ORIGINAL RESEARCH

Induction of Labor with Oral Misoprostol vs Oxytocin: A Comparative Study

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Abstract

Objective: To compare the effectiveness of oral misoprostol versus intravenous oxytocin for induction of labor.

Methodology: This was a single-center, prospective comparative study done at a tertiary care academic health center from January 2018 to June 2019, where a total of 266 term pregnant women who were candidates for induction of labor were assessed and selected to enter the study. The women were assigned to one of the two groups according to the mode of induction, oral misoprostol, or intravenous oxytocin. The misoprostol group received 25 µg of oral misoprostol solution every 2 hours for a maximum of six doses, and the oxytocin group received an infusion drip starting from 6 mIU/minute, which gradually increased every 30 minutes up to a maximum of 37 mIU/minute. Women who went into active labor within 24 hours of the first dose in the misoprostol group and 12 hours in the oxytocin group were considered successful induction.

Results: The successful induction rate was more with oral misoprostol than with oxytocin (64.3% vs 58.8%). More women delivered vaginally with oral misoprostol as compared to oxytocin (59.1% vs 50.4%). Induction to active labor time and induction to delivery time was significantly shorter for the oxytocin group than the misoprostol group (5.96 ± 2.59 and 7.75 ± 2.90 vs 10.15 ± 5.66 and 12.53 ± 6.33 hours; *p*-value <0.001).

Conclusion: Oral misoprostol is a safe and effective drug with low complications for induction of labor in women with an unfavorable cervix compared to oxytocin.

Keywords: Induction, Labor, Maternal and perinatal outcome, Misoprostol, Obstetric outcome.

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Introduction

Over the past several decades, the incidence of labor induction for shortening the duration of pregnancy has continued to rise.[1] In developed countries, the proportion of infants delivered at term following induction of labor can be as high as one in four deliveries.[1] Unpublished data from the World Health Organization (WHO) global survey on maternal and perinatal health, which included 373 healthcare facilities in 24 countries and nearly 3,00,000 deliveries, showed that 9.6% of all the deliveries involved labor induction.[1] In Nepal, a study done at Paropakar Maternity and Women's Hospital, the overall induction rate was found to be 7.2%.[2]

Historically, most trials have studied the vaginal route of administration of misoprostol for induction of labor. However, owing to concerns about the risk of uterine hyperstimulation with vaginal misoprostol, more recent trials have focused on studying lower doses of vaginal misoprostol and the oral route for its administration.[3] In 2012, the International Federation of Gynecology and Obstetrics (FIGO) recommended an oral dose of 25 µg misoprostol solution every 2 hours to induce labor, citing the 2011 WHO recommendations for labor induction.[4] The WHO strongly recommended this regimen by rating the quality of evidence as moderate and included data from the 2006 Cochrane Review by Alfrevic and Weeks.[1,5,6]

In 2014, a Cochrane review of oral misoprostol for induction of labor, which included nine trials comparing oral misoprostol with placebo, showed that women using oral misoprostol were more likely to give birth vaginally within 24 hours.[7]

The optimal dosing of misoprostol in oral form with minimal side effects is an important topic of discussion and has been the focus of various studies. The doses and dosing intervals used in the studies vary widely. Considering these differences, the aim of our study was to find the rate of successful induction with an optimal dose of oral misoprostol with minimal side effects. Among the women who delivered vaginally, we also compared the time to achieve vaginal delivery between the oral misoprostol group and the oxytocin group.

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Methodology

This study was an observational prospective comparative study conducted in the Department of Obstetrics and Gynecology at a tertiary care center in Nepal, over a period of 18 months, from January 1, 2018 to June 30, 2019, among women who were candidates for induction of labor and were between 38 and 42 gestational weeks. Ethical clearance was obtained from the Institutional Review Board of the college. Using the standard formula for sample size calculation, taking a confidence interval of 95% and margin of error of 5%, we calculated the sample size to

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be 133 in each of the two groups. The women of age 18–45 years with term singleton pregnancy, cephalic presentation with normal fetal heart rate, and a Bishop's score of 6 or less were included in the study. Those who were unwilling to participate, had a previous cesarean section, antepartum hemorrhage, or cephalopelvic disproportion were excluded from the study.

A total of 485 women were induced in the hospital during the study period, among which 266 women met the inclusion criteria and were assessed. Written informed consent was taken from each participant and confidentiality was maintained. The women were randomly assigned to one of the two groups after randomization was carried out using odd–even number technique. The women who were designated with odd numbers were assigned to group I, who received oral misoprostol as induction agent, and those designated with even numbers were assigned to group II, who received intravenous oxytocin as induction agent.

In the misoprostol group, a tablet of 200 µg from the pharmaceutical company Cipla was dissolved in 200 mL of water and 25 mL was administered every 2 hours until adequate contractions were achieved, or for a maximum of six doses. If contractions did not occur within 12 hours (six doses), no further doses were given and the patients were observed for the next 12 hours. If the patient did not go into active labor within 24 hours of the first dose, they were regarded as failed inductions. Women who had onset of labor within 24 hours but did not enter active labor were augmented with inj. oxytocin 5 U in 500 mL of ringers lactate (RL) in titrating doses after 6 hours of the last dose of misoprostol.

