

Effects of intravaginally inserted controlled-release dinoprostone and oxytocin for labor induction on umbilical cord blood gas parameters

Doğum eylemi indüksiyonunda kullanılan intravajinal dinoproston ve oksitosin'in umbilikal arter kan gazı parametreleri üzerine etkilerinin karşılaştırılması

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Abstract

Objective: To compare the effects of oxytocin and dinoprostone used in labor induction on fetal blood gas parameters.

Material and Methods: This prospective randomized trial involved 108 women who completed 37 gestational weeks and who required labor induction prior to normal vaginal birth. Labor was induced in 57 women with an intravenous low dose oxytocin regimen and in 51 with intravaginal dinoprostone (PGE₂). Following childbirth, umbilical artery blood gas was analyzed, with pH, pCO₂, pO₂, HCO₃ and base excess (BE) compared in the two groups.

Results: Mean age and obstetrical data (gravity, parity, gestational weeks and birthweight) were similar in the two groups (p>0.05). All infants had 1 and 5 minute APGAR scores ≥7. Umbilical artery blood pH was similar in the oxytocin and dinoprostone groups (7.31±0.07 vs. 7.31±0.05, p=0.780), as were the other blood gas parameters (pCO₂, pO₂, base excess and HCO₃; p>0.05 each).

Conclusion: Induction of labor with either oxytocin or dinoprostone in women with uncomplicated term pregnancies had no adverse effects on umbilical artery blood gas parameters.

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Key words: Oxytocin, dinoprostone, umbilical artery blood gas, labor induction, pH

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Özet

Amaç: Bu çalışmada amacımız, doğum indüksiyonunda kullanılan iki metod olan oksitosin ve dinoprostonun fetal kan gazı parametreleri üzerine olan etkilerinin karşılaştırılmasıdır.

Gereç ve Yöntemler: Bu prospektif randomize çalışmaya 37 gebelik haftasını doldurmuş ve doğum eylemi indüksiyonu uygulanan ve vajinal yoldan doğumu gerçekleştiren 108 olgu alındı. Eylem indüksiyonu için 57 olguya intravenöz yolla oksitosin, 51 olguya ise intravajinal dinoproston (PG E₂) uygulandı. Doğumu takiben umbilikal arter kan gazı analizi yapıldı ve her iki indüksiyon metodu için bazı parametreler (pH, pCO₂, pO₂, HCO₃ and baz açığı (BE)) incelendi.

Bulgular: İki grup arasında ortalama yaş ve obstetrik değişkenler (gravida, parite, gebelik haftası ve doğum ağırlığı) benzer saptandı (p>0.05). Tüm olgularda 1. ve 5. dakika Apgar skoru ≥7 idi. Umbilikal arter kan pH değeri oksitosin grubunda 7.31±0.07 iken ; dinoproston grubunda 7.31±0.05 olarak izlendi (p=0.780). Diğer kan gazı parametreleri değerlendirildiğinde de (pCO₂, pO₂, baz açığı ve HCO₃) iki grup arasında belirgin farklılık saptanmadı (p>0.05).

Sonuç: Komplike olmayan term gebeliklerde doğum eylemi indüksiyonunda kullanılan iki metod olan oksitosin ve dinoprostonun fetal kan gazı parametreleri üzerine olumsuz etkisi yoktur.

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Anahtar kelimeler: Oksitosin, dinoproston, umbilikal arter kan gazı, doğum eylemi indüksiyonu, pH

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Introduction

Induction of labor refers to the process whereby uterine contractions are initiated by mechanical or pharmacological methods before the onset of spontaneous labor (1). Induction of labor is advised in situations when the pregnancy is dangerous for the mother or fetus; or when induction is beneficial for both. Induction of labor decreases operative labor and minimizes risks to the fetus (2). Labor is induced in 20% of all pregnancies (3).

