Maternal and Neonatal Effects of Single-Dose Epidural Anesthesia with Lidocaine and Morphine for Cesarean Delivery

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Abstract

Two per cent lidocaine (18-20 ml) with epinephrine 1:200,000 plus 4 mg of morphine was given as a single epidural injection over 3 minutes for elective cesarean section in 60 healthy mothers at term. It provided effective, safe and adequate analgesia in the postoperative period. There was no evidence of neonatal depression related to the epidural morphine as judged by Apgar scores at 1 and 5 minutes and umbilical venous *p*H at birth. Maternal and umbilical venous levels of morphine were measured and found to be low at birth. However, this study was done only in healthy mothers not in labor and having a term fetus. We do not recommend using this technique in complicated obstetric patients.

Single-dose epidural analgesia with lidocaine and morphine for cesarean delivery is a common anesthetic in Thailand. There are some reports[1-4] using epidural morphine to alleviate labor pain but to date there are none regarding this technique for cesarean delivery. Previous studies[4,5] showed that the plasma morphine levels in mothers receiving epidural morphine reached a peak within 30 minutes which often corresponded to the time of delivery. The objectives of our study were :

1. To observe the analgesic and side effects of single-dose epidural analgesia with lidocaine and morphine in the mother during and following elective cesarean section.

2. To observe the neonatal effects from this technique.

3. To measure maternal and umbilical venous serum morphine levels at delivery.

METHOD

The protocol was approved by the Ethics Committee for Human Investigation, Faculty of Medicine, Chulalongkorn University. Informed consent was obtained from each patient. Sixty healthy parturients with uncomplicated singleton preg-

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nancies, not in labor and scheduled for elective cesarean section were included in this study. Their gestational age by date was between 38-42 weeks. The indications for section were previous cesarean section (65%), cephalopelvic disproportion (31.7%), and elderly primigravida (3.3%). No premedication was given to any patient. Prior to epidural blockade, the patients were prehydrated intravenously with full strength saline solution 15 ml/kg within 30 minutes. The single-dose epidural anesthesia was conducted, using the paramedian approach, with the standard loss-of-resistance technique at L3-4 interspace by one researcher (SN). The mother was placed in the lateral recumbent position and the epidural space was entered with a 18-gauge short-bevelled Tuohy needle. If attempt at aspiration proved negative for 10 sec, 3 ml of 2 per cent lidocaine with epinephrine 15 micrograms was injected as a test dose, and if no evidence of subarachnoid block or intravascular injection was present within 5 minutes, a therapeutic dose was injected as a single bolus but was given slowly over a period of 3 minutes. The drugs used was 18-20 ml of 2 per cent lidocaine, depending on the height of the patient, with freshly added epinephrine to a concentration of 1:200,000 plus preservative free morphine sulfate 4 mg. After completion of the block the mother was turned on her back with left uterine displacement. Five liter per minutes of oxygen was given by a clear plastic face mask until delivery of the baby.

The sensory level of anesthesia to pinprick was measured every 2 minutes before surgery. Non-invasive blood pressure measurement, heart rate, and pulse oximetry monitored by ESCORT 100 (Medical Data Electronics, Arleta, CA 91331-4329) were recorded every 1 minute before delivery then every 4 minutes till the end of the operation. Hypotension was defined as systolic blood pressure less-than 100 mmHg and bradycardia as heart rate less than 60/min. The time after completing the block till the baby was delivered was the epidural-to-delivery time.

Maternal and neonatal assessments

During surgery maternal complaints of discomfort, need for drug supplementation and the cardiovascular changes were recorded. The supplementary drugs were inhaled 50 per cent nitrous oxide in oxygen or intravenous fentanyl 50-75 micrograms (after the delivery). If an anesthetic level of T6 was not obtained, general anesthesia with endotracheal intubation was induced without the use of opioids.

