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ORIGINAL ARTICLE

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Oxytocin infusion in labor: the effect different indications and the use of different diluents on neonatal bilirubin levels

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Abstract *Objective:* To investigate the relationship of neonatal bilirubin levels to oxytocin infusion and the diluent used for oxytocin infusion. *Materials and methods:* The study was carried out as a prospective, randomized study in Istanbul University Cerrahpasa School of Medicine,Department of Obstetrics and Gynecology between January to December in 1995 . A total of 80 patients managed with oxytocin during labor, enrolled to the study. These patients randomly divided into isotonic % 0.9 saline (Group 1) and 5% glucose solutions (Group 2) by a consecutive order using a balanced block randomization scheme. Forty multiparous patients delivering without oxytocin infusion formed the control group (Group 3). The details of maternal age, gestational age, labor duration, mode of delivery, birth weight of the babies, total volume of fluid administered until delivery and total oxytocin dose were noted in each case. Sodium and initial bilirubin levels were measured in the cord blood. Later on, capillary blood bilirubin and hematocrit concentrations were measured on day 1 and 2 in the newborn nursery. The groups were compared according to these parameters. *Results:* The data of 29 patients in Group 1, 36 patients in Group 2 and 40 patients in Group 3 were suitable for analysis. The difference between study and control groups regarding the rate of hyponatremia, neonatal hyperbilirubinemia and neonatal jaundice was not statistically significant. Cord plasma sodium levels, cord plasma bilirubin levels and day 1 and 2 hematocrit and plasma bilirubin levels were not statistically different between the groups. Unrespectable of the diluent used, the cord plasma bilirubin levels and day 2 plasma bilirubin levels were significantly higher in the accelerated group. *Conclusion:* No significant effect of oxytocin infusion was revealed on neonatal hyperbilirubinemia unless oxytocin was for the augmentation of labor.

Keywords Oxytocin · Induction · Hyperbilirubinemia · Neonatal

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Introduction

Chemical hyperbilirubinemia, a serum bilirubin of 2.0 mg/dl or more, is almost universal in newborns during the first week of life. It has been suggested that there has been an increase in the incidence of neonatal hyperbilirubinemia that might be due to the use of oxytocin in the management of labor. A higher incidence of neonatal hyperbilirubinemia associated with the use of oxytocin has been found by some authors, whereas some others could not demonstrate such an association [3, 13]. The use of different diluents for the oxytocin infusion was suggested to reduce the incidence of neonatal hyperbilirubinemia as a result of hemolysis of fetal erythrocytes [8].

The aim of this study is to investigate the association of neonatal bilirubin levels to oxytocin infusion with different diluents and indications and the likelihood to prevent neonatal hyperbilirubinemia due to oxytocin infusion with changing the diluent for oxytocin.

Materials and methods

The study was conducted and completed as a prospective, randomized study in Istanbul University Cerrahpasa School of Medicine, Department of Obstetrics and Gynecology between January to December in 1995. A total of 80 patients managed with oxytocin during labor either for labor induction or augmentation, enrolled to the study. 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 in either of the groups. The eligibility criteria for the study were 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. The Bishop score on the pelvic examination was at least 6 or higher. These patients randomly divided into isotonic % 0.9 saline (Group 1) and 5% glucose solutions (Group 2) by a consecutive order using a balanced block randomization scheme. 10U oxytocin was placed in 500 cc of 5% glucose or isotonic saline. In group 1 and 2, the oxytocin infusion was initiated at a rate of 4 mU/min and increased by an additional 4 mU/min in every 20 minutes until effective uterine contractions were accomplished (regular pattern of contractions in every 2 or 3 minutes with an intensity of at least 50 mmHg) and continued until the third phase of labor was completed. Forty multiparous patients delivering without oxytocin infusion formed the control group (Group 3).

The details of maternal age, gestational age, labor duration, mode of delivery, birth weight of the babies, total volume of fluid administered until delivery and total oxytocin dose were recorded in each case. Oral fluid intake was not restricted in any of the patients.

The patients delivering with forceps or vacuum extraction and cesarean section were discarded from the study (10 cesarean deliveries and 1 vacuum extraction in group 1 and 4 cesarean deliveries in group 2) and further evaluations were not carried out on these patients.

Sodium and initial bilirubin levels were measured in the cord blood. Later on, capillary blood bilirubin and hematocrit concentrations were measured on day 1 and 2 in the newborn nursery. Umbilical cord blood samples were obtained 10 ml from the placental site of divided umbilical cord in the delivery room into heparin tubes and plasma was separated immediately. Neonatal capillary blood was obtained by heel prick at the age of one day and two days. Sodium measurement was carried out by flame photometry and the bilirubin was measured by spectrophotometry. The personnel in charge of the assays were not informed of the groups to which the patients belong.

Later on the groups were compared due to the parameters studied. The statistical analysis was performed with SPSS 10.0 (SPSS Inc. 1989–1999) program. ANOVA test and Pearson correlation coefficient analysis were utilized. $p<0.05$ was accepted as statistically significant.

