

# Segmental Epidural Anesthesia Have No Effect on Neonatal Serum Bilirubin Concentrations and Neonatal Jaundice

## SEGMENTAL EPİDURAL ANESTEZİ YENİDOĞAN SERUM BİLİRUBİN DÜZEYLERİNİ ETKİLEMEMEKTE VE YENİDOĞAN SARILIĞI RİSKİNİ ARTIRMAMAKTADIR

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### Summary

**Objective:** In this study we examined neonatal hyperbilirubinemia and jaundice among the newborns delivered by caesarean section with segmental epidural anesthesia with bupivacaine hydrochloride and the newborns delivered by caesarean section with general anesthesia.

**Methods:** The patients who had delivered by caesarean section at 38-40 weeks under general anesthesia (Group-A, n=66) and under segmental epidural anesthesia (Group-B, n=76) under elective circumstances were included into this prospective study. The neonatal blood samples for serum bilirubin determinations were drawn at the first and fifth days after deliveries and compared.

**Results:** There were no significant difference on bilirubin levels between two groups and the incidence of hyperbilirubinemia cases did not differ statistically ( $p>0.05$ ). The percentage of the newborns who needed phototherapy displayed no significant differences between the deliveries by caesarean section under general or segmental epidural anesthesia.

**Conclusions:** Segmental epidural anesthesia with bupivacaine hydrochloride does not increase the neonatal serum bilirubin levels and have no effect on neonatal jaundice.

**Key Words:** Epidural anesthesia,  
Neonatal hyperbilirubinemia,  
Neonatal jaundice

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### Özet

**Amaç:** Bu çalışmada prospektif olarak bupivacaine hidroklorid'in yeni doğan serum bilirubin seviyelerine ve yenidoğan sarılığına yol açıp açmadığını araştırdık.

**Yöntemler:** 38-40. gebelik haftalarında genel anestezi (n=66) veya epidural anestezi (n=76) altında ve elektif koşullarda sezeryan uygulanan hastalar prospektif olarak araştırıldı. Neonatal serum bilirubin düzeyleri postpartum 1. ve 5. günlerde ölçülerek gruplardaki bulgular incelendi.

**Bulgular:** Bilirubin seviyeleri gruplar arasında farklı değildi ve hiperbilirubinemi gelişimi iki grup arasında istatistiksel fark taşımamaktaydı ( $p>0.05$ ). Fototerapi gören bebekler açısından gruplar arasında anlamlı fark saptanmadı.

**Sonuçlar:** Bupivacaine hidroklorid kullanılan segmental epidural anestezi yenidoğan sarılığı açısından risk faktörü özelliği taşımamaktadır.

**Anahtar kelimeler:** Epidural anestezi,  
Neonatal hiperbilirubinemi,  
Neonatal sarılık

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Neonatal jaundice is a frequent problem in neonatology and can be influenced by many factors. There has been concern about this increasing incidence of what used to be called "physiological" jaundice of the newborn and there have been suggestions that this is due to some change in clinical practice. It has long been known

that much higher levels of unconjugated bilirubin are likely to develop in babies who are born before term, due to immaturity of glucuronyl transferase enzyme system. The other reasons mentioned for the increased incidence of neonatal hyperbilirubinemia include the increased use of oxytocin for inducing labor (1-2), abnormal

deliveries (forceps, breech and ventouse) (3), fasting of the baby (4), and certain drugs used by mother during pregnancy (5). Birth weight and the duration of spontaneous labor have been shown to have no significant effect on this incidence, whereas a highly significant association between increasing duration of labor and the subsequent development of neonatal hyperbilirubinemia has been seen when labor is induced artificially (1).

The role of epidural anesthesia with bupivacaine hydrochloride as a causative factor in neonatal hyperbilirubinemia is still open to discussion. Some previous studies have found it to be associated with jaundice (6,7) while others have not (8,9). However, in most of these studies researchers have concerned on the mothers received segmental epidural analgesia during the first stage of the labor. In a recent study, De Amici et al (10) mentioned that among all newborns delivered by caesarean section, some had a more intense physiological jaundice and it was likely that anesthetic technique could be included among factors with possible influence on neonatal jaundice. In the present prospective study we therefore examined neonatal hyperbilirubinemia among all newborns delivered by caesarean section with segmental epidural anesthesia with bupivacaine hydrochloride and compared to deliveries by caesarean section with general anesthesia.

