Short Communication

Oxytocin and neonatal hyperbilirubinemia: A prospective cohort study

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Abstract

Objective: To study the incidence of neonatal jaundice requiring phototherapy in babies exposed to maternal oxytocin for induction of labor and to compare the increase in neonatal jaundice in oxytocin group with the jaundice in babies born of spontaneous labor. **Materials and Methods:** This prospective cohort study was conducted in the neonatal unit of a tertiary care center in Trivandrum, Kerala over a period of 6 months. After exclusion, 308 babies were divided in two groups, Group A (babies exposed to maternal oxytocin for induction of labor) or Group B (babies born of spontaneous labor with oxytocin use for augmentation of labor). Babies were observed daily for clinical jaundice till discharge. **Results:** Incidence of neonatal jaundice in Group A was 52% and in Group B was 12% with relative risk 4.3 (95% confidence interval: 2.69-6.73). **Conclusion:** Our study shows that maternal oxytocin used for induction of labor increase the incidence of neonatal jaundice, and it is logical to prevent hyperbilirubinemia by reducing the dose of oxytocin.

Key words: *Induction, Neonatal jaundice, Oxytocin, Spontaneous labor*

Hyperbilirubinemia is often a benign condition of the neonates which can affect about 60% of the term and 80% of the preterm infants [1]. One of the possible reasons for increased incidence of neonatal hyperbilirubinemia (NNH) in healthy term babies is the widespread use of oxytocic drugs in the management of labor. This association between maternal oxytocin use and NNH is well-documented in studies [2]. Fetal erythrocytes are less deformable after oxytocin-induced labor than after spontaneous labor. *In-vitro* studies showed a time related and dose related reduction in erythrocyte deformability in response to oxytocin administration [1].

We have observed that the use of phototherapy in healthy term babies without risk factors (ABO or Rh incompatibility, cephalhematoma, low birth weight [LBW], and sepsis, etc.) for neonatal jaundice has been increased in our unit. Since oxytocin is often administered intravenously to induce or accelerate labor, we have felt that it is mandatory to make a critical appraisal of the association between maternal oxytocin use and the incidence of NNH in our unit. We have planned this study with the objective of estimation of the incidence of NNH requiring phototherapy in babies exposed to maternal oxytocin for induction of labor and comparison of incidences of NNH in the babies exposed to maternal oxytocin and in babies born of spontaneous labor.

MATERIALS AND METHODS

This prospective cohort study was conducted in the neonatal unit of a tertiary care hospital where facilities for newborn intensive care is available. The study was conducted over a period of 6 months (01-02-2014 to 31-07-2014) after obtaining clearance from the Institutional Ethical Committee. Informed written consent was obtained from the parents of the eligible neonates before recruitment. Our study did not affect obstetricians' decision in giving oxytocin. All healthy term (≥37 weeks) normal birth weight babies born during the study period were eligible for inclusion in the study. Babies with ABO and Rh blood group settings, cephalhematoma, LBW (LBW i.e., birth weight <2500 g) babies, who required extensive resuscitation, suspected/probable sepsis, and babies whose siblings required exchange transfusion for NNH were excluded from the study.

Recruited babies were grouped in two groups, either Group A (babies exposed to maternal oxytocin for induction of labor) or Group B (babies born of spontaneous labor with oxytocin use for augmentation of labor only). The dose of oxytocin used for induction of labor was 5-10 IU, whereas dose for augmentation of labor was <5 IU. Babies from both groups were observed daily for clinical jaundice till discharge. Blood for serum bilirubin was obtained from a peripheral vein, in babies with clinical jaundice. Serum bilirubin was estimated by automated total bilirubin method (using diazotized sulfanilic acid). Phototherapy was started on those babies whose serum bilirubin was above the photo zone, as in the nomogram clinical management of jaundice [3]. Observer assured that breast feeding was established in those babies who received phototherapy.

The data were entered prospectively into a Microsoft Excel sheet and the results were analyzed using SPSS statistics version 20. The incidence of neonatal jaundice in each group was analyzed independently, and their relative risk (RR) and 95% confidence interval (CI) were calculated. The statistical test used for analysis was Chi-square test/Fisher's exact test. p values reported are 2 tailed, and a $p \leq 0.05$ is considered statistically significant.

RESULTS

Of the 402 healthy term babies born during the study period, 308 babies were enrolled in the study after excluding 94 babies (27 and 14 babies with ABO and Rh incompatibility respectively, 24 LBW babies, 16 babies with suspected or probable sepsis, 7 babies with cephalhematoma, and 6 sick babies). Of 308 babies, 161 were exposed to maternal oxytocin (Group A) and 147 babies were born of spontaneous labor (Group B). There were 81 males and 80 females in Group A while in Group B, there were 82 males and 65 females. The mean birth weight in Group A was 3150±446 g and in Group B was 2950±386 g. Mean gestational age in Group A was 38.0±1.23 weeks and in Group B was 38.20±2.56 weeks.

Mean maternal oxytocin dose in Group A and Group B was 8.24±2.66 IU and 3.18±1.34 IU, respectively. In Group A, 84 babies and 18 babies in Group B developed jaundice requiring phototherapy. None of the babies required exchange transfusion during the study period. Mean peak bilirubin level on post natal day 3 in Group A was 19.1±3.56 mg% and in Group B was 12.4±2.68 mg/dl. The incidence of neonatal jaundice in Group A and in Group B was 0.52 and 0.12, respectively, with RR of 4.3 (95% CI: 2.69-6.73), showing a significant association ($p<0.0001$).

DISCUSSION

Bilirubin toxicity remains a significant problem despite recent advances in the care of neonates with jaundice. Kernicterus, though infrequent, is the cause of 10% of the mortalities and at least 70% of the long-term morbidities in these neonates [4]. Oxytocin crossing the placenta affected deformability was shown in the *in-vitro* studies, with the finding of both a time-related and dose-related effect of oxytocin on erythrocyte deformability in the range of oxytocin concentrations found in maternal blood during induction of labor with oxytocin [3]. These *in-vitro* results also help to explain the clinical observations that the NNH after induction of labor is related to the dose and the duration of oxytocin administration. Our study also supported this increase in erythrocyte destruction during oxytocin-induced labor.

The vasopressin-like action of oxytocin causes activation of electrolyte and water transport across the erythrocyte membrane with consequent osmotic swelling, which is a well-recognized cause of reduced erythrocyte deformability and leads to more rapid erythrocyte destruction. In the neonate, whose hepatic enzymes are unable to cope with the increased bilirubin production, clinical hyperbilirubinemia ensues. Oxytocin is an important therapeutic agent in obstetrics and probably its use cannot be stopped and thus its effect on erythrocytes also cannot be prevented. However, it would be logical to prevent the hyperbilirubinemia by reducing the dose of oxytocin.

CONCLUSION

Our study implies that maternal oxytocin used for induction of labor is responsible for the higher bilirubin values. It is logical to prevent hyperbilirubinemia by reducing the dose of oxytocin, as oxytocin has shown a dose-related response in developing neonatal jaundice.

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