The women in group II received oxytocin 5 U in 500 mL of RL in titrating doses (minimum dose of 10 drops/minute, i.e., 6 mIU/minute and maximum dose of 60 drops/minute, i.e., 37 mIU/minute). In the absence of ideal uterine activity in 12 hours starting from the first dose of administration of the drug, the patients were considered as failed inductions.

The active phase of labor was considered as cervical dilatation of 4 cm or more. At least three, contractions of moderate intensity in 10 minutes were considered adequate.[8] The time taken to reach active labor was recorded and compared between both groups. A successful induction was considered when women in either group went into the active phase of labor within the given time frame, i.e., 24 hours for those induced with oral misoprostol and 12 hours for those induced with intravenous oxytocin. The women who delivered by cesarean section before the designated time, i.e., 24 hours for misoprostol group and 12 hours for oxytocin group due to other reasons such as meconium-stained liquor and fetal heart rate changes, were excluded while calculating the successful induction rate.

The mode of delivery and induction to delivery time was compared between both the groups after excluding the women who went into active labor after 24 hours in the misoprostol group and after 12 hours in the oxytocin group.

The data were analyzed using Statistical Product and Service Solutions (SPSS) software sheet version 22. Variables such as age, Bishop's score, induction to active labor time, and induction to delivery time were presented as means and standard deviations. The comparison of means of numeric data was done using independent sample *t*-test. The comparison of the differences in percentages of categorical data such as parity, gestational week, body mass index, induction to active labor time, induction to delivery time, mode of delivery, neonatal complications, and maternal complications, was done using Chi-square test. A *p*-value <0.05 was considered as statistically significant.

Results

In the final 266 women who were induced and analyzed during the study period, the baseline demographic characteristics and Bishop's score did not differ significantly between the two groups (Tables 1 and 2). It was observed that around two-third of the inductions were done for postdated pregnancy in both groups. Other common indications included intrauterine growth retardation (IUGR)/oligohydramnios, diabetes mellitus, and hypertensive disease of pregnancy. Successful inductions were compared between the two groups after excluding the patients who were delivered by lower segment cesarean section (LSCS) with indications other than failed induction before the assigned time. More women in the misoprostol group had successful inductions as compared with the oxytocin group though the difference was not statistically significant (Table 3).

Table 1: Demographic details of study subjects

	Misoprostol (n = 133)	*Oxytocin (n = 133)*	*p-value*
Maternal age (years)			
<20	2 (1.5%)	5 (3.8%)	0.52
20–24	51 (38.3%)	41 (30.8%)	
25–29	61 (45.9%)	62 (46.6%)	
30–34	16 (12.0%)	20 (15.0%)	
>34	3 (2.3%)	5 (3.8%)	
Mean age ± SD (years)	25.93 ± 3.96	26.04 ± 4.11	0.832
Maternal parity			
0	82 (61.7%)	85 (63.9%)	0.237
1	47 (35.3%)	38 (28.6%)	
2	4 (3.0%)	9 (6.8%)	
3	0 (0%)	1 (0.8%)	
Period of gestation (weeks)			
38	13 (9.8%)	24 (18.0%)	0.12
39	22 (16.5%)	26 (19.5%)	
40	89 (66.9%)	69 (51.9%)	
41	8 (6.0%)	13 (9.8%)	
42	1 (0.8%)	1 (0.8%)	

Table 2: Bishop's score of study subjects

	Misoprostol (n = 133)		*Oxytocin (n = 133)*			
Bishop's score	*Mean*	*Standard deviation*	*Mean*	*Standard deviation*	*t-test*	
	3.68	0.86	3.63	0.80	0.443	0.658

Table 3: Successful inductions

Failed induction	*Misoprostol group (n = 115)*	*Oxytocin group (n = 119)*	*p-value*
Yes	41 (35.7%)	49 (41.2%)	0.385
No	74 (64.3%)	70 (58.8%)	

Table 4: Induction to active labor time

Induction to active labor time (hours)	*Misoprostol group (n = 74)*		*Oxytocin group (n = 70)*			
<6	21 (28.4%)		34 (48.6%)			
>6– <12	25 (33.8%)		36 (51.4%)			
>12– <24	28 (37.8%)		0			
Total	74		70			
Mean onset time of active labor (hours)	*Mean*	*SD*	*Mean*	*SD*	*t-test*	*p-value*
	10.15	5.66	5.96	2.59	5.66	<0.001

