Original Research Article

Misoprostol and Oxytocin in induction of labor

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Abstract

Background: Induction of labor is defined as the process of artificially stimulating the uterus to start labor. It is usually performed by administering oxytocin or prostaglandins to the pregnant woman or by manually rupturing the amniotic membranes.

Objective: Main objective of the study was to find out are there any differences in maternal and neonatal / fetal outcomes after induction labor with misoprostol and oxytocin beyond 37 weeks of gestation.

Materials and methods: This was a hospital-based study carried out in 431 inductions of labor during the study period. Total 327 women met the criteria and were enrolled into study. Misoprostol of 25 µg was inserted in posterior fornix of vagina or oxytocin infusion was started from 2.5 units on whom induction was decided. Maternal and fetal/ neonatal outcomes were observed. Collected data were analyzed using SPSS and MS Excel.

Results: Analysis of onset of labor led to the finding that mean onset of labor was much rapid in oxytocin (7.2 h) than misoprostol (12.7 h). However, there is similarity in induction–delivery interval in both groups. Overall, the rate of normal delivery and caesarean section was found to be 64.8% and 38.2%, respectively. Fetal distress was found as the most common reason for caesarean section. The overall occurrence of maternal complication was found to be similar in misoprostol and oxytocin groups, nausea/vomiting being the most common complication followed by fever. Besides this, the most common neonatal complication found in overall cases was meconium stained liquor.

Conclusion: It was found that misoprostol was used most frequently for induction of labor compared to oxytocin. The onset of labor was found to be rapid in oxytocin than misoprostol. However, the occurrence of side effects was found to be similar in both misoprostol and oxytocin groups.

Key words

Fetal outcome, Induction of labor, Maternal outcome, Misoprostol, Neonatal outcome, Oxytocin.

Introduction

There were 25,642,200 births in India in 2012 [1]. Four million women give birth each year in the United States with more than 20 percent of them undergoing an induction of labor [2]. There were 698,512 live births in England and Wales in 2013. More than one in five births followed labor induction [3]. As such, induction is one of the most common procedures performed during a woman's pregnancy. Despite this, the fastest and most effective method of inducing labor is unknown [4, 5].

Induction of labor is defined as the process of artificially stimulating the uterus to start labor. It is usually performed by administering oxytocin or prostaglandins to the pregnant woman or by manually rupturing the amniotic membranes [4].

Over the past several decades, the incidence of labor induction for shortening the duration of pregnancy has continued to rise. In developed countries, the proportion of infants delivered at term following induction of labor can be as high as one in four deliveries. Unpublished data from the WHO Global Survey on Maternal and Perinatal Health, which included 373 health-care facilities in 24 countries and nearly 300 000 deliveries, showed that 9.6% of the deliveries involved labor induction. Overall, the survey found that facilities in African countries tended to have lower rates of induction of labor (lowest: Niger, 1.4%) compared with Asian and Latin American countries (highest: Sri Lanka, 35.5%) [4].

Over the years, various professional societies have recommended the use of induction of labor in circumstances in which the risks of waiting for the onset of spontaneous labor are judged by clinicians to be greater than the risks associated with shortening the duration of pregnancy by induction. These circumstances generally include gestational age of 41 completed weeks or more, prelabor rupture of amniotic membranes, hypertensive disorders, maternal medical complications, fetal death, fetal growth restriction, chorioamnionitis, multiple pregnancy, vaginal bleeding and other complications. Although currently available guidelines do not recommend this, induction of labor is being used more and more at their quest of pregnant women to shorten the duration of pregnancy or to time the birth of the baby according to the convenience of the mother and/or health-care workers [6, 7].

During induction of labor, the woman has restricted mobility and the procedure itself can cause discomfort to her. To avoid potential risks associated with the procedure, the woman and her baby need to be monitored closely. This can strain the limited health-care resources in under-resourced settings. In addition, the intervention affects the natural process of pregnancy and labor and may be associated with increased risks of complications, especially bleeding, caesarean section, uterine hyper stimulation and rupture and other adverse outcomes [8].

