J Surg Med. 2024;8(1):17-21.
https://doi.org/10.28982/josam.7799

JOSAM

Journal of Surgery and Medicine

e-ISSN: 2602-2079

Research article
https://jsurgmed.com/

Assessment of maternal and fetal outcomes according to induction methods following negative oxytocin challenge test

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Ethics Committee Approval
The study was approved by the Etlik Zubeyde Hanim Women's Health Training and Research Hospital Local Ethics Committee (Approval Date/No: February 22, 2017/02).
All procedures in this study involving human participants were performed in accordance with the 1964 Helsinki Declaration and its later amendments.

Conflict of Interest
No conflict of interest was declared by the authors.

Financial Disclosure
The authors declared that this study has received no financial support.

Previous Presentations
The study is published as a preprint in Research Square (https://doi.org/10.21203/rs.3.rs-1232960/v1).

Published
2024 January 22

Abstract

Background/Aim: There is insufficient information about how long fetal well-being will last after a negative oxytocin challenge test (OCT) and the factors affecting this process. We aim to evaluate maternal and perinatal outcomes in high-risk patients who had negative OCTs and to investigate the effects of methods of induction on the development of fetal distress.

Methods: The study was designed as a retrospective cohort study. Data of patients who were hospitalized in the perinatal intensive care unit due to high-risk pregnancies between January 2016 and December 2016 were reviewed retrospectively. The patient's gestational age, gravidity, parity, and body mass index (BMI), risk factors leading to the OCT, labor induction methods used following a negative OCT, time from negative OCT to delivery, mode of delivery, and indications for cesarean section were recorded. In addition, data regarding fetal sex, birth weight, birth height, labor complications, Apgar scores at minutes 1 and 5, admission to the neonatal intensive care unit (NICU), indications for NICU admission, length of NICU stay, and stillbirth were also recorded.

Results: OCT was performed on 551 patients and was negative in 447 patients. Among patients with a negative OCT, labor induction was preferred in 427 (95.5%) patients. When fetal distress development was assessed according to the induction method used following a negative OCT, fetal distress developed in 9.1% of 427 patients who underwent labor induction.

Conclusion: When outcomes were considered in pregnant women with a negative OCT, it was observed that there were no fetal deaths and a limited number of newborns with low Apgar scores. Further randomized studies are needed to draw definitive conclusions.

Keywords: fetal outcomes, labor induction, oxytocin challenge test, maternal outcomes

How to cite: Aytekin O, Aksakal SE, Altay MM. Assessment of maternal and fetal outcomes according to induction methods following negative oxytocin challenge test. J Surg Med. 2024;8(1):17-21.

Introduction

Detection of fetal hypoxia during labor to minimize fetal death and neurologic sequelae related to fetal asphyxia is highly important. Electronic fetal monitoring (non-stress test [NST]), contraction stress test (CST), fetal biophysics profile, amniotic fluid index, Doppler sonography, fetal scalp blood testing, umbilical cord blood gas analysis, and neonatal Apgar scores are commonly used parameters in the assessment of intrauterine fetal state and distress [1–7]. The oxytocin challenge test (OCT) is one of the CST methods and is commonly used to monitor the fetus during the antepartum period. OCT is a test used to evaluate fetal well-being based on uterine contractions in suspected placental insufficiency. The negative OCT test was defined as the presence of accelerations in fetal heart rate, normal variability, and absence of slowdown in uterine contractions [8]. Freeman et al. [9] used the CST for follow-up in 679 post-term cases and observed no perinatal mortality. In other studies, it was shown that the perinatal mortality rate was lower than 0.1% during follow-up within the first week following a negative CST [10–13].

Delivery is induced due to maternal (preeclampsia, cardiac or renal disease), fetal (intrauterine growth retardation), or combined causes (uncontrolled diabetes mellitus, premature rupture of membrane, or post-term pregnancy) [14]. There are several methods of induction. However, no method has been shown to be superior to others [15]. Our study aimed to evaluate maternal and perinatal outcomes in high-risk patients (preeclampsia, intrauterine growth retardation, gestational diabetes mellitus, post-term pregnancy, and oligohydramnios, among others.) who had negative OCTs. The secondary aim was to investigate the effects of methods of induction on the development of fetal distress.

Materials and methods

The hospital records of all patients hospitalized in the perinatal intensive care unit due to high-risk pregnancies between January 2016 and December 2016 were reviewed retrospectively. There were 950 high-risk pregnancies. Of these, 551 patients underwent OCT and met the patient selection criteria. A total of 447 individuals with negative test results were included in the study. This study was approved by the Ethical Committee of the University of Health Sciences Turkey, Etlik Zübeyde Hanim Women's Health Training and Research Hospital (Approval Date/No: February 22, 2017/02).