Results

The data of 29 patients in Group 1, 36 patients in Group 2 and 40 patients in Group 3 were eligible for analysis. Hyponatremia (Cord plasma sodium =135 mmol/ml) was present in 5.7% of all cases. Neonatal hyperbilirubinemia (Day 2 plasma bilirubin = 2 mg/dl) was observed 95.7% of the cases whereas the rate neonatal jaundice (Day 2 plasma bilirubin =10 mg/dl) was 8.7% in the whole group. The difference between study and control groups with respect to the rate of hyponatremia, neonatal hyperbilirubinemia and neonatal jaundice was not statistically significant.

The baseline characteristics of the groups were presented in Table 1. The difference of the number of parity and labor duration between groups was statistically significant ($p<0.001$).

In 33 (50.8%) patients the oxytocin was administered for labor induction and in 32 (49.2%) patients it was for augmentation of labor. In group 1, 15 patients (51.7%) were induced with oxytocin, while 14 were augmented (48.3%). In group 2, 18 patients were induced (50%) while 18 were augmented (50%).

Cord plasma sodium levels, cord plasma bilirubin levels and day 1 and 2 hematocrit levels and plasma bilirubin levels were not statistically different between the groups (Table 2). Unrespectable of the diluent used the cord plasma bilirubin levels and day 2 plasma bilirubin levels were significantly higher in the accelerated group (Table 3).

In the correlation analysis, no correlation was detected between total oxytocin dose and total diluent dose with the metabolic parameters studied.

Table 1 The baseline characteristics of the groups

	Group 1 *n*=29	Group 2 *n*=36	Group 3 *n*=40	F	P
Maternal Age (year)	26.27±4.67	26.22±4.20	24.75±5.38	1.198	0.306
Gestational weeks	39.03±1.97	39.05±2.31	39.47±1.13	0.682	0.508
Parity	0.79±1.14	1.00±1.04	1.55±0.78	5.636	0.005*
Birth weight (g)	3305.35±593.22	3455.83±683.17	3435.12±459.11	0.600	0.551
Labor duration (min)	292.75±205.48	328.28±210.74	542.75±344.96	9.149	0.000**
Fluid volume (cc)	266.78±206.73	287.72±199.84	–	0.161	0.690
Oxytocin dose (mU)	5335.7±4134.8	5754.5±3997.0	–	0.161	0.690

Table 2 The distribution of metabolic parameters between the groups

	Group 1 *n*=29	Group 2 *n*=36	Group 3 *n*=40	F	P
Cord Plasma Sodium (mmol/ml)	141.03±4.70	139.80±5.90	140.00±3.55	0.598	0.552
Cord Plasma Bilirubin (mg/dl)	1.89±0.91	1.61±0.76	1.69±0.53	1.206	0.304
Day 1 Plasma Bilirubin (mg/dl)	2.00±0.98	2.13±0.60	2.97±2.62	1.914	0.156
Day 1 Hematocrit	59.46±6.07	59.83±4.20	59.43±5.68	0.042	0.959
Day 2 Plasma Bilirubin (mg/dl)	5.90±3.12	5.22±2.04	6.82±3.16	2.187	0.120
Day 2 Hematocrit	58.30±6.60	60.20±6.88	56.63±5.20	2.275	0.111

Table 3 The characteristics of labor and the distribution of metabolic parameters according to the oxytocin indication

	Induced group *n*=33	Accelerated group *n*=32	F	P
Duration of labor (min)	345.62±185.71	278.75±225.16	1.68	0.200
Total fluid administered (cc)	378.33±232.92	181.12±95.28	18.95	0.000**
Total oxytocin dose (U)	7.56±4.65	3.62±1.90	18.95	0.000**
Cord Plasma Sodium (mmol/ml)	140.12±5.44	140.59±5.42	0.123	0.727
Cord Plasma Bilirubin (mg/dl)	1.49±0.71	1.99±0.90	6.065	0.017*
Day 1 Plasma Bilirubin(mg/dl)	1.90±0.61	2.39±0.87	3.939	0.055
Day 1 Hematocrit	59.21±5.16	60.50±4.39	0.598	0.444
Day 2 Plasma Bilirubin(mg/dl)	4.73±2.14	6.56±2.64	5.665	0.023*
Day 2 Hematocrit	59.56±6.39	59.50±7.56	0.001	0.978

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 [9]. These are delayed cord clamping, delivery by vacuum extraction and use of forceps, breech delivery, the use of oxytocin for labor induction or augmentation and administration of epidural analgesia, especially bupivacaine, to the mother [3, 9, 10]. 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 [5, 6, 11, 12, 13, 14].

Although not all the surveys have demonstrated an association between the use of oxytocin and hyperbilirubinemia, Buchan showed that infants delivered following oxytocin induction had evidence of hemolysis [15]. 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 [3].