Among the factors influencing the method used to induce labor are cervical and membrane status, parity, and patient and provider preferences (4). The ideal method should be safe, painless, inexpensive, comfortable and effective. The most common pharmacological agents are oxytocin and prostaglandins (PGE₁ and PGE₂) (5). Oxytocin is a safe and efficient starter of uterine contractions, but its success is associated with the condition of the cervix at the start of the labor. Dinoprostone (PGE₂) is used to turn an unfavorable to a favorable cervix before the induction of labor (6, 7).

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If labor is not induced under acceptable indications and surroundings, the uterus may be overstimulated, causing it to contract too frequently. Too many contractions may lead to changes in fetal heart rate and result in fetal distress (2). We therefore compared the effects of oxytocin and dinoprostone on fetal blood gas parameters.

Material and Methods

This study involved women pregnant for ≥ 37 weeks who did not experience spontaneous uterine contractions, had a cervical Bishop score ≤ 3 , and were in need of labor induction. Women with fetal distress before labor induction, as determined by fetal monitoring; with a pathological umbilical artery or pathological findings on Doppler examination; with intrauterine growth retardation; or with maternal disease (e.g. thyroid dysfunction, diabetes, hypertension, preeclampsia, or cardiac disorders) were excluded. We enrolled 160 consecutive pregnant women fulfilling the above criteria; these women were randomized 1:1 to labor induction with oxytocin or dinoprostone using numbers generated randomly by a computer. Indications for labor induction were postterm pregnancy (n=81), premature rupture of membranes (n=50), non-assurance on non-stress tests (n=11), and oligohydramnios (amniotic fluid index < 60 mm in all four quadrants; n=18). Seven women withdrew consent prior to the initiation of medication and were removed from the study.

Labor was induced in one group with intravenous low dose oxytocin (Synpitan® amp) and in the other with Propess®, a hydrogel polymer matrix containing 10 mg dinoprostone, administered intravaginally. Each woman in the oxytocin group received an intravenous infusion of 2 mU/min oxytocin, which was doubled at 15-min intervals until the appropriate contraction pattern (at least 200 Montevideo Units) was achieved. The infused dose was increased to a maximum of 20 mU/min and afterward kept constant, even after an ideal pattern was reached. If a contraction pattern had not been induced after 18 hours or if spontaneous labor did not start within 18 hours of receiving oxytocin, a cesarean section was performed.

In patients randomized to dinoprostone, fetal heart rate and uterine activity were monitored continuously, starting 15 to 30 minutes before treatment. A polymer matrix containing dinoprostone was placed intravaginally on the posterior fornix, releasing PGE₂ at a constant rate of 0.3 mg/h over 12 hours. As hyperstimulation may occur after placement of the insert, fetal heart rate and uterine activity were monitored continually, from the time of insertion to 15 minutes after removal. The insert was removed by pulling the cord at the start of active labor or at the time of uterine hyperstimulation. If active labor did not start within 12 hours of insertion, the insert was removed and oxytocin infusion was begun.

Five patients in the dinoprostone group were removed from the study, 3 due to spontaneous dislocation of the insert and 2 due to hyperstimulation. Three patients in the oxytocin group elected to stop oxytocin infusion and were removed from the study. Eleven patients in the dinoprostone group were switched

to oxytocin for progression of labor. An additional 11 patients were removed from the dinoprostone group, 6 for fetal distress and 5 for cephalopelvic disproportion and malpresentation; and 15 patients were removed from the oxytocin group, 7 for fetal distress, 5 for labor dystocia and 3 for non response to oxytocin. All 26 of these patients underwent cesarean sections. The remaining 108 patients, 51 in the dinoprostone group and 57 in the oxytocin group, were included in the study. The study flow chart is shown in Figure 1.

Following vaginal birth, the umbilical cord was clamped, and a 2 cc blood sample was drawn from the umbilical artery within 30 seconds. Blood gas samples were analyzed for pH, pCO₂, pO₂, HCO₃ and base excess (BE), while obeying the rules of cold chain. One and 5 minute APGAR scores of each newborn were recorded.

This study protocol was approved by the Local Ethics Committee of our Hospital, and all subjects provided informed consent.