Patient selection

Patients who had ≥34 weeks of gestation, singleton pregnancy with vertex presentation, and a negative OCT result were included in the study. Patients who had a history of cesarean delivery, uterine surgery, suspected cephalopelvic disproportion, inconclusive and hyper-stimulated or suspected OCT results, and a fetus with major congenital anomalies were excluded. The research included patients who had at least one of the risk factors listed below.

The following definitions were used when assessing risk factors:

- Oligohydramnios was defined as amnion fluid index <50 mm,
- Polyhydramnios was defined as the deepest vertical pocket >80 mm,
- The decreased fetal movement was defined as experiencing fewer or no fetal movements by the mother,
- Intrauterine growth retardation was defined as estimated fetal weight <3rd percentile according to the gestational week or confirmation by birth weight,
- Non-reactive NST was defined as lacking fetal heart rate acceleration at a 40-min period in NST monitoring,
- Preterm pregnancy was defined as gestational age between 34 – 36 6/7 weeks,
- Term pregnancy was defined as gestational age between 37 – 40 6/7 weeks,
- Post-term pregnancy was defined as gestational age ≥41 weeks,
- Gestational diabetes mellitus (GDM) was defined as the presence of elevation in at least two values by 100 g glucose and in at least one value by 75 g glucose in an oral glucose tolerance test,
- Preeclampsia was defined as arterial blood pressure >140/90 mm Hg and the presence of at least one of the following: proteinuria, thrombocytopenia, hepatic dysfunction, pulmonary edema, or cerebral and visual symptoms [16].

In the OCT, ten units of oxytocin in 500 milliliters (mL) of normal saline were given at a rate of 15 mL/hour using an infusion pump. The dose was doubled at 20-minute (min) intervals until achieving three uterine contractions with sufficient intensity in a 10-min period. The OCT was considered negative in patients who showed three uterine contractions with moderate intensity lasting 40–60 seconds but not late deceleration [17].

If an induction of labor is decided following an OCT, the appropriate method was selected according to the patients' Bishop scores. In our clinic, oxytocin (SYNPITAN®, DEVA, Turkey), Dinoproston (PROPESS Ovul®, FERRING, Switzerland), transcervical balloon catheter (COOK® Cervical Ripening Balloon, Cook Medical, Ireland), and Foley balloon catheter (Latex Foley Catheter®, Weel Lead Medical, China) were used for inducing labor. Ten units of oxytocin (SYNPITAN®) in 500 mL normal saline were given at a rate of 15 mL/h using an infusion pump; the dose was doubled at 20-min intervals until achieving three uterine contractions with sufficient intensity in a 10-min period. Dinoprostone was given via a slow-release vaginal delivery system (PROPESS Ovule®). It was removed in patients who achieved active labor, those with membrane rupture, and those who failed to induce labor within 12 hours. A transcervical balloon catheter and a Foley balloon catheter were administered through the cervix, as shown in studies in the extra-amniotic region [18,19].

The patient's gestational age, gravidity, parity, and body mass index (BMI), risk factors leading to the OCT, labor induction methods used following a negative OCT, time from negative OCT to delivery, mode of delivery, and indications for cesarean section were recorded. In addition, data regarding fetal sex, birth weight, birth height, labor complications, Apgar scores at minutes 1 and 5, admission to the neonatal intensive care unit (NICU), indications for NICU admission, length of NICU stay, and stillbirth were also recorded.

Statistical analysis

All statistical analyses were performed using the Statistical Package for the Social Sciences (SPSS) for Windows version 22.0. Descriptive values are expressed as arithmetic mean (standard deviation), median, and percent. The Chi-square test

was used to analyze independent quantitative data, and Fisher's exact test was used when terms for the Chi-square test were inappropriate. A *P*-value <0.05 was considered statistically significant.

Results

It was found that the OCT was performed on 551 patients between January 2016 and December 2016. It was seen that the OCT was negative in 447 (81.1%) patients, positive in 50 patients (9.1%), and inconclusive in 54 (9.8%) patients. It was found that the mean maternal age was 25.7 (5.1) years, and the mean gestational age was 39.2 (1.5) weeks. The mean gravidity was 1.8 (1.1), and the mean BMI was 29.1 (4.2) kg/m^2 in 447 patients with a negative OCT.

