Original Article

Comparing Efficacy of Dinoprostone alone with Dinoprostone and Concurrent Oxytocin for Induction of Labour in Primigravidas at Term and Foetomaternal Outcome

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Abstract

Objective: in this study we compared the efficacy of conventional dinoprostone alone and concurrent oxytocin with dinoprostone in reducing induction delivery interval in primigravida at term. Minimizing induction delivery interval will result in improved maternal satisfaction with birth process and less hospital cost by reducing hospital stay.

It was hypothesized that the concurrent method of labour induction would lead to shorter induction to delivery time without any adverse foetal or maternal effects.

Study Design: a randomized controlled trial.

Place & duration of study: department of Obstetrics and Gynaecology, PAEC General Hospital, Islamabad from August 1st, 2009 to January 31st, 2010.

Methodology: eighty pregnant women at term were randomly assigned to either dinoprostone and concurrent oxytocin group (Group A, n=40) or dinoprostone alone with placebo group (Group B, n=40). Induction delivery interval, mode of delivery, maternal complications (e.g. hyperstimulation) and foetal complications (e.g. NICU admission and APGAR score after birth of neonate) were studied.

Results: It was found that induction to delivery interval in concurrent oxytocin group (Group A) was

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significantly reduced as compared to dinoprostone alone group (Group B). In group 'A' 22.5% patients delivered in 3-5hrs while in only 7.5% patients induction delivery interval was 10-16hrs as compared to group 'B' where 25% patients delivered in 10-16hrs (p value 0.026). The operative delivery i.e. lower segment caesarean section (LSCS) was performed in 27.5% and 32.5% patients in group 'A' and group 'B' respectively.

Hyperstimulation rate in group 'A' was slightly higher (5% patients) than group 'B'(2.5% patient). There was no statistically significant difference in APGAR score and Neonatal Intensive Care Unit (NICU) admissions in babies born in both groups.

Conclusion: induction delivery interval in concurrent method of induction was significantly less as compared to dinoprostone alone group without increasing foetomaternal risks.

Keywords: term, Primigravida, Dinoprostone, Induction of labour, Induction delivery interval, Concurrent oxytocin

Introduction

Labour induction is the artificial initiation of uterine contractions prior to the spontaneous onset for purpose of accomplishing delivery of foetoplacental unit.[1] Induction is done when benefits of vaginal delivery outweigh the potential maternal and foetal risks of awaiting spontaneous labour.[2] This is a common procedure carried out in 9.5% to 33.7% of all term pregnancies.[3] The studies on elective induction of labour have shown its association with adverse outcomes such as prolonged first stage, failure to progress, intrapartum haemorrhage, admission to NICU and increased rate of assisted vaginal birth. [4] These complications in induction of labour can be significantly minimized by taking appropriate actions including selection of right patients for induction, close foetomaternal monitoring during labour, selection of appropriate agent for preparing cervix and poor Bishop score together with agents of labour augmentation.[5] The condition of cervix or favourability is important in the success of labour induction as predicted by modified Bishop Score.[6]

Cervical ripening and maturation is of fundamental importance and a pre-requisite for successful induction of labour. Cervical ripening is a complex process that results in physical softening and distensibility of the cervix, ultimately leading to partial cervical effacement and dilatation.[7] Various methods have been developed for preparing the cervix.[8] Cervical ripening can be achieved by pharamacological interventions using oxytocin and prostaglandin delivered orally or vaginally. Prostaglandins act on the cervix to enable its ripening by number of different mechanisms. Vaginal prostaglandins are recommended for initiation of cervical ripening or labour induction for both unfavourable and favourable cervix.[9] PGE_2 increases cervical favourability and rate of successful vaginal birth with no increase in assisted vaginal delivery. [10]

