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Evaluation of the Effect of Different Anesthetic Techniques on Neonatal Bilirubin Levels

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Abstract

Objectives: The aim of the present study was to determine whether different anesthetic techniques applied for vaginal delivery and cesarean section affect neonatal bilirubin levels in the first 24 hours of life.

Materials and Methods: A total of 511 neonates delivered by vaginal route or cesarean section were included in the study. The neonates were classified according to method of delivery and anesthetic agents as group A (cesarean section / general anesthesia with sevoflurane), group B (cesarean section / spinal anesthesia with bupivacaine hydrochlorur), group C (vaginal delivery with episiotomy / local anesthesia with prilocaine hydrochloride) and group D (vaginal delivery/ no anesthesia). The levels of neonatal serum bilirubin in the groups were compared.

Results: There was no difference between group A and group B when compared in terms of neonatal bilirubin levels ($p = 0.98$). Depending on the use of prilocaine hydrochloride as local anesthetic agent in the vaginal delivery, there was no significant difference between the groups C and D ,who had vaginal delivery, in terms of the neonatal bilirubin levels ($p = 0.99$). The serum levels of bilirubin in cesarean section groups were significantly higher than those of the vaginal delivery groups ($p < 0.001$).

Conclusion: Prilocaine hydrochloride used for episiotomy is not effective on neonatal hyperbilirubinemia. However, cesarean section with sevoflurane and bupivacaine hydrochloride seems to result in increased bilirubin levels.

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Introduction:

Jaundice is one of the most common causes of health problems, contributing to 60% of term and 80% of preterm infants in the first week of life (1). Hyperbilirubinemia may lead to neurotoxicity. There is no defined safe level of bilirubin (2). So, early detection and treatment of neonatal hyperbilirubinemia is important in the prevention of bilirubin-induced encephalopathy (3). However, neonatal jaundice is sometimes harmless. Monitoring bilirubin levels over multiple hospital visits and readmitting infants to the hospital for phototherapy may cause anxiety to the parents and could adversely affect the parent–infant relationship. Furthermore these hospital visits and treatments increase overall health care costs (4).

It has long been known that hyperbilirubinemia is likely to develop in the neonates who are born before term, due to immaturity of glucuronyl transferase enzyme system. The other reasons are preterm labor as well as blood group incompatibility, more liberal use of oxytocin for inducing labor, certain drugs used by the mother and abnormal deliveries such as (forceps, breech and ventouse)(5,6).

It is expected that anesthetic agents cross the placenta considering the time from induction of anesthesia to clamping of the umbilical cord. Therefore, it is likely that anesthetic technique could be included among factors with possible influence on neonatal jaundice (7). Recently, Alkan et al. showed that bupivacaine was not effective on neonatal bilirubin levels. However, sevoflurane increased bilirubin levels (8). Demiraran et al. (6) mentioned that bupivacaine was more effective than sevoflurane considering neonatal hyperbilirubinemia. The studies related to the effect of anesthesia and particular techniques in neonatal hyperbilirubinemia are often limited by cesarean sections (5,7). Up until now, there are a few studies on vaginal deliveries related to hyperbilirubinemia (8). In addition, studies related to this issue compared general, epidural, spinal and total intravenous anesthesia. However, as far as we could see, none of these have been mentioned for local anesthesia for episiotomy in the vaginal deliveries. Prilocaine hydrochloride is a local anesthetic agent that could be used for episiotomy. This agent may lead to methemoglobinemia (9). So, the use of prilocaine is not recommended for babies who are younger than 3 months old (10). We could not find any studies about the effect of prilocaine on neonates born by vaginal route in literature.

Therefore, in this study, we aimed to determine the effects of the local anesthesia with prilocaine hydrochloride in vaginal deliveries on neonatal hyperbilirubinemia in the first 24 hours of life. Besides, it compares with both general anesthesia given with sevoflurane and spinal anesthesia with bupivacaine hydrochloride in cesarean section.

