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Comparison of the use of dinoprostone and oxytocin for induction in cases with Bishop score of ≤4

Özlem Yörük, Ayşegül Öksüzoğlu, Yaprak Engin Üstün, Ayla Aktulay, Elif Gül Yapar Eyi, Salim Erkaya

Zekai Tahir Burak Maternal Health Training and Research Hospital, Ankara, Turkey

Abstract

Objective: The aim of this study is to compare the efficiency, reliability, and maternal and perinatal complications of dinoprostone and oxytocin for induction of labor, both separately and together, in women with a Bishop score of ≤4.

Methods: A total of 279 primigravida patients, diagnosed with oligohydramnios and prolonged pregnancy, over 37 weeks of gestation with a Bishop score of ≤4 and had been admitted to our hospital's delivery unit for labor induction between January and April 2013 were divided into three groups. Thirty-four patients who were administered intravaginal dinoprostone formed the 1st group. The 2nd group consisted of 204 patients who were administered intravenous oxytocin. The 41 patients in the 3rd group were initially administered dinoprostone and subsequently oxytocin. Age, body mass index (BMI), the duration of the latent and active phases of labor, presence of meconium, and changes in the NST were recorded for each pregnant woman. Delivery method, birth weight and gender of the neonates were also recorded. Indications for caesarean section and maternal and neonatal complications were investigated.

Results: When these three groups were compared, no difference was found in terms of age, gravida, parity, BMI and duration of pregnancy. However; comparison of the 3 groups for latent and active phases indicated that the active phase to be significantly shorter in the patients administered dinoprostone (p=0.001). When compared for the caesarean section ratios, 1st and 3rd groups were found to have higher ratios than the 2nd group (p=0.000). No difference was noted among the 3 groups in terms of maternal and perinatal outcomes.

Conclusion: Although dinoprostone increases caesarean section ratio, it decreases the active phase of labor and does not affect maternal and fetal morbidity. The labor induction method to be chosen may change depending on the patient and option of the physician doing the evaluation.

Key words: Dinoprostone, labor induction, oxytocin.

Bishop skoru 4 ve altında olan gebelerde doğum indüksiyonunda dinoproston ve oksitosin kullanılmasının karşılaştırılması

Amaç: Çalışmamızın amacı term veya günaşımı gebeliklerde serviksi olgunlaştırma ve doğum eylemi indüksiyonunda sık kullanılan ajanlardan dinoproston ve oksitosin kullanımlarının ayrı ayrı ve birlikte kullanımlarının etkinliğini, güvenirliliğini, maternal ve perinatal komplikasyonlarını karşılaştırmaktır.

Yöntem: Hastanemiz doğum ünitesinde 2013 Ocak-Nisan aylarında oligohidroamnios ve günaşımı gebelik tanılarıyla doğum indüksiyonu için yatırılmış 37 gebelik haftası üzerinde, Bishop skoru ≤4 olan primigravid 279 hasta 3 gruba ayrıldı. İntravajinal dinoproston uygulanan 34 hasta grup 1'i, intravenöz oksitosin uygulanan 204 hasta grup 2'yi oluşturdu. Grup 3'ü oluşturan 41 hastaya ise önce dinoproston, takibinde ise oksitosin uygulandı. Gebelerin yaşı, vücut kitle indeksleri (VKİ), doğum eyleminin latent ve aktif fazlarının süresi, mekonyum varlığı, NST değişiklikleri kayıt edildi. Olguların doğum şekilleri, bebeklerin doğum kilosu ve cinsiyetleri not edildi. Sezaryen endikasyonları ile anneye ve yenidoğana ait komplikasyonlar araştırıldı.

Bulgular: Bu üç grup karşılaştırıldığında aralarında yaş, VKİ ve gebelik süresi açısından fark bulunamadı. Ancak 3 grup latent süre ve aktif süre açısından karşılaştırıldığında dinoproston uygulanan hastalarda aktif sürenin anlamlı olarak daha kısa olduğunu bulduk (p=0.001). Bu üç grup sezaryen oranı açısından karşılaştırıldığında grup 1 ve 3'de grup 2'ye göre anlamlı olarak daha fazla sezaryen uygulandığı görüldü (p=0.000). Maternal ve perinatal sonuçlar açısından 3 grup arasında fark bulunmadı.

Sonuç: Sonuç olarak dinoproston sezaryen oranlarını artırmasına rağmen doğumun aktif dönemini kısaltmakta, maternal ve fetal morbiditeyi etkilememektedir. Doğum indüksiyonu için kullanılacak yöntemin seçimi, hastaya ve değerlendirmeyi yapacak olan hekimin tercihine göre değişebilir.

