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RESEARCH ARTICLE

UMBILICAL CORD BLOOD GAS VALUES IN PREGNANT WOMEN APPLIED OXYTOCIN AND VAGINAL DINOPROSTONE FOR LABOR INDUCTION

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ABSTRACT

The current study aims to compare the umbilical cord blood gas parameters, neonatal and maternal outcomes in pregnant women induced with oxytocin and dinoprostone. Women at term with a Bishop score 4 and 6 were randomized into two groups to undergo induction of labor with either high-dose oxytocin administered intravenously (n = 93) or dinoprostone-only vaginal suppository without oxytocin augmentation (n = 93). The umbilical cord was clamped. Arterial blood gas values were evaluated in less than 30 minutes after sampling pH, base excess, pCO2, pO2 and HCO3 were measured.. APGAR scores were determined by a neonatologist at first and fifth minutes after birth. All resuscitated babies were either transferred to the NICU or the neonatology service. There were no significant differences in cesarean section and vaginal delivery rates between the oxytocin and dinoproston-only groups.(p > 0,05). There were no significant differences amongst oxytocin and dinoproston-only groups in terms of pH values, PCO2, HCO3, Base-E, lactate levels, number of parities,1-and 5-minute Apgar scores, and the need for neonatal intensive care unit (NICU). (p > 0,05). In colclusion, we suggest that under proper indicatons, oxytocin and dinoprostone have no adverse effects on perinatal outcomes and all umbilical cord blood gas parameteres.

INTRODUCTION

Labor induction is one of the most common interventions in the obstetrics practice. At least 19.8% of deliveries in the developed countries are assumed to be induced.[1] Labor induction is a process where mechanical and pharmacological methods are used to start the spontaneous onset of labor.[2] The ideal method should be safe, painless, comfortable, effective and low-cost. Oxytocin is a common, effective and credible induction agent in favorable cervices. [3,4] If the cervix is unfavorable, prostaglandins are the most commonly opted pharmacological agents. Prostaglandin analogues such as dinoprostone (PGE_2) and misoprostol (PGE_1) are commonly used in labor induction for cervical ripening and stimulation of uterine contractions leading to a successful vaginal delivery. Dinoprostone has been approved by the FDA for use in cervical ripening in term and near term pregnancies. [5-8] Although many studies have shown that oxytocin and prostaglandin E_2 do not affect neonatal outcomes their effects on umbilical cord blood gas parameters and neonatal outcomes is still controversial.[3,4,9,10] and there are few studies examining all the cord parameters. The purpose of the current study is to compare umbilical cord blood gas parameters and neonatal outcomes in oxytocin and prostaglandin administered pregnancies.

MATERIAL AND METHODS

This study is a prospective randomized study of pregnant women who received labor induction at the Unit of Obstetrics and Gynecology of Manisa Merkezefendi State Hospital between April 2014 and February 2015. The study was approved by the "scientific researches ethics committee" of the medical faculty of Celal Bayar University. 186 women who received induction of labor on the 37th gestational week and above were included in the study. Over 37th gestational week, singleton gestations with normal fetal heart rate and bishop score 4-6 before induction, were included in the study. Pregnancies with fetal malpresentation cases, history of antepartum hemorrhagia; cardiopulmonary, renal or pancreatic insufficiency, pregnancies with an estimated fetal weight above 4500 gr, pregnancies with previous myomectomy and/or c/s delivery or any contraindications for vaginal delivery, multiple pregnancies, placenta previa, hypersensivity to

Dinoprostone are excluded from the study. The study group was divided into two groups as "oxytocin group" with high dose oxytocin infusion and "dinoprostone group" with continuous release of 10mg dinoprostone in form of vaginal suppository. Randomization was done via closed envelopes containing numbered cards for indications. Indications for labor induction were IUGR cases with an estimated fetal weight of less than 10 percentile at 37 weeks or with a s/d ratio of> 3.0 or RI> 0.6, the GDM-originated macrosomia cases, with an estimated risk of birth weight over 4000 gr according to the Hadlock formula, preeclampsia, post-term pregnancy and oligohydramnios (amniotic fluid index <5 cm). [11] Fifteen patients from the oxytocin group and 10 from the dinoprostone group were excluded from the study because of rejection for further intervention after the induction protocol started. The flow of participants before and after randomization is summarized in **Figure 1.**