When the induction methods used were assessed, among patients with a negative OCT, it was seen that labor induction was preferred in 427 (95.5%) patients, and spontaneous delivery occurred in 20 patients (4.5%). In addition, it was found that labor induction was performed using dinoprostone in 237 (53%) patients, oxytocin alone in 117 (26.2%) patients, Cook balloon catheter with oxytocin inductions in 47 (10.5%) patients, and Foley balloon catheter with oxytocin inductions in 26 (5.8%) patients (Table 1).

Table 1: Labor induction methods used in patients with a negative OCT

Labor induction method used	n	%
No induction	20	4.5%
Labor induction	427	95.5%
Dinoprostone	237	53.0%
Oxytocin	117	26.2%
Cook Balloon + Oxytocin	47	10.5%
Foley Balloon + Oxytocin	26	5.8%

Of the patients, 310 (72.6%) gave birth via vaginal delivery (VD) and 117 (27.4%) via cesarean section (C/S). When indications for C/S were assessed, it was found that C/S was performed due to fetal distress in 39 (33.3%) patients, non-progressive labor in 74 (63.2%) patients, placental abruption in two (1.7%) patients, umbilical cord prolapse in one (0.9%) patient, and risk for chorioamnionitis in one (0.9%) patient.

When the causes of fetal distress following OCT were assessed according to the risk factors prompting OCT, it was seen that C/S was performed in 10 (5%) patients who underwent OCT due to oligohydramnios, comprising 25.6% of all cases with fetal distress, followed by six (15.4%) patients with post-term pregnancy plus oligohydramnios, and six (15.4%) patients with post-term pregnancy alone. A significant difference was detected in oligohydramnios, preeclampsia, polyhydramnios, and gestational cholestasis between groups with or without fetal distress when they were assessed according to the risk factors prompting OCT (Table 2).

When fetal distress development was assessed according to the induction method used following a negative OCT, it was seen that fetal distress developed in 25.0% of 20 patients (n=5) who did not undergo labor induction and 9.1% of 427 patients (n=39) who underwent labor induction (Table 2). No significant difference was detected in fetal distress development according to the use of labor induction. When the induction methods used were assessed, it was seen that the dinoprostone group (n=237) had the highest rate of fetal distress development (10.5%). No significant difference was detected in fetal distress development according to the induction method used (*P*=0.257, *P*=0.906, *P*=0.077, *P*=0.792; Table 2).

Table 2: Fetal distress development following a negative OCT according to risk factors and induction methods in the induction group

Risk factor prompting OCT	Fetal distress (+) n=39 (9.1%)	Fetal distress (-) n=388 (90.9%)	Total n=427	*P*-value
Oligohydramnios	10(5%)	166 (95%)	176	0.038 $^{X^2}$
Post-term and oligohydramnios	6 (11%)	48 (89%)	54	0.589 $^{X^2}$
Post-term	6 (11%)	48 (89%)	54	0.589 $^{X^2}$
IUGR and Oligohydramnios	2 (5%)	36 (95%)	38	0.386 $^{X^2}$
Decreased fetal movements	3 (8%)	33 (92%)	36	0.862 $^{X^2}$
IUGR	4 (12%)	27 (88%)	31	0.449 $^{X^2}$
Non-reactive NST	3 (13%)	19 (87%)	22	0.452 $^{X^2}$
Preeclampsia	3 (33%)	6 (67%)	9	0.011 $^{X^2}$
Gestational Diabetes Mellitus	0 (0)	3 (100%)	3	0.582 $^{X^2}$
Polyhydramnios	1 (50%)	1 (50%)	2	0.044 $^{X^2}$
Gestational cholestasis	1 (50%)	1 (50%)	2	0.044 $^{X^2}$
Labor induction method				
Dinoprostone	25 (10.5)	212 (89.5)	237	0.257 $^{X^2}$
Oxytocin	11 (9.4)	106 (90.6)	117	0.906 $^{X^2}$
Cook Balloon + Oxytocin	1 (2.1)	46 (97.9)	47	0.077 $^{X^2}$
Foley Balloon + Oxytocin	2 (7.7)	24 (92.3)	26	0.792 $^{X^2}$

OCT: oxytocin challenge test, $^{X^2}$ Chi-square test

Perinatal outcomes

When NICU admission and its indications were assessed, it was seen that 397 neonates (93%) did not require NICU admission. Of the neonates who required NICU admission, it was found that 53.3% (n=16) were admitted due to neonatal respiratory distress, 33.3% (n=10) due to neonatal jaundice, 10% due to prematurity, and one (3.3%) due to brachial plexus injury.

