Original Article

The Impact of Labor Oxytocin Use on Newborn Liver Enzymes

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Received April 2024; Revised and accepted September 2024

Abstract

Objective: Oxytocin is commonly used during labor and delivery for induction of labor and prevention of postpartum hemorrhage. While previous studies have explored the effects of labor oxytocin use on maternal and neonatal outcomes, there is a paucity of research on its impact on newborn liver enzyme function. This study aimed to assess the effects of labor oxytocin use on liver enzyme function in newborns.

Materials and methods: A case-control study was conducted. The case group consisted of 70 newborns whose mothers received oxytocin during labor, while the control group consisted of 70 newborns whose mothers did not receive oxytocin. Complete blood count (CBC), lactate dehydrogenase (LDH), creatine phosphokinase (CPK), aspartate aminotransferase (AST), alanine aminotransferase (ALT), and total and indirect bilirubin levels were measured in all newborns on the second day of life.

Results: The levels of AST and total and indirect bilirubin were found to be higher in the case group than in the control group (51 vs. 42, 7.8 vs. 4.6, and 7.4 vs. 4, respectively; $p < 0.005$). The levels of CPK and LDH were also higher in the case group ($p < 0.005$). However, the difference in ALT levels was not significant between the study groups.

Conclusion: The observed increase in liver enzymes in this study can indicate the effect of maternal oxytocin on the newborn's liver function. While the changes in liver enzyme levels due to oxytocin use were not found to be high enough to cause liver damage, the increase in CPK and LDH levels could potentially elevate bilirubin levels due to hemolysis. Further research is needed to confirm these findings and explore the underlying mechanisms.

Keywords: Oxytocin; Labor; Delivery; Newborn; Liver Enzymes; Bilirubin; Hemolysis

Introduction

Oxytocin is a peptide hormone by multifaceted role in human physiology. Oxytocin has an essential metabolic role and influences human behavior and the reproductive system in both women and men. Endogenous oxytocin is secreted from the hypothalamus and stored in the pituitary gland, releasing into the bloodstream when necessary, thereby affecting the oxytocin receptor organs (1).

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Oxytocin receptors are widely distributed in various tissues, with the highest concentration found in the breast and uterus in females and the male's penis. During childbirth, oxytocin stimulates uterine contractions, and after childbirth, it facilitates lactation. Oxytocin secretions are triggered by several physiological stimuli, including labor, infant suckling, exercise, sexual stimulation, and stress (2).

Exogenous oxytocin is a high-consumption drug in the delivery room, often used to stimulate the uterine muscles and cause contractions. It is typically administered intravenously for labor augmentation or induction, and its half-life is 3-6 minutes. The uterine response to oxytocin is almost immediate and dissipates within 40-45 minutes after administration (3). The primary purpose of induction is to hasten labor and prevent adverse maternal outcomes, such as maternal underlying diseases, prolonged labor, or unreliable heart rate in post-term or growth-restricted fetuses. In high doses, oxytocin has antidiuretic effects, while in smaller amounts, it causes vasodilator effects and transient hypotension (4).

Although oxytocin is often considered safe during labor and birth, its use has been associated with potential adverse effects on the mother and the fetus, such as uterine tachysystole and impairment of fetal heart rates. These complications can occur due to the reduction or interruption of blood flow to the fetus during labor stimulation, resulting in higher percentages of intrapartum fever, lower pH of umbilical cord, and a greater need for advanced neonatal resuscitation (5).

Oxytocin can cross the placental circulation and enter the fetal bloodstream in small amounts. It is metabolized in the liver by multiple amino peptidases, including oxytocinase, which increases in both liver and adipose tissue concentration (6). Some sources suggest that oxytocin can affect liver hormones and hinder the maturation of liver enzymes involved in bilirubin excretion causing physiological jaundice (bilirubin below 12) in newborns. Aminotransferases, including ALT (Alanine aminotransferase) and AST (Aspartate aminotransferase), are sensitive indicators of liver cell damage. When liver cell damage occurs, these enzymes are released into the blood, aiding in the diagnosis of acute hepatocellular diseases such as hepatitis (both drug-induced and other causes) (7), although, the limited number of studies investigated the effect of oxytocin on liver function.

In this study, we aim to measure the impact of oxytocin on the liver enzymes of the newborns.

Materials and methods

Study was a descriptive, case control study and was performed in Alborz, Iran. Participating were 140 mothers who were hospitalized in labor room for natural delivery in one of the public hospitals of city. Mothers put in two groups of cases and control. The samples in both control and control groups were included in the study available methods. Based on Garosi's article and considering the statistical power of 80% and significance level of 0.05, the number of people in each group was determined to be 70. Using the formula for calculating the sample size in descriptive studies (8).

Mothers in cases group were received 5-10 unit of oxytocin infusion into 1000 mL of ringer lactate serum during their labor in the active phase. The mean time of oxytocin infusion was variable depended on onset of labor pains in mothers and birth. The initiation of oxytocin in mothers started after the active phase and continued until the stabilization of good labor and delivery.

All births end by vaginal manner without applying forceps or vacuum while babies were in cephalic position. Data related to the study, including demographic information using medical records of babies and mothers, results of laboratory tests and interviews with mothers was achieved.

Inclusion criteria were: Babies born over 73 weeks based on first trimester ultrasound, weight over 2500, and born from mothers, without liver problems and any special drug in prenatal period use that received oxytocin during labors. Infants who did not have enough information recorded in their records or had diseases and abnormalities, low Apgar scores were excluded from the study. The control group was selected from the same hospital and department with the conditions mentioned above: weight over 2500, age over 37 weeks, absence of disease, and enough medical information.