Dinoprostone (PGE_2) has been approved by the FDA for cervical ripening in women at or near term with mean induction delivery interval of 15.6 h $\pm$ 0.7 (standard error of the mean).[11] The current

recommendations of Royal College of obstetricians and gynaecologist on the induction of labour are vaginal tablets in preference to gel formulations.[12] Misoprostol is prostaglandin E_1 analogue which has effect on uterine contractility and can be used as a cervical ripening agent.[13] Oral and titrated dose of misoprostol can be used for cervical ripening and labour induction.[14] It does not reduce the rate of caesarean delivery and also increases the rate of tachysystole and hyper-stimulation.[15]

Although useful, oxytocin alone is not always successful for induction of labour.[16] Women undergoing labour mostly do not desire a prolong process. Various clinical trials are being done to assess the ability of using separate and simultaneous oxytocin and PGE_2 analogues for induction of labour in reducing induction delivery interval without increasing foetomaternal complications.[17] It has been reported that combination of oxytocin induction preceded by dinoprostone insert is safe and significantly shortens the induction to delivery time.[18]

The costs are also reduced because less time is spent in labour and delivery units.[17] Simultaneous use of oxytocin and prostaglandin preparations pose no increased risk of adverse events.[19] Concurrent oxytocin infusion with prostaglandin administration can be used for cervical ripening and induction of labour.[20,21]

The purpose of this study was to find an appropriate method for shorter induction delivery interval in a woman with unripe cervix associated with fewer chances of foetomaternal complications.

Methodology

This randomized controlled study was conducted in Pakistan Atomic Energy Commission (PAEC) hospital Islamabad from August 1st, 2009 to January 31st, 2010. The study was restricted to Primigravidas with singleton pregnancy at term (≥ 37 weeks), with intact membranes, cephalic presentation, Bishop score ≤ 6 and without any contraindication to normal vaginal delivery (e.g. placenta & vasa praevia, transverse lie, active genital herpes etc) or history of previous surgery on uterus i.e. Caesarean section/myomectomy or hysteroscopy. Intrauterine foetal death and gross foetal anomaly were also excluded from the study. An informed written consent was taken from all women and ethical committee approved the study.

Eighty patients were randomly allocated to group 'A' and group 'B' (40 each). An intracervical extra-amniotic catheter was inserted in all participants one night before to promote cervical ripening. All patients in both groups received 3 mg dinoprostone pessary for labour induction at 0400 hours. Those randomized to oxytocin arm (Group A) received oxytocin infusion being started at 1milliunit/minute (3ml/h) and was doubled every 30 minutes to a maximum of 32milliunit/minute to achieve effective uterine contractions (3 moderate in 10 minutes) without foetal heart rate abnormality. Patients who were assigned to placebo (Group B) received identical volume of saline infusion. The time of insertion of the first pessary was considered the starting point of the induction. After 6 hours, infusion was stopped from both groups and vaginal assessment was performed to guide further management. When Bishop Score was improved to

>8, amniotomy was performed (in both groups) followed by augmentation with oxytocin in group 'B' (if necessary according to departmental protocol) while oxytocin infusion was continued in group 'A'. We allowed a maximum of two dinoprostone pessaries/day. The main objective of our study was to reduce the time interval between induction and delivery while looking for associated complications such as uterine hyperstimulation, assisted vaginal and abdominal deliveries and condition of baby at birth. Uterine hyperstimulation (tachysystole) was considered as 4 or more contractions in 10-min duration for 30min or contractions of >2min duration or repeated contractions within 60sec of normal duration with or without FHR changes. Baby was assessed post-delivery for APGAR score and need for NICU admission was evaluated. The data was collected on a special proforma where all variables were defined and quantitative variables were tested by descriptive statistics as mean and standard deviation and also applying t-test on SPSS version 16. The p-value of <0.05 was considered to be statistically significant.

Results

It was found that induction to delivery interval of 22.5% patients was 3-5hours, 35% patients delivered in 5-8hours while in only 7.5% induction delivery interval was 10-16 hours in group 'A' as compared to group 'B' where 25% patients delivered in 10-16hours reflecting significant difference (p-value 0.026) between two groups as shown in Table-I. There was significant difference (p-value 0.019) in response to mode of induction between two groups with improved Bishop score (7-8) in 27.5% patients in group 'A' after 6hours while in group 'B' 45% patients had Bishop score 5-6 after 6hours assessment (Figure 1).