Study Protocol

Patients in the oxytocin group received an infusion of Oxytocin (Synpitan® , Deva, İstanbul, Turkey)starting at 4 mIU / min in a 500 ml saline infusion and increasing 4 mIU every 30 min until regular uterine contractions (4-5 contractions / 10 min) were achieved. [12,13] In the dinoprostone group, patients were treated with 10 mg intravaginal dinoprostone (Propess®, Vitalis, Ankara, Turkey), which consists a hydrogel polymer matrix (0.3 mg / hr) and provides a dinamic release of dinoprostone and after 12 hours of application or in the first phase of labor- transition from latent phase to active phase (At least 3 regular contractions present within 10 minutes for 60 seconds and 4 cm cervical dilatation are defined as transition from active phase to latent phase). Patients in the dinoprostone group were not administered concurrent oxytocin infusion. In the oxytocin group, i.v. oxytocin infusion was applied until delivery. In the study, cervical dilatation and maturation, which was considered to be a failed induction after 12 hours of oxytocin infusion and/or intravaginal dinoprostone application, were induced with c/s. Demographic data (maternal age, BMI, gestational week, gravida, parity), bishop score and birth indications were recorded. APGAR scores of the 1st to 5th minutes of the newborns were recorded. Before and after the induction of labor, USG examination and fetal biometric measurements were performed and the pregnants were examinated vaginally every 2 hours. Continuous fetal heart rate (FHR) monitoring was performed during induction. Variable deceleration or FHR of >160/min, sinusoidal pattern, late decelaration, low persistence of variability were accepted as non-response FHR patterns.[14] Patients with tachysystole and hyperstimulation syndrome (tachysystole refers to at least six uterine contractions per 10 minutes in two consecutive 10-minute periods. A single uterine contraction, which lasts at least 2 minutes, is defined as uterine hypertonus.) Were managed with left lateral position, cutting of oxytocin infusion, 500ml i.v. bolus crystalloid infusion, and oxygen inhalation with mask; and c/s rates, maternal and fetal outcomes and hospitalization times were evaluated as secondary outcome in terms of the safety of induction. After delivery, the umbilical cord was clamped within 30s and a 2cc arterial blood sample was taken in a heparinized insulin syringe. pH, pCO2, pO2 and HCO3 were measured with pH and gas analyzer (AVL, Compact3, Australia) at 37°C. Arterial blood gas values were examined within the next half an hour after sampling. The 1st and 5th minute APGAR scores were assessed by a neonatalogist after delivery. All infants who were resuscitated were hospitalized to neonatal services or newborn intensive care unit.

Sample size estimation

On the basis of our pilot study, a total sample size of 146 (73 per group) women was required to provide 85% power and a 5% significance level to show a difference of 25% between groups for successful vaginal delivery within 24 h. Assuming nearly a 20% drop-out rate, a total of 186 women would need to be recruited.

Statictical Analysis

Statistical Package for the Social Sciences version 19.0 (SPSS Inc., Chicago, IL, USA) was used for statistical analysis. The normality of quantitative variables was tested by the Kolmogorov- Smirnov test. A comparison was made between these factors among the two groups of women by means of the Student's t-test and Mann-Whitney U-test, respectively. The $\chi 2$ test or Fisher's exact test was used to express qualitative variables as frequencies and to analyze percentages. Statistical significance was accepted as $p < 0.05$.

RESULTS

Seventy eight patients from the oxytocin group and 83 patients from the dinoprostone group were analyzed. The demographic characteristics of the subjects included in the study are given in **Table 1**.

Table 1 Demographic data, indications of labor induction, and median bishop scores of the study groups

	Oxytocin (n:78)	Dinoprostone-Only (n:83)	P-value
Maternal age, years	28.6±4.5	28±4.6	0.377
BMI, kg/m2	27.3±4.1	26.4±3.5	0.120
Gestational age at labor induction, weeks	39.8±1.3	39.7± 1.4	0.742
Gravidity	1.8 (1-4)	16 (1-5)	0.074
Parity	1 (0-3)	0.8 (0-4)	0.118
Nulliparous, n (%)	23 (29.4)	30 (36.2)	0.372
Multiparous, n (%)	55 (70.6)	53 (63.8)	0.372
Bishop score at labor induction	5.21±0.7	5.17±0.7	0.762
Indication of labor induction			
Oligohydramnios n (%)	20 (25.6)	25 (30.1)	ns
Post-term pregnancy n (%)	39 (50)	35 (42.2)	ns
Intrauterine growth retardation n (%)	7 (9)	9 (10.8)	ns
Preeclampsia n (%)	9 (11.5)	10 (12)	ns
Diabetes n (%)	3 (3.8)	4 (4.8)	ns

There is no significant difference between demographic data. Nineteen of the 78 patients in the oxytocin group and 20 of the 83 patients in the dinoprostone group delivered with c/s due to an indication of induction of labour (IOL) failure. There was no significant difference in c/s and normal vaginal delivery rates between oxytocin and dinoprostone groups. **(Table 2)**. When the APGAR scores of 1st and 5th minutes of newborns are evaluated; Oxytocin and dinoprostone groups did not show any significant differences (7.72 ± 0.95 vs 7.54 ± 1.456 P =

