Original Article

Misoprostol versus Dinoprostone for induction of labor in PROM: A Randomized Controlled Trial

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Abstract

Objective: To compare the efficacy of misoprostol (PG E1 analog) and dinoprostone (PGE2) for induction of labor in prelabour rupture of membranes (PROM).

Methodology: This randomized controlled trial study was conducted at the Department of Obstetrics & Gynecology, Mardan Medical Complex, Mardan from 1st January 2019 to 30th June 2019. A total of 214 women (107 in each group) presenting with PROM within 72 hours with gestational age between 34 to 41 weeks having 15-45 years of age were included. Group A women received 25 mcg of tablet misoprostol and Group B women received 3mg of dinoprostone placed aseptically in the posterior vaginal fornix. Both groups were followed for 24 hours after the first dose for induction to the delivery interval. Efficacy was considered when induction to the delivery interval was less than 12 hours.

Results: The mean age of women in Group A was 28.89 ± 4.58 years and in Group-B was 26.64 ± 5.80 years. The majority of patients 153 (71.50%) were between 15 to 30 years. The mean gestational age in group A was 38.86 ± 1.03 weeks and in group B, it was 38.97 ± 1.03 weeks. In a group, A 60 patients (56.07%) were delivered in less than 12 hours after induction while in group B, only 37 patients (34.58%) were delivered in less than 12 hours with a highly significant p-value of 0.02.

Conclusion: This study concluded that misoprostol (PGE1 analog) is more effective as well as cheaper than dinoprostone (PGE2) for induction of labor among women with prelabour rupture of membranes (PROM).

Keywords: Dinoprostone. Misoprostol, Prelabour rupture of membranes, PROM, Prostaglandin E_1 analog, Prostaglandin E_2.

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Introduction

Prostaglandins are hormones that are naturally produced in the uterus. Female reproductive system studies with knockout mice have confirmed a role for prostaglandins in reproduction and parturition.[1] They soften the cervix and stimulate contractions in labor.[2]

Misoprostol, a prostaglandin E1 analog, is an inexpensive synthetic prostaglandin. Studies have suggested that vaginal prostaglandin E1 analog is an

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effective agent for cervical ripening and labor induction, particularly in women with unfavorable Bishops score i.e. less than 6. Advantages of misoprostol include its effectiveness in low doses, lower cost, and ease of administration with lesser gastric irritation and above all, it requires no cold chain storage.[3] Prostaglandin E1 analog have been used off-label vaginally, orally, and sublingually since the 1980s for cervical ripening and labor induction.[4,5] A meta-analysis of 62 studies, completed by Hofmeyr et al, found that a PGE1analog, 25-µg tablet placed vaginally every 4hr had similar efficacy to intravaginal or intracervical PGE_2 with regards to delivery time.[5]

Prelabor rupture of the membrane (PROM) at term is defined as spontaneous rupture of the membranes after 37 weeks of the gestations and before the onset of the regular painful uterine contractions.[6]It occurs in about 10% of women beyond 36 weeks of gestation.[7] About 80% of the women at term with PROM go into spontaneous labor within 24-48 hours. Some patients (10-25%) have a latent period of more than 24 hours from PROM to the onset of labor. The chances of infection increase, if the latent period exceeds 24hours.[8]

Early induction of labor not only increases the maternal satisfaction but also helps in decreasing the risk of chorioamnionitis, the need for neonatal antibiotic therapy and neonatal intensive care admission. [9,10] Induction of labor is indicated, when it is agreed that the fetus or mother will benefit from delivery.[11] There is no consensus on the management of women with PROM between 34+ and 37+ weeks. The American Congress of Obstetricians and Gynecologists guidelines recommend induction of labor if PROM occurs at or beyond 34+ weeks of gestation.[12] induction of labor aims to achieve a safe vaginal delivery. The methods which are commonly available for induction are non pharmacological and pharmacological use of drugs like oxytocin and prostaglandins.[13]

In a study conducted by Chaudhuri S et al, the time from induction to delivery was 10.75 hours in the misoprostol group and 9.37 hours in the prostaglandin group while the cesarean section rate did not differ significantly between them (7.61% vs 15.30%).[14] In another study, induction to the delivery interval was less than 12 hours in 50% when induced with prostaglandin E1 (misoprostol) and 33.3% with prostaglandin E2 (dinoprostone).[15]

The present study is designed to compare the efficacy of vaginal prostaglandin E1 and prostaglandin E2 tablets in terms of induction of labor among women presenting with prelabour rupture of fetal membranes. Prelabor rupture of membranes is not uncommon in our population and prompt response to its treatment in terms of induction of labor is of utmost importance to reduce the occurrence of adverse fetal and maternal outcomes.

