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# Comparison of high and low doses of oxytocin protocols in multiparous pregnant women in terms of labor durations and fetal-maternal complications

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## Abstract

**Objective:** Our aim is to compare high and low doses of oxytocin protocol applied during labor induction in terms of reliability and efficacy in multiparous pregnant women with Bishop score ≥6.

**Methods:** Pregnant women between 37 and 41 weeks of gestation who had singleton and alive fetuses in vertex presentation, whose labor did not start spontaneously, who had no history of uterine surgery and no fetal congenital anomaly, who had Bishop score 6 and higher were included in this single center, randomized, prospective study with the indications of Category II trace, oligohydramnios and rational/psychosocial factor after obtaining their informed consent forms. A total of 164 multiparous pregnant women were separated into two groups during admission by simple randomization with opaque envelopes according to onset and increasing doses of oxytocin. In the groups which received low and high doses of oxytocin, labor durations, delivery types, newborn measurements, meconium presence, the presence of cord on neck, blood gas analyses, placental weights, maternal complications (postpartum bleeding, need for postpartum transfusion, puerperal fever, grades III–IV perineal lacerations and uterine rupture) and early newborn morbidity (respiratory distress, birth trauma, shoulder dystocia and neonatal hyperbilirubinemia) were compared.

**Results:** When 75 pregnant women administered high doses of oxytocin and 75 pregnant women administered low doses of oxytocin were compared, no difference was observed between the groups in terms of the durations of phase I, phase II and phase III of labor, cesarean section rates, and maternal and perinatal complications (p>0.05). Although there was an increase in the rate of dark meconium by high dose induction protocol (p=0.01), the difference could not be established due to the limitations of the study in terms of intrapartum hypoxia which can be associated with 5-minute Apgar score being below 5 and acidemia in umbilical artery, pH being below 7, and base excess being 12 mmol/L and above.

**Conclusion:** There is no difference between high or low doses of oxytocin induction in multiparous pregnant women in terms of labor duration, cesarean section rate, and maternal and perinatal complications.

**Keywords:** Induction, labor, parity, oxytocin.

## *Özet:* Multipar gebelerde yüksek ve düşük doz oksitosin protokollerinin doğum eylem süreleri ve fetal-maternal komplikasyonlar açısından karşılaştırılması

**Amaç:** Amacımız, doğum indüksiyonunda uygulanan yüksek ve düşük doz oksitosin protokolünün multipar, Bishop skoru 6 ve üzerinde olan gebelerde, güvenirlilik ve etkinlik açısından karşılaştırılmasıdır.

**Yöntem:** Tekil, canlı, verteks prezentasyonunda, doğumu kendiliğinden başlamamış, daha önce geçirilmiş uterin cerrahisi olmayan, fetal konjenital anomali saptanmayan, 37–41. gestasyonel hafta arasında, Bishop skoru 6 ve üzerinde olan gebeler bilgilendirilmiş onam sonrası Kategori II trase, oligohidramnios, rasyonel/psikososyal faktör endikasyonları ile tek merkezli, randomize, prospektif çalışmaya dahil edildi. Çalışmadaki 164 multipar gebe, oksitosin başlama ve artış dozuna göre basit randomizasyon ile opak zarflarla kabülde seçilerek iki gruba ayrıldı. Düşük ve yüksek doz oksitosin alan grupların, doğum eylemi süreleri, doğum şekli, yenidoğan ölçümleri, mekonyum varlığı, boyunda kordon mevcudiyeti, kan gazı analizleri, plasenta ağırlıkları, maternal komplikasyonları (postpartum kanama, postpartum transfüzyon gereği, puerperal ateş, III.–IV. derece perine laserasyonları ve uterin rüptür) ve erken yenidoğan morbiditesi (solunum sıkıntısı, doğum travması, omuz distosisi, neonatal hiperbilirubinemia) karşılaştırıldı.

