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Labor induction: comparison between oxytocin and dinoprostone

Eylem indüksiyonu: oksitosin ve dinoprostonun karşılaştırılması

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Abstract
Labor induction is one of the most frequent procedures in pregnant women. The optimal regimen for preinduction cervical ripening and labor induction is not established. The aim of the present study was to compare the efficacy and safety of vaginal dinoprostone and intravenous oxytocin administration for labor induction. The medical records of the patients who had induction of labor at Okmeydanı Teaching and Research Hospital, Department of Obstetrics and Gynecology from January 2010 to June 2011 were evaluated retrospectively. The first group (143 patients) received a single dose of sustained- released dinoprostone 10 mg, which was inserted high into the vaginal fornix. The second group (151 patients) received intravenous oxytocin (synpitan). Maternal and fetal outcomes were compared. There were no significant differences between the two groups for parity, birth weight, fetal gender and mode of delivery. 195 (66.3%) of patiens had vaginal delivery and 99 (33.7%) had cesarean delivery. The median time from start of induction of labor to vaginal birth was longer when a prostaglandin E2 was used for labor induction than it was when oxytocin was used (20.1 hours vs 16.1 hours) ($p<0.01$). No maternal death or uterine rupture occurred. Neonatal weight, admission to neonatal unit, 1 and 5-minute Apgar score <7, did not differ significantly between two groups ($p>0.05$). Oxytocin is safe, effective and cost-effective treatment. The current study shows that sustained-released Dinoprostone which is an FDA (U.S. Food and Drug Administration) approved drug; is an alternative method for the induction of labor although it is not cost effective.
Keywords: Cervical ripening; dinoprostone; labor induction; oxytocin.

Özet
Eylem indüksiyonu gebelerde en sık uygulanan prosedürlerden birisidir. Servikal olgunlaşma ve eylem indüksiyonu için uygun tedavi rejimi tam olarak belirlenmemiştir. Çalışmamızın amacı, eylem indüksiyonu için kullanılan vajinal dinoproston ve intravenöz oksitosinin etkinlik ve güvenilirliğini karşılaştırmaktır. Ocak 2010-Haziran 2011 tarihleri arasında Okmeydanı Eğitim ve Araştırma Hastanesi, Kadın Hastalıkları ve Doğum Kliniği'nde eylem indüksiyonu yapılan 294 hastanın dosya kayıtları retrospektif olarak incelendi. Olgular iki gruba ayrıldı. Birinci gruptaki 143 hastaya; 10 miligram kontrollü salınımlı dinoposton posterior vaginal fornikse yerleştirildi. İkinci gruptaki 151 hastaya ise intravenöz oksitosin uygulandı. Maternal ve fetal sonuçlar karşılaştırmalı olarak incelendi. Her iki grup arasında parite, doğum kilosu, fetal cinsiyet ve doğum şekli açısından anlamlı fark saptanmamıştır. 195 (%66.3) hasta vajinal, 99 (%33.7) hasta ise sezaryen doğum yapmıştır. Çalışmamızda, indüksiyon başlangıcından vajinal doğuma kadar geçen süre oksitosin grubunda (16.1 saat) Dinoproston grubuna (20.1 saat) göre anlamlı olarak daha kısa bulundu. Çalışmamızda hiçbir grupta, uterin rüptür ve maternal kayıp izlenmedi. Her iki grup arasında yenidoğan yoğun bakım ihtiyacı, 1. ve 5. dakika Apgar skorları açısından istatistiksel olarak anlamlı fark saptanmadı. ($p>0,05$). Oksitosin güvenilir ve efektif ve maliyet-performansı uygun bir ajandır. Araştırmamıza gore, maliyet-performans uygun olmasada, FDA (Amerikan Gıda ve İlaç Dairesi) onaylı kontrollü salınımlı Dinoproston, eylem indüksiyonu için alternatif bir metottur.
Anahtar kelimeler: Dinoproston; eylem indüksiyonu; oksitosin; servikal olgunlaşma.

Introduction

Induction of labor refers to iatrogenic stimulation of uterine contractions to accomplish delivery prior to the onset of spontaneous labor. Labor induction is one of the most frequently used procedures in pregnant women. The prevalence of labor induction has doubled over the past two decades. This increase is partly related to a rise in the number of medically and obstetrically indicated inductions; however, it appears that marginally indicated and elective inductions account for a large proportion of this increase. Indications vary, but most obstetricians use labor induction for prolonged pregnancy because it has been shown to reduce perinatal mortality when used after 41 weeks of ge
station (1). The optimal regimen for preinduction cervical ripening and labor induction has not been established. Although local application of prostaglandin E2 (PGE2) has been considered effective for cervical ripening and shortening delivery time (2,3), this procedure is very expensive and thus unavailable to obstetricians in many developing or underdeveloped countries. Oxytocin is the agent most frequently used for the induction of labor (4,5). Oxytocin infusion is also effective for cervical ripening; however, a Cochrane meta-analysis has concluded "prostaglandin agents probably overall have more benefits than oxytocin alone" (6).

