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Perioperative Analgesia with Subarachnoid Fentanyl–Bupivacaine for Cesarean Delivery

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Addition of fentanyl to bupivacaine administered for spinal anesthesia for cesarean delivery was evaluated in 56 ASA physical status 1 term parturients. Preservative-free saline was added to 0, 2.5, 5, 6.25, 12.5, 25, 37.5, or 50 μg fentanyl to make a 1 ml total volume, which was injected intrathecally prior to bupivacaine in a double-blind, randomized fashion. Vital signs, sensory level, motor block, pain score, and side effects were recorded every 2 min for the first 12 min and then at 15, 30, 45, and 60 min and at 30-min intervals until the patient complained of pain. At delivery maternal vein, umbilical artery, and umbilical vein blood gases were obtained. Apgar scores at 1 and 5 min were recorded. Early Neonatal Neurobehavioral Scales (ENNS) were performed on days 1 and 2. Side effects and opioid requirements were recorded for the first 24 h. All of the patients in the control group reported a pain score greater than 0 during surgery and 67% required intraoperative opioids. None of the patients who received ≥6.25 μg fentanyl required intraoperative opioids. Complete analgesia (time from injection to first report of pain) lasted 33.7 ± 30.8 min (mean ± SD) in the control group and increased to 130 ± 30 min ($P < 0.05$) with addition of 6.25 μg fentanyl. Duration of effective analgesia (time from injection to first parenteral opioid) was 71.8 ± 43.2 min in the control group and increased ($P < 0.05$) to 192 ± 74.9 min with addition of 6.25 μg fentanyl. Increasing the doses of fentanyl above 6.25 μg did not further increase duration of complete or effective analgesia. Twenty-four–hour opioidic requirements were not affected by addition of fentanyl. UV and UA blood gases were within normal limits. No differences were found between groups in Apgar scores or ENNS. Results indicate that the addition of 6.25 μg fentanyl to hyperbaric bupivacaine for spinal anesthesia improves intraoperative analgesia and provides analgesia into the immediate postoperative period with no adverse effects on mother or neonate. (Key words: Analgesics, opioid: fentanyl. Anesthesia, obstetric: cesarean section. Anesthetics, local: bupivacaine; Anesthetic technique, spinal: bupivacaine; fentanyl.)

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SPINAL ANESTHESIA is commonly employed for cesarean delivery in the United States. Advantages of spinal anesthesia include the simplicity of the technique and the rapid onset of anesthesia. Disadvantages of spinal anesthesia include its limited duration of action and lack of postpartum pain relief. The ability of epidural opioids to provide prolonged postpartum pain relief is one of the advantages of epidural anesthesia.[1–7],†† Fentanyl in doses of 50–100 μg administered epidurally has been shown to provide analgesia for 3–4 h after injection.[5] No decrease in respiratory rate has been observed following administration of epidural fentanyl (up to 100 μg) to pregnant patients.[5–8] However, the ventilatory response to inhaled CO_2 has not been studied in these patients. In surgical patients using much larger doses of epidural fentanyl, 200 μg, depression of the CO_2 response curve has been reported, although resting respiratory parameters have been unchanged.[9] However, this effect is transient and normal responses to CO_2 can be expected by 3 h. Although epidural morphine provides prolonged postoperative pain relief of up to 24 h duration, there is also a prolonged duration of depression of the CO_2 response curve and respiratory depression has been reported.[2,10],‡‡ Due to the risk of delayed respiratory depression with epidural morphine and our inability to provide prolonged respiratory monitoring, fentanyl is the most commonly used epidural opioid at our institution. For these same reasons, we undertook this double-blind, randomized investigation to evaluate the potential of fentanyl administered in the subarachnoid space to improve intraoperative and perioperative analgesia in the immediate postcesarean period.

Methods

The protocol was approved by the Committee for the Protection of Human Subjects from Research Risks of the Brigham and Women's Hospital. Written informed consent was obtained from all patients. Fifty-six ASA physical status 1 patients scheduled for elective, repeat

†† Dougherty TB, Baysinger CL, Gooding DJ: Epidural hydromorphine for postoperative analgesia after delivery by cesarean section. Regional Anesthesia 11:118–122, 1986

‡‡ Leicht CH, Hughes SS, Dailey PA, Shnider SM, Rosen MA: Epidural morphine sulfate for analgesia after cesarean section: A prospective report of 1,000 patients (abstract). ANESTHESIOLOGY 65:A366, 1980