There is a broad range of methods available for induction of labor. The choice of method may depend on national guidelines and local protocol, as well as individual clinical factors. The advantages and disadvantages of different methods vary [9].

From a clinical perspective, the decision about which method to use for induction of labor can be influenced by the woman's readiness for

labor, for example whether or not membranes have ruptured spontaneously or whether or not the cervix remains undilated at the start of the induction process. Different methods used for inducing labor have different mechanisms of action, and vary in terms of how quickly birth is achieved and the likelihood of causing complications in women with different clinical characteristics. Thus, the choice of method will take into account the reason for induction and its urgency. The woman's obstetric and medical history is also considered. For example, there is evidence that women may be more sensitive to drugs that stimulate the uterus if they have had a previous birth, and women who have a scar from a previous caesarean birth are at increased risk of uterine rupture, which can result in hysterectomy and fetal death [9].

General principles related to the practice of induction of labor [4]:

- Induction of labor should be performed only when there is a clear medical indication for it and the expected benefits outweigh its potential harms.
- In applying the recommendations, consideration must be given to the actual condition, wishes and preferences of each woman, with emphasis being placed on cervical status, the specific method of induction of labor and associated conditions such as parity and rupture of membranes.
- Induction of labor should be performed with caution since the procedure carries the risk of uterine hyper stimulation and rupture and fetal distress.
- Wherever induction of labor is carried out, facilities should be available for assessing maternal and fetal well-being.
- Women receiving oxytocin, misoprostol or other prostaglandins should never be left unattended.
- Failed induction of labor does not necessarily indicate caesarean section.
- Wherever possible, induction of labor should be carried out in facilities where caesarean section can be performed.

Different methods also have different direct costs, and some methods require continuous monitoring of the woman throughout labor. Women may wish to experience a natural onset of labor, and there is evidence that an induced labor can have a negative impact on their overall experience of childbirth.8 Some methods of induction are painful or unpleasant, and some are associated with distressing side effects, such as headache or nausea. Women may also have preferences about which method is used and may prefer non-pharmacological approaches. On the other hand, women will want their baby to be born safely, and timely induction may improve outcomes for women and babies.5 Women facing decisions about induction of labor require up-to-date information about the range of options available, including alternative and complementary methods [9].

For an induction to be successful, the cervix needs to have undergone the changes that will ensure the uterine contractions are effective in the progressive dilation and effacement of the cervix. Assessing the ripeness of the cervix is done by means of a scoring system devised by Bishop in 1964. Induction is carried out by oxytocin in case cervix is favorable, that is, Bishop score of 6 or more, whereas in case the cervix is unfavorable, then usually a PG is placed in vagina or cervix to ripen the cervix to initiate the uterine contraction [10].

PGs have been used for IOL since 1960s. The most effective agent found is intravaginal or intracervical prostaglandin-E (PGE). PGs improve the rate of normal delivery and lower the rate of caesarean section. In comparison to other PGs, misoprostol is found to be cheap, widely available, stable at room temperature and has few side effects. Oxytocin is widely used for IOL, alone or in combination with other agents. Risks associated with the use of oxytocin infusion include fetal hypoxia and asphyxia,

uterine rupture, fluid retention, PPH and amniotic fluid embolism [10].

Materials and Methods

This was a hospital-based observational study which was carried out at P.K. Das Institute of Medical Sciences, Vaniyamkulam, Kerala during the period from August 2016 to January 2018 for a period of 6 months. The sample population for the study was those patients in whom IOL was decided after admission in the hospital for delivery.