Material & Methods:

The study was approved by Ethics Committee of Celal Bayar University. It is a study that included ASA I-II status, uncomplicated pregnants who had delivered by cesarean section under elective circumstances (n=189) and uncomplicated pregnants who had vaginal deliveries (n=322) at the Departments of Obstetrics between June-2012 and March-2013. Exclusion criteria were Rh incompatibility, positive direct Coombs test results, fetal anomalies, fetal growth retardation, APGAR scores of <8 at 1 min and <10 at 5 min and the pregnant who had delivered preterm (<37 weeks) or history of maternal drug useage which has known to influence neonatal bilirubin levels. Indications for cesarean section were often previous uterine incisions, less frequently cephelopelvic disproportion, malpresentation and patient preference.

The neonates were classified according to the method of delivery and anesthetic agents as:

group A (cesarean section / general anesthesia with sevoflurane),

group B (cesarean section / spinal anesthesia with bupivacaine hydrochloride),

group C (vaginal delivery with episiotomy / local anesthesia with prilocaine hydrochloride), and

group D (vaginal delivery/ no anesthesia) .

For induction, propofol 2 mg/kg and atracurium besylate 0,5 mg/kg were given intravenously in cesarean section for general anesthesia group. After muscular relaxation, endotracheal intubation was performed. To maintenance of anesthesia, 50% O2, 50% N2O and 1-2% minimum alveolar concentration of sevoflurane were used. The time from the start of general anesthesia to clamping of the cord was 6-8 minutes. For cesarean section with spinal anesthesia group, 1000 ml 0.9% NaCl was given in 30 minutes. Hydration was continued with 0.9% NaCl 10ml/kg/h. Spinal anesthesia was performed by using 26 gauge spinal needle into L3-4 or L4-L5 intervertebral space, in the sitting or lateral decubitus position. After free flow of cerebrospinal fluid, heavy bupivacaine hydrochloride 0.5% 2cc and fentanyl 15 mcg were injected. The period from the beginning of the spinal anesthesia to clamping of the cord was 8-10 minutes. Prilocaine hydrochloride (2%) 5 cc was injected into the muscular perineal area for episiotomy in group C. The cord was clamped in 8-10 minutes after injection. No anesthetic agent used in group D.

The blood samples taken from the heel in the Hematocrit pipette were centrifuged and then, measured by B-105 digital bilirubinometer, (Erma Inc., Japan) with spectrophotometric method. Considering exclusion and inclusion criteria (maternal and gestational age, birth weight and sex of neonatal, route of delivery, anesthetic agents) bilirubin levels in the first 24 hours were recorded from patient files.

Obtained data were analyzed by using descriptive statistical methods (frequency count, mean and standard deviation), t test for independent groups, chi-square test for categorical variables, pearson correlation test for relationships between variables, one-way analysis of variance (ANOVA) and post hoc tukey test performed to compare difference between groups. P values less than 0.05 were accepted as significant.

Results:

In total, of 511 pregnant women were included in the study, there were no significant difference between groups in terms of birth weight and sex of neonates ($p = 0.89$ and $p = 0.90$, respectively).The maternal age was significantly lower in group C (vaginal delivery/local anesthesia with bupivacaine hydrochloride) than those of group A (cesarean section/general anesthesia with sevoflurane), group B (cesarean section / spinal anesthesia with bupivacaine hydrochloride) and group D (vaginal delivery /no anesthesia) ($p = 0.007$, $p = 0.001$ and $p < 0.001$, respectively). Gestational age was lower in cesarean section groups (group A and B) than those of the vaginal delivery groups (group C and D) but the difference was not significant statistically (38.8 ± 1.1 and 39.2 ± 1.3 weeks respectively, $p=0.65$).There was no difference between group A and group B in cesarean groups in terms of gestational age ($p=0.86$). Likewise, a significant difference was not found between group C and group D in vaginal delivery groups for gestational age ($p=0.77$). Demographic data is given in table 1.

