Effects of General and Regional Anesthesia on the Neonate (A Prospective, Randomized Trial)

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Abstract

Anesthetic methods used during cesarean section have advantages and disadvantages to both mothers and infants and may result in short and long term neonatal effects.

Objective : To determine the effects of general and regional anesthesia on the infants, a prospective, randomized trial was performed in Siriraj Hospital, Mahidol University.

Material and Method : 341 uncomplicated pregnant women who were to be delivered at term by Cesarean section were recruited and randomized to receive general anesthesia, GA (103); epidural anesthesia, EA (120) and spinal anesthesia, SA (118). The immediate fetal and neonatal effects were assessed by cord blood gas analysis and the infant's Apgar scores. The Neurologic and Adaptive Capacity Scores (NACS) was performed within 4 hours after birth by two pediatricians who were blind to the anesthetic method.

Result : Maternal age, weight, height, duration of the operation and infants' birth weight were not different among the study groups. In the EA and SA group, maternal systolic blood pressure decreased more than 20 per cent from the baseline in more than half. The infants' Apgar scores at 1 and 5 minutes were 8.3 ± 1.9; 8.2 ± 1.6; 6.7 ± 2.8, and 9.7 ± 0.9; 9.8 ± 0.7; 9.2 ± 1.6 in EA, SA and GA group respectively. The adaptive capacity, active tone, passive tone, general assessment and primary reflexes of the NACS were not statistically different.

Conclusion: Apgar scores of the infants whose mothers received general anesthesia were lower than infants whose mothers received regional anesthesia but the NACS were not statistically different among the three study groups.

Key word : Anesthesia - General - Regional - Effect - Neonate

Epidural (EA) and spinal anesthesia (SA) for cesarean section have advantages and disadvantages to both mothers and neonates. Compared to general anesthesia (GA), regional anesthesia offers reduced maternal mortality, the ability to use fewer drugs, more direct experience of childbirth, decreased blood loss and provides excellent postoperative pain control. The disadvan-

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tages of regional anesthesia include maternal hypotension, intraoperative discomfort, post-dural-puncture headache and the risk of neurologic and cardiac toxicity from local anesthetics[1]. Fetal and neonatal side effects range from profound to subtle and transient to persistent after birth. Fetal neurological toxicity is rare but change in the fetal heart rate (FHR) pattern during regional anesthesia has been reported. If those anesthetic techniques were complicated with maternal hypotension, it may result in neonatal depression[2]. The adverse effects on later intelligence, neuromuscular physiology, learning ability and behavior have not been reported beyond infancy in children whose mothers received acceptable doses of analgesic, sedative or anesthetic drugs during labor and delivery. Brackbill[3] and Scanlon[4] described a delay in habituation to sound and decrease in muscle tone of neonates, which they considered were due to maternal anesthesia and analgesia, however, long term significances of these effects is unknown. For different obstetric conditions, one anesthetic technique will be more preferable than the others. The choice of anesthesia for cesarean section is the technique that minimizes the risk to both mother and fetus especially in a high risk pregnancy. The objective of this study was to determine effects of general and regional anesthesia an infant delivered from an uncomplicated pregnancy. The neonatal effects were determined with cord blood acid-base analysis, Apgar scores and neonatal behavior assessed by using the Neurologic and Adaptive Capacity Scores[5].

MATERIAL AND METHOD

A prospective, randomized trial was performed in the Department of Obstetrics and Gynecology, Siriraj Hospital. Three hundred and forty-one uncomplicated pregnant women who would be delivered at term by cesarean section were recruited. Randomization was done by a random number to receive GA (103), EA (120) or SA (118) after informed consent. The exclusion criteria was patients with obstetric conditions that were a contraindication to any of the anesthetic techniques. All patients were anesthetized by anesthesiologists according to a planned protocol:

General anesthesia composed of 0.3 M sodium citrate orally before oxygenation, crashed induction, Sellick's maneuver and intubation with 7 mm endotracheal tube. Halothane 0.5 per cent, nitrous oxide and oxygen 50 per cent were given until the baby was delivered then halothane was turned off and either Fentanyl (1 mcg/kg) or Morphine (0.1 mg/kg) was given. The ventilation was controlled at the rate of 12 bpm at the tidal volume 10 ml/kg with pancuronium bromide as the muscle relaxant.