### Methods

The pregnant women who had delivered with caesarean section under general anesthesia at 38-40 weeks of uncomplicated pregnancy (Group-A, n=66) and who had delivered by caesarean section at 38-40 weeks under elective circumstances and under segmental epidural anesthesia (Group-B, n=76) were included into this prospective study between 2001 and 2002. The patients in the two study groups elected randomly depending to the patients desire of the anesthetic technique. The patients who had delivered preterm (<37 weeks), the patients who had used certain drugs during pregnancy, the labours in which oxytocin was used, abnormal deliveries were not included into the study. The patients who had hypertension, diabetes or anemia (hematocrit levels with < %30 at

birth) findings during pregnancy were also excluded from the study. Cephalopelvic disproportions, malpresentations, previous uterine incisions, primigravida after 35 years of age, placenta previa were the major elective indications for caesarean operation in our study group. All operations were performed by the same group of residents.

The patients who delivered by caesarean section received segmental epidural anesthesia. For providing epidural anesthesia, the patients positioned in lateral decubitus position and with the insertion of tuohy needle to the epidural space at the height of Lumbal 3, 10 ml bolus doses of 0.5% plain bupivacaine hydrochloride injected. Then the tuohy needle replaced with the catheter. The anesthetic level checked with pinprick test. Optimum height of the anesthesia was accepted as the height of Th 5-6 before starting the operation. This is followed by repeated bolus doses (2.5 ml of %0.5 plain bupivacaine hydrochloride) of the same anesthetic concentration into the epidural space when the optimum anesthetic level was not provided. The total dose of bupivacain hydrochloride per parturient varied from 10 to 15 ml. To avoid aortocaval compression, the maternal posture during the first 30 min after commencing anesthesia was tilted at least 15° left lateral. During this time the patients received 500 ml of Ringer solution to protect from vasodilatation and hypotensive effect of anesthesia.

For general anesthesia, thiopental sodium 8-10 mg/kg and succinyl choline 1 mg/kg were given to the patients intravenously for initial induction. After intubation, 40% O<sub>2</sub> and sevoflurane up to 0.60 MAC in 60-70% N<sub>2</sub>O were given for anesthesia of the patients.

Neonatal serum bilirubin levels were determined at the ages of 24 hrs and 5 days in 142 infants. The sexuality, weight, fifth minute APGAR scores, hematocrit levels of the neonates were recorded. The neonates who needed phototherapy were also noted. The results in Group-A and Group-B were compared.

Statistical analysis was performed by Statistical Package for Social Sciences (SPSS) version 10.0 for Windows (SPSS Inc, USA). The values

**Table 1.** The percent of the neonates in Group-A and Group-B who needed phototherapy or who did not

		Group-A	Group-B	Total
The neonates who did not need phototherapy	Count	36	26	62
	%within count	58.1%	41.9%	100%
	%of total	25.4%	18.3%	43.7%
The neonates who needed phototherapy	Count	30	50	80
	%within count	37.5%	62.5%	100%
	%of total	21.1%	35.2%	56.3%
Total	Count	66	76	142
	%within count	46.5%	53.5%	100%
	%of total	46.5%	53.5%	100%

P=0.99, not significant

**Table 2.** Outcome of the neonates in Group-A and Group-B

	Group-A	Group-B	P value
Bilirubin level Day 1 (mg/dl)	7.4±3.1	7.4±2.9	0.970 (NS)
Bilirubin level Day 5 (mg/dl)	11.3±3.2	11.7±3.2	0.617 (NS)
Weight(kg)	3331.8±502.6	3222.6±376.6	0.300 (NS)
Hematocrit(%)	54.6±5.7	54.3±6.1	0.855 (NS)
APGAR (5.min)	9.9±0.3	9.8±0.3	0.919 (NS)

Note : Data are means ± SD unless otherwise indicated

NS: Not Significant

were expressed as mean ± standard deviation. The means were compared by student-t test. The percentages were compared by chi-square test. P value lower than 0.05 was accepted as significant.

### Results

There was no complication during the operations. The mean age of the patients in general anesthesia (GA) group was 27.8±3.9 and in the epidural anesthesia (EA) group was 28.4±4.1 years (p>0.05). Cephalopelvic disproportions (EA;33, GA;28), malpresentations (EA:11,GA;12), previous uterine incisions (EA;27,GA;23), primigravida after 35 years of age (EA;2,GA;2) and placenta previa (EA;3,GA;1) were the major elective indications for caesarean operation in our study group. The mean time from incision to deliveries during the procedures was 7 minutes (min:5, max:14). There were 76 male and 66 female neonates in the groups and no difference was found between the sexuality of the neonate and the need of phototherapy (p>0.05). None of the newborns needed ex-

change transfusion because of hyperbilirubinemia. The percent of the newborns who needed phototherapy displayed no significant differences between the two groups (Table 1).