The aim of the present study was to compare the efficacy and safety of vaginal dinoprostone and intravenous oxytocin administration for labor induction.

Material and Methods

The medical records of patients who underwent labor induction at Okmeydanı Teaching and Research

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Hospital, Department of Obstetrics and Gynecology, from January 2010 to June 2011 were evaluated retrospectively. The protocol was approved by the hospital ethics committee.

Criteria for eligibility were as follows: ≥ 38 weeks of gestation, a reassuring fetal heart rate (FHR) pattern, an unfavorable cervix (Bishop score ≤ 4), cephalic presentation, and intact amniotic membranes. Exclusion criteria included the following: any contraindication to vaginal delivery, previous Cesarean delivery or uterine scar, previous cervical surgery, a sonographically estimated fetal weight > 4.500 g, multiple pregnancy, grand multiparity (parity > 5), placenta previa or vaginal bleeding, any contraindication to prostaglandin use, suspected chorioamnionitis, and an abnormal FHR pattern. Demographic data included age, weight, height, gravidity, parity, and gestational age at admission and the indication for labor induction.

The treatment modality was chosen by the gynecological specialist. The first group (143 patients) received a single dose of sustained-released dinoprostone (10 mg; Propess; Vitalis, Ankara, Turkey), which was inserted high into the vaginal fornix. The drug remained in the vagina for up to 12 hours. Dinoprostone ovul is a controlled-release hydrogel pessary containing 10 mg prostaglandin E2. The second group (151 patients) received oxytocin (Synpitan, Deva, Istanbul, Turkey). The oxytocin dose regimen comprised a low-dose protocol (initial dose of 2 mu/min, with increases of 2 mu/min as often as 20 min up to 36 mu/min). All women were monitored for maternal pulse, temperature, respiratory rate, and blood pressure. External FHR monitoring was performed, and the study continued if the results showed a reassuring pattern. The same examiner performed a vaginal examination at 4-hour intervals to assess the progress of labor.

In the case of uterine hyperstimulation, oxytocin was discontinued, and a left-lying position, nasal oxygen, and intravenous hydration were indicated. All women included in the study were hospitalized. Patients were followed up with electronic FHR monitoring (EFM) and vaginal examination. In our study, uterine hyperstimulation was defined as either a series of single contractions lasting 2 minutes or more or a contraction frequency of five or more in 10 minutes. Postpartum hemorrhage (PPH) was defined as blood loss greater than 500 mL during vaginal delivery or greater than 1,000 mL with a Cesarean delivery. In the present study, we evaluated changes in the Bishop score, total labor time, and the duration of latent and active phases of labor, cases delivered vaginally or abdominally within 12 hours, maternal and fetal side effects, and complications for each study group.

Data were analyzed using NCSS (Number Cruncher Statistical System) 2007 and PASS 2008 statistical software (Kaysville, UT, USA). A χ^2 test and Fisher's exact test were used to analyze categorical variables. A Student's t-test was used to analyze normally distributed continuous variables. P-values less than 0.05 were deemed statistically significant.

Results

A total of 294 women were recruited to the study. Of these, 151 patients (51.4%) received oxytocin treatment and 143 (48.6%) received vaginal controlled-release dinoprostone. The indications for labor induction are provided in Table 1.

Table 1. Indications for induction.

Indications	n	%
Post-term pregnancy	118	40.1
Premature rupture of membranes	53	18
Oligohydramnios	43	14.6
Preeclampsia	32	10.9
Chronic hypertension	31	10.5
Intrauterine growth restriction	28	9.5
Gestational diabetes mellitus	17	5.8

No significant differences were found between the two groups with regard to parity, birth weight, fetal gender, and mode of delivery. The difference in maternal age was significant (P=0.028). A total of 159 patients (66.3%) underwent vaginal delivery and 99 (33,7%) underwent a Cesarean delivery. The decision to perform a Cesarean delivery was determined based on our usual obstetric practice, and the indication for the Cesarean section was recorded (failure to progress in established labor, fetal distress, failure to progress during labor, or umbilical cord prolapse). Fetal distress was the most common Cesarean indication in both groups. The mean latent phase duration was shorter in the oxytocin group as compared with the sustained-released dinoprostone group (10.4 vs 14.2 hours). The median time from the start of labor induction to vaginal birth was longer when prostaglandin E2 was used for labor induction than that when oxytocin was used (P<0.01; Table 2).