Epidural anesthesia composed of preloading with 1000 ml of Ringer lactate solution and a single shot epidural block with 18-20 ml of 2 per cent lidocaine with adrenaline 1:200000 *via* Touhey's needle. Oxygen 6 litres/minute was given *via* a variable-performance oxygen mask until the baby was delivered.

Spinal block patients received preloading of 1000 ml of Ringer lactate solution and spinal block with 5 per cent lidocaine 1.2 ml *via* spinal needle number 25 or 23. Oxygen was given in the same manner as in the epidural group. Vasopressor (Ephedrine) was given in the regional groups when the systolic blood pressure decreased more than 20 per cent of the baseline. Other medications were all recorded.

Following delivery, one and five minute Apgar scores were assigned by one of the three trained obstetric registered nurses. The umbilical cord was clamped at two sites before the infant's first breath, blood was sampled from the umbilical vein and determined for *p*H, PO_2, PCO_2, HCO_3 and oxygen saturation. Within 2 to 4 hours after birth, the infants were evaluated for the Neurologic and Adaptive Capacity Scores by one of the two pediatricians who was blind to the technique of anesthesia, the inter-observer variation had been reduced to the minimum. The results were tested for statistical significance among the groups by using the ANOVA. Statistical significance was considered at $P<0.05$.

RESULT

Three hundred and forty-one patients were randomized into GA, EA and SA groups. The technique of anesthesia in 39 patients was changed due to technical difficulty. The maternal age, weight, height, duration of the operation and birth weight were not different among the study groups. The different techniques of anesthesia resulted in different duration of time from the start of anesthesia to the time to start operation but the surgeons took the same duration of time from the start of incision to delivery (Table 1). In the SA and EA groups,

systolic blood pressure of mothers decreased more than 20 per cent of the baseline in half of the cases, 52 per cent and 37 per cent decreased to below 90 mmHg. The Apgar scores of infants delivered from mothers who received GA were significantly lower than those in the EA or SA group and when cord blood gas analysis was compared among the study groups, pH was significantly lower, PO_2 and PCO_2 was higher in GA group than in the EA or SA group. For the neuro-behavioral assessment, the three study groups showed no significant difference in total NACS (Table 2).

DISCUSSION

Placental transfer of local anesthesia depends on maternal factors (dosage, degree of protein binding, blood *p*H), placental factors (surface of placental exchange, placenta thickness) and fetal factors (maternal-fetal gradient of *p*H, fetal hepatic metabolism, redistribution of cardiac output in cases of fetal hypoxia[2]. Fetal neurotoxicity from regional anesthesia is rare, but maternal hypotension resulting from regional anesthesia may cause fetal or neonatal depression. In this study, epidural anesthesia when compared to spinal or general

Table 1. Demographic data (Mean ± S.D).

Demographic variables	General anesthesia (n=103)	Epidural anesthesia (n=120)	Spinal anesthesia (n=118)	P value
Maternal age (yr)	29.2±5.2	29.2±5.9	29.5±5.2	NS
Maternal weight (kg)	65.7±9.5	65.4±8.8	66.4±12.0	NS
Maternal height (cm)	153.8±5.6	153.8±11.1	154.7±6.0	NS
Time in minute(Mean ± S.D.)				
Start anes. to start operation	1.5±2.6	9.7±3.9	7.9±3.8	0.0001
Start operation to delivery	11.0±10.9	10.7±5.4	10.2±8.0	NS

Table 2. Result of the study.