Power and Statistical Analyses

The primary end point of our study was a comparison of blood gas parameters in the two groups. We calculated the minimal sample size for this trial using G*power ver. 3.1.3 software (Germany). We estimated a minimum of 49 patients per group, assuming an effect size of 0.6, a Type I error (α) of 0.05 and a statistical power of 90%. Assuming an overall loss rate of 40%, however, with 20% of patients undergoing cesarean section and 20% lost for other reasons, we planned to enroll 160 subjects (80 per group).

Data were analyzed using SPSS ver. 17.0 software. Before statistical analysis, the normal distribution of continuous data was tested using the Shapiro-Wilk test. All the parameters except for gravidity and parity were distributed normally ($p > 0.05$). Normally distributed parameters were expressed as mean \pm SD and compared using independent sample T tests, non-normally distributed parameters were expressed as median (IQR) and compared using Mann-Whitney U tests. A p value ≤ 0.05 was considered statistically significant.

Results

The mean age of all women enrolled in this study was 26.0 ± 5.1 years, and the mean gestational age was 39.8 ± 1.0 weeks.

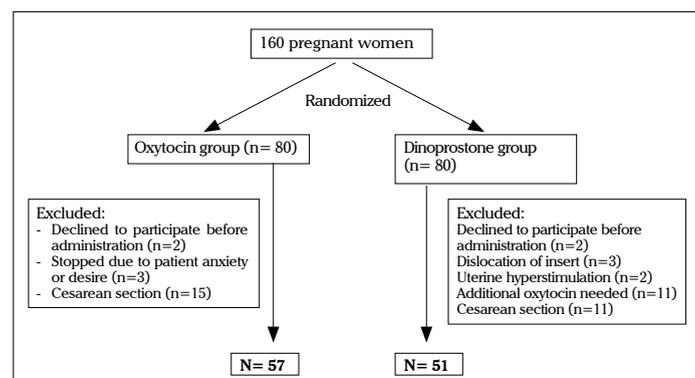


Figure 1. The flow chart of the study

Indications for labor induction in the dinoprostone group included postterm pregnancy in 27 women, premature rupture of membranes in 18, oligohydramnios in 3 and non reassuring NST in 3; whereas indications in the oxytocin group were postterm pregnancy in 29, premature rupture of membranes in 22, oligohydramnios in 4 and non-reassuring NST in 2. The demographic and obstetrical data of the two groups were comparable ($p > 0.05$ each; Table 1). All infants had 1 and 5 minute Apgar scores ≥ 7 .

Comparisons of umbilical arterial blood gas pH, pCO_2 , pO_2 , HCO_3 and BE showed no differences between the oxytocin and dinoprostone groups ($p > 0.05$ each; Figure 2).

Discussion

The initiation of labor has become a routine procedure in gynecology and obstetrics clinics. Indications for labor induction include postterm pregnancy, early rupture of membranes, fetal distress, intrauterine growth restriction, fetal death, placenta detachment, preeclampsia, maternal disease and chorioamnionitis (2). We compared the effects of two different methods of labor induction on fetal blood gas parameters. To exclude the effects of fetal distress, we excluded women with chronic maternal disease, complications of pregnancy or fetal distress, and included only uncomplicated pregnancies ending with vaginal birth. Evaluations included Apgar scores and umbilical artery blood gas parameters of the newborn to determine whether acidemia had occurred.