**Bulgular:** Yetmiş beş yüksek doz ve 75 düşük doz oksitosin uygulanan gebe karşılaştırıldığında, doğum eyleminin I. evresi, II evresi ve III. evresinin süreleri; sezaryen doğum oranları, maternal ve perinatal komplikasyonlar açısından gruplar arasında fark izlenmedi (p>0.05). Yüksek doz indüksiyon protokolü ile koyu mekonyum oranında artış belirlense de (p=0.01), beşinci dakika Apgar skorunun 5'in altında olması ve umbilikal arterde asidemi, pH'ın 7'nin altında olması ve baz fazlasının 12 mmol/L ve üstü olması ile ilişkilendirilebilen intrapartum hipoksi açısından farklılık, çalışmanın sınırlılığı nedeni ile belirlenemedi.

**Sonuç:** Multipar gebelerde yüksek ya da düşük doz oksitosin indüksiyonu arasında, eylem süresi, sezaryen doğum oranı, maternal ve perinatal komplikasyonlar açısından fark yoktur.

**Anahtar sözcükler:** İndüksiyon, eylem, parite, oksitosin.

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## Introduction

Labor induction is the stimulation of uterine contractions through any mechanical procedure, pharmacological or non-pharmacological agents or complementary methods independent from spontaneous onset of labor or the rupture of amniotic membranes.[1] The rate of labor induction increases over the years, it increased from 9.5% in 1990 to 23.2% in 2011.[2] Families declining fetal risks by informed consent form which may occur during late term and postterm pregnancies and their induction preferences, using cervical maturing agents, increased experience of clinician on the use of induction, wide use of fetal monitorization enabling monitorization during induction and rational/psychosocial factors are among the basic reasons for the increase of labor induction rate.[3]

Although there are many pharmacologic agents involved in the labor induction, oxytocin is the most common one among them. This hormone, which is in polypeptide structure secreted in a pulsatile way from the posterior lobe of hypophysis proceeding through the axons of neurons and synthesized from the supraoptic and paraventricular nuclei of hypothalamus, was first used intravenously for labor induction by Theobald et al.[4] The use of synthetic oxytocin in labor induction is carried out by various protocols with different initial doses, incremental intervals, amounts and maximum rates. While many clinics perform their own protocols, being unable to establish a single common protocol indicates that it has been still unclear which protocol is the most appropriate and which dose minimizes perinatal and maternal complications.

Our purpose is to compare the effect of high and low doses of oxytocin induction protocols in multiparous and term pregnancies on the durations of labor phases and fetal and maternal complications.

## Methods

The pregnant women at 37 and higher weeks of gestation, who were hospitalized at the Obstetrics Clinic of Zekai Tahir Burak Women's Health Training and Research Hospital between January 2012 and May 2014, who were positive for fetal cardiac activity, had no history of cesarean section or uterine surgery and no pelvic deformation, who were not established with the diagnosis of active genital herpes, at head presentation, had no comorbid disease, who were not on medication or underwent delivery yet, and who had Bishop score being 6 and higher were included in the study.[5] The week of gestation and the date of last menstrual period of pregnant women who were included in the study with Category II trace, oligohydramnios and rational/psychosocial factor indications were determined by early ultrasonographic findings. The presence of additional problems was evaluated during admission by detailed anamnesis, physical examination, laboratory examinations (complete blood count, blood glucose, urea, creatinine, alanine aminotransferase, aspartate aminotransferase, bleeding profile, blood type and complete urinalysis) and ultrasonography. In all pregnant women, cervical dilation and cervical effacement were recorded by performing vaginal examination.