Demographic variables	General anesthesia (n=103)	Epidural anesthesia (n=120)	Spinal anesthesia (n=118)	P value
Systolic blood pressure (SBP) in mothers during the operation (Per cent of cases)				
decrease SBP> 20%	15.8	51.3	56.8	<0.001
SBP < 90 mmHg	11.7	37.2	52.1	<0.001
Apgar scores of the infants				
1 minute (Mean ± S.D.)	6.7±2.8	8.3±1.9	8.7±0.6	0.001 (GA/EA,SA)
5 minute (Mean ± S.D.)	9.2±1.6	9.7±0.9	9.8±0.7	0.004 (GA/EA,SA)
Cord blood gas analysis				
*p*H	7.29±0.05	7.31±0.06	7.30±0.06	0.045 (GA<EA)
PO_2 (mmHg)	39.05±20.3	32.52±13.1	29.46±15.8	0.0001 (GA>EA,SA)
PCO_2 (mmHg)	52.7±7.3	48.0±9.2	50.3±8.9	0.003 (GA>SA>EA)
HCO_3 (mEq/L)	25.5±2.6	24.4±2.6	25.3±6.2	NS
BE	-1.65±2.67	-1.97±2.32	-1.98±2.17	NS
Oxygen saturation (%)	59.6±19.6	53.0±19.6	45.8±20.8	0.0001 (GA>EA>SA)
Neurological and Adaptive Capacity Scores				
Total score	34.4±3.4	34.9±4.2	34.8±3.7	NS

NS = non significant at P < 0.05

anesthesia, had the least effect on maternal blood pressure. Systolic blood pressure of mothers in the SA and EA groups decreased more than 20 per cent from baseline in half and below 90 mmHg in 52 per cent in SA and 37 per cent in EA group respectively. Fetal effects of maternal anesthesia would be demonstrated by an abnormal FHR pattern or low Apgar scores. Analysis of FHR tracings by a blinded perinatologist revealed no changes after lidocaine or bupivacaine epidural anesthesia and no significant differences between the groups at any time in basal FHR, short or long term variability, or the incidence of accelerations or decelerations[6]. The effect on the infants' Apgar scores has been studied. One of a retrospective studies found that infants who were delivered from mothers with epidural block had better Apgar scores[7]. The result was confirmed by a study done by Ratcliffe in 1993. In the study, neonates delivered following spinal anaesthesia were more acidaemic (pH = 7.249) ($P < 0.05$) than those delivered following epidural (pH = 7.291) or general anaesthesia (pH = 7.296) despite measures taken to minimize hypotension and the percentage of neonates with Apgar scores ≥ 7 at 1 minute was 96 per cent after epidural anaesthesia, 93 per cent after spinal anaesthesia and 75 per cent after general anaesthesia. The difference between epidural and general anaesthesia was significant ($P < 0.05$)[8]. In our study, Apgar scores were significantly lower in the GA than SA or EA group which was similar to the study done by Evans et al[9]. Infants in the GA group who were initially depressed at birth recovered rapidly. This depression may result from an interference of fetoplacental circulation because cord blood pH was lower although PO_2 was higher in the GA group. Evans suggested that general anesthesia rather than asphyxia or aortocaval compression was responsible for most of the depressed infants born by elective cesarean section[9]. In neonates delivered by urgent cesarean section such as uterine dystocia or failure of labor to progress, and those delivered by section because of fetal distress, general anesthesia was associated with higher rates of low Apgar scores as well as greater requirements for intubation and artificial ventilation, 12.5 per cent and 1.4 per cent of infants had Apgar scores at 1 and 5-minute of 4 or less respectively[10]. In infants with a gestational age of 32 week or less who were delivered by cesarean section under general anesthesia, 43 per cent and 10 per cent had low 1 and 5-minute Apgar scores compared to 22 per cent and 3.8 per cent of epidural anesthesia. General anesthesia was associated with a higher risk of low 1-minute score (0-3) after controlling for confounding factors (relative odds 2.92, [95%CI; 1.99, 4.27])[11]. In Thailand, the study by Werungkabutr that reported the neonatal outcome after anesthesia for cesarean section was not a randomized trial. They reported Apgar scores of 10 in 96.8 per cent, 100 per cent and 96.8 per cent of neonates from mothers who received general, spinal and epidural anesthesia respectively. But since 86-95 per cent of their patients received general anesthesia, the criteria for choosing anesthetic technique might have the effect on the infants' Apgar scores[12]. Abboud found that neonates delivered with GA scored significantly lower on some of the NACS items than those delivered with either EA or SA. In addition, neonates delivered with EA scored lower than those delivered with SA on supporting reaction and motor activity at 2 hours ($P \leq 0.05$) but all neonates had high scores. When they followed these infants for 24 hours there were no significant differences between each group[13]. In our blind, randomized trial using a NACS as the neuro-behavioral assessment, we found no differences among our study groups. In the study comparing 2 per cent lidocaine to 0.5 per cent bupivacaine epidural anesthesia, neonates in the lidocaine group scored as well as those in the bupivacaine group on all parameters of the Early Neonatal Neurobehavioral Scores (ENNS). In fact, on one parameter, sucking response at 24 hours, the neonates in the lidocaine group scored significantly higher than those in the bupivacaine group[14]. Cord venous concentrations of lidocaine were the only drug variables that correlated with performance on the autonomic items; the higher the concentration, the poorer the Brazelton Neonatal Behavioral Assessment Scale (BNBAS), all of the cluster scores showed significant improvement with age except for the regulation of state. Those data suggested that the difference in performance on the BNBAS associated with lidocaine is very subtle and that other perinatal factors can influence performance on the BNBAS more than the type of local anesthetic used[15].