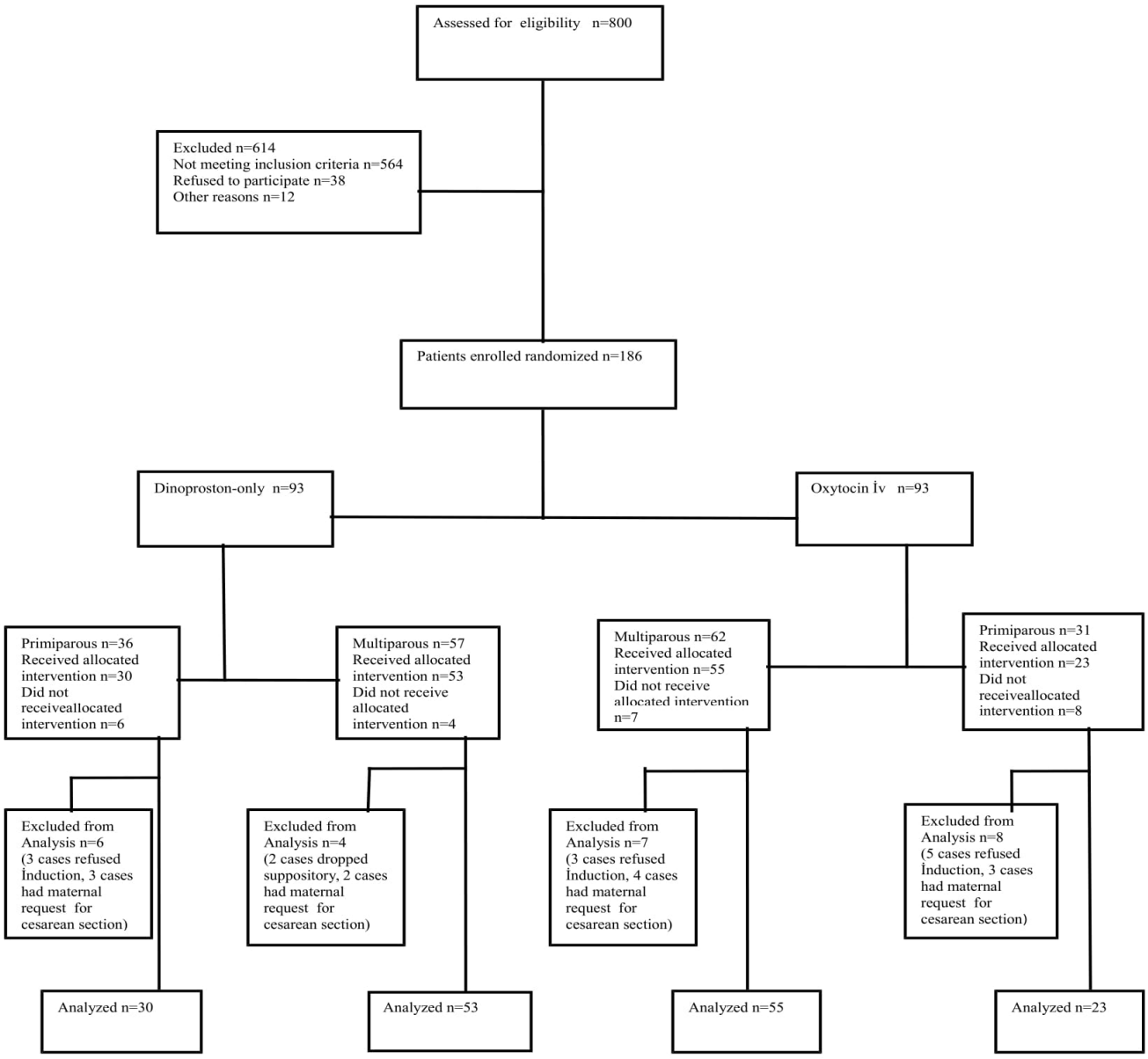

Figure 1 Diagram showing the flow of participants before and after randomization

Table 2 Indications to Cesarean Section and rates of vaginal and operative vaginal delivery (no, %)

	Oxytocin (n:78)	Dinoprostone -Only (n:83)	P-value
Suspected fetal distress n (%)	4(5.1%)	5(6%)	ns
Failed induction n (%)	6(7.7%)	4(4.8%)	ns
Fetal malpresentation n (%)	2(2.6%)	3(3.6%)	ns
Failure to progress during the first stage of labor n (%)	5(6.4%)	7(8.4)	ns
Failure to progress during the second stage of labor	2(2.6)	1(1.2)	ns
Total Cesarean Section	19	20	
Vacuum extraction-assisted vaginal delivery n (%)	4 (5.1)	3 (3.6)	ns
Non operative vaginal delivery n (%)	55 (70.5)	60 (73.2)	ns
Total vaginal delivery	59	63	

Abbreviation: ns, not significant.