Anahtar sözcükler: Dinoproston, eylem indüksiyonu, oksitosin.

Correspondence: Özlem Yörük, MD. Zekai Tahir Burak Kadın Sağlığı Eğitim ve Araştırma Hastanesi, Ankara, Turkey.
e-mail: özlemese@gmail.com

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Introduction

The induction of labor is to initiate regular uterine contractions mechanically or by pharmacological methods in order to provide labor following the progressive cervical dilatation before spontaneous labor begins.[1] The induction of labor is suggested for cases where maintaining pregnancy poses risk for mother or fetus. Approximately 20-30% of all pregnant women are induced.[2,3]

Although oxytocin is a safe and effective inducer of uterine contractions during the induction of labor, it has less or no effect on cervical maturity. In cases where cervix is not appropriate, it is generally hard or takes long to induce labor, and the rates of attempted labor and caesarean labor increase. Prostaglandin preparations are used to prepare cervix which is not appropriate for induction. Recently, dinoprostone which is applied vaginally and provides regular low-dose and controlled prostaglandin E2 release is frequently used for labor induction. This new design also has a retraction system, so it can be easily and quickly retracted at the end of 12 hours of dosing or in the beginning of active labor.

Since the use of prostaglandin E1 (misoprostol) for labor induction is not approved in our country by the regulations of Turkish Drug and Medical Device Institution of the Ministry of Health, we planned a study in order to compare the use of dinoprostone and oxytocin, which we assumed economic, on patients with Bishop score of ≤4.

Methods

The patient files of 279 primigravida patients, diagnosed with oligohydramnios and prolonged pregnancy, over 37 weeks of gestation with a Bishop score of ≤4 and had been admitted to our hospital's delivery unit for labor induction between January and April 2013 were examined retrospectively.

After uterine was separated into 4 quadrants by Phelan technique,[4] pockets with amniotic fluid were measured on vertical plane, and their total amount was recorded as amniotic fluid index (AFI). It was considered as oligohydramnios when obtained total value was below 5 cm. Since the oligohydramnios is associated with bad perinatal outcomes, labor induction is initiated in many pregnancies which are at or near term.

Pregnancies which were 41 weeks and 4 days and above were considered as prolonged pregnancy according to our clinical protocols.

The patients were divided into 3 groups. In the first group consisting of 34 pregnants, 10 mg dinoprostone (Propess® ovule, Vitalis, Ankara, Turkey) was placed into posterior vaginal fornix and their labors were followed up. Propess ovule was kept in the freezer between -10°C and -20°C as stated in the prospectus, and applied by taking out of the freezer just before the application. After applied, they were treated as medical waste. Low-dose oxytocin protocol was applied to 204 pregnants constituting the second group (Synpitan®, Deva, İstanbul, Turkey). Synpitan ampule was kept in the room temperature below 25°C. The third group included 41 patients who were initially applied dinoprostone but could not get into active labor at least 12 hours because of displacement of dinoprostone and oxytocin induction was started.

High risky pregnants (diabetes mellitus, hypertension, multiple pregnancy, intrauterine growth retardation etc.) and cases with early membrane rupture and fetal anomaly were excluded from the study.

The weeks of the gestation were recorded. Gestational ages of patients who could not remember the date of last menstrual period were determined according to first trimester or early second trimester ultrasonography. Ages and body mass indexes (BMI) of the pregnants were recorded.

The duration of the latent and active phases of labor, presence of meconium, and changes in the NST were recorded for each pregnant woman.

Dinoprostone was placed into ovule posterior fornix horizontally. The presence of contractions with frequent intervals less than two minutes and lasting more than 90 seconds was considered as hyperstimulation and dinoprostone vaginal ovule was removed and the pregnant was turned to her left side, oxygen was applied with 500 ml crystalloid solution infusion and nasal cannula or mask.[5]

As intravenous infusion, oxytocin (Synpitan®, Deva) was started at 2 mU/min as 5 units of intravenous within 500 cc 5% dextrose and it was increased 2 mU/min every 20 minutes until it reached 36 mU/min. Total induction duration was recorded.

The duration until cervix effacement was 70% and dilatation was 4 cm was deemed as the latent phase of the delivery while the duration until cervix effacement

and dilatation were both full was deemed as the active phase of the delivery; and both durations were recorded.

The patients were monitored during labor. In NST evaluation, fetal heart rate acceleration at least for 15 seconds and 15 beat/min in 20 minutes was considered as reactive, while decreases at least for 15 seconds and 15 beats were considered as deceleration, and non-presence of these accelerations and decelerations were considered as non-reactive.[5] NST was carried out by Philips 50A or Corometrics model 170 monitors by using external ultrasonographic transducer. AFI was measured by using Mindray M5 3.5 MHz linear probe.