When bilirubin levels were compared, the serum levels of bilirubin in cesarean section groups (6.2 ± 1.6 mg/dL) were significantly higher than those of the vaginal delivery groups (5.4 ± 0.9 mg/dL) ($p<0.001$).

There was no difference between group A and group B when compared in terms of neonatal bilirubin levels in the first 24 hours of their life ($p=0.98$). The serum levels of bilirubin in each group are given in table 2. Depending on the use of local anesthesia, there was no significant difference between the groups C and D ,who had vaginal delivery, in terms of the neonatal bilirubin levels ($p=0.99$).

The correlation between the characteristics showing significantly differences among the groups and the neonatal bilirubin levels were evaluated. The serum levels of bilirubin were decreased with increase in the gestational age, but, the negative correlation was not statistically significant ($r = -0.06$, $p = 0.12$). There was positive correlation between maternal age and bilirubin levels. However, this correlation was not statistically significant, either ($r = 0.07$, $p = 0.08$).

Discussion:

In our study, to the best of our knowledge, the effect of local anesthesia on neonates

was questioned the first time ever. We found no difference between neonates born by vaginal delivery with local anesthesia for episiotomy and those who anesthesia weren't applied in terms of bilirubin levels. We determined that the total bilirubin levels in the first 24 hours for cesarean groups were significantly higher than vaginal delivery groups. However, we didn't find any difference between anesthesia with sevoflurane and bupivacaine hydrochloride in terms of neonatal bilirubin levels.

It has been shown that there was no correlation between cesarean section and neonatal hyperbilirubinemia by Phuapradit et al. (11). Recently, Alkan et al (8) have emphasized that the route of delivery had no effect on neonatal transcutaneous bilirubin levels during the first 24 hours. However, Gale et al (12) reported a significant correlation between cesarean section and increased bilirubin levels. In their study similar to our study, it has been shown that preterm labor, vacuum, forceps, low birth weight and maternal age increase neonatal bilirubin levels in the first 24 hours of life.

Prilocaine hydrochloride is in the list of drugs or toxins that can cause methemoglobinemia (9). As a result of prilocaine hydrocholoride usage as local anesthesia on infants in the first 3 months of their life, methemoglobinemia has been mentioned in the literature (10). Infants are particularly vulnerable to hemoglobin oxidation because of their cytochrome b5 reductase level to becoming approximately 50% of the adult value (9,13). Therefore, it is not recommended to use on babies who are younger than 3 months old because of the risk of methemoglobinemia (10). However, we determined that prilocaine hydrochloride as local anesthesia had no harmful effect on neonatal bilurubin levels. So, this result may be due to the use of a low dose of drug and injection to the mothers. Clark and Landaw reported that the neonatal jaundice associated with maternal anesthesia, especially bupivacaine hydrochloride, may be explained by the observations that local anesthetic agents (lidocaine, mepivacaine) cross the placenta, bind to red cell membrane and reduce its filterability, resulting in shortened red cell survival (14). In our study, we found that neonatal bilirubin levels increased due to spinal anesthesia with bupivacaine hydrochloride.

Alkan et al. (8) mentioned that transcutaneous bilurubin levels in sevoflurane group were significantly higher than bupivacaine hydrochloride group. Whereas, Ozçakır et al (5) founded out that different anesthesiology strategies had no effect on neonatal jaundice by comparing sevoflurane against bupivacaine hydrochloride. Demiraran et al. (6) reported that there was no difference on total bilurubin levels between sevoflurane and bupivacaine hydrochloride on the first day postpartum. Our findings supported these two recent studies that Sevoflurane doses were the same in both Demiraran's and our study (1-2 minimum alveolar concentration). Alkan et al. (8) used lower dose of sevoflurane (up to 0.8 minimum alveolar concentration). However, this difference in results could be explained by the length of time existd between the delivery of a baby and anesthesia.