In the recovery room if more analgesia was required, fentanyl 50-75 micrograms was given intravenously. One hour after dissipation of local anesthetic blockade the individual patient's pain was assessed by visual analogue scale (VAS, 0-10 cm) and McGill Pain Score (0=no pain, 1= mild pain, 2=discomfort, 3=distressing, 4=horrible, 5=excruciating). Side effects of epidural morphine and the late analgesic requirements were also recorded for 48 hours postoperatively. The analgesics given in the ward were intramuscular morphine 0.15 mg/kg or oral non-opioid analgesics (acetaminophen or naproxen sodium) as required every 4 hours depending on the severity of pain. Newborn assessment was made with 1-minute and 5-minute Apgar scores and neonatal neural and adaptive capacity scores (NACS)[6] wihtin 2 hours and after 24 hours postdelivery. No neonates required naloxone reversal for apnea.

Immediately after delivery, maternal venous blood samples were obtained from the non-infusion arm and the umbilical venous blood samples from a double clamped section of umbilical cord. The serum was separated and frozen at-10 C for later analysis of morphine base. Umbilical venous *p*H was measured. All of the samples were analyzed for serum morphine base at the same time by a specific radioimmunoassay technique using Coat-A-Count Serum Morphine kits (Diagnostic Products Corporation, Los Angeles, CA 90045), with a sensitivity of 0.12 ng/ml at a range of 0.12-200 ng/ml and with cross-reactivity to morphine -3- glucuronide, morphine -6- glucuronide and codeine at 0.03 per cent, 0.15 per cent and 0.06 per cent respectively. Results were expressed as mean±SD or percentage. The mean serum morphine concentrations of the mothers and neonates delivered within and after 25 minutes of epidural injection were evaluated statistically by two-tailed T-test. Multiple regression analysis was used to evaluate the correlation between the epidural-to-delivery time and the ratio of serum morphine levels of the neonates and the mothers. A P value of < 0.05 was considered significant.

RESULTS

The maternal parameters are given in Table 1. Four of the sixty patients obtained an in-

Table 1. Demographic data of 60 parturients studied.

	Range	Mean ± SD
Age (yr)	18 - 40	30.30 ± 4.48
Body weight (kg)	55 - 85	67.81 ± 7.69
Height (cm)	148 - 165	155.68 ± 4.05

Table 2. Maternal effects of single-dose epidural anesthesia with morphine.

	No. of parturients	%
Proceed to general anesthesia	4/60	6.7
Complaint of discomfort during surgery	27/56	48.2
Need for supplementation of analgesia	13/56	23.2
Intraoperative complications		
- hypotension	16/56	28.6
- bradycardia	2/56	3.6
- shivering	3/56	5.4
Postoperative pain relief		
- no analgesics required	15/60	25
- immediate postop fentanyl IV (50-75 ug)	4/60	6.7
- analgesic requirement after 12 h	45/60	75
morphine IM	12/60	20
oral analgesics only	33/60	55
Postoperative complications of epidural morphine		
- pruritus	27/60	45
- nausea/vomiting	21/60	35

Table 3. Maternal pain assessment postoperatively.

Pain assessment	No. of parturients	%
- VAS (0-10)		
0	20/60	33.3
more than 0-2	23/60	38.3
more than 2-4	13/60	21.7
more than 4-6	3/60	5
more than 6-8	1/60	1.7
more than 8	0/60	0
- McGill Pain Score (0-5)		
0	21/60	35
1	24/60	40
2	11/60	18.3
3	4/60	6.7
more than 3	0/60	0

adequate sensory level (less than T6) and required general anesthesia. Thirteen of the 56 successful epidural cases (23%) needed supplementation during the operation. The incidence of hypotension, bradycardia and shivering were 28.6 per cent, 3.6 per cent and 5.4 per cent respectively (Table 2). In the recovery room four of the patients who gave the VAS more than 4 and the McGill Pain score of 3 experienced severe pain and required supplement fentanyl 50-75 microgram intravenously which together with the epidural morphine then provided adequate analgesia for at least 12 hours. The VAS at 1 hour after dissipation of the blockade was 4 or less in 93.3 per cent of the patients corresponded with the McGill pain score which was 2 or less in the same percentage (Table 3). The mean analgesic duration of epidural morphine was 23.8 ± 13.6 h. Fifteen of the patients (25%) required no analgesics postoperatively (Table 2). Only minimal side effects of epidural morphine (Table 2 : mild pruritus 45 per cent and nausea/vomiting 35%) were found. Since a urinary catheter was retained in each patient for at least 24 hours, urinary retention could not be evaluated.

