Original Article

Comparative Analytical Study of Dinoprostone Gel and Hyaluronidase Injection for Induction of Labour in Term Primigravida in Tertiary Rural Medical Centre of Western Uttar Pradesh

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Abstract

Objective: To compare the efficacy of intracervical dinoprostone gel and hyaluronidase injection for induction of labour in term primigravida.

Materials and methods: This is a hospital based analytical prospective interventional study conducted in a rural tertiary care centre over a period of 18 months. A total of 70 patients who required induction of labour for one or another reason with Bishop score of less than 6 were included in the study. All the cases were randomly divided into two groups, Group A received dinoprostone gel and Group B received hyaluronidase injection. Chi square test & unpaired T test were applied for statistical analysis.

Results: Time interval from induction to active phase of labour was comparatively shorter in group A than in group B (10.74 ± 6.17 vs 15.94 ± 7.1) and the difference was significant (p= 0.001). Time interval from induction to delivery time was comparatively shorter in group A than group B (14.84 ± 8.86 vs 21.33 ± 7.86) and difference was significant (P= 0.009). Maternal complications were more common in group A as compared to group B.

Conclusion: This study showed that labour could be accelerated significantly by intracervical injection of hyaluronidase. Hyaluronidase injection has less maternal and fetal side-effects as compared to dinoprostone gel and can be a good choice for induction of labour.

Keywords: Induction of Labour; Dinoprostone Gel; Intracervical Hyaluronidase Injection; Bishop Score

Introduction

Induction of labour implies, the intentional initiation of uterine contractions after the period of viability for many obstetrical, maternal and fetal indications either by medical or mechanical methods. It primarily refers to attempt to produce regular uterine contractions along with cervical changes to begin the active phase of labour (1). In obstetrics it is one of the commonest procedures and about 20% of pregnant women will have labour induced for variety of reasons (2), the most common being prolonged pregnancy (3). If induction is successful, it reduces the number of

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caesarean deliveries significantly, as compared to expectant management.

Labour induction with unfavourable cervix is a difficult and lengthy procedure for both mother as well as an obstetrician. Many a times its failure leads to maternal exhaustion and outcome is caesarean delivery. Therefore, there is need of good cervical ripening agent for induction of labour in unfavourable cervix and further assessment of action of ripening agent can be documented by Bishop's score as this is the most crucial indicator for successful vaginal delivery. We have several proved effective cervical ripening methods, which has been applied for long time, including various mechanical and pharmacological methods. Dinoprostone (PGE2), is an FDA-approved drug for a long time that leads to cervical ripening, initiates uterine contractions, and thus facilitates vaginal delivery, but not exempted from side effects and contraindications. We have tried to utilize another drug, hyaluronidase, which has not been used for induction of labour but can be incorporated in this series of drugs because it acts on cervical tissue as per its composition. Hyaluronidase is a locally acting enzyme which hydrolyzes hyaluronic acid and causes depolymerisation of the conjunctive components of the cervix (collagen, hyaluronic acid and chondroitin) and acted upon as a reducing cellular adhesion of collagen of the cervix, causing softening and effacement of cervix (4).

Therefore, we planned this study to evaluate the efficacy of local intracervical hyaluronidase injection in ripening of cervix with respect to presently accepted safe drug Dinoprostone (PGE2) intracervical gel in full term primi gravida cases, requiring induction of labour for one or other reasons with unfavourable cervical findings.

Materials and methods

It is a hospital based analytical prospective interventional study conducted in the Department of Obstetrics and Gynaecology, Uttar Pradesh University of medical Sciences, Saifai, Etawah (U.P) from Jan2018- June2019. Ethical clearance for the study was taken from institutional ethical committee. Inclusion criteria for the study includes primigravida having singleton pregnancy with vertex presentation between 37 to 42 weeks gestation with absence of spontaneous contraction and Bishop score of equal to or less than 6. There was no contraindication for the administration of prostaglandin and/or for vaginal delivery. 70 patients admitted in labour ward who fulfil the inclusion criteria were enrolled in the study after taking written and informed consent. They were randomly divided in two equal study groups – Group A, received dinoprostone gel and Group B, received intra cervical Injection of Hyaluronidase. After performing general as well as systemic examination, non-stress test was performed prior to induction in all the study subjects. Initial Bishop's score was noted in both the groups at time of initiation of induction.