Gale et al. (12) in a large population study, showed that a high bilirubin level was significantly associated with male sex, vacuum or forceps, short gestation, lower birth weight, and older maternal age . Therefore, we attempted to standardize the groups in terms of these conditions. Aside from, maternal and gestational age being different between groups, we showed that differences were not statistically significant. Most of the previous studies investigated the effects of anesthesia in cesarean section groups (5-7). The studies include vaginal deliveries in which anesthetic agents were not applied as a control group were extremely rare (8). In our study, we obtained significant difference for sevoflurane and bupivacaine hydrocholoride, but not for prilocaine hydrocholoride compared to vaginal delivery without anesthesia.

It has been known that oxytocin that stimulate uterine motility increase neonatal bilirubin levels (15). We didn't question the use of oxitocin in our study groups. Although, it is expected that the use of oxytocin is the most common in vaginal delivery, bilirubin levels of vaginal delivery

group were lower than cesarean section group. Restrictions of our study may be that bilirubin evaluation was limited to the first 24 hours because the mothers and babies were not hospitalized for a long time. In other studies, long term tracking is restricted to five days and it confirms the values of the first day (5).

Conclusion :

We found that local anesthesia with prilocaine hydrochloride did not effects bilirubin levels in neonates born by vaginal deliveries. Although, in the first 24 hours higher levels of bilirubin of neonates in cesarean section groups were observed significantly than vaginal delivery groups. We didn't observe any significant difference between sevoflurane and bupivacaine in terms of bilirubin levels of neonates.

Conflicts of interest:

The author(s) declared no potential conflicts of interest with respect to the research, authorship, and/or publication of this article.

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Table 1: Maternal and neonatal demographic data in groups (mean± SD)

	Cesarean delivery		Vaginal Delivery	
	General Anesthesia Group A (n=140)	Spinal Anesthesia Group B (n=49)	Local Anesthesia Group C (n=238)	No Anesthesia Group D (n=84)
Maternal age (year)	28.07±4.78	29.30±5.23	26.29±5.22	29.94±5.66
Neonatal Birth weight (g)	3275±405	3251±452	3297±423	3280±418
Neonatal Sex (male/female)	71/69	26/23	129/109	47/37
Neonatal Age (week)	38.9±1.1	38.4±1.1	39.2±1.3	39.3±1.3

SD: Standard Deviation

Table 2: Neonatal bilirubin levels according to applied anesthetic technique in the maternal delivery groups

Bilirubin (mg/dl)	General anesthesia	Spinal anesthesia	Local anesthesia	No anesthesia	P values
Total bilirubin levels in the first 24 hours	6.2±1.6a	6.3±1.7a	5.4±0.8b	5.4±1.2b	<0.0001

Different letters indicates statistical importance between the groups. One-way Analysis of Variance (ANOVA) was applied to results. SD: Standard Deviation, P <0.0001