Table 1. Demographic, clinical and blood gas characteristics in the oxytocin and dinoprostone groups

	Oxytocin (n=57)	Dinoprostone (n=51)	P value
Age*	26.4±5.9 (18-37)	25.5±4.3 (19-40)	0.576
Gravidity†	2.0 (2) (1-8)	1.0 (1) (1-5)	0.034
Parity†	1.0 (1) (0-3)	0 (1) (0-2)	0.195
Gestational weeks*	39.7±1.2 (37.1-41.3)	40.0±0.8 (38.1-41.7)	0.469
Birthweight (g)*	3382±457 (2555-4490)	3473±385 (2820-4320)	0.335
pH*	7.31±0.07 (7.10-7.47)	7.31±0.05 (7.18-7.38)	0.780
pCO_2 (mmHg)*	43.14±8.67 (22.1-65.2)	44.16±7.74 (22.1-59.7)	0.579
pO_2 (mmHg)*	18.84±8.29 (4.1-41.2)	18.70±7.40 (6.7-40.1)	0.981
BE (mmol/L)*	-3.76±2.50 (-12-0)	-3.28±2.92 (-13-2)	0.479
HCO_3 (mmol/L)*	21.71±1.19 (19.8-25.6)	21.86±1.68 (19.2-25.4)	0.620

*Mean±SD (min-max), †Median (Interquartile range) (min-max)