The mean weight of the neonates in Group-A and Group-B is not statistically different (3331.8±502,6 versus 3222.6±376.6 respectively) (p>0.05). The mean hematocrit levels were also similar in Group-A and Group-B (54.6±5.7 versus 54.3±6.1 respectively) (p>0.05). The mean APGAR scores on the fifth minute after deliveries were similar in both of the groups (9.9±0.3 versus 9.8±0.3 respectively) (p>0.05). There was no difference between the mean bilirubin levels detected on the first day (7.4±3.1 versus 7.4±2.9 respectively) and on the fifth day (11.3±3.2 versus 11.7±3.2 respectively) (p>0.05). (Table 2)

### Discussion

Different causative factors of neonatal hyperbilirubinemia has been reported during the years. Prematurity, abnormal deliveries, certain drugs

used by the mother during pregnancy were reported as the risk factors. One other reason for neonatal hyperbilirubinemia mentioned in prospective studies was oxytocin use during labour. Chalmers et al (1) have found the incidence of neonatal jaundice higher in infants born after oxytocin administration than among others in 10591 deliveries. Joupilla et al (9). showed that neonatal serum bilirubin levels were higher when oxytocin was used during labour.

Segmental epidural anesthesia with bupivacaine hydrochloride has been shown to be a safe and effective obstetric anesthetic method, however, it has also been suggested to be one of the causative factors of neonatal jaundice (6). Clark and Landaw (7) incubated cord blood with lidocaine, mepivacaine, bupivacaine, or buffer and determined red blood cell filterability and found that only bupivacaine at either 1 or 2 micrograms/ml prolonged filterability by an average of 58 to 65% over red cells treated with buffer alone. They also determined red cell survival in 13-day-old rats injected with bupivacaine hydrochloride or buffer and revealed that at 2 h after injection, buffer-treated animals had a red cell survival of 96.9 +/- 3.3%, whereas 2-h survival was reduced to 82.6 +/- 8.7% for the animals injected with bupivacaine. Authors concluded that the neonatal jaundice associated with maternal anesthesia, especially bupivacaine hydrochloride, may be related to the observations that these agents cross the placenta, bind to the red cell membrane and reduce its filterability, resulting in shortened red cell survival. Johnson et al (11) suggested that bupivacaine hydrochloride crosses the human placenta by passive diffusion rather than active transport and was influenced by the degree of maternal and fetal protein binding differences and quite possibly by placental accumulation. This relationship of placental transfer has important clinical implications, especially under pathologic circumstances, when either maternal or fetal serum protein concentrations might vary widely from normal. For example, in severe preeclampsia with reduced maternal protein binding, greater placental transfer of bupivacaine hydrochloride might occur. Also, it is quite clear that,

during the period of fetal acidosis, bupivacaine hydrochloride transfer might be increased by alarge factor. In addition, the placenta's ability to

Sequester bupivacaine hydrochloride in large quantities may allow it to act as a depot to expose the fetus to concentrations of bupivacaine hydrochloride well after maternal concentrations have dissappeared. Here, we performed a prospective study on healthy term newborns to ensure avoidance of these negative conditions.

In a recent study, De Amici et al (10) mentioned that among all newborns delivered by caesarean section, some had a more intense physiological jaundice and it was likely that anesthetic technique could be included among factors with possible influence on neonatal jaundice. However, Joupilla et al (9) have found no statistically significant differences in the neonatal serum bilirubin levels at different times between the epidural and control groups, nor did the incidence of neonatal hyperbilirubinemia cases differ between the groups (9). Similarly, Gale et al (8) have failed to demonstrate a causative connection between bupivacaine hydrochloride and neonatal jaundice in newborns whose mothers received an epidural block with bupivacaine hydrochloride during labor and delivery. In these studies researchers have concerned on the mothers received segmental epidural analgesia during the first stage of the labor. Epidural analgesia for labour and delivery involves an initial incremental injection of 8-12 ml of a relative dilute local anesthetic solution (%0.25 bupivacaine hydrochloride). This is followed by either repeated bolus doses of the same local anesthetic concentration when pain recurs or a continuous infusion of an even more dilute local anesthetic solution into the epidural space. In caesarean operations more concentrate solution (%0.5 bupivacaine hydrochloride) of bupivacaine hydrochloride is necessary for segmental epidural anesthesia. In this study, we examined the relation between neonatal hyperbilirubinemia and bupivacaine hydrochloride in neonates delivered by caesarean section with segmental epidural anesthesia or by general anesthesia, however, no difference was found.

In conclusion our findings support the clinical studies which have not demonstrated an association between segmental epidural anesthesia with bupivacaine hydrochloride and neonatal jaundice.

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