Table 5: Induction to delivery time for vaginal deliveries

Induction to delivery time (hours)	*Misoprostol group (n = 68)*		*Oxytocin group (n = 67)*			
<6	14 (20.6%)		21 (31.3%)			
>6– <12	19 (27.9%)		41 (61.2%)			
>12– <24	33 (48.5%)		5 (7.5%)			
>24	2 (2.9%)		0			
Total	68		67			
Mean delivery time (hours)	*Mean*	*SD*	*Mean*	*SD*	*t-test*	*p-value*
	12.53	6.33	7.75	2.90	5.66	<0.001

Table 6: Induction outcome and maternal complications

Mode of delivery	*Misoprostol group (n = 115)*	*%*	*Oxytocin group (n = 133)*	*%*	*p-value*
Normal delivery	66	57.4	67	50.4	0.135
LSCS	47	40.9	66	49.6	
Instrumental vaginal delivery	2	1.7	0	0	
Postpartum hemorrhage	–	–	2	1.5	0.498
Tachysystole/Hyperstimulation	2	1.5	9	6.8	0.031

In all the women who went into active labor, i.e., 74 women in the misoprostol group and 70 women in the oxytocin group, the time to reach active labor was assessed and compared. The mean onset of active labor was 10.15 ± 5.66 hours in the misoprostol group and 5.96 ± 2.59 hours in the oxytocin group, which was found to be significantly less in the oxytocin group (*p*-value <0.001). The mean delivery time in women who had delivered vaginally was 12.53 hours in the misoprostol group whereas it was 7.75 hours in the oxytocin group (Tables 4 and 5).

Out of 133 women in the misoprostol group, 85 women delivered vaginally, including two instrumental deliveries. Eighteen cases out of 133 went into active labor only after 24 hours of the first dose of misoprostol and hence were excluded from the misoprostol-only group (Table 6).

Discussion

The optimal dosing of oral form of misoprostol with minimal side effects is a vital context of discussion and has been focused in various studies, with the doses and dosing intervals used varying greatly. In this study, 25 µg of misoprostol solution was given every 2 hours for a maximum of six doses. WHO, with moderate-quality evidence, recommends the use of 25 µg of oral misoprostol solution two hourly for a maximum of 12 doses citing the Cochrane review in 2006 by Alfrevic and Weeks.[1,6] In 2012, the International FIGO recommended an oral dose of 25 µg of misoprostol solution every 2 hours to induce labor, which was again revised in 2017 with similar recommendations.[4] The doses and dosing interval used in this study for oral misoprostol aimed to decrease the incidences of hyperstimulation and to achieve successful induction with the lowest possible dose. The doses used in this study for oxytocin were according to the high-dose regimen recommendation from American College of Obstetricians and Gynecologists.[9]

The demographic and clinical characteristics of the women in this study, including maternal age, parity, gestational age, and Bishop's score, were comparable between the two groups.

Our study found that there were more vaginal deliveries in patients receiving oral misoprostol as compared with those receiving oxytocin. Also, the vaginal delivery rate increased significantly with oral misoprostol when the labor was augmented with oxytocin after 24 hours. In a study done by Aalami-Harandi et al., they used 12 doses of 25 µg of oral misoprostol and found that the misoprostol-receiving patients had a significantly higher rate of vaginal deliveries at time intervals of 18 and 24 hours during the study period when compared with oxytocin receiving patients.[10]

We observed that the patients receiving oxytocin required significantly less time to enter active labor and deliver when compared to oral misoprostol. When comparing the maternal complications, an increased incidence of hyperstimulation was seen in patients receiving oxytocin. Similar findings were observed by Aalami-Harandi et al. and they concluded that the patients receiving oxytocin took less time to reach active labor compared with patients receiving oral misoprostol.[10]

While comparing the mode of delivery in our study, 59.1% of women receiving oral misoprostol only and 50.4% of women receiving oxytocin delivered vaginally. The vaginal delivery increased to 63.3% in the misoprostol group when augmented with oxytocin. Misoprostol acted as a cervical priming agent in those cases. Asokan and Santhosh, in their study, used titrated oral misoprostol increasing the dose by 12.5 µg every 3 hours from 25 µg onward for a maximum of six doses. They found a significant increase in vaginal deliveries with oral misoprostol as compared with oxytocin.[11] The reason behind a decreased number of vaginal deliveries in our study population as compared with their study with oral misoprostol could be because of the difference in the doses used. The delivery rate could have been increased in our study had we used the dosage recommended by WHO.

Also, we found that the incidence of tachysystole with oxytocin was more when compared with misoprostol. Rouzi et al. reported no incidence of hyperstimulation or tachysystole in their study using 12 doses of 25 µg of oral misoprostol.[12] On the contrary, Asokan and Santhosh and Aalami-Harandi et al. reported an increased incidence of hyperstimulation with misoprostol as compared with oxytocin though the difference was not statistically significant.[10,11]

Conclusion

Based on the results of this study, we found oral misoprostol to be a safe and effective drug for inducing labor in term pregnant women. Oral misoprostol has an increased rate of vaginal delivery as compared with oxytocin. The vaginal delivery rate increases furthermore when oxytocin is added. However, further studies are required to determine the effective dose and dosing interval for this method of induction.

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