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Oxytocin and Neonatal Hyperbilirubinemia: A Cohort Study.

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ABSTRACT

Hyperbilirubinemia is among the most common problems encountered in term and pre term newborns. Several studies have reported an association between oxytocic drugs and neonatal hyperbilirubinaemia. The aim of this cohort study was to determine the correlation between using oxytocin during labor and neonatal hyperbilirubinaemia in newborns. This cohort study with a prospective design was conducted on 168 newborn infants of mothers who referred to Sanandaj Besat Hospital and were managed with oxytocin during labor either for labor induction or augmentation. These 168 newborn infants were compared with 180 newborn infants of mothers without oxytocin therapy for incidence of hyperbilirubinaemia. Mothers of two groups were matched for age, parity, gestational age and birth weight. Data were analyzed using SPSS, qui square and T- test. According to the results of this study the incidence of hyperbilirubinaemia in newborns was 8.9 percent (39 cases). There was no significant association statistically between neonatal hyperbilirubinemia and using oxytocin for induction of labor (p=0.44). Using oxytocin to manage labor may not affect neonatal bilirubin levels when oxytocin is used in usual duration and dose.
Keywords: oxytocic drugs, labor induction, bilirubin levels

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INTRODUCTION

Hyperbilirubinemia is among the most common problems encountered in term and pre term newborns [1, 2]. It is a cause of concern for the parents as well as for the pediatricians [3]. Hyperbilirubinemia is observed in 60% of term and 80% of preterm infants in the first week of life and is the most common reason for readmission after early hospital discharge [3, 4]. In majority of cases it is benign and does not require treatment. Early initiation of treatment is cost effective and highly effective in preventing the neurological sequelae [5]. The neonatal hyperbilirubinemia practice guidelines published in 2004 by the American Academy of Paediatrics (AAP) expresses the paediatric community's concern regarding bilirubin-induced neurological pathology [6].Common risk factors for hyperbilirubinemia include fetal-maternal blood group incompatibility, prematurity, and a previously affected sibling [7].The incidence of neonatal hyperbilirubinemia is increasing that might be due to the use of oxytocin in the management of labor [8, 9]. One of the possible reasons for increased incidence of neonatal hyperbilirubinemia in healthy term babies is the widespread use of oxytocic drugs in the management of labor [10]. Although oxytocin is widely accepted as a safe & effective initiator of uterine contractions, some studies have reported an association between oxytocic drugs and neonatal hyperbilirubinaemia [11]and some others reported no association between oxytocic drugs and neonatal hyperbilirubinaemia [8,9].

This hypothesis was remained controversial for decades. Investigations were introduced since 1978 to answer to this question that does oxytocin can induce or exacerbate neonatal hyperbilirubinemia? [12]. In 1979 possible pathogenesis of oxytocin-induced hyperbilirubinaemia in newborn infant was described[13].One year later the effect of induction of labor on the neonatal bilirubin levels was investigated in a prospective randomized study but there was no evidence of an association between induction of labor with oxytocin and jaundice during the neonatal period [14].

This theoretically and practically important subject was evaluated again by several studies [8, 11, 15, 16]. Some of them found that the use of isotonic saline rather than 5% glucose solution as vehicle for oxytocin infusion in labor appears to be associated with lower neonatal bilirubin levels [17] and other not found significant effect of oxytocin infusion on neonatal hyperbilirubinemia unless oxytocin was for the augmentation of labor [8] but authors in some reviews have been proposed that oxytocin which was use to labor induction is a risk factor for neonatal icterus [1, 18].

The aim of this cohort study was to determine the correlation between using oxytocin during labor and neonatal hyperbilirubinaemia in newborns in Sanandaj Besat Hospital, Iran.

METHODS

The study was conducted and completed as a cohort study with a prospective design in Kurdistan University of medical sciences, department of obstetrics and gynecology between December 2004 and June 2005. A total of 168 newborn infants of mothers were managed with oxytocin during labor either for labor induction or augmentation enrolled to the study and were compared with 180 newborn infants of mothers without oxytocin therapy for incidence of hyperbilirubinaemia. Mothers of two groups were matched for age, parity, gestational age and birth weight.