Delivery types, birth weights and genders of neonates were recorded. Caesarean indications and maternal and fetal complications were screened. Bleeding after delivery or caesarean more than normal with uterine relaxation was considered as atonic bleeding. Conditions such as the need for resuscitation during at delivery, fifth minute Apgar score below 7, presence of encephalopathy (lethargy, stupor, hypotonia, and abnormal or insufficient reflex findings including lack of sucking reflex), development of multiple organ dysfunction (encephalopathy and involvement of at least one organ), need for mechanical ventilation, breathing to start late, and the pH value of blood gas lower than 7.2 were considered as perinatal asphyxia. The diagnosis of temporal fetal tachypnea was established by tachypnea started within the first 6 hours after birth and continued at least for 12 hours as well as respiration increase in chest radiography, vascular congestion, and observing fluid accumulation at fissures and costophrenic angle, and the lack of other diseases having similar findings.

Statistical Analysis

Distribution of numerical data was analyzed by Kolmogorov-Smirnov test. The difference of variables displaying normal distribution among 3 groups was analyzed by one-way analysis of variance. Paired comparisons afterwards were done by Tukey test. The difference of variables not displaying normal distribution among 2 groups was analyzed by Mann-Whitney U test while it was analyzed for 3 groups by Kruskal-Wallis test, and then paired comparisons were done by Dunn test. The data was expressed as mean±standard deviation or median (minimum-maximum). The correlation among qualitative variables was analyzed by Pearson chi-square test and Fisher exact test. The analyses were carried out by SPSS for Windows 20.0 (SPSS Inc., Chicago, IL, USA). $p<0.05$ was considered as the statistical significance limit.

Results

The 279 patients included to this study constituted 8.9% of 3133 deliveries carried out within 3 months. Mean age of the patients was found as 26.2±5.3. When the three groups were compared, no difference was found among them in terms of age, BMI and weeks of gestation. However, there was significant difference among them in terms of latent duration and active duration. These results are given in **Table 1.**

While meconium was seen in 26 patients (12.7%) in the Group 2, it was seen in 6 patients (11.5%) in the Group 3; but there was no patient with meconium in the Group 1. There was no significant difference among three groups in terms of meconium (p=0.077).

Abnormal NST findings were observed in 6 patients (17.6%) in the Group 1, in 35 patients (17.2%) in the Group 2 and in 12 patients (29.3%) in the Group 3. When analyzed in terms of abnormal NST findings, there was no difference among 3 groups (p=0.490).

It was seen that caesarean section was applied to 18 patients (52.9%) in the Group 1, 70 patients (34.3%) in

Table 1. Demographic and clinical data of the groups*.

	Group 1 (N=34)	Group 2 (N=204)	Group 3 (N=41)	p
Age (year)	26.2±4.6	26.1±5.1	24.8±5.5	0.480
BMI† (kg/m²)	29.8±4.7	29.9±4.9	31.6±7.4	0.259
Duration of pregnancy (day)	287.3±3.5	288.0±3.3	287.6±3.2	0.185
Latent period (min)	858.97±524.96	639.49±569.89	1665.24±1341.71	0.000
Active period (min)	154.11±132.86	229.60±184.81	246.87±269.20	0.001

*Values are given as mean±standard deviation. †**BMI:** body mass index.

the Group 2, and 28 patients (68.3%) in the Group 3. When these three groups were compared for caesarean rates, it was seen that the rate was higher in Group 1 and Group 3 than Group 2 (p=0.000). In terms of caesarean indications, there was no significant difference among 3 groups (p=0.275). These indications are shown in **Table 2.**

While the caesarean rate at our hospital's delivery unit was 39.7% in general, our primary caesarean rate was 18%.

When neonate weights were analyzed, it was seen that there was no significant difference among groups (it was 3461±428 g in Group 1, 3469±414 g in Group 2, and 3451±408 g in Group 3; p=0.110). It was seen that 2 neonates were followed up at intense care unit due to perinatal asphyxia and they were discharged from the hospital as were.

The most common problem when using dinoprostone was miscarriage in 12 (29.2%) out of 41 patients constituting Group 3. Hyperstimulation associated with dinoprostone was observed in 6 patients (14.6%).

Maternal complications in our study were observed in 8 patients (2.8%). There was atonia which was recovered by treatment in 4 patients (1.4%), infection in 1 patient (0.3%) and the need for blood transfusion in 3 patients (1.0%). During this period, atonia was seen in 9 (0.28%) out of 3133 patients, 7 patients (0.22%) needed blood transfusion.