Table I. Distribution of Delivery intervals among groups A & B (p-value 0.026)

Induction Delivery Interval (In hours)		Group A (7.46 ± 2.76)	Group B (8.82 ± 2.57)	Total (8.14 ± 2.74)
3.01-5 hrs	Count	9	3	12
	Col %	22.5%	7.5%	15.0%
5.01-8 hrs	Count	14	12	26
	Col %	35.0%	30.0%	32.5%
8.01-10 hrs	Count	14	15	29
	Col %	35.0%	37.5%	36.2%
10.01-12 hrs	Count	1	7	8
	Col %	2.5%	17.5%	10.0%
12.01-16 hrs	Count	2	3	5
	Col %	5.0%	7.5%	6.2%
Total	Count	40	40	80
	Col %	100.0%	100.0%	100.0%

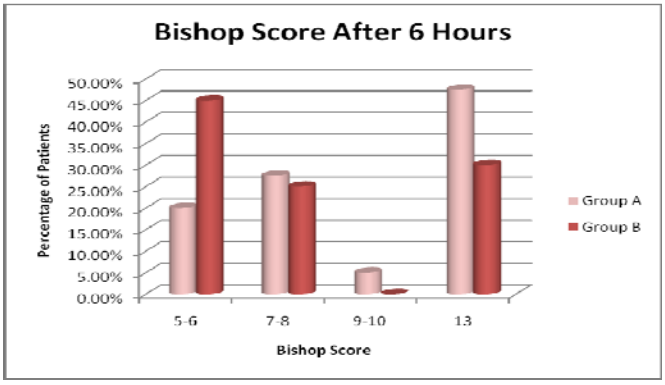

Figure 1. Bishop score after 6 hours

Number of Patients in Group A = 40

Number of Patients in Group B = 40

Consequently, 92.5% patients in group 'A' went in labour with first dose of dinoprostone while second dose was required in 52.5% patients in group 'B' (Figure 2). Regarding mode of delivery, in concurrent

oxytocin group (Group A) 10% patients had assisted vaginal delivery (AVD) i.e. usage of vacuum or forceps and 27.5% had LSCS, while in group 'B', 5% patients were delivered through AVD and 32.5% had LSCS. Hyperstimulation rate in group 'A' was slightly higher i.e. 5% (2 patients) than group 'B' which was 2.5% (1 patient).

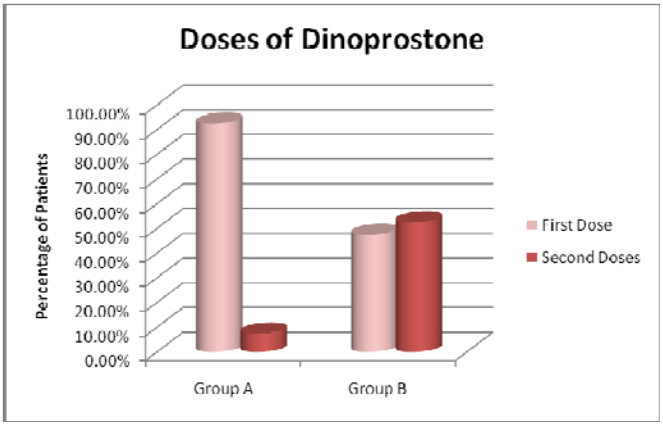

Figure 2. Distribution of number of doses required for response to labour induction:

Number of Patients in Group A = 40

Number of Patients in Group B = 40

The neonatal outcomes were equally favourable in each group. There was no statistically significant difference in APGAR score (p-value 0.672 at 1 minute and p-value 0.559 at 5 minutes) and NICU admissions (p-value 0.5) in babies born in both groups.