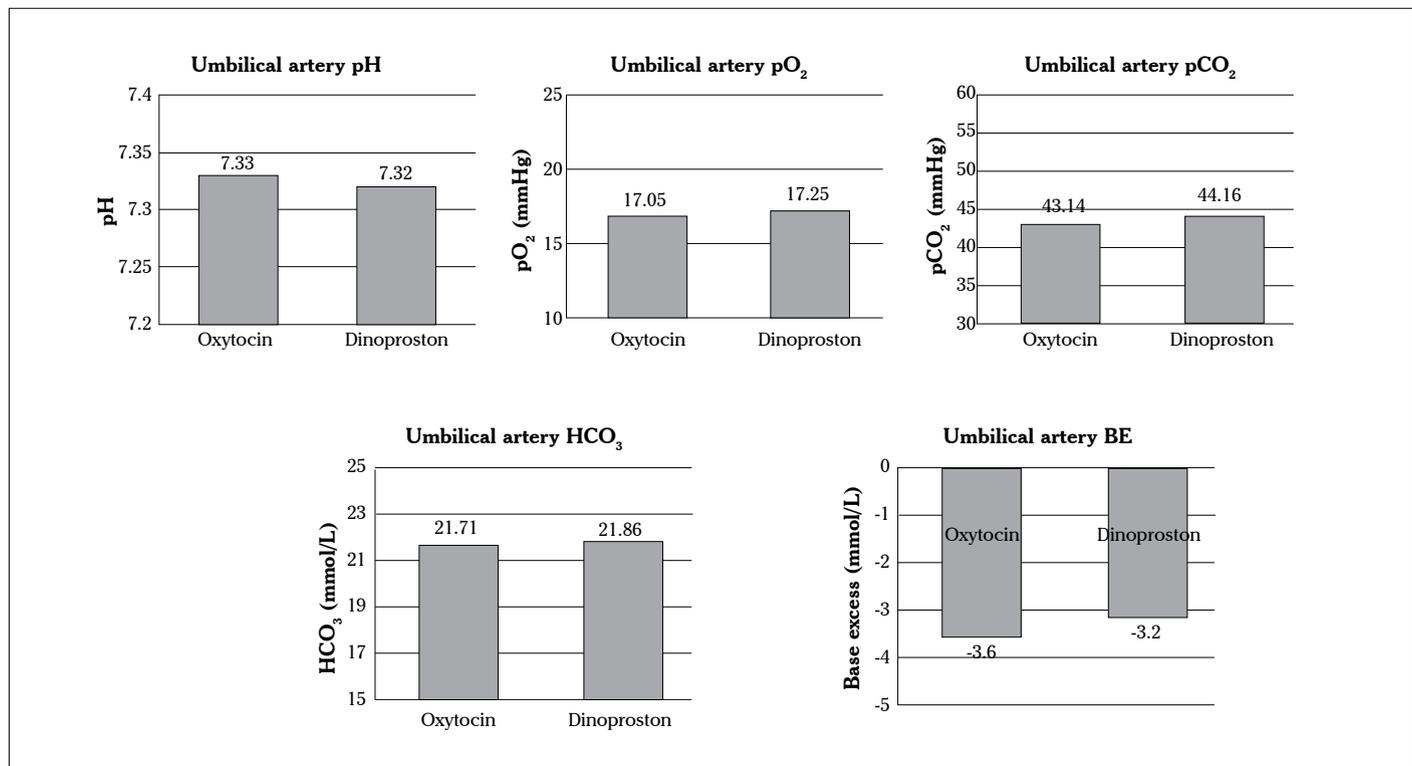


Figure 2. Umbilical artery blood gas parameters in the oxytocin and dinoprostone groups. (A) pH, (B) pO_2 , (C) HCO_3 concentration, (D) base excess (BE)

Low Apgar scores are indications of fetal depression and hypotonicity and can be affected by many other parameters other than asphyxia. The acid/base status of umbilical artery blood gas may be an alternative to Apgar score in evaluating neonatal status and in managing any neonatal assistance required. Umbilical artery pH has been shown to be an objective measurement of fetal acid/base balance (8). Fetal acidemia has been defined as $\text{pH} \leq 7.20$ and pathological fetal acidemia as $\text{pH} \leq 7.0$. Risks of fetal morbidity and mortality were found to be increased at umbilical artery $\text{pH} \leq 7.0$, whereas no morbidity was observed in term babies with umbilical artery $\text{pH} > 7.0$ (9). Intravenous administration of oxytocin is the method most frequently used to induce labor (10). Although treatment with oxytocin does not increase fetal morbidity, uterine hyperstimulation may result in fetal distress, uterine rupture and/or water intoxication (10). Uterine perfusion decreases during contractions, and increased uterine activity has negative effects on uteroplacental and fetoplacental circulation (11). Intravenous oxytocin was shown to result in hyperstimulation in 8.3-11.1% of women and fetal distress in 15.9-18%, suggesting that oxytocin application during labor may trigger fetal oxidative stress (5, 12). However, oxytocin did not have any negative effects on pH and did not increase perinatal risk (11, 13). When we investigated the effects of oxytocin-induced labor on fetal acid-base status, we observed an acid-base balance in the umbilical cord, a finding supported by intrapartum cardiotocographic findings and Apgar scores. Thus, the use of oxytocin to assist labor does not have negative effects on the fetus (11, 13).

Intracervical or intravaginal application of dinoprostone (PGE_2) is also frequently used to induce labor (5, 6, 10). Long term treatment with low-dose controlled dinoprostone was well tolerated by both the mother and the fetus (14), with uterine hyperstimulation rates of 7.4-7.8% and fetal distress rates of 10.9-26% (5, 12). In comparison, we observed lower uterine hyperstimulation (2.6%) and fetal distress (7.7%) rates in our dinoprostone group, whereas the fetal distress rate in our oxytocin group was 9.3%. In addition, about 19% of women in whom cervical maturation was established with dinoprostone have been reported to require oxytocin for the progression of labor (12, 15). In comparison, we found that this rate was 14.1%. Few studies to date have compared the effects of oxytocin and dinoprostone on fetal umbilical artery blood gas parameters. A comparison in 91 pregnant women showed no differences in methods of delivery or neonatal Apgar scores (16), although that umbilical artery blood pH was lower after PGE_2 than after oxytocin treatment (16). Arterial and venous umbilical cord gas parameters have been found to be unaffected by oxytocin augmentation or induction (11, 13). Moreover Apgar scores, which indicate the well being of newborn infants, were shown to be statistically similar in women induced with dinoprostone and oxytocin (5, 12). We found that all Apgar scores were ≥ 7 , all umbilical artery pHs were above 7.10, and none of the newborns experienced fetal acidosis. Umbilical artery blood gas parameters did not differ significantly in our oxytocin and dinoprostone groups, indicating that their safety and effectiveness were similar for labor induction.

Conclusion

We found that both labor induction agents, oxytocin and dinoprostone, did not have any unfavorable effects on fetal blood gas in uncomplicated term pregnancies.

Conflict of interest

No conflict of interest was declared by the authors.

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