Pregnant women were separated into two groups for high dose and low dose through a simple randomization by selecting from closed opaque envelopes: The low dose group was initially administered 5 units of synthetic oxytocin (Synpitan® amp. Deva, Istanbul, Turkey) intravenously in 500 cc isotonic at the dose of 2 milliunit/min (mU/min) and the dose was increased for 2 mU/min every 15 minutes and it was infused by external cardiotocography until a sample was obtained with contraction frequency once every 2–3 minutes and contraction duration for 60–90 seconds. The maximum oxytocin dose was determined as 40 mU/min. The patients were monitored by hourly vaginal palpation and continuous cardiotocography.[6,7] The high dose group was initially administered 5 units of Synpitan® amp. intravenously in 500 cc isotonic at the dose of 4 mU/min and the dose was increased for 4 mU/min every 15 minutes and it was infused by external cardiotocography until a sample was obtained with contraction frequency once every 2–3 minutes and contraction duration for 60–90 seconds. Similarly, maximum oxytocin dose was determined as 40 mU/min.[6] The patients were monitored by hourly vaginal palpation and continuous cardiotocography.

In the cardiotocographic evaluation, normal basal fetal heart rate limits were considered as 110–160 beat/min. Basal heart rate above 160 beat/min was accepted as fetal tachycardia, below 100 beat/min as fetal bradycardia, and uterine contraction more than 5 in 10 minutes within two consecutive periods or contractions starting once every minute was accepted as tachysystole. Together with tachysystole, irregularity in fetal heart beat was evaluated separately. When abnormal fetal heart trace (late deceleration, sever variable deceleration)

or abnormal uterine contraction (tachysystole) was identified, it was monitored by discontinuing oxytocin infusion first. Decelerations lower than 110 beat/min in more than 2 minutes and less than 10 minutes in fetal heart beats in the presence of Category II trace or in the presence of type I trace in the beginning, repeating decelerations and repeating variable decelerations were evaluated as "unreliable fetal condition".[8]

Hourly progress for cervical dilations of patients from 4 cm to 10 cm was marked on time graph; amniotomy was carried out after palpation if the head was located on cervix and in case of possible vasa praevia in membranes. The duration from 4 cm to 10 cm of cervical dilation was considered as phase I, the duration from 10 cm up to delivery was considered as phase II, and the period from delivery to the separation of placenta was considered as phase III and all three phases were evaluated separately. About 10–20 cm of the cord within first 10 minutes after delivery was clamped on both sides and blood samples were collected from umbilical artery by heparinized blood gas injectors and they were examined within first 30 minutes. After separated from the placenta, the newborn was weighed and the weight was recorded. Apgar score, weight, height, head circumference, and early newborn morbidity (respiratory distress, birth trauma, shoulder dystocia, neonatal hyperbilirubinemia) of the newborns were compared. Intrapartum and postpartum complications were identified and recorded. As postpartum maternal complications, hemoglobin (Hb) and hematocrit (Hct) decreases, uterine rupture, grades III–IV perineal lacerations, postpartum fever, postpartum bleeding and transfusion at prepartum and postpartum 6th hour were evaluated.

The statistical analyses of the study were performed by BM® SPSS® Statistics 20 for Mac (IBM Corp., Los Angeles, CA, USA), and the tables of the results were prepared with Microsoft® Excel® for Mac 2011 (Microsoft Corp., Santa Rosa, CA, USA). In the evaluation of the data, mean ± standard deviation was used. In the comparison of the groups for the data obtained from the measurements, t-test was used for independent groups if the data were homogenous according to Shapiro-Wilk test, which is one of the normality tests, and Mann-Whitney U test was used if they were not homogenous. In the evaluation of repeating measurements, t-test and Wilcoxon test were used for dependent groups. In the comparison of multi-groups, one-way ANOVA was used if they were distributing homogenously and Bonferroni, one of the post hoc tests, was used for double comparisons; if they were not distributing homogenously, Kruskall-Wallis test was used and Mann-Whitney U test was used for double comparisons. Chi-square test was performed for frequency comparisons between the groups. The association between continuous data was evaluated by Pearson and Spearman correlation tests. The results were evaluated within 95% confidence interval and according to $p<0.05$ significance level.

