaginal group.
D+V= Diarrhea+ Vomiting

Conclusion

The aim of the study was to compare safety and efficacy of 25µg sublingual misoprostol versus vaginal misoprostol for preinduction cervical ripening and induction of labor. The following conclusions were drawn:

- There was a significant difference in medication established labor interval in both groups. The average interval from start of induction to established labor was shorter in sublingual than vaginal group.
- The response to a single dose of misoprostol was more in the sublingual group (n=134) than the vaginal group (n=102).
- The incidence of maternal complications like diarrhea, nausea, shivering and pyrexia were more in the vaginal (28.74%) as compared to the sublingual group (14.57%).
- There was no significant difference in neonatal outcome in either group.

To conclude, misoprostol is a promising drug for labor induction. Sublingual misoprostol is better than when used vaginally.

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