Despite the earlier studies that have suggested that oxytocin use during labor was a significant determinant for neonatal hyperbilirubinemia, recent studies oppose this assumption. Seidmann et al, found that oxytocin infusion did not have contribution to neonatal hyperbilirubinemia in their prospective study on 1177 patients [3]. Linn et al, reported that some factors like the use of epidural anesthesia, parity, the use oxytocin and white race that had been proposed to contribute the neonatal hyperbilirubinemia did not affect neonatal bilirubin levels in their study on 12,023 patients [1]. Maissels et al, reported that breastfeeding and the percentage of weight loss after birth were the major determinants for the neonatal jaundice rather than oxytocin infusion in the healthy newborns [2]. Like these studies, we found that oxytocin infusion did not cause neonatal hyperbilirubinemia.

The commonly used way of administration of oxytocin as diluted in 5% glucose solution supposed to increase the risk of transplacental hyponatremia due to the infusion of large volumes of salt-free fluid into the mother and neonatal hypoglycemia and neonatal hyperbilirubinemia as a consequence.

In our study, the quality and the quantity of the diluents used to administer the oxytocin infusion was found not to affect the neonatal bilirubin levels. There was not a significant difference in cord plasma sodium levels between the groups, which indicated that hyponatremia did not contribute significantly to the hyperbilirubinemia in the neonatal period.

Our data is inconsistent with the results of Omigbodun et al, who had proposed the use of 5% dextrose might be major determinant for the neonatal hyperbilirubinemia since we found no difference between the isotonic saline and 5% dextrose groups in the induction and augmentation groups [8]. D'Souza et al suggested restricting the fluids that were used for oxytocin to prevent neonatal hyperbilirubinemia but we could not detect any correlation between the total volume of diluent administered and the intensity of neonatal bilirubin levels [4].

In our study, the higher rate of parity in Group 3 may be attributed to the prospective and randomized study design. Interestingly, the oxytocic effect in groups 1 and 2 almost shortened the labor duration in half although the parity was dramatically high in group 3. Another remarkable finding in our study is the higher incidence of neonatal bilirubin levels in the augmentation of labor group even though the total dose of oxytocin is less than the induction of labor group. Lange et al, did not report any difference between induced or augmented groups with oxytocin in their study with 739 patients [7].

Conclusion

We did not detect any significant effect of oxytocin infusion and the different diluents used for oxytocin administration on neonatal hyperbilirubinemia. Our study indi-

cates that the oxytocin use in the management of labor may affect neonatal bilirubin levels when oxytocin is used for the augmentation of labor even though the duration and the dose of oxytocin infusion are less than the induction of labor group.

References

1. Linn S, Schoenbaum SC, Manson RR, Rosner B, Stubblefield PG, Ryan RJ (1985) Epidemiology of neonatal hyperbilirubinemia. Pediatrics 75:770–774
2. Maissels MJ, Gifford K, Antle CE, Leib GR (1988) Jaundice in the healthy newborn infant: a new approach to an old problem. Pediatrics 81:505–511
3. Seidman DS, Ergout Z, Part I, Laor A, Revel, Vilk S, Stevenson DK, Gale R (1999) Predicting the risk of jaundice in full-term healthy newborns. J Perinatol 19:564–567
4. D'Souza SW, Liebermann B, Cadman J, Richards B (1986) Oxytocin induction of labor. Hyponatremia and neonatal jaundice. Eur J Obstet Gynecol Reprod Biol 22:309–317
5. Johnson JD, Aldrich M, Angelis P, Stevenson DK, Smith DW, Herschel MJ, Papagrafolis C, Valales T (1984) Oxytocin and neonatal hyperbilirubinemia. Studies of neonatal bilirubin production. Am J Dis Child 138:1047–1050
6. Davies DP, Gomersall R, Robertson R, Gray OP, Turnbull AC (1973) Neonatal jaundice and maternal oxytocin infusion. BMJ 3:476–477
7. Lange AP, Secher NJ, Westergaard JG, Shougard I (1982) Neonatal jaundice after labor induced or stimulated by prostaglandin E2 or oxytocin. Lancet i:991–994
8. Omigbodun AO, Akindele JA, Osotimehin BO, Fatinikun T, Fajimi JL, Adeye JA (1993) Effect of saline and glucose infusions of oxytocin on neonatal bilirubin levels. Int J Gynecol Obstet 40:235–239
9. Friedman L, Lewis PJ, Clifton P, Bullpitt CJ (1978) Factors influencing the incidence of neonatal jaundice. BMJ i:1235–1237
10. Roberts G, Weaver A (1974) Labour and neonatal jaundice. Lancet i:935
11. Ghosh A, Hudson FP (1972) Oxytocic agents and neonatal hyperbilirubinemia. Lancet ii:823
12. Sims DG, Neligan GA (1975) Factors affecting the increasing incidence of severe non-haemolytic neonatal jaundice. Br Obstet Gynecol 82:863–867
13. Jeffares MJ (1977) A multifactorial survey of neonatal jaundice. Br Obstet Gynecol 84:452–455
14. Boylan P (1976) Oxytocin and neonatal jaundice. BMJ iii: 564–565
15. Buchan PC (1979) Pathogenesis of neonatal hyperbilirubinemia after induction of labor with oxytocin. BMJ ii:1255