Perinatal outcomes were assessed by stratifying according to gestational age: ≥41 weeks and between ≥37 and <41 weeks. It was found that of the 311 newborns with gestational age between ≥37 and <41 weeks, 46.9% were boys, and 53.1% were girls. It was found that the mean birth weight was 3011 (383) g, and the mean birth length was 49.2 (2.4) cm. The median Apgar scores were 9 and 10 at minutes 1 and 5, respectively. Again, it was found that of the 108 newborns with gestational age ≥41 weeks, 45.4% were boys, and 54.6% were girls. The mean birth weight was 3394 (349) g, and the mean birth length was 51.2 (1.5) cm. The median Apgar scores were 9 and 10 at minutes 1 and 5, respectively. It was seen that 31 newborns required NICU admission, including six newborns with gestational age <37 weeks. Prematurity was the underlying cause of NICU admission in 50% of six newborns with gestational age <37 weeks. In the remaining 25 newborns with gestational age ≥37 weeks, respiratory distress was the underlying cause of NICU admission in 45.1% (Table 3).

When the relationship between the time from OCT to delivery and fetal distress was assessed, fetal distress development was detected after OCT in 39 patients. Of these 39 patients, fetal distress developed within the first 24 hours in 24 (10.4%) and between hours 24 and 72 in 15 (8.2%). No fetal distress development was detected beyond 72 hours after the OCT (*P*=0.388). When Apgar scores were assessed in infants born following a negative OCT, it was found that Apgar scores were <7 at minute 1 in 10 newborns and four newborns at minute 5. When the relationship between the time from the OCT to delivery and Apgar scores was assessed, it was seen that there was no significant difference between Apgar scores <7 and >7 (*P*=0.416) (Table 4).

Table 3: Perinatal outcomes according to gestational age in the induction group

		Gestational age ≥37 – <41 weeks n=311	Gestational age ≥41 weeks n=108	*P*-value
		Mean (SD)/n (%)	Mean (SD)/n (%)	
Birth weight (g)		3011 (383)	3394 (349)	<0.001 [t]
Birth length (cm)		49.2 (2.4)	51.2 (1.5)	<0.001 [t]
Sex	Boy	146 (46.9)	49 (45.4)	0.777 [X²]
	Girl	165 (53.1)	59 (54.6)	
Apgar score on minute 1		8.9 (0.6)	8.8 (0.6)	0.594 [t]
Apgar score on minute 5		9.9 (0.5)	9.8 (0.5)	0.480 [t]
Perinatal complications				
None		310 (99.7)	107 (99.1)	0.450 [X²]
Shoulder dystocia		1 (0.3)	1 (0.9)	
Length of hospital stay (days)		3.0 (1.7)	3.8 (2.5)	0.449 [t]
NICU admission				
None		292(93.9)	102 (94.4)	0.391 [X²]
Yes		19 (6.1)	6 (5.6)	
Cause of NICU admission				
Neonatal jaundice		7 (36.8)	3 (50.0)	
Neonatal respiratory distress		11 (57.9)	3 (50.0)	
Brachial plexus injury		1 (5.3)	0 (0.0)	
Prematurity		0 (0.0)	0 (0.0)	

[X²] Chi-square test, [t] Student T test

Table 4: Relationship between time from OCT to delivery, fetal distress and Apgar score at minute 5 in the induction group

Time from OCT to delivery	Fetal distress (-)	Fetal distress (+)	*P*-value	APGAR ≥7	APGAR <7	*P*-value
	n (%)	n (%)		n (%)	n (%)	
0–24 hours	208 (89.6)	24 (10.4)	0.388 [X²]	231 (99.6)	1 (0.4)	0.416 [X²]
24–72 hours	167 (91.8)	15 (8.2)		179 (98.4)	3 (1.6)	
>72 hours	13 (100)	0 (0.0)		13 (100)	0 (0.0)	

OCT: oxytocin challenge test, [X²] Chi-square test

Discussion

This descriptive study investigated perinatal outcomes in pregnant women with a negative OCT. It was found that labor was induced in 95% of pregnant women with a negative OCT, dinoprostone and oxytocin were the most commonly used methods of labor induction, and delivery was via vaginal delivery in 72.6% and via C/S in 27.4%. No significant difference was detected in fetal distress rates between patients who did and did not undergo labor induction. In addition, there was no significant difference in fetal distress rates across the induction methods used. Of the patients, 7% were admitted to the NICU, most commonly due to respiratory distress and jaundice. No significant relationship was detected between fetal distress development, time from the OCT to delivery, and Apgar scores at minute 5.