**Table 1.** Demographic factors of the study group.

| Criteria | Groups | n | Mean | Standard deviation | p |
|---|---|---|---|---|---|
| Age | Low | 75 | 29.40 | 5.33 | |
| | High | 75 | 28.45 | 4.87 | 0.258 |
| | Total | 150 | 28.93 | 5.11 | |
| Height | Low | 75 | 160.61 | 5.66 | |
| | High | 75 | 161.11 | 6.18 | 0.611 |
| | Total | 150 | 160.86 | 5.91 | |
| Weight gained | Low | 69 | 8.29 | 3.65 | |
| | High | 71 | 8.42 | 3.8 | 0.834 |
| | Total | 140 | 8.36 | 3.72 | |
| BMI | Low | 75 | 30.51 | 4.75 | |
| | High | 75 | 30.45 | 4.73 | 0.932 |
| | Total | 150 | 30.48 | 4.72 | |
| Week of gestation | Low | 75 | 39.42 | 1.21 | |
| | High | 75 | 39.69 | 1.19 | 0.176 |
| | Total | 150 | 39.56 | 1.2 | |
| Ultrasonographic week of gestation | Low | 75 | 39.37 | 1.17 | |
| | High | 75 | 39.68 | 1.16 | 0.101 |
| | Total | 150 | 39.53 | 1.17 | |

## Results

The maternal demographic data are shown in **Table 1**. Accordingly, there was no statistically significant differ-

**Table 2.** The durations (minute) of the labor phases I, II and III in high- and low-dose oxytocin groups.

| Phases | Groups | n | Mean | Standard deviation | p |
|---|---|---|---|---|---|
| Phase I | Low | 69 | 227.32 | 136.41 | |
| | High | 71 | 216.25 | 117.27 | 0.607 |
| | Total | 140 | 221.71 | 126.73 | |
| Phase II | Low | 69 | 12.91 | 9.95 | |
| | High | 71 | 13.34 | 10.41 | 0.805 |
| | Total | 140 | 13.13 | 10.15 | |
| Phase III | Low | 69 | 8.29 | 3.65 | |
| | High | 71 | 8.42 | 3.8 | 0.834 |
| | Total | 140 | 8.35 | 3.71 | |

ence between the groups in terms of age, height, weight gained during pregnancy, body mass index (BMI) at admission and in the beginning of pregnancy, week of gestation and first trimester ultrasonographic findings.

When the association of high and low doses of induction protocols with the durations of delivery phases were evaluated, no statistically significant difference was found between two groups in terms of phase I (227.32±136.41 in low-dose group and 216.25±117.27 in high-dose group), phase II (12.91±9.95 in low dose group and 13.34±10.41 in high-dose group) and phase III (8.29±3.65 in low dose group and 8.42±3.80 in high-dose group) (**Table 2**). When the distribution of delivery type to the groups was analyzed, it was found that the rate of vaginal delivery with episiotomy was 29.3%, the rate of spontaneous vaginal delivery was 62.7% and the rate of cesarean section was 8% in the group which was applied low-dose induction while they were 42.7%, 52.0% and 5.3%, respectively, in the group which was applied high-dose induction; there was no statistically significant difference between two groups in terms of delivery type (p=0.224).

In terms of the distribution of cesarean section (C/S) indications to the groups, fetal distress was 2.6% and non-progressive labor was 5.4% in the low-dose induction group; in high-dose induction group, fetal distress was 2.65% and cephalopelvic disproportion was 2.65% as C/S indication. There was no statistically significant difference between two groups in terms of C/S indications (p=0.548). According to the values obtained by complete blood count at prepartum and postpartum 6th hour, Hb values decreased from 11.90±1.40 to 10.88±1.35 in low-dose group and from 12.01±1.46 to 11.02±1.49 in high-dose group while Hct values decreased from 35.56±3.47 to 32.91±3.38 in low-dose group and from 36.15±3.41 to 33.26±3.80 in high-dose group, indicating a significant difference (p=0.00). There was no statistically significant difference between the groups (p=0.76) (**Table 3**). Uterine rupture, grades III–IV perineal lacerations and postpartum fever were not observed as postpartum maternal complications. Due to postpartum uterine atony causing reduction in hematocrit values, a woman in low-dose oxytocin group was applied transfusion. There was no statistically significant difference between the groups in terms of maternal complications (p=0.50).