Group A patients were given dinoprostone gel (PGE2) (0.5 mg) intracervically and Group B patients were given injection Hyaluronidase (1500 IU) in anterior and posterior lip of the cervix. Bishop's score was reassessed after 8 hours of giving first dose of inducing agent. If favourable (Bishop's score > 6), augmentation of labour was done otherwise second dose of ripening agent was repeated as per their respective protocols. Cases who had not achieved the favourable Bishop's score after second dose of ripening agent, were considered as induction failure. Primary outcome measures were assessed in terms of change in Bishop's score (at 8 and 16 hours), requirement of one or two doses of ripening agent, time taken for induction to active phase and induction to vaginal delivery intervals. Secondary outcome measures were assessed in terms of vaginal deliveries, number of caesarean sections for failed induction, side effects to mother and fetus especially uterine hyper stimulation, occurrence of postpartum bleeding and meconium-stained liquor and neonatal outcome with reference to Apgar at 1 minute and 5 minutes and need for admission to the neonatal intensive care unit.

Statistical analysis: Chi square test & unpaired T test were applied for statistical analysis of qualitative data .P value of less than 0.05 was taken as statistically significant via analytical tool pack of Microsoft excel -2010 home edition.

Results

In our study total 70 cases with indication of induction of labour were enrolled and divided randomly into two groups according to ripening agent used. Group –A incorporates cases being induced with intracervical dinoprostone gel and group –B having cases induced with hyluronidase injection. Both the study groups were similar in demographic profile i.e., age, parity, gestational age, socioeconomic background etc. Both study groups

were comparable in age parameter and maximum number of subjects was of younger age group i.e. 18-25 years (Table 1). Mean age was 24.09 ± 3.51 and 22.71 ± 1.71 in group A and B respectively. Near about 54.29% cases of group A and 60%cases of group B belongs to lower socioeconomic as our institute is a referral rural tertiary care unit (Table 1). The most common indication for induction was post-dated pregnancy followed by pre-eclampsia in both groups (Table 2).

Mean Bishop's score at the time of initiation of induction was 3.71 ± 0.46 and 3.63 ± 0.55 in group A and B respectively. 2 cases in group A and 1 case in group B delivered by caesarean section before completion of eight hours of first dose of ripening agent.

Mean Bishop's after 8 hours of 1st dose of ripening agent was 6.12 ± 2.02 (n=33) and 5.56 ± 1.65 (n=34) in group A and B respectively (Table 3).

Second dose of ripening agent was repeated in 15 (42.85%) and 18 (51.43%) cases in group A and B respectively as shown in (Table 4). Mean Bishop's score in cases who required 2nd dose of ripening agent (after 1st dose of ripening agent) was 4.06 ± 0.45 and 4.16 ± 0.51 in group A and B respectively (Table 5). In group A, 3 cases delivered vaginally and 2 cases by caesarean section before completion of eight hours of second dose of ripening agent. Mean Bishop's after 8 hours of 2nd dose of ripening agent was 5.6 ± 1.71 (n=10) and 5 ± 1.14 (n=18) in group A and B respectively (Table 5).

In group A, 21 cases delivered vaginally and 8 cases delivered by caesarean section while in group B, 19 cases delivered vaginally and 2 cases delivered by caesarean section (Table 6).

Time interval from induction to active phase of labour is comparatively shorter in group A than group B (10.74 ± 6.17 vs 15.94 ± 7.1) and difference was significant (p= 0.001). Time interval from induction to delivery time is comparatively shorter in group A than group B (14.84 ± 8.86 vs 21.33 ± 7.86) and difference was significant (P= 0.009) (Table 7).

Maternal complications were more common in group A as compared to group B. Uterine hyperstimulation was seen in five cases (14%) in group A and none in group -B. Meconium-stained liquor was seen in fifteen cases (42.85%) and ten cases (28.57%) in group A and group B respectively. Postpartum haemorrhage was seen in four cases (11.41%) and one case (2.85%) in group A and group B respectively.

Number of NICU admission were more in group A as compared to group B (17.24% vs 14.28%), but result was statistically not significant (Table 8).