In conclusion, we found that infants whose mothers received general anesthesia had lower Apgar scores than infants whose mothers received epidural or spinal anesthesia. The effects on neo-

natal behavior may not be clinically significant, long-term neurological effects in the infants may be difficult to assess because of the interference of other factors such as socioeconomics, and parental education on the infant's developmental outcome. Although this study was done in uncomplicated pregnancies at term, neonatal depression at birth is not uncommon in infants whose mothers received general anesthesia. From the results of our study, epidural anesthesia may be beneficial to infants who will be delivered from mothers who were complicated with high risk conditions.

(Received for publication on December 19, 1997)

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ผลของยาดมสลบและยาชาขณะผ่าตัดคลอดต่อทารกแรกเกิด

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การใช้ยาชาหรือยาดมสลบขณะทำการผ่าตัดคลอดมีทั้งผลดีและผลเสียต่อมารดาและทารก คณะผู้วิจัยได้ทำการศึกษาทารกซึ่งคลอดจากมารดาโดยการผ่าตัด 341 ราย โดยการสุ่มตัวอย่างมารดาเป็น 3 กลุ่ม คือ general (GA) 103 ราย, epidural (EA) 120 ราย หรือ spinal anesthesia (SA) 118 ราย ในระยะแรกเกิดทารกทุกรายจะได้รับการประเมินผลของยาชาหรือยาดมสลบโดยการตรวจ cord blood gas และคะแนนแอพการ์ (Apgar score) หลังจากนั้น 2–4 ชั่วโมง กุมารแพทย์ซึ่งไม่ทราบวิธีการใช้ยาชาหรือยาดมสลบจะประเมินระบบประสาทและพฤติกรรมของทารกด้วย Neurologic and Adaptive Capacity Score (NACS) ผลการวิจัยพบว่า อายุ น้ำหนัก ส่วนสูง ระยะเวลาที่ทำการผ่าตัด รวมทั้งน้ำหนักแรกเกิดในกลุ่มที่นำมาศึกษาทั้ง 3 กลุ่มไม่แตกต่างกัน มารดาที่ได้รับ EA และ SA จะมีความดันโลหิตต่ำกว่ากลุ่มที่ได้รับ GA อย่างมีนัยสำคัญทางสถิติ โดยกลุ่มที่ได้ EA หรือ SA จะมีความดันโลหิตซิสโตลิคต่ำกว่าร้อยละ 20 จากความดันโลหิตเดิมมากกว่าร้อยละ 50 นอกจากนี้ร้อยละ 52 ของมารดาที่ได้รับ SA และร้อยละ 37 ที่ได้รับ EA จะมีความดันซิสโตลิคต่ำกว่า 90 มม.ปรอท ทารกที่มารดาได้รับ GA มีคะแนนแอพการ์ต่ำกว่ามารดาที่ได้รับ EA หรือ SA อย่างมีนัยสำคัญทางสถิติ อย่างไรก็ตามจากการประเมินทารกด้วย NACS คณะผู้วิจัยไม่พบความแตกต่างในทารกทั้ง 3 กลุ่ม การใช้ epidural anesthesia ในมารดาขณะผ่าตัดคลอดอาจช่วยลดการขาดออกซิเจนของทารกซึ่งคลอดจากมารดากลุ่มเสี่ยงได้

คำสำคัญ : ยาสลบ – ยาดม – ยาชา – ผล – ทารกแรกเกิด

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