There was also no statistically significant difference between two groups in terms of placental weight, newborn weight and height, newborn's head circumference, 1-minute and 5-minute Apgar scores, cord blood gas analyses, negative logarithm of hydrogen ion concentration (pH), partial pressure of carbon dioxide ($PCO_2$), and

**Table 3.** Hemoglobin (Hb) and hematocrit (Hct) values at admission and postpartum 6th hour in high- and low-dose oxytocin induction (mean+standard deviation).

| | Parameter | Status | Mean | Standard deviation |
|---|---|---|---|---|
| Low-dose | Hb | Admission | 11.90 | 1.40 |
| | | 6th hour | 10.88 | 1.35 |
| | Hct | Admission | 35.56 | 3.47 |
| | | 6th hour | 32.91 | 3.38 |
| High-dose | Hb | Admission | 12.01 | 1.46 |
| | | 6th hour | 11.02 | 1.49 |
| | Hct | Admission | 36.15 | 3.41 |
| | | 6th hour | 33.26 | 3.80 |
| | | Final | 30.45 | 4.73 |

**Table 4.** Placental weight and newborn's measurements and analysis results of umbilical artery blood gas in high- and low-dose oxytocin induction groups.

| Criteria | Groups | N | Mean | Standard deviation | p |
|---|---|---|---|---|---|
| Placental weight (g) | Low | 75 | 638.13 | 107.25 | |
| | High | 75 | 640.27 | 105.36 | 0.902 |
| | Total | 150 | 639.2 | 105.96 | |
| Newborn weight (g) | Low | 75 | 3314.27 | 544.35 | |
| | High | 75 | 3254.93 | 488.56 | 0.483 |
| | Total | 150 | 3284.6 | 516.33 | |
| Newborn Height (cm) | Low | 75 | 49.87 | 5.49 | |
| | High | 75 | 50.4 | 1.62 | 0.421 |
| | Total | 150 | 50.13 | 4.04 | |
| Newborn's head circumference (cm) | Low | 75 | 34.75 | 1.1 | |
| | High | 75 | 34.67 | 1.07 | 0.653 |
| | Total | 150 | 34.71 | 1.08 | |
| Cord pH | Low | 40 | 7.27 | 0.08 | |
| | High | 44 | 7.28 | 0.08 | 0.283 |
| | Total | 84 | 7.28 | 0,08 | |
| Cord $PCO_2$ (mm Hg) | Low | 40 | 47.96 | 11.56 | |
| | High | 44 | 43.97 | 8.35 | 0.071 |
| | Total | 84 | 45.87 | 10.15 | |
| Cord $PO_2$ (mm Hg) | Low | 40 | 26.14 | 9.3 | |
| | High | 44 | 24.32 | 6.16 | 0.289 |
| | Total | 84 | 25.19 | 7.82 | |
| Cord $HCO_3$ (mEq/L) | Low | 40 | 21.29 | 1.88 | |
| | High | 44 | 20.97 | 2.16 | 0.478 |
| | Total | 84 | 21.12 | 2.03 | |
| 1-minute Apgar | Low | 75 | 7.33 | 0.53 | |
| | High | 75 | 7.35 | 0.48 | 0.872 |
| | Total | 150 | 7.34 | 0.5 | |
| 5-minute Apgar | Low | 75 | 9.33 | 0.53 | |
| | High | 75 | 9.35 | 0.48 | 0.872 |
| | Total | 150 | 9.34 | 0.5 | |

bicarbonate concentration ($HCO_3$) (**Table 4**). There was no case with umbilical artery pH being 7 and below. The comparison of cord entanglement to the neck between the groups is summarized in **Table 5**. Accordingly, there was no statistically difference between the groups (p=0.164). When the comparison characteristics of meconium at delivery was evaluated between the groups, it was seen that 13.3% of the pregnant women in low-dose group had thin meconium and there was no dark meconium in this group, while 1.3% of the pregnant women in high-dose group had thin meconium and 1.3% of them had dark meconium. Accordingly, thin meconium was found less in high-dose group, and there was only one case with dark meconium. The difference in the rate of total amnion with meconium was found to be statistically significant (p=0.012). There was also no difference between the groups in terms of neonatal hyperbilirubinemia and birth trauma which appear as respiratory distress, cephalohematoma and clavicle fracture (**Table 5**).