In our study, delivery was via C/S in 117 (27.4%) patients. When C/S indications were assessed, fetal distress was the most common indication (33.3%). In the study of Różańska-Waledziak et al. [8], 69 (33.8%) of 204 patients with negative OCT underwent C/S. The authors found that abnormal heart traces comprised 37.6% of C/S indications. The C/S rate in our study was in agreement with the study mentioned above.

Our study observed fetal distress findings during follow-up and labor in 39 (9.1%) of 427 pregnant women who were followed after a negative OCT. This rate indicated that OCT was not effective in predicting fetal distress during labor. In a study by Schifrin et al. [20], fetal distress findings during labor were observed in three (3%) of 101 patients with a negative OCT. The difference may be attributed to the difference in sample sizes. Again, Apgar scores at minute 1 were <7 in 10 of 100 newborns, three of which had Apgar scores <7 (3%) at minute 5. In our study, Apgar scores at minute 1 were <7 in 10 of 427 patients, four of whom had Apgar scores at min 5 of <7 (0.9%). In a study by Hayden et al. [21], fetal distress findings during labor were observed in five of 97 patients with a negative OCT. The authors provided no data regarding Apgar scores, diagnoses, and labor induction methods.

Our study used labor induction methods in 427 of 447 patients with a negative OCT, and fetal distress was observed in 9.1%. No significant difference was found in fetal distress development across the induction methods. In a study by Cammu et al. [22], labor was induced in 7,683 nulliparous pregnant women, and fetal distress findings were observed in 2.6% of patients. However, the study had some limitations, including the selection of low-risk pregnancies, excluding post-term and low-birth-weight pregnancies, and a lack of data regarding fetal well-being before induction. In a study by Vahratian et al. [23], labor was induced in 429 low-risk, nulliparous pregnant women, and fetal distress findings were observed in 5.1% of patients. The authors assigned patients into two groups: (1) labor was directly induced using oxytocin in 286 patients and (2) using oxytocin following cervical preparation with a Foley balloon catheter in 143 patients. The fetal distress rate was 7% among patients who underwent cervical preparation with a Foley balloon catheter and 4.2% in the oxytocin group [23]. Again, the study was conducted on low-risk term pregnant women, and no test was performed to assess fetal well-being before induction. In our study, the fetal distress rate was 7.7% in the Foley balloon catheter and oxytocin group and 9.4% in the oxytocin group. Again, this study, like other studies, was applied to term pregnant women with low risk, and no test was applied for fetal well-being before induction. However, our study was limited by the small number of patients in the Cook balloon catheter and Foley balloon catheter groups and patients who did not undergo labor induction.

During follow-up from OCT to delivery, no stillbirths were observed in 427 pregnant women with a negative OCT. In a study by Evertson et al. [24], seven cases of stillbirth (1%) were observed during a one-week follow-up among 680 pregnant women with a negative OCT. The authors reported that causes of stillbirth included cord injury in three cases, placental detachment in one case, multiple anomalies in one case, and undefined in two cases, suggesting that fetal deaths were not due to disruption of fetal well-being. In a study on 1,337 high-risk pregnant women, Nageotte et al. [25] reported only one fetal death within seven days following a negative CST. Again, in a study on 679 women who underwent CST due to post-term pregnancy, no fetal death was observed by Freeman et al. [9]. In another study, CST was used to assess fetal well-being in 337 pregnant women with a previous history of stillbirth, and no fetal deaths were observed [10].

Our study also has limitations. The fact that all groups underwent induction, including high-risk patients, limited the ability to determine whether disruption of fetal well-being was caused by the risk status of patients or the induction method used.

Our study has some strengths. In studies about outcomes after negative OCT, fetal mortality rates were investigated during one-week follow-up in general [9,10,24,25]. However, our study evaluated fetal distress and Apgar scores in addition to fetal mortality. Low-risk pregnancies were preferred in studies that investigated outcomes according to induction methods, and no data were provided regarding fetal well-being before induction [22,23].

Conclusions

When outcomes are considered in pregnant women with a negative OCT, there are no fetal deaths and a limited number of newborns with low Apgar scores. It could be suggested that OCT is an effective method to predict fetal well-being but may not provide data regarding fetal distress development during labor. The induction methods used after negative OCT and the time until delivery have no effect on the development of fetal distress. Further randomized studies are needed to draw definitive conclusions.

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