Confounding factors related to the mother of this study in the part related to mothers include the use of misoprostol in induction of labor, and maternal liver problems such as pre-eclampsia, HELLP (acronym stands for hemolysis, elevated liver enzymes, and low platelet count), fatty liver of pregnancy and the confounding factors of newborns, including neonatal metabolic diseases, asphyxia and congenital liver problems of the newborn, and individuals with these factors were not included in the study. The blood sample of newborns was taken from a vein in the first 48 hours of birth. The data was analyzed using

software and applying statistical tests at a significance level of less than 0.05. Descriptive and analytical statistical methods including independent t-test were used to analyze the results.

This research was approved by Alborz University of Medical Sciences. All mothers gave informed consent to participate in the study. Mothers' information was kept confidential.

Results

The results of the study are given in this section. The average age of the mothers was 24.7± 2 years, and the average gestational age was 39 weeks and 1 day. Each mother had an average of 2 children, and their average education level was 14 years. Mothers in the case group underwent uterine induction or augmentation for an average of 4 hours and 20 minutes, with a dose of oxytocin ranging from 5-10 units per 1000 ml serum infusion. Two mothers required more than 10 hours of induction, but none needed the use of forceps or vacuum during delivery.

Immediately after birth, all babies were given skin-to-skin contact and breast milk feeding in the mother's ward. Healthy babies remained with their mothers, while affected babies were cared for in the same ward. The newborn blood test results are presented in Table 1, which indicates that mothers who received oxytocin during labor had significantly higher levels of bilirubin (T, ID), LDH, CPK, and AST. However, these increases were not significant enough to exceed the normal laboratory range.

Discussion

In our investigation, the administration of labor oxytocin was found to result in an increased bilirubin level in the serum of newborns, 48 hours following birth. In alignment with a systematic review, oxytocin utilization during labor was linked to increased bilirubin levels on the second day after birth, but not in the first day or umbilical cord serum (9). The dose-related effects of maternal labor oxytocin on neonatal hyperbilirubinemia have been reported in several studies (8, 10).

The vasopressin-like action of oxytocin may lead to osmotic swelling and deformation in red blood cells, causing their early destruction in the baby's immature liver, which has limited enzyme production and function. However, the mechanism by which oxytocin increases bilirubin is not entirely clear (9). Although a slight increase in bilirubin does not indicate liver enzyme damage, hemolysis could be a potential cause. Oxytocin-induced labor also resulted in increased levels of LDH, CPK, and AST in neonates.

In a study involving buffaloes, daily oxytocin injections of 6 units for six months led to significantly higher levels of liver enzymes AST and ALT, and C-reactive protein, compared to the control group, indicating a role for oxytocin in increasing metabolic parameters and hormones, potentially posing a risk to animal health (11). However, in our study, oxytocin was administered for a shorter duration during labor and postpartum, and no effects were observed on ALT levels.

The non-specific nature of LDH and its widespread presence in the body makes it difficult to determine if an increase is due to oxytocin use, erythrocyte lysis, or other clinical causes in newborns (12). A separate study suggested an association between oxytocin and the development and progression of fatty liver, supporting the possibility of effects on liver function (6).

Table 1: Comparison of newborn test scores in case and control groups48 h after birth

Variables	Intervention group	Control group	P-value*
Birth weight (grams)	3250±250	3100±140	>0.05
Baby gender			>0.05
Female	34	37	
Male	36	33	
ALT (U/L)	17 (12-22)	15 (12-20)	>0.05
AST (U/L)	51 (41-60)	42 (33-52)	<0.05
Total Bilirubin (mg/dl)	7.8 (6- 10.8)	4.6 (4.1-5.6)	<0.05
Indirect Bilirubin (mg/dl grams)	7.4 (5.6-10.8)	4 (4- 5)	<0.05
LDH (U/L)	1007 (888-1188)	903 (806-1005)	<0.05
CPK (IU/L)	483 (331- 479)	353.5 (286- 419)	<0.05

ALT: Alanine aminotransferase, AST: Aspartate aminotransferase, LDH: Lactate dehydrogenase, CPK: Creatine phosphokinase

It is important to note that oxytocin levels naturally increase at the onset and during labor, peaking when the baby's head is delivered, but the amount of oxytocin that persists and is transmitted to the newborn is unclear (3). Due to the short half-life of oxytocin and its pulsatile release pattern, interpreting results related to oxytocin is challenging.

While the safety of oxytocin during labor cannot be definitively established, it is recommended to use minimal doses and follow conservative, specific protocols based on the symptoms of both mother and baby (13).

To the best of our knowledge, our study is the first to investigate oxytocin levels during pregnancy in liver function.

Conclusion

The present study found that oxytocin caused an increase in serum bilirubin of newborns and higher levels of specific liver parameters. Further research with a larger sample size is necessary to accurately determine the cause-and-effect relationship between oxytocin and liver function and its potential impact on newborn health.

Conflict of Interests

Authors declare no conflict of interests.

Acknowledgments

The authors are grateful to all the mothers who participated in this study and allowed their infants to be included in the study.

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Citation: Abodollahi S, Poorbahri Ghesmat S, Khoshnam Rad M, Behrouzi K. **The Impact of Labor Oxytocin Use on Newborn Liver Enzymes.** J Family Reprod Health 2024; 18(3): 160-3.