Inclusion and exclusion criteria

Inclusion criteria

Included patients who were at least 18 years of age with a full term (≥37 weeks), singleton gestation in cephalic presentation. Both nulliparous and multiparous women were included. Women were required to have intact membranes, a Bishop score of ≤6 and cervical dilation ≤2cm to be eligible. Women with HIV, and women with medical conditions requiring an assisted second stage were also excluded.

Exclusion criteria

Excluded patients with grand multiparity (>5 deliveries), women with previous lower segment cesarean section (LSCS), antepartum hemorrhage and prelabor rupture of membrane (PROM).Women were excluded if there was a contraindication to a vaginal delivery or to misoprostol, fetal demise, or major fetal anomaly.

Data collection tools

Structured questionnaire and patient's record file was used as a tool for collection of information. Bishop's scoring and Apgar scoring system was used to check cervix status and neonatal outcome, respectively.

Data collection technique/ methods

Before administration of drugs, women were asked to empty the bladder. Bishop's scoring was done. In case of IOL with misoprostol, 25 μg was inserted in the posterior fornix of the vagina. Doses of 25 μg were repeated every 6 h according to the requirement of the patient with maximum up to two doses.

In case of IOL with Oxytocin infusion was started from 5 units given with 500 ml of normal saline at 10 drops per minute. The rate was increased by 10 drops per minute in every 30 min. This was done until a good contraction pattern (three contractions in10 min each lasting >40 s) was established maximum up to60 drops per minute. Uterine contractions (for10 min) and fetal heart rate (for 1 min) were monitored hourly by staff nurses. Fetal Heart Sound (FHS) was monitored every 30 min in case of infusion of Oxytocin.

All eligible women were observed for the occurrence of any side effects (vomiting, diarrhea, pyrexia, tachycardia, tachysystole, hyper stimulation and uterine rupture). After delivery, neonatal condition was observed. Finally, overall maternal and neonatal outcomes were recorded. Collected data were compiled, managed, analyzed and presented using Statistical Package for Social Sciences (SPSS) software and MS Excel. As this was a non-randomized observational study in which the method of IOL for each woman was determined on clinical grounds, no formal comparisons were made between the treatment groups.

Trained research staff, uninvolved with the clinical care, collected all induction, labor and delivery information, maternal demographics, and maternal and neonatal outcomes.

Ethics Committee

Protocol approval was obtained from institutional ethics committee of P.K. Das Institute of Medical Sciences. An informed consent was obtained from all the subjects before participation in the study.

Results

There were 431 inductions of labor during the study period. And 327 women met the criteria and were enrolled into study.

The majority of the population fell under the age group of 20-25 years (190, 58.4%) followed by 26-30 years (79, 24.3%). Gestational age varied from 37 weeks to 44 weeks, out of which the highest proportion of patients were found in 41 weeks (160, 49%) (**Table – 1**).

Table - 1: Demographic distribution

Table - 1a: Age of Mother

Group	N (%)
Below 20	53 (14)
20-25	190 (58.4)
26-30	79 (24.3)
31-35	5 (3.3)

Table - 1b: Gestational age.

Weeks	N (%)
37	2 (0.6)
38	18 (5.5)
39	16 (5)
40	115 (34.9)
41	160 (49)
42	6 (1.8)
43	5 (1.6)
44	5 (1.6)

Out of 327 patients, 183 (56%) were induced with misoprostol and 144 (44%) were induced with oxytocin (**Table – 2**).

Table - 2: Treatment disposition.

Treatment	N (%)
Misoprostol	183 (56)
Oxytocin	144 (44)

The modes of delivery after induction are depicted in **Table - 3**. After induction, out of 327 cases, the rate of normal delivery was 64.8%, caesarean section 34.2% and vacuum delivery 1%. In both misoprostol and oxytocin groups majority of the women had normal delivery.

It was found that second dose of misoprostol was required in 69 (37.9%) cases (**Table - 4**). Among those, the requirement of additional misoprostol dose was much higher in nulliparous women (n = 56, 40.6%) than in multiparous women.

Table - 3: Modes of delivery.