**Table 5.** The data on meconium, cord entanglement on the neck, birth trauma and hyperbilirubinemia of newborn.

| | | Cord entanglement | | | | |
|---|---|---|---|---|---|---|
| **Group** | **Number-Percentage** | **N/A** | **1 time** | **2 times** | **3 times** | **Total** |
| Low | Sayı | 59 | 12 | 3 | 1 | 75 |
| | Percentage | 78.7 | 16.0 | 4.0 | 1.3 | 100 |
| High | Sayı | 49 | 19 | 7 | 0 | 75 |
| | Percentage | 65.3 | 25.3 | 9.3 | 0.0 | 100 |
| Total | Sayı | 108 | 31 | 10 | 1 | 150 |
| | Percentage | 72 | 20.7 | 6.7 | 0.7 | 100 |
| Chi-square value=5.107; p=0.164 | | | | | | |
| | | **Meconium** | | | | |
| **Group** | **Number-Percentage** | **N/A** | **Thin** | **Dark** | **Total** | |
| Low | Number | 65 | 10 | 0 | 75 | |
| | Percentage | 86.7 | 13.3 | 0.0 | 100.0 | |
| High | Number | 73 | 1 | 1 | 75 | |
| | Percentage | 97.3 | 1.3 | 1.3 | 100.0 | |
| Total | Number | 138 | 11 | 1 | 150 | |
| | Percentage | 92.0 | 7.3 | 0.7 | 100.0 | |
| Chi-square value=8.827; p=0.012 | | | | | | |
| | | **Acidosis** | | | | |
| **Group** | **Number-Percentage** | **N/A** | **Respiratory** | **Metabolic** | **Total** | |
| Low | Number | 36 | 4 | 0 | 40 | |
| | Percentage | 90.0 | 10.0 | 0.0 | 100.0 | |
| High | Number | 40 | 2 | 1 | 43 | |
| | Percentage | 93.0 | 4.7 | 2.3 | 100.0 | |
| Total | Number | 76 | 6 | 1 | 83 | |
| | Percentage | 91.6 | 7.2 | 1.2 | 100.0 | |
| Chi-square value=1.771; p=0.412 | | | | | | |

| | | Newborn complications | | | | | |
|---|---|---|---|---|---|---|---|
| **Group** | **Number-Percentage** | **N/A** | **Trauma** | **Shoulder dystocia** | **Hyperbilirubinemia** | **Respiratory distress** | **Total** |
| Low | Number | 71 | 1 | 0 | 0 | 3 | 75 |
| | Percentage | 94.7 | 1.3 | 0.0 | 0.0 | 4.0 | 100.0 |
| High | Number | 67 | 4 | 1 | 3 | 0 | 75 |
| | Percentage | 89.3 | 5.3 | 1.3 | 4.0 | 0.0 | 100.0 |
| Total | Number | 138 | 5 | 1 | 3 | 3 | 150 |
| | Percentage | 92.0 | 3.3 | 0.7 | 2.0 | 2.0 | 100.0 |
| Chi-square value=8.916; p=0.063 | | | | | | | |