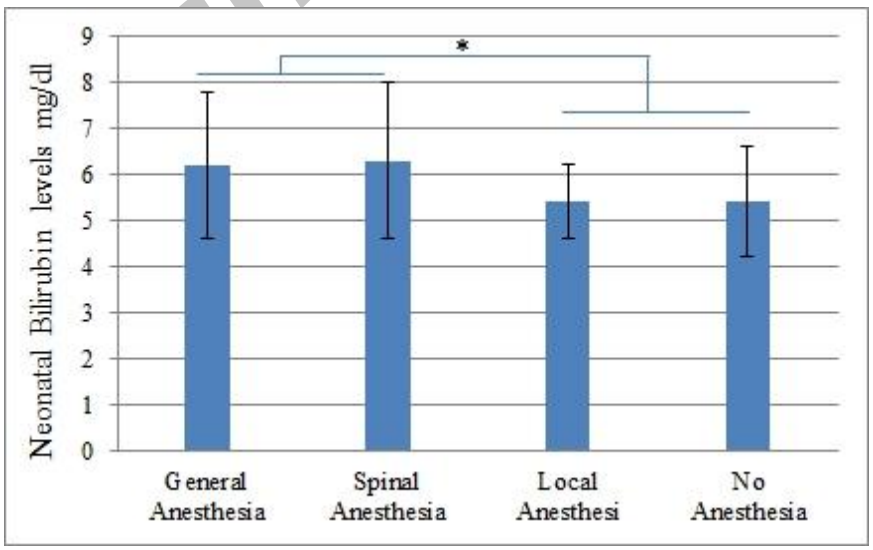

Figure 1: Neonatal bilirubin levels (mg/dl) according to applied anesthetic technique in the maternal delivery groups. One-way Analysis of Variance (ANOVA) was applied to results. Mean±SD, * P <0.0001

References:

1. Chowdhury AD, Hussey MH, Shortland DB. Critical overview of the management of neonatal jaundice in the UK . Public Health . 2007 Feb ;121 (2):137–43.

2. Amin SB, Lamola AA. Newborn jaundice technologies: unbound bilirubin and bilirubin binding capacity in neonates. Semin Perinatol. 2011 Jun;35(3):134-40.

3. Petrova A, Mehta R, Birchwood G, Ostfeld B, Hegyi T. Management of neonatal hyperbilirubinemia: pediatricians' practices and educational needs. BMC Pediatr. 2006; 6:6.

4. Kemper K, Forsyth B, McCarthy P Jaundice, terminating breast-feeding, and the vulnerable child. Pediatrics. 1989; 84(5): 773–8

5. Ozcakır HT, Lacin S, Baytur Y, Luleci N, Inceboz U. Different anesthesiologic strategies have no effect on neonatal jaundice. Arch Gynecol Obstet 2004; 270: 179–81.

6. Demiraran Y, Albayrak M, Seker IS, Kaynak G, Iskender A, Sezen GY, Ozdemir I. Effect of anesthesiological strategies on neonatal bilirubin levels during cesarean section: a prospective and randomized trial. Arch Gynecol Obstet . 2011; 284:1059–65

7. De Amici D, Delmonte P, Martinotti L, Gasparoni A, Zizi S, Ramajoli I, et al. Can anesthesiologic strategies for caesarean section influence newborn jaundice? A retrospective and prospective study. Biol Neonate. 2001; 79: 97–102.

8. Alkan S, Tıras U¸ Dallar Y, Sunay D. Effect of anaesthetic agents administered to the mothers on transcutaneous bilirubin levels in the neonates. Acta Pædiatrica. 2010; 99: 993–6

9. Rehman HU. Methemoglobinemia. West J Med. 2001 Sep; 175(3):193-6.

10. Ozdogan H, Osma S, Aydin GB, Dinc A, Ozgun G. Methemoglobinemia presenting in a circumcised baby following application of prilocaine: a case report.J Med Case Rep. 2010; 4:49.

11. Phuapradit W, Chaturachinda K, Auntlamai S. Risk factors for-neonatal hyperbilirubinemia. J Med Assoc Thai .1993; 76:424–8.

12. Gale R, Seidman DS, Dolberg S. Epidemiology of neonatal jaundice in the Jerusalem population. J Pediatr Gastroenterol Nutr .1990; 10:82–6.

13. Wright RO, Lewander WJ, Woolf AD. Methemoglobinemia: etiology, pharmacology, and clinical management. Ann Emerg Med. 1999; 34(5):646–56.

14. Clark DA, Landaw SA. Bupivacaine alters red blood cell properties: a possible explanation for neonatal jaundice associated with maternal anesthesia. Pediatr Res. 1985; 19:341–3

15. Meisel P, Meisel M. Do drugs in pregnancy modify neonatal jaundice?. Zentralbl Gynakol. 1993; 115(7):301-8.