Table 2. Time from start of induction to vaginal birth.

	Time (hours)		P-value
Induction Agent	**Min-Max**	**Mean±SD**	
Oxytocin (n=103)	5.5-28.0	16.17±5.61	0.001**
Dinoprostone (n=91)	7.5-30.0	20.10±6.43	
Total (n=195)	5.5-30.0	18.02±6.31	

*Student t Test **p<0.01*

No significant difference was found in maternal outcome between the two groups regarding postpartum hemorrhage (500 mL) or uterine hyperstimulation. No significant differences were observed in adverse treatment, adverse effects, or complications between the groups (P>0.05). No maternal death or uterine rupture occurred. Neonatal weight, admission to the neonatal unit, and 1- and 5-minute Apgar score < 7, did not differ significantly between the two groups (P>0.05; Table 3).

Discussion

The optimal approach to labor induction should be effective, non-invasive, free of adverse effects, and cost effective (7). Induction of labor for medical or obstetrical reasons produces excellent success if the

cervix is ripe or the patient is easily inducible. Cervices that remain firm and inelastic or closed have a high rate of failed induction (20–50%). When patients with an unripe cervix deliver vaginally, they have a prolonged labor and a higher incidence of instrumental delivery (8). There are still no definite conclusions regarding labor induction. Prostaglandin E2 (PGE2) is an efficacious agent that shortens the time from induction to delivery, improves success rates, and reduces morbidity associated with labor induction. Although PGE2 may cause abnormal uterine contractions or FHR traces, abnormal psychomotor or physical development has not been reported in children born to mothers who received a vaginal PGE2 insert to stimulate cervical ripening (9). Vaginal PGE2 has been reported to provide a reasonable, effective, and reliable option to induce labor in an outpatient setting (10,11). Oxytocin with or without an amniotomy and PGE are the most widely used agents for labor induction; however, comparative studies regarding their efficacy and safety are scant and controversial (12).

Table 3. Maternal adverse effects, complications and neonatal outcomes.

OUTCOMES	Oxytocin	Dinoprostone	Total	P-value
Fever	4 50(%)	16 (53.3%)	20 (52.6%)	1.000
Nausea	2 25(%)	4 (13.3%)	6 (15.8%)	0.587
Diarrhea	0 0(%)	3 (10%)	3 (7.9%)	1.000
Hypotension	2 (25%)	3 (10%)	5 (13.2%)	0.279
Vomiting	0 (0%)	4 (13.3%)	4 (10.5%)	0.560
Postpartum hemorrhage	12 (24%)	13 (22.8%)	25 (23.4%)	0.884
Admission to NICU	7 (23.3%)	10 (25%)	17 (24.3%)	0.672
Apgar score at 1 min	7.81±0.82	7.84±0.91	7.82±0.86	0.759
Apgar score at 5 min	8.75±0.82	8.65±0.92	8.70±0.87	0.337

Data was given as n (%) and ± SD, NICU: neonatal intensive care unit

Our study was designed to compare the use of oxytocin and dinoprostone. In our study, the induction to vaginal delivery interval was significantly longer in the dinoprostone group. We also found no significant difference in the mode of delivery. The Cochrane database review, which was based on five trials and compared intravenous oxytocin and vaginal PGE in the induction of labor (13-17), suggested that induction failed within 12-48 hours less frequently with vaginal PGE than with oxytocin. Ramsey et al. (18, 19) found that fetal cardiotocographic abnormalities associated with PGE2 were less frequent and less severe than those associated with PGE1. The results reported by Kunt et al. were consistent with our study and demonstrated that the changes in FHR were similar in the PGE2 and oxytocin groups (20). In the present study, maternal and fetal complication rates were not significantly different between the two treatment groups. Additionally, the treatments were safe. Sifleler et al. found no statistically significant differences in hyperstimulation rates among misoprostol, oxytocin, and dinoprostone (21). In other studies, hyperstimulation rates for dinoprostone were reportedly higher than hyperstimulation rates for misoprostol (22, 23, 24). In the present study, one advantage is the relatively large study population, which included nulliparous and multiparous women. An important limitation of our study, however, was that the treatment modality was chosen by a gynecological specialist. Thus, the present study reports a clinical observation.

In conclusion, oxytocin is an FDA (United States Food and Drug Administration)-approved drug that is cost effective and, based on evaluations of maternal and fetal complications and outcomes, seems safe to use. The current study shows that sustained-released dinoprostone, which is an FDA-approved drug, is an alternative agent for the induction of labor, although it is not cost effective. We also believe that any of these protocols must be applied at hospitals under close follow-up.

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