Methodology

This is a randomized controlled trial conducted in the Department of Obstetrics & Gynecology, Mardan Medical Complex affiliated with Bacha Khan Medical College Mardan from 1st Jan 2019 to 30th June 2019. All pregnant women with age group of 15-45 years and period of gestation between 34 to 41 weeks assessed by LMP irrespective of parity, presenting with PROM within 72 hours were included in the study. Women with a history of failed induction, history of oxytocin infusion or misoprostol intake, twin pregnancy, cardiac problems and history of previous cesarean section were excluded. The sample size was 107 in each group using 50% proportion of efficacy in misoprostol group and 33.3% efficacy in prostaglandin group for induction of labor, 95% confidence interval and 80% power of the test using WHO sample size estimation software. The non-probability convenience sampling technique was adopted for this study.

The study was conducted after approval from the hospital's research and ethical committee. All women meeting the inclusion criteria were enrolled in the study through labour ward. The purpose of the study was explained to the patients and written informed consent was obtained. A detailed history was taken regarding age, parity, and time since PROM. Obstetrical examination was done to confirm the PROM. All included patients were randomly allocated in two groups by the lottery method. In Group A, 50 women were induced with tab misoprostol 25µg through intravaginal route under aseptic technique and repeated 4 hours apart if needed for a maximum of 3 doses. Similarly, group B women were induced with 3mg of dinoprostone tablet placed vaginally under aseptic precaution, repeated 6hrs apart for a maximum of 2 doses. The patients were advised to remain in a recumbent position for 30 minutes in both groups after administration of drugs. Both groups were followed after induction for 24 hours. Efficacy was documented as an induction to delivery interval time less than 12

hours. All observations and therapeutic interventions were done under the supervision of an expert obstetrician. All the above mentioned information including name, age, gravidity, parity, gestational age, induction to the delivery time, and mode of delivery were recorded in a predesigned proforma.

Data collected and analyzed in SPSS version 20.0. Mean and standard deviation were calculated for quantitative variables like maternal age, gestational age, and induction to delivery time. Frequencies and percentages were calculated for categorical variables like parity, Gravidity, mode of delivery and efficacy. Chi square test was used to compare the efficacy in both groups while keeping a *p value of < 0.05* as statistically significant.

Results

Total number of patients recruited randomly in this study was 214. They were divided into two groups A and B (107 in each group). The majority of patients 153 (71.50%) were between 15 to 30 years of age. Mean age of women in group A was 28.89 ± 4.58 years and in group B was 26.64 ± 5.80 years (Table I).

Gestational age was 34 to 41 weeks with mean gestational age of 38.87 ± 1.02 weeks. The majority of the patients 159 (74.30%) were between 39 to 41 weeks of gestation. In group A, mean gestational age was 38.86 ± 1.03 weeks whereas in group B, it was 38.97 ± 1.03 weeks. Similarly, distribution of patients according to parity & gravidity in both groups is also shown (Table II). A study showed in misoprostol group 76.29% delivered vaginally and 32.71% undergone cesarean section while in dinoprostone group 47.60% delivered vaginally and 52.34% by cesarean section. Overall, 57.28% of patients delivered vaginally while 42.52% of patients delivered by cesarean section in both groups (Table III).

Table IV shows time interval from induction to delivery. Time interval less than 12 hours from induction to delivery was considered as efficacy. In misoprostol group it was less than 12 hours in 60 (56.07%) and 37 (34.58%) with dinoprostone group. Thus, misoprostol had faster effect as compare to dinoprostone as an inducing agent with statistically highly significant *p-value* of 0.02 vs. 0.27.

Discussion

Induction of labour is defined as the process of artificially stimulating the uterus to start labour. Traditionally labour is induced by oxytocin infusion but

Table I: Age distribution (n=214)

Age (years)	Group A (n=107)			Group B (n=107)			Total (n=214)		
	No. of patients	%age	Mean ± SD	No. of patients	%age	Mean ± SD	No. of patients	%age	
15-30	72	67.29	28.89 ± 4.58	81	75.70	26.64 ± 5.80	153	71.50	27.41± 5.39
31-45	35	32.71		26	24.30		61	28.50	

Table-II: Patients distribution according to gestational age, parity & gravidity

Variables		Group A (n=107)		Group B (n=107)		Total (n=214)	
		No. of patients	%age	No. of patients	%age	No. of patients	%age
Gestational Age (weeks**)**	34-38	29	27.10	26	24.30	55	25.70
	39-41	78	72.90	81	75.70	159	74.30
Parity	Primiparous	26	24.30	26	24.30	52	24.30
	Multiparous	81	75.70	81	75.70	162	75.70
Gravidity	Primigravida	29	27.10	26	24.30	55	25.70
	Multigravida	78	72.90	81	75.70	159	74.30

Table III: Patients distribution according to mode of delivery (n=214).