Discussion

In present study, most of the cases belonged to 18–25-year age group. Mean age of cases is about 24.09 ± 3.51 in group A. Mean gestational age is 40.24 ± 1.03 in group A. It was similar to study conducted by Kandemir O et al where mean patient age and gestational age was 25.22 ± 4.9 and 40.21 ± 1.2 respectively which is comparable (5).

In our study, mean Bishop's score at the time of initiation of induction was 3.71 ± 0.46 in group A, which was similar to study conducted by study Hend S Saleh et al (6), who reported initial bishop score of 3.6 ± 1.4. A study by Kandemir o et al (5) reported initial mean Bishop's score of 2.47 ± 0.2.

Table 1: Demographic profile of patients

Demographic variables		Group A (n=35)	Group B (n=35)	P value
Age group (years)	18-25	27 (77.14%)	33 (94.28%)	0.10*
	26-30	06 (17.14%)	02 (5.71%)	
	31-35	02 (5.71%)	00 (0%)	
Socioeconomic status	Lower	19 (54.29%)	21 (60%)	0.79*
	Lower middle	14 (40.00%)	13 (37.14%)	
	Upper middle	02(05.71%)	01 (2.86%)	
Booking status	Booked	20 (57.14%)	17 (48.57%)	0.47*
	Unbooked	15(42.85%)	18 (51.42%)	
Gestational age (in weeks)	37-37wk6day	02 (5.71%)	01 (2.86%)	0.94*
	38-38wk6day	01 (2.86%)	02 (5.71%)	
	39-39wk6day	05 (14.26%)	04 (11.42%)	
	40-40wk6day	05 (14.26%)	05 (14.26%)	
	41-42wk	22 (62.86%)	23 (65.71%)	

Chi square test, * not significant

Table 2: Distribution of cases according to indications for induction of labour

Indication for induction	Group A (n=35)	Group B (n=35)	P value
Post-dated pregnancy	18 (51.42%)	20 (57.14%)	0.57*
Pre-eclampsia	11(31.43%)	06 (17.14%)	
Cholestasis of pregnancy	01 (2.86%)	01 (02.86%)	
Others	05 (14.28%)	08 (22.86%)	

Chi square test, * not significant

Table 3: Bishop's score changes

Mean Bishop's score	Group A	Group B	P value
Initial Bishop's score	3.71 ± 0.46 (n=35)	3.63 ± 0.55 (n=35)	0.42*
Bishop's score after 8 hours of 1st dose of ripening agent	6.12 ± 2.02 (n=33)	5.56 ± 1.65 (n=34)	0.06*

Chi square test, * not significant

In present study, second dose of ripening agent was repeated in 42.85% cases in group A. Similar results were seen in study conducted by Bashutheen NS et al where second dose of ripening agent was required in 41.50% (7). In a study conducted by Hend S Saleh et al, second dose of ripening agent was required in 23 % cases (6).

Table 4: Bishop's scoring in cases requiring second dose of ripening agent

Mean Bishop's score	Group A	Group B	P value
Mean Bishop's score who required second dose of ripening agent	4.06 ± 0.45 (n=15)	4.16 ± 0.51 (n=18)	
Bishop's score after 8 hours of 2nd dose of ripening agent	5.60 ± 1.71 (n=10)	5.0 ± 1.14 (n=18)	0.51*

Chi square test, * not significant

In our study, mean Bishop's after 8 hours of 1st dose of ripening agent was 6.12 ± 2.02 (n=33) in group A. There was increase in mean Bishop's score by 2.41 in group A after 8 hours of first dose of ripening agent, the difference was not significant. A study conducted by Parate S et al (8) showed increase in mean Bishop's score by 3.06 after single dose instillation of Dinoprostone gel.

In our study, mean Bishop's after 8 hours of 2nd dose of ripening agent was 5.6 ± 1.71 (n=10) in group A. In study done by Parate et al[8], mean bishop's score after second dose instillation was 8.79 ± 2.04.

In present study, 51.72% delivered vaginally after single dose of ripening agent in group A. similar results were shown by Mukopadhyay et al where 72 % cases delivered vaginally after single dose of dinoprostone (9).