The neonatal variables were as follows (Table 4) : the epidural-to-delivery time was 25.0 ± 8.27 minutes and the umbilical venous *p*H was 7.30 ± 0.02. 1 - minute and 5 - minute Apgar scores of all neonates were 8 or over (Table 5). Immediately after the delivery no clinical sign of neonatal respiratory depression or compromise was observed. The 2-hour and 24-hour follow-up periods of the neonates were normal using NACS except in three, two who developed transient tachypnea of the newborn and one who developed mild respiratory distress (Table 6) thought to be the result of difficulty during delivery. All three of these neonates received oxygen therapy for 2-5 days and recovered uneventfully.

In this study the patients were divided into 2 groups. Group 1 the babies were delivered within 25 minutes of completing epidural injection and group 2, after 25 minutes. Table 7 shows the serum morphine levels of the two groups of mothers and the corresponding umbilical venous levels. Although the neonatal serum morphine levels of both groups appeared to be lower than their mothers, there were no statistically significant differences between the two groups of mothers and umbilical veins ($P > 0.05$, two-tailed

Table 4. Neonatal effects of single-dose epidural anesthesia with morphine.

	Range	Mean ± SD
Epidural-to-delivery time (min)	12 - 51	25.0 ± 8.27
Umbilical vein *p*H	7.27 - 7.37	7.30 ± 0.02

Table 5. 1 - minute and 5 - minute Apgar scores of the 60 neonates.

Apgar score	Number of neonates	
	1 min	5 min
8	3	0
9	30	3
10	27	57

Table 6. Three complicated newborns.

Case No.	7	10	28
Problem	TTNB	mild RDS	TTNB
Epidural-to-delivery time (min)	20	22	22
Umbilical vein *p*H	7.337	7.283	7.32
Apgar scores 1 - min	10	8	10
5 - min	10	9	10
Umbilical venous morphine level (ng/ml)	7.8	10	11
Maternal morphine level (ng/ml)	12	10.5	12

TTNB = Transient tachypnea of the newborn
RDS = Respiratory distress syndrome

Table 7. Maternal and neonatal serum morphine levels at delivery

Epidural-to-delivery time (min)	No.	Maternal morphine level (ng/ml)	Umbilical venous morphine level (ng/ml)
within 25	34	4.3 - 26 (15.29 ± 4.84)	4.6 - 16 (9.85 ± 2.13)
after 25	26	2.3 - 21.5 (13.70 ± 4.24)	5.8 - 18 (10.23 ± 2.61)

No statistical significant differences at $P < 0.05$, two - tailed T-test

T-test). In addition, by using multiple regression analysis, there was no correlation between the epidural-to-delivery time and the ratio of serum morphine levels of the umbilical veins and the mothers ($P > 0.05$).

DISCUSSION

This study showed that giving epidural morphine at the time of the epidural injection for cesarean section did not appear to have any ill effects on the normal term neonates and yet did produce in most patients satisfactory postoperative analgesia. Also it was a good opportunity to measure maternal and umbilical venous morphine levels at birth which could be correlated with the clinical appearance of the mothers and neonates. The epidural morphine used in this study was 4 mg which was the lowest effective dosage for adequate analgesia after lower abdominal surgery[7].

In Thailand the single-dose epidural technique for cesarean delivery may have the advantages of the ease and economy as compared to the catheter technique. The clinical data of Crawford et al[8] showed that the single-dose epidural technique for cesarean delivery may decrease the total dosage of local anesthetics from 27-84 per cent. On the contrary, the total dosage of lidocaine in the study of Crochetiere et al[9] by giving a bolus of 20 ml of 2 per cent lidocaine through the needle at the rate of 5 ml/30 sec followed by incremental doses through the catheter to achieve a sensory level to T4 was not different from the incremental catheter technique. Thus the single-dose epidural technique for cesarean delivery may decrease the total dosage of local anesthetics but at the risk of failure to get adequate level of analgesia for operation as four of our patients required additional general anesthesia with endotracheal tube. All of the four patients were observed to experience tightness at the buttock during the injection.