Discussion

Induction of labour is performed in approximately 9.5%-33.7% of all pregnancies.[3] Considerable research is being done concerning induction of labour with concurrent method of induction as compared to sequential method. This study was conducted to compare the time interval and foetomaternal effects in women receiving concurrent oxytocin infusion with dinosprostone with women to whom oxytocin was given 6 hours after dinoprostone. The primary outcome of the study was reduction in induction delivery interval, in group A.

It was hypothesized that induction delivery interval can be shortened by using concurrent oxytocin infusion with dinoprostone as concluded by a study of Khan RA et al[21] where induction delivery interval was less along with higher rate of vaginal deliveries in concurrent method of labour induction. These effects were also observed in this study. Concurrent oxytocin with dinoprostone is also associated with a better birth process satisfaction score.[20]

At the time of initiation of this study, no studies regarding comparison of concurrent oxytocin infusion with dinoprostone and dinoprostone alone were available in local literature, to our knowledge.

However, Tan PC et al[20], concluded in a randomized placebo controlled trial that concurrent oxytocin infusion with dinoprostone pessary did not significantly increase vaginal delivery rate within 24 hours (48.6% vs. 35.9%; p=0.07) but in our study higher proportion of patients delivered within 6 hours in concurrent group (47.5% vs. 30%) which is also supported by the study of Christensen FC et al.[19]

According to the study of Tan PC et al[20], concurrent oxytocin with dinoprostone reduced the requirement for repeat dose of dinoprostone (37% vs. 61.2%) that is also proved in the current study (7.5% vs. 52.5%) as shown in Figure-II. Christensen FC et al[19] found mean induction to delivery interval of 972 minutes (16.2 hours) in concurrent group versus 1516 minutes (25.2 hours) in delayed group (p=0.001). In this study, we have also observed mean induction to delivery interval of 7.46 hours±2.76 (standard deviation to mean) in concurrent oxytocin with

dinoprostone group and 8.82 hours±2.57 (standard deviation to mean) in placebo controlled dinoprostone alone group (p=0.026). There was no difference observed in caesarean section rate between two groups in the studies of Tan PC et al[20] and Christensen FC et al[19] that is also true in this study. Similarly the change of Bishop Score at 6 hours in concurrent oxytocin group was significantly greater than delayed group (p=0.01) as found in this study also (47.5% vs. 30%) as shown in Figure-I. There was no case of hyperstimulation seen in the study of Christensen FC et al[10] but in our study 5% of patients had hyperstimulation in concurrent group as compared to 2.5% in placebo controlled group.

Christensen FC et al[19] found similar values of APGAR scores at 5 minutes in two groups as observed in this study where we found no differences of APGAR scores between two groups. Regarding foetal and neonatal outcomes, 100% neonates were alive and healthy and no foetal loss was found in this study. The mean baby birth weight of group 'A' and group 'B' had no significant difference. The NICU admission rate was also comparable in both groups and no difference in neonatal morbidity was noticed in both groups.

The study of Mahalakshmi R et al[2] have shown that labour induction results in failed induction, increased risk of operative delivery and longer stay at hospital but it was not the case in this study.

Conclusion

In summary, induction to delivery interval was shortened when oxytocin was administered concurrently with sustained release dinoprostone and resulted in higher proportion of vaginal deliveries with no significant increase of adverse effects. The shorter induction delivery interval also allows shorter hospital stay, which is also considered as an added advantage of this technique. The small sample size (N=80) of the study limits any definite conclusion regarding important adverse effects of concurrent oxytocin (secondary outcome of the study).

As mentioned earlier, the major limitation of this study is that its small sample size (N=80) does not provide sufficient power to obtain definitive data concerning the incidence of hyperstimulation or the caesarean delivery rate. There is thus a need for further studies on larger scale to firmly establish the safety of concurrent oxytocin and dinoprostone.

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"The purpose of education is to teach one to think intensively and critically."
Martin Luther King