Mode	Group A (n=107)		Group B (n=107)		Total (n=214)	
	No. of patients	%age	No. of patients	%age	No. of patients	%age
NVD	72	67.29	51	47.66	123	57.48
CS	35	32.71	56	52.34	91	42.52

Table-IV: Induction to delivery interval (n=214).

Time (hours)	Group A (n=107)			Group B (n=107)		
	No. of patients	%age	*P value*	No. of patients	%age	*P value*
< 12	60	56.07	***0.02***	37	34.58	0.27
>12	47	43.93	0.10	70	65.42	0.48

*Efficacy=***<** 12*hours;P value <0.05% -significant*

its relative ineffectiveness in women with unfavorable cervix has instigated a search for methods to improve cervical ripening. There are several techniques available for cervical ripening. However, prostaglandins remain the single most effective means of achieving cervical ripening and inducing labour providing good clinical effectiveness and patient satisfaction.[16]

Dinoprostone (PGE2) is registered for labour induction in many countries. However, it is expensive and needs cold chain maintenance. Misoprostol (PGE1- analogue) has many advantages. It is stable at room temperature, inexpensive and it can be given via several routes (oral, vaginal, sublingual, and buccal). These properties make misoprostol a good agent for induction of labour, particularly in settings where the use of prostaglandin E2 is not possible owing to lack of availability, facilities for storage, or financial constraints.[17]

This study was conducted to compare the efficacy of misoprostol and dinoprostone for induction of labor in prelabour rupture of membranes. The mean age of women in group A was 28.89 ± 4.58 years and in group B was 26.64 ± 5.80 years. The majority of the patients 153 (71.50%) were between 15 to 30 years of age.

Induction to delivery interval was less than 12 hours in 60 (56.07%) when induced with misoprostol and 37 (34.58%) with dinoprostone (p-value = 0.02 vs.0.27 respectively). In a study conducted by Chaudhuri S et al, the time interval from induction to delivery was 10.75 hours in the misoprostol group and 9.37 hours in the dinoprostone group. The cesarean section rate did not differ significantly among them (7.61% vs. 15.30%).[14] In another study, induction to delivery interval was less than 12 hours in 50% with misoprostol and 33.3% with dinoprostone.[15] The significant difference of induction to delivery interval have been also observed by Oza A et al, which was 11.26 hours in misoprostol group and 14.72 hours in dinoprostone group (P=0.004).[18] Similar results regarding induction to delivery interval were found by Frohn et al (16.4 ± 10.2 versus 22.0 ± 12.9 hours) and Abraham et al (13.5 versus 21.5 hours).[19,20]

Our study shows that vaginal deliveries were 67.29 % in misoprostol group which is comparable to a study conducted by Oza et al (68%) while dinoprostone group was not comparable to this study (47.6% versus 80%). Cesarean section rate was 32.7%. This Cesarean section rate of misoprostol group is again comparable to Oza et al (32%) and Anjali, Sunita et al (22%) . In dinoprostone group cesarean section rate was 52.34% again not comparable to above mentioned studies (20% and 12% respectively). [18, 21] Main indications for cesarean section are fetal distress and induction failure. In our study, the increased rate of cesarean section seen in the dinoprostone group could be attributed to the lack of cold chain maintenance in our setup.

In the 2010 Cochrane review of 38 clinical trials comparing vaginal misoprostol with placebo or other pharmacologic methods in a broad population of women undergoing induction, there was no difference in the rate of vaginal births, although misoprostol was associated with a higher rate of vaginal delivery in 24 hours. Misoprostol was associated with reduced use of epidural analgesia and oxytocin augmentation but was also associated with more uterine tachysystole and meconium-stained amniotic fluid compared with vaginal dinoprostone.[5]

Misoprostol effectively induces labour with the vaginal route of administration. Misoprostol is especially relevant for Pakistan where economic resources are scarce and high temperatures prevail. This drug is cheap as compared to other prostaglandins licensed for pregnancy termination, induction of labour and treatment, and prevention of post-partum hemorrhage. It is heat stable so is easily stored at room temperatures and it has few systemic side effects. Although formulated for oral usage, but rapidly absorbable via sublingual, vaginal and per rectal route.[22]

Conclusion

Induction of labour confers benefits in various maternal and fetal conditions like PROM. Misoprostol and dinoprostone have a significant role as inducing agents. However, both drugs have their pros and cons. This study concluded that efficacy of misoprostol is more than dinoprostone for induction of labor in terms of induction to delivery interval among women with prelabor rupture of membranes. As tab misoprostol is associated with fetal distress more than dinoprostone, one should only use tab misoprostol in a setup where close fetal monitoring is possible. It is suggested that with judicious use and proper dosage, complications like uterine hyper stimulation, fetal distress and postpartum hemorrhage can be prevented.

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