Although Mehta et al[10] showed that in laboring patients injecting the full dose of local anesthetic epidurally through the needle had superior analgesia than injecting half through the needle and half through the epidural catheter, the other study[9] failed to confirm its efficiency when using a bolus epidural technique for cesarean delivery. In our study, forty-eight per cent of the patients experienced pain during surgery, most likely visceral pain, similar to the results reported

by Alahuhta et al[11] using the incremental catheter technique. 23 per cent of our patients needed supplementation during the operation. It appears that within the first hour epidural morphine did not improve the quality of analgesia from epidural local anesthesia. The incidence of intraoperative hypotension in our study (28.6%) was much lower than that of a previous report (52.2%) with similar technique[9]. The reason for this may be because the anesthetic level was somewhat lower between T4-T6.

For pain relief after cesarean section, epidural morphine 4 mg was found to provide effective analgesia with a mean duration of 24 hours. Twenty-five per cent of the patients needed no analgesics throughout the postoperative period with the level of pain assessment using VAS and McGill Pain Scores being very low. An additional 55 per cent required only oral analgesics. But in the recovery room, there were four patients who had severe pain and required intravenous fentanyl 50-75 microgram for pain relief following which all four had adequate pain relief for at least 12 hours. The delay in onset of effective epidural analgesia of 2 to 3 hours noted in these cases has also been reported by Youngstrom et al[5]. Since the analgesic onset of epidural morphine takes up to 1 hour after injection[7], it is not surprising that some patients experienced pain during the cesarean section and the three patients in the postanesthesia care unit (PACU). It is possible to improve analgesia by adding 50 microgram of fentanyl epidurally[12,13] to the local anesthetic solution with morphine which would be expected to give good analgesia certainly by about 9 minutes following injection[14]. However, if fentanyl combined with morphine are used epidurally before delivery, further studies are required to confirm its efficiency and safety. In our study we found only mild side effects of epidural morphine 4 mg with the incidence being lower than that reported in a previous study also utilizing epidural morphine 4 mg[15].

All the neonates were delivered within 1 hour after the epidural block and no signs of depression were observed at delivery. Three infants later developed transient tachypnea of the newborn and mild respiratory distress, which appeared unrelated to anesthesia. The levels of serum morphine base of the three infants were 7.8, 10 and 11 ng/ml, at 20, 22 and 22 minutes postinjection (Table 6). Since Youngstrom et al[5] reported the peak plasma morphine levels of 13.1 $\pm$ 0.6 ng/ml, at the time of 20.4 $\pm$ 2.3 minutes postinjection in the mother, in our study (for statistic analysis) we divided the patients in two groups : those who delivered their babies within 25 minutes postinjection and the others, after 25 minutes. There were no statistically significant differences between the two groups of mothers and corresponding umbilical venous levels. While the level of the serum morphine base in the umbilical venous blood was lower than in the mothers, the difference was not statistically significant. From this study, we believe that the single-dose epidural technique with morphine can be used for cesarean section in selected patients, according to the ease, effectiveness, and the economic point compared to the catheter technique.