The indication for labor induction was the primary arrest of labor in the latent phase whereas the indication for labor augmentation was the secondary of arrest of labor in the active phase, with or without intact amniotic membrane. Study criteria for these mother includes: singleton term (37–42 weeks) pregnancy with no Rhesus negative blood group and no known medical disease (Hypertension, Diabetes mellitus etc.) or fetal problem (intrauterine growth restriction, macrosomia, fetal anomaly etc.) complicating the ongoing pregnancy. We fallow up either two groups two weeks after birth for neonatal hyperbilirubinemia. As such, significant jaundice was defined as jaundice requiring phototherapy and/or exchange transfusion within the first seven days of life, and thus newborns with physiological or mild jaundice not requiring therapy were excluded from this analysis. Investigations obtained in all cases with significant jaundice included maternal and neonatal blood groups, Coombs test, serial levels of total serum bilirubin, direct bilirubin, hemoglobin and hematocrit, reticulocyte count, and peripheral blood smear. Data were analyzed with SPSS using qui square and T- test.

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RESULTS

According to the results of this study incidence of hyperbilirubinaemia in newborn infants was 8.9 percent (39 cases). Demographic data of subjects were summarized in table 1.

Results showed that incidence of neonatal jaundice were not significantly higher in oxytocin group than comparison group (table 2).

Results also showed that there was no significant association between neonatal hyperbilirubinemia and using oxytocin for induction of labor statistically (p=0.44).

Table 1: Demographic information of mothers and their newborn infants of two groups

Demographic information	Oxytocin group	Comparison group	*P*
Mean age	25.8 Y ± 8.13	24.9 Y ± 7.45	< 0.05
Parity	1.7 ±0.92	2.07 ± 1.36	< 0.05
Gestational age	38. 8 ± 1.9	39. 1 ± 1.6	< 0.05
Birth weight (g)	3265 ± 485 g	3405 ± 567 g	< 0.05
Newborn Sex	51% Female 49 % Male	52% Female 48 % Male	< 0.05

Table 2: Correlation between oxytocin and neonatal hyperbilirubinemia

Groups	Neonatal hyperbilirubinemia was occurred	Neonatal hyperbilirubinemia was not occurred
Oxytocin	17 cases (10.11%)	151 cases (89.88%)
Comparison	14 cases (7.77%)	166 cases (92.22 %)

DISCUSSION

The primary cause of neonatal hyperbilirubinemia is a lack of hepatic glucuronyl- transferase enzymes in the newborn infant. The general limits of hyperbilirubinemia vary as a function of the gestational age and the race of the infant. Some perinatal events concerning the delivery have been reported to be associated with an increased incidence of hyperbilirubinemia [1, 18- 20].

The prevalence of neonatal jaundice requiring therapy in this study was 9 percent. This prevalence was similar to the reports of developed country [3] and some developing country include India [21], Thailand [22] and Australia[23] but was lower than previous study in Pakistan[24].

According to the result of this study neonatal hyperbilirubinemia was higher in oxytocin group but this association was not significant. Earlier studies on neonatal hyperbilirubinemia and the use of oxytocin for the management of labor have produced conflicting results, but it has been widely accepted that oxytocin infusion during labor, increased the risk of neonatal hyperbilirubinemia [8,9,25-27].

Although not all the surveys have demonstrated an association between the use of oxytocin and neonatal jaundice, Buchan showed that infants delivered following oxytocin induction had evidence of hemolysis[28]. In addition, oxytocin group had decreased erythrocyte deformability that was ascribed to osmotic swelling produced by the action of oxytocin on the erythrocyte membrane resulting in increased water intake. The other mechanisms that have been proposed to explain the higher incidence of neonatal hyperbilirubinemia and oxytocin administration are trauma to the fetal erythrocytes as a result of uterine activation, vasoconstrictive effect of oxytocin on uterine blood vessels, alterations in erythrocyte deformability due to the anti-diuretic activity of oxytocin and hyponatremia caused by the administration of large quantities of electrolyte-free diluents for oxytocin infusion [9].

As above was noted previous studies have suggested that oxytocin use during labor was important risk factor for neonatal hyperbilirubinemia, recent studies rejected this hypothesis. A study that was printed in 1999, found that oxytocin infusion did not have contribution to neonatal hyperbilirubinemia in their prospective study on 1177 patients[9]. Another study that was conducted on 12,023 newborn infants had been proposed that oxytocin did not affect neonatal bilirubin levels in their subjects [29]. In spite of this

results, some review article in recent years have been noted that oxytocin is a risk factor for neonatal icterus[1,18], but it is logical to prevent hyperbilirubinemia by reducing the dose of oxytocin, as oxytocin has shown a dose-related response in developing neonatal jaundice [9].

Although we found no significant effect of oxytocin infusion on neonatal hyperbilirubinemia, but the oxytocin use in the management of labor may not affect neonatal bilirubin levels when it is used in usual dose and duration.

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