Discussion

One of the major delivery problems for a pregnant near term is the condition of cervix. When cervix is rigid, induction of labor by inappropriate methods generally will cause bad results. Patient should be informed about the indication of labor induction, and informed consent form should be received. The suitability of maternal pelvic bone structure for vaginal delivery should be evaluated; fetal weight and presentation should certainly be known. WHO stated the indications of labor induction in the guide published in 2011. Induction of labor is suggested when the weeks of gestation is above 41 and early membrane rupture is present. It is suggested to use intravenous oxytocin alone or oral misoprostol (25 µg, with intervals of 2 hours) or low-dose vaginal misoprostol (25 µg, with intervals of 6 hours) when low-dose vaginal prostaglandins cannot be provided during the induction of labor. WHO states that balloon can be applied or the combination of oxytocin and balloon when prostaglandin or misoprostol cannot be provided.[6]

Mechanical or pharmacological agents are used for the induction of labor. Mozurkewich et al. reviewed 283 studies on the methods used for the induction of labor between 1980 and 2010, and found that dinoprostone and misoprostol are more effective than other methods for carrying out the delivery within 24 hours, and that mechanical methods cause less hyperstimulation than these two methods, but lead to more maternal and neonatal infection morbidity.[7]

Oxytocin infusion for the induction of labor may fail even when combined with amniotomy if cervix is not suitable. The caesarean rates increases in unsuccessful inductions.[8-10] Calder et al. showed that delivery duration, maternal fever, caesarean and fetal asphyxia increase when amniotomy was applied together with oxytocin to patients whom cervices are not prepared compared to patients with ripened cervices.[11]

Dinoproston has been used since 1970, and it stimulates myometrial contractions as well as ripening cervix. When compared with other induction methods, it is reported that less and equal amount of maternal and fetal complications are observed.[12-14]

It was reported by Perry and Leaphart that placing dinoprostone ovule into intra-cervical decreased the period up to delivery without any increase in caesarean rate, infection morbidity or any other labor complications.[15]

Table 2. Caesarean indications of the groups.

	Group 1 (N=34)	Group 2 (N=204)	Group 3 (N=41)
Fetal distress, n (%)	6 (33.3)	31 (44.3)	11 (39.3)
Cephalopelvic disproportion, n (%)	10 (55.8)	21 (30.0)	8 (28.6)
Dystocia, n (%)	2 (11.1)	10 (14.3)	7 (7.1)

In the literature, the studies comparing intravenous oxytocin and dinoprostone use during the induction of labor showed that dinoprostone causes less delivery failure than oxytocin and it is more effective and reliable method,[16-18] the study conducted by Koç et al. comparing oxytocin and dinoprostone reported that labor occurred in a short time by oxytocin and caused less cesarean delivery even there is no statistical significance.[19]

In our study, we found that active labor phase was significantly shorter although latent duration was longer in dinoprostone group compared to oxytocin group (p=0.000). Mazouni C et al. indicated in their study that there was no maternal and fetal morbidity in patients applied dinoprostone while the caesarean rate was 3.5 times more.[20]

The caesarean rates vary between 7-27% by dinoprostone use in the literature.[21,22] In our study, we observed that delivery by caesarean was higher in Groups 1 and 3 than the oxytocin group (p=0.000). High caesarean rate (68.3%) in Group 3 shows that the caesarean rate will increase in pregnants who are applied dinoprostone but need to undergo other methods for some reasons. For caesarean indications, we did not detect any difference among the groups in terms of fetal distress and non-progressive labor. However, cephalopelvic disproportion was observed only in 55.6% (n=10) of the Group 1 applied dinoprostone, which was higher than other two groups but the difference was statistically not significant (p=0.275).

We believe that the high caesarean rate in all 3 groups is caused for the low number of patients in the groups and medicolegal concerns.

In the studies, hyperstimulation rate based on dinoprostone use varies between 8.3% and 16%.[23,24] In our study, hyperstimulation rate was 14.6%.

It was seen that 2 neonates were followed up at intense care unit due to perinatal asphyxia and they were discharged from the hospital as were. No perinatal and early neonatal mortality was observed.

We believe that our study has weak points which should be emphasized. One of them is the inevitable methodological issues which are seen in all retrospective studies. Other one is the disproportionality in patient number affecting statistical analysis.

Conclusion

Dinoprostone is a method approved by FDA for the induction of labor at term pregnancies. Even though it increases caesarean rates, it decreases the active period of labor, and does not affect maternal and fetal morbidity. The method to be used may differ according to the preference of patient and physician. However, patient and fetus should be kept under close observation. Supporting to study greater patient groups will increase the reliability of results.

Conflicts of Interest: No conflicts declared.

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