Table 5: Distribution of cases according to need of second dose of ripening agent

Second dose repeated	Group A (n= 35)	Group B (n= 35)	P value
Yes	15 (42.85%)	18 (51.43%)	0.47*
No	20 (57.14%)	17 (48.57%)	

Chi square test, * not significant

In our study, time interval from induction to delivery in group A was 14.84 ± 8.86. Study done by Bernstein et al reported 15.6 ± 7.7 as induction to delivery time (10). Another study done by Parate S et al (8) and Hend S saleh et al (6) reported induction to delivery time of 13.14 ± 6.24 and 14.7 ±0.8 respectively.

In our study, the incidence of thick meconium-stained liquor was 42.85% in group A. The maternal side effects observed were chills, tachysystole, hyperstimulation, vomiting, diarorhea, fever and PPH. In the Dinoprostone group the major side effects were vomiting – 8.50% and PPH in 11.42% cases while in hyaluronidase group PPH was seen in only 2.85% cases.

In our study number of NICU admission were 17% in group A. Studies conducted by Kandemir et al (5) and Ramya D et al (11) shows 2.22% and 10.6% NICU admission.

Table 6: Distribution of cases according to mode of delivery

Mode of delivery		Group A (n= 29)	Group B(n=21)	P value
Vaginal	After 1st dose of ripening agent	15 (51.72%)	16 (76.19%)	0.33*
	After 2nd dose of ripening agent	06 (20.68%)	03 (14.28%)	
LSCS	After 1st dose of ripening agent	05 (17.24%)	01(4.76%)	0.74*
	After 2nd dose of ripening agent	03 (10.34%)	01 (4.76%)	

Chi square test, * not significant

Table 7: Distribution of cases showing labour outcomes

Labour outcomes (hours and minutes)	Group A (n= 21)	Group B (n= 19)	P value
Induction to active phase of labour (Mean ± SD)	10.74 ±6.17	15.94 ± 7.1	0.001*
Induction to delivery time (Mean ± SD)	14.84 ± 8.86	21.33 ± 7.86	0.009*

Chi square test, * not significant

Table 8: Distribution of cases according to Neonatal outcome

Neonatal outcome	Group A (n= 29)	Group B (n= 21)	P value
NICU admission	05 (17.24%)	03 (14.28%)	0.77*
Healthy baby	24 (82.75%)	18 (85>71%)	

Chi square test, * not significant

In our study, in hyaluronidase group Bishop's score at the time of induction and final Bishop's score was 3.63 ± 0.55 and5.56 ± 1.65 respectively. In a study conducted by F.G.C.surita et al (12), they compared the effect of intracervical hyaluronidase with foley catheter for cervical ripening and reported Bishop's score at the time of induction and final Bishop's score of 2.97 ± 1.81 and 5.73 ± 1.99 respectively.

Dr Rajini Priya et al (13) studied effect of local injection of hyaluronidase on cervical dilatation in labour and found that the primigravida who received intracervical hyaluronidase injection, the mean labour time from 4 cm dilatation to delivery of baby is 2 hrs and 20 minutes. All the primigravida and multigravida delivered within five hours of intracervical hyaluronidase injection.

In our study, maternal and fetal complications were less in hyaluronidase group as compared to dinoprostone group. Study conducted by Dr Rajini Priya et al, there were no maternal complications in hyaluronidase group. Time taken from induction to delivery of fetus was longer in hyaluronidase group. This may reflect the fact that hyaluronidase takes longer to achieve its optimal effect.

Hyaluronidase injection for cervical ripening proved to be safe, with very few maternal or fetal side effects but due to invasive procedure it might be not an acceptable method for induction when other noninvasive methods are there. As very few studies had been done on hyauronidase, so more studies are required, mainly with respect to its use as it is very safe in terms of complications occurred with prostaglandins.i.e hyperstimulation. So, Hyaluronidase can be a good alternative in women with scared uterus requiring induction in view of successful VBAC.

Conclusion

This study showed that labour could be accelerated significantly by intracervical injection of hyaluronidase. Hyaluronidase injection has less maternal and fetal side-effects as compared to dinoprostone gel for induction of labour. There are only few studies which shows positive role of hyaluronidase injection but recently there is no study done. But in view of increasing number of caesareans we should explore more and more options for induction of labour other than prostaglandins. So, hyaluronidase can be a good choice in this series of drugs in future but needs more studies.

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