0.362 and 9.81 ± 0.80 vs 9.66 ± 1.14 P = 0.356). Also there was no significant difference between oxytocin and dinoprostone groups in pH, pCO2, pO2, HCO3 and BE values in umblical artery blood gas analyzes. (P> 0.05).

Three of the neonates in the oxytocin group and 2 of the neonates in the dinoprostone group were admitted to the neonatal intensive care unit and no significant difference was found between the groups **(Table 3)**.

Table 3.Blood gas characteristics in the ocytocin and dinoprostone groups and and neonatal outcomes (no, %)

	Oxytocin (n:78)	Dinoprostone -Only(n:83)	P-value
pH	7.27±0.06	7.25±0.11	0.347
pCO2 (mmHg)	54.6 ±64.7	48.8 ±12.4	0.446
BE (mmol/L)	-3.84±4.31	-3.35±5.35	0.526
HCO3 (mmol/L)	19.72±2.58	19.47±2.46	0.531
laktat	3.99±2.25	4±2.95	0.904
Apgar score 1′ < 7	7.72±0.95	7.54±1.45	0.362
Apgar score 5′ < 7	9.81±0.80	9.66±1.14	0.356
NICU transfer n (%)	3 (3.8)	2 (2.4)	0.599

All newborns admitted to intensive care unit were discharged together with their mothers in good health.

DISCUSSION

Labor induction methods are commonly practiced in instances such as early rupture of membranes, post-term pregnancy, fetal death, preeclampsia and several maternal diseases. [15] Intravenous oxytocin is one of the fundamental labor induction methods.[13,14] Oxytocin reduces uterine blood flow, however negative effects on perinatal outcomes and blood pH have not yet been identified. [16,17] Dinoprostone, on the other hand, is a pharmacological agent preferred in unfavorable cervices and might have disadvantages such as early deceleration, tachysystole and prolonged hospital stay. [18,19] Despite plentiful studies comparing dinoprostone and oxytocin, very few have compared effects of these pharmacological agents on umbilical cord blood gas parameters and apgar scores. Wang *et al*. have compared pharmacological agents with mechanical stimulation but found no differences in terms of NICU rates and apgar scores. However, patients with a blood gas pH< 7.1 were significantly higher in the dinoprostone group. [20] In their studies comparing oxytocin and dinoprostone, Akay *et al*. have found no significant differences in the apgar scores. [7] Lyndrup *et al*. have neither found no significant differences in the apgar scores between the oxytocin and dinoprostone groups in their study investigating 91 pregnant women, nevertheless the blood gas pH values were lower in the dinoprostone group. [21] Hidalgo-Lopezosa *et al* found no differences in apgar scores between pregnancies treated with oxytocin, however in most patients found pH values as low as 7.2. [22] Differently, keskin *et al* have reported no significant differences in the apgar scores as well as cord gas pH values, pCO2 (mmhg), HCO3 (mmhg) and BE (mmol/L). [16] There are few studies examining all the cord parameters. İn this study, we have compared all cord blood paramaters oxytocin and dinoprostone induced pregnant women. in our study no significant differences were demonstrated between the two groups in terms of apgar scores, blood pH as well as pCO2 (mmhg), HCO3 (mmhg), BE (mmol/L) and lactate values. in most studies, despite the low pH value of labor induction with dinoprostone, we found no significant differences were demonstrated between the dinoprostone and the oxytocin groups.

Moreover, our study has also investigated the NICU admission rates amongst pharmacologically induced pregnancies. Özkan *et al*. have reported a NICU admission rate of 5.4% in babies of 56 dinoprostone induced women. [19] Wang *et al*. found no significant differences in NICU admissions between the dinoprostone and the mechanically assisted group; NICU admission rate was found to be 3.4% in the dinoprostone group. [20] Akay *et al*. reported a rate of 4.1% NICU admission in the dinoprostone group, however no significant differences between the two groups were revealed. [20] The current study revealed the NICU admission rate in both the dinoprostone and the oxytocin group to be 3.8%, and 2.4% no statistical differences were found.

CONCLUSIONS

In conclusion, in most studies, despite the low pH value of labor induction with dinoprostone, we found no significant differences were demonstrated between the dinoprostone and the oxytocin groups. We suggest that under proper indicatons, oxytocin and dinoprostone have no adverse effects on perinatal outcomes and umbilical cord blood gas parameteres and dinoprostone can still be used safely in labor induction

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Acknowledgements

None

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