Mode of delivery	Misoprostol N (%)	Oxytocin N (%)	Total N (%)
Normal	123 (67.3)	89 (62)	212 (64.8)
Caesarean	60 (32.7)	52 (36)	112 (34.2)
Vacuum	0 (0)	3 (2)	3 (1)

Table - 4: Details of additional misoprostol dose.

Is there requirement for additional misoprostol dose	N (%)
Yes	69 (37.9)
No	114 (62.1)
Total	183

Table - 5: Time taken for labor induction.

Induction Method	Sample size (n)	Mean (SD) (h)
Misoprostol	183	12.7 (1.2)
Oxytocin	144	7.2 (0.7)

Table - 6: Induction to delivery time.

Induction Method	Sample size (n)	Mean (SD) (h)
Misoprostol	183	19.1 (2.8)
Oxytocin	144	18.4 (3.2)

Table - 7: Maternal complications.

	Misoprostol n (%)	Oxytocin n (%)
Nausea / Vomiting	18 (41)	13 (45.8)
Diarrhoea	4 (9)	2 (6.9)
Headache	11 (25)	2 (6.9)
Fever	6 (13.5)	8 (27.2)
Shortness of breath (SOB)	1 (2.5)	1 (3.1)
Post-partum hemorrhage (PPH)	4 (9)	3 (10.1)
Overall occurrence, n (%)	44 (24.5)	29 (20.2)

The mean (standard deviation (SD)) onset of action for oxytocin was 7.2 h (0.7 h), whereas it was 12.7 h (1.2 h) for misoprostol (**Table - 5**). Similarly, the mean (SD) induction–delivery interval was found to be 19.1 h (2.8 h) in

misoprostol-given group, whereas it was 18.4 h (3.2 h) in oxytocin-given group (**Table - 6**).

Table - 8: Apgar score.

Induction method	Mean Apgar score (SD)
Apgar score at 2 min	
Misoprostol	5.2 (1.0)
Oxytocin	4.7 (0.6)
Apgar score at 5 min	
Misoprostol	8.2 (0.7)
Oxytocin	7.9 (0.4)

Table - 9: Neonatal complications.

	Misoprostol n (%)	Oxytocin n (%)
Irregular FHR	2 (1.8)	2 (2)
Fetal bradycardia	1 (0.9)	3(3)
MSL	71 (61.9)	59 (58.3)
Suction/ oxygen resuscitation	36 (31.2)	27 (26.7)
Baby unit admission	5 (4.2))	10 (10)
Overall occurrence	115 (63)	101 (70.1)

FHR: Fetal heart rate; **MSL:** Meconium Stained Liquor.

Maternal complications had been observed in more than 20% of patients in both the groups. Nausea and vomiting are the most common complications observed followed by headache and fever. The occurrence and distribution of maternal complications is presented in **Table - 7**.

For neonatal outcome, Apgar score was used. Neonates mean (SD) Apgar score at 2 min was 5.2 (1.0) and 4.7 (0.6) for misoprostol- and oxytocin treated cases, respectively, whereas it was 8.2 (0.7) and 7.9 (0.4), respectively, at 5 min (**Table - 8**). The occurrence and distribution of neonatal/ fetal complications is presented in **Table - 9**. Meconium stained liquor (MSL) was the most frequently encountered fetal complication in patients followed by requirement of suction for resuscitation, baby unit admission, irregular fetal heart rate (FHR) and fetal bradycardia.

Discussion

There is a potential risk for the health of mother and infant if pregnancy continues beyond term and because of which IOL is desired [11]. In a study conducted in Norway, it was found that IOL and post-term pregnancy are the prognostic factors for poor outcome [12]. Even though routine IOL at 41 weeks of gestation is suggested to reduce perinatal mortality, induction is associated with other obstetric complications [13].