## Discussion

The purpose of labor induction is to carry out vaginal delivery and to prevent deaths at term. With the evaluation of 22 studies performed on 9383 women, comparing pregnancies at and above 41 weeks of gestation through an expectant approach, it is seen that the labor induction decreases relative risk (RR) (which is 0.31) for perinatal deaths from 0.12 to 0.88 within 95% confidence intervals;[1] however, evidence based data on the induction performed at term pregnancy up to 41 weeks of gestation could not be revealed in the presence of Category II trace, oligohydramnios, and rational/psychosocial factors. Therefore, success possibility and C/S risk should be evaluated certainly if it is planned to perform induction. The parameters referred for the risk evaluation are Bishop score, parity, vaginal delivery underwent previously, BMI, age, estimated birth weight and diabetes. By adding Bishop score being 6 and higher, which indicates that cervix is convenient for delivery, to the most significant parameter, "presence of previous delivery", which shows that further deliveries can be carried out vaginally, it was aimed to evaluate induction success and fetal maternal outcomes. Bishop score is a scale system, developed in 1964, to predict the success of elective induction in which cervical dilation, effacement, position, level and consistency are graded up to 13 points by grading from "0" to "2" or "3".[9] If Bishop score is 9 or higher, it is considered that "vaginal delivery can be achieved independent from the induction". In Bishop scoring system developed by Burnett in 1966, total score is 10 where each item can be graded up to "2" points.[5] In this system used for multiparous pregnancies, score 6 and above indicates that vaginal delivery would be achieved. Therefore, assessment with Bishop score before induction is preferred to predict the agent to be used in the induction and the success of induction.[10]

In our study, there was no statistically significant difference between two groups in terms of maternal demographics, maternal BMI at the time of oxytocin induction and gestational age. Zhang et al. reported that the ages of patients who were administered low-doses of oxytocin were significantly higher than the patients who were administered high-doses of oxytocin.[11] In this prospective randomized controlled study, multiparous pregnant women were separated into two groups, oxytocin protocol similar to the protocol in our study was used, but unlike our study, they concluded that the augmentation with high-dose of oxytocin reduced the phase I of delivery by 0.7–1.1 hours in multiparous pregnant women and that there was no difference in phase II of delivery. It was not an induction study which was used to stimulate uterine contractions before labor; it was an augmentation study which was defined as the study for increasing current contractions since cervical dilation and fetal descending were insufficient. In this augmentation study, there was no statistically significant difference between high- and low-dose of oxytocin protocols in terms of C/S rates. Patka et al. confirmed the results of Zhang et al., and they found no statistically significant difference between the groups in terms of C/S rates while reporting that labor duration was reduced in pregnant women who underwent high-dose of oxytocin induction.[12] Similar to our study, Hourvitz et al. reported no significant difference between the delivery phases of pregnant women who underwent high- and low-dose of oxytocin induction.[13] However, Hourvitz et al. used lower doses of oxytocin in their protocols. In the review of Wei et al. analyzing 10 studies, it was reported that labor duration was reduced by 1.54 hour through high-dose oxytocin augmentation.[14]

Oxytocin, which is the most common agent used in labor induction on pregnant women with appropriate Bishop score, was used in various protocols with different initial doses, incremental intervals, amounts and maximum rates. In low-dose protocol, the initial dose of oxytocin is 1 or 2 mU/min, incremental interval is 30 minutes and dose increments vary from 1 mIU to 2 mU. In low-dose protocol, the dose that labor is set is 8–12 mU/min, and maximum dose before re-evaluation is reported as 30 mU/min. For high-dose protocol, the initial dose of oxytocin is either 4 or 6 mU/min, incremental interval is 15–30 minutes and dose increment varies from 4 to 6 mU/min. The dose that labor is set is usually 8–12 mU/min and maximum dose before re-evaluation is reported as 30 mU/min in the literature.[6,7,10] It is still unclear which protocol is the most suitable for which patient and which dose minimizes fetal and maternal complications.[15] In our study, we found no statistically significant difference between high- and low-dose oxytocin protocol in terms of phases I (active phase), II and III of labor, delivery type and C/S rate.