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REFERENCES

1. Hughes SC, Rosen MA, Shnider SM, Abboud TK, Stefani SJ, Norton N. Maternal and neonatal effects of epidural morphine for labor and delivery. Anesth Analg 1984; 63: 319-24.
2. Lirzin JD, Jacquinot P, Dailland P, et al. Controlled trial of extradural bupivacaine with fentanyl, morphine or placebo for pain relief in labour. Br J Anaesth 1989; 62: 641-4.
3. Booker PD, Wilkes RG, Bryson THL, Beddard J. Obstetric pain relief using epidural morphine. Anaesthesia 1980; 35: 377-9.
4. Nybell-Lindahl G, Carlsson C, Ingemarsson I, Westgren M, Paalzow L. Maternal and fetal concentrations of morphine after epidural administration during labor. Am J Obstet Gynecol 1981; 139: 20-1.
5. Youngstrom PC, Cowan RI, Sutheimer C, Eastwood DW, Yu JCM. Pain relief and plasma concentrations from epidural and intramuscular morphine in post-cesarean patients. Anesthesiology 1982; 57: 404-9.
6. Amiel-Tison C, Barrier G, Shnider SM, Levinson G, Hughes SC, Stephani SJ. A new neurologic and adaptive capacity scoring system for evaluating obstetric medications in full-term newborns. Anesthesiology 1982; 56: 340-50.
7. Hjortso E, Vester-Andersen T, Moller IW, Lunding M. Epidural morphine for postoperative pain relief. Acta Anaesth Scand 1982; 20: 528-30.
8. Crawford JS, Davies P, Lewis M. Some aspects of epidural block provided for elective Caesarean section. Anaesthesia 1986; 41: 1039-46.
9. Crochetiere CT, Trepanier CA, Cote JJ. Epidural anaesthesia for caesarean section : comparison of two injection techniques. Can J Anaesth 1989; 36: 133-6.
10. Mehta P, Theriot E, Mehrotra D, et al. Technique of injection, maternal position and spread of anesthetic in epidural anesthesia. Anesthesiology 1983; 59: A410.
11. Alahuhta S, Kangas-Saarela T, Hillmen AI, Edstrom HH. Visceral pain during caesarean section under spinal and epidrual anaesthesia with bupivacaine. Acta Anaesthesiol Scand 1990; 34: 95-8.
12. Preston PG, Rosen MA, Hughes SC, et al. Epidural anesthsia with fentanyl and lidocaine for cesarean section : Maternal effects and neonatal outcome. Anesthesiology 1988; 68: 938-43.
13. Halonen PM, Paatero H, Hovorka J, Haasio J, Korttila K. Comparison of two fentanyl doses to improve epidural anaesthesia with 0.5% bupivacaine for caesarean section. Acta Anaesthesiol Scand 1993; 37: 774-9.
14. Naulty JS, Datta S, Ostheimer GW, Johnson MD, Burger GA. Epidural fentanyl for post-cesarean delivery pain management. Anesthesiology 1985; 63: 694-8.
15. Asantila R, Eklund P, Rosenberg PH. Epidural analgesia with 4 mg of morphine following caesarean section : effect of injected volume. Acta Anaesthesiol Scand 1993; 37: 764-7.

ผลกระทบต่อมารดาและทารก จากการฉีดยาชาผสมมอร์ฟีนเข้าในช่องเอปิดูรัล ครั้งเดียว เพื่อการผ่าตัดคลอดทางหน้าท้อง†

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การศึกษาเชิงพรรณาเกี่ยวกับผลของการใช้ 2% lidocaine ร่วมกับ epinephrine 1:200,000 (18–20 มล.) และผสมกับมอร์ฟีน 4 มิลลิกรัม ฉีดเข้าในช่อง epidural ครั้งเดียว สำหรับการผ่าตัดคลอดทางหน้าท้องตามปกติในหญิงมีครรภ์ครบกำหนดที่ทั้งมารดาและทารกในครรภ์มีสุขภาพแข็งแรงจำนวน 60 ราย ผู้ป่วย 4 ราย มีระดับการชาไม่พอเพียงและต้องการการวางยาสลบทั่วไป ระหว่างการผ่าตัดผู้ป่วย 13 ราย (23.2 %) ที่มีระดับการชาพอเพียงยังต้องการยาสลบเพิ่ม อุบัติการของความดันเลือดตก หัวใจเต้นช้าและหนาวสั่น คิดเป็น 28.6 %, 3.6 % และ 5.4 % ตามลำดับ ระยะหลังผ่าตัด epidural morphine ระงับปวดได้อย่างมีประสิทธิภาพนาน 24 ชั่วโมง ผลข้างเคียงในมารดาพบไม่รุนแรง เมื่อแรกคลอดทารกทุกรายไม่พบถูกกดการหายใจหรือมีภาวะความเป็นกรดในเลือดจาก umbilical vein ผิดปกติ แต่พบทารก 3 ราย มีการประเมินทาง neurobehavioral ผิดปกติที่ 2 และ 24 ชั่วโมง หลังคลอด สาเหตุของความผิดปกติไม่น่าเกี่ยวข้องกับการดมยา ระดับซีรั่มมอร์ฟีนของมารดาและทารกภายในและหลังจาก 25 นาทีเมื่อฉีดยาเสร็จ ไม่พบมีความแตกต่างกันอย่างมีนัยสำคัญ (M1/M2 (mean ± SD) = 15.29 ± 4.84/13.70 ± 4.24 ng/ml, UV1/UV2 = 9.85 ± 2.13/10.23 ± 2.61 ng/ml ; P > 0.05)

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