From this study it's understood that Misoprostol is more commonly preferred over oxytocin for IOL in our hospital. Misoprostol is safe, cost-effective and easy to administer and store because of which it has become a drug of choice in poor nations, and 25 μg intra vaginal misoprostol has been included in the World Health Organization (WHO) complementary list as drug for IOL [10]. The gestational age of the patient varied from 37 weeks to 44 weeks in our study which is similar to other studies.

Kelly and Tan [14] and Escudero and Contreras [15] reported that oxytocin is an effective method of labor induction. In these studies, the time duration from initiation of induction to delivery was shorter in groups induced with oxytocin, and majority delivered within 24 h after intravenous oxytocin induction. In our study, the mean onset of action for oxytocin was found to be rapid than misoprostol. Furthermore, this study shows that there is not much difference in induction–delivery interval between two drugs. The induction–delivery interval in misoprostol group was similar to another study [16], whereas this differs from other studies where shorter induction–delivery interval was seen in misoprostol than oxytocin.

The overall success rate of normal delivery and caesarean section was found to be 64.8% and 34.2%, respectively. Normal delivery in patients administered only by misoprostol was little higher (67.3%) than oxytocin (62%) group. According to different studies, the incidence of

normal delivery was similar to this study [17, 18]. Most of the other studies [19-23], have found that caesarean section rate was significantly less in misoprostol than other methods for induction. A study reported that though more incidences of caesarean section were encountered with oxytocin, it appeared to be safe [14]. However, another study reported that the incidence of caesarean section was similar in both oxytocin and misoprostol groups, no differences were observed between groups in perinatal and post-partum adverse outcomes and misoprostol use was considered safe [15]. This incidence of caesarean was almost similar in both misoprostol (32.7%) and oxytocin groups (36%) in our study.

Heffner, et al. [24] reported that IOL, age of mother and gestational age over 40 weeks were some factors that increased the risk for caesarean delivery. As we studied different reasons for caesarean section, it was seen that the most common reason for caesarean was found to be fetal distress which is similar to a study [18]. In another study, failed induction was found to be the second highest indication for caesarean like in this study [24].

IOL is not free from unwanted effects. This study indicates that both misoprostol and oxytocin were associated with several complications. Overall, maternal morbidity resulting from misoprostol was found to be nausea/vomiting, diarrhea, headache, fever, shortness of breath (SOB) and PPH with nausea/vomiting being the most common followed by fever. Several studies [25, 26] have reported uterine hyper stimulation and tachysystole with misoprostol, but in this study, no such cases were found. According to different studies, there is less risk of hyper stimulation with lower dose of misoprostol, but it also decreases the effectiveness for labor induction [25-27].

Regarding neonatal outcomes, the overall occurrence of MSL was found to be higher. Other complications seen were requirement of suction for resuscitation, baby unit admission, irregularity in FHR, fetal bradycardia and Apgar score of <7. In this study, very less difference was seen in Apgar score between misoprostol and oxytocin group.

According to Chitrakar [20], a 25 μg intra vaginal misoprostol reduces passage of meconium in fetus and is safe. A study by Hofmeyr and Gülmezoglu [28] also suggests that even though administration of misoprostol increases the passes of meconiumin the fetus, neonatal adverse effect is less even at higher doses.

Thus, we see that the use of misoprostol and oxytocin during IOL is associated with maternal and fetal adverse effects, and we believe that it is the clinician's judgement that determines the safety while minimizing the risks. So, any differences observed between the treatment regimens may also have been influenced by the decision process taken to determine which women underwent each regime. Similarly, this study was a single-centred study. Inclusion of multi-centre data could have made the analysis much more representative.

Conclusion

It was found that misoprostol was the most frequently used rug for IOL as compared to oxytocin in our hospital set up. There is no much difference in induction-to delivery interval within these drugs, whereas the onset of labor was found to be rapid in oxytocin than misoprostol. However, the occurrence of side effects was found to be similar in both misoprostol and oxytocin groups.

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