Among the member countries of Organisation for Economic Co-operation and Development (OECD), the rates of C/S in our country are unfortunately at the third rank following Brazil and China and at the first rank in European countries.[16] About one out of two

women deliver by C/S. In our study, among multiparous pregnant women with Bishop score 6 and higher, we performed C/S to 4 (5.3%) of 75 pregnant women who underwent high-dose oxytocin and 6 (8%) of pregnant women who underwent low-dose oxytocin due to fetal distress and cephalopelvic disproportion. Satin et al. reported that cesarean section rate increased due to fetal distress indication in pregnant women who underwent high-dose oxytocin.[17] Xenakis et al. found in their study that 18.8% of pregnant women who were administered high-dose oxytocin and 20% of pregnant women who were administered low-dose oxytocin had fetal distress; contrarily, there are publications reporting that C/S rates decrease and vaginal delivery rates increase in pregnant women who were administered high-dose oxytocin.[18] In our study, we found no statistical difference between low- and high-dose oxytocin induction in terms of C/S indications. As maternal complications, we investigated postpartum bleeding (one case), postpartum transfusion need (one case), puerperal fever, grades III–IV perineal lacerations and uterine rupture, and we found no statistical difference between two groups. While one case in low-dose induction group had transfusion need during postpartum period, there was no statistical difference between the groups although hematocrit and hemoglobin levels decreased at prepartum and postpartum 6th hour in both groups. Except the postpartum transfusion need in low-dose induction group, we observed no maternal complication in both groups. Similar to our study, Xenakis et al. evaluated the parameters of postpartum bleeding and postpartum transfusion need as maternal complications and they found no statistically significant difference between two groups.[17] In the study of Zhang et al., the authors investigated grades III–IV perineal lacerations and they found no statistically significant difference between two groups.[11]

In terms amnion with meconium in high- and low-dose oxytocin groups, thin meconium was observed in 13.3% of the cases in low-dose induction group but there was no dark meconium while the rates were 1.3% and 1.3%, respectively, in the high-dose induction group. Accordingly, thin meconium was found less in high-dose group, and there was only one case with dark meconium. Statistically, total rate of amnion with meconium was significantly higher in low-dose group similar to the augmentation study of Zang et al.[11] Five-minute Apgar score below 5 which can be the indication intrapartum hypoxia that can be associated with dark meconium, pH level below 7 and base excess being 12 mmol/L and above were not found in study groups. The number of cases required for perinatal hypoxia evaluation being out of study scope was the limitation of the study. In our study, we found shoulder dystocia (1.3%) and brachial plexus injury as a result in one of the pregnant women who underwent high-dose induction, cephalohematoma in two babies, caput succedaneum in one case and clavicle fracture in case as birth trauma while we found caput succedaneum in one of the pregnant women who underwent low-dose induction; there was no statistically significant difference between two groups. Similar to our study, Xenakis et al. evaluated the parameter of shoulder dystocia as perinatal complication, and they found no statistically significant difference between high- and low-dose oxytocin induction.[18] Zhang et al. also found no statistically significant difference between high- and low-dose groups in terms of birth traumas similar to our study.[11] In our study, we observed neonatal hyperbilirubinemia in three (4%) of the pregnant women who underwent high-dose induction. We did not found neonatal hyperbilirubinemia in the pregnant women who underwent low-dose oxytocin induction. Newborns with neonatal hyperbilirubinemia did not have predisposing factors such as cephalohematoma or caput succedaneum, and they were discharged following about one-week phototherapy. In their study, Woyton et al. also categorized the relationship between oxytocin use and neonatal hyperbilirubinemia and compared these two groups.[19] Similar to Woyton et al., Johnson et al.[20] separated pregnant women into two groups, which were oxytocin and no oxytocin group, and they found no statistically significant difference between two groups. In their study, they attributed the reason for the lack of neonatal hyperbilirubinemia in pregnant women induced by oxytocin to not administering oxytocin in hypoosmolar fluids and therefore not observing hyponatremia, and erythrocytes not swelling and thereby being hemolyzed. In studies suggesting that oxytocin leads to neonatal hyperbilirubinemia, the reason is attributed to the use of hypoosmolar fluid.[19–20]

## Conclusion

In multiparous pregnant women with Bishop score 6 and higher, high- and low-dose induction did not make a difference in terms of C/S rates and maternal and perinatal complications; high-dose oxytocin does not reduce delivery duration compared to the low-dose oxytocin.

**Conflicts of Interest:** No conflicts declared.

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