TABLE 1. Patient Parameters

Fentanyl dose (μg)	0	2.5	5	6.25	12.5	25	37.5	50
No. of patients	9	6	8	7	7	6	7	5
Height (inches)	63.9 ± 3.3	65.0 ± 2.0	63.3 ± 3.8	63.9 ± 2.5	64.8 ± 2.6	63.2 ± 1.9	64.3 ± 1.4	64.3 ± 1.0
Weight (lb)	167.0 ± 28.5	149.7 ± 23.3	163.0 ± 29.1	165.4 ± 16.4	161.9 ± 32.5	175.0 ± 23.3	176.8 ± 21.1	167.7 ± 14.9
Age (yr)	28.5 ± 5.7	30.6 ± 4.0	31.5 ± 3.0	31.5 ± 5.3	33.4 ± 3.5	31.2 ± 2.6	31.8 ± 5.8	32.7 ± 4.3
Induction to delivery time (min)	17.4 ± 4.4	17.7 ± 2.9	16.8 ± 4.4	17.7 ± 3.3	15.9 ± 3.5	18.7 ± 3.9	19.2 ± 2.2	21.0 ± 2.6
Surgical time (min)	56.7 ± 8.9	55.5 ± 12.8	54.1 ± 25.0	53.1 ± 11.9	46.6 ± 10.5	55.7 ± 6.3	56.3 ± 4.1	49.6 ± 10.9

Values are mean ± SD.

cesarean delivery participated in the study. All patients received 30 ml of a clear antacid preoperatively. No parenteral opioids or benzodiazepines were administered preoperatively. Before induction all parturients received a minimum of 1,500 ml of lactated Ringer's solution through a large-bore iv catheter. With the patient in the right lateral decubitus position, a subarachnoid puncture was performed with a 26-G spinal needle through a midline approach at the L2–3 or L3–4 interspace. Preservative-free normal saline was added to 0, 2.5, 5, 6.25, 12.5, 25, 37.5, or 50 μg of fentanyl to make a total volume of 1 ml, which was injected after free flowing cerebrospinal fluid (CSF) was obtained. The fentanyl solution was prepared by an anesthesiologist not involved with data collection. The dose of fentanyl was selected in a randomized fashion. Immediately thereafter, a dose of 0.75% bupivacaine in 8.25% dextrose was administered according to the height of the patient. This dose was 1 ml (7.5 mg) for patients 5 feet tall with the addition of 0.1 ml (0.75 mg) for every 1 inch increase in height. The amount of fentanyl injected was unknown to the anesthesiologist injecting the drug and evaluating the patient's responses. The patient was turned supine, a wedge was placed under the right hip to effect uterine displacement, and oxygen was administered by face mask at 6–8 l/min.

After injection blood pressure, pulse, respiratory rate, sensory level to pinprick, motor block, pain score, and occurrence of side effects were recorded every 2 min for the first 12 min and then at 15, 30, 45, and 60 min after injection and, thereafter, at 30-min intervals until the patient complained of pain. Motor block was assessed with the Bromage score: 1 = unable to move feet or knees, 2 = able to move feet only, 3 = just able to move knees, 4 = full flexion of knees and feet. Pain was evaluated using a 10-cm linear visual analog scale with 0 corresponding to no pain and 10 to the worst pain imaginable. The duration of complete analgesia (time from subarachnoid injection to the first report of pain [pain score greater than 0]) and effective analgesia (time from subarachnoid injection to first administration of parenteral opioid) was recorded. The side effects evaluated were pruritus, somnolence, nausea, shivering, euphoria or dysphoria, and chest tightness. They were scored as follows: 0 as not present; 1 as present, no treatment required; and 2 as present, therapy given. Intravenous droperidol, 0.625 mg, was used to treat nausea. Intravenous naloxone, 0.04 mg, was administered for pruritus. Diazepam was administered only if the patient requested decreased intraoperative awareness. The presence of side effects and the opioid requirements in the first 24 h were recorded.

At the time of delivery, maternal vein and umbilical artery and vein blood gases were obtained. Apgar scores at 1 and 5 min were recorded. Neonatal neurobehavior assessments with the Early Neonatal Neurobehavioral Scale (Scanlon, ENNS) were performed between 2 and 4 h of life and between 46 and 48 h of life.[11]

Parametric data were evaluated for statistical significance using an analysis of variance with correction for multiple comparisons. Differences in the incidence of side effects were evaluated with a Scheffe *F*-test and a Fisher's exact test. A P value < 0.05 was considered to be statistically significant.

Results

Patient Variables

There were no significant differences in patient height, weight, age, gravidity, or parity in the control or any of the dosage groups (table 1). There were no differences between groups in local anesthetic dosage, which was based on patient height. There were no significant differences between groups in induction to delivery interval or surgical times. Diazepam was requested by four patients in the control group, two patients in the 5 μg fentanyl group, and one patient in the 25 μg fentanyl group.

Sensory and Motor Blockade

There were no significant differences in the onset time of sensory or motor blockade between the control and any of the dosage groups (table 2). All patients had a T4 sensory level and complete motor blockade within 10 min of injection. There were some minor differences in the duration of sensory blockade. The number of segments regressed at 60 min was prolonged in the 50 μg fentanyl group compared with control. At 90 min there were dif-

ferences between the control group and the 12.5 μg, 37.5 μg, and 50 μg fentanyl groups. However, by 120 min there were no differences between groups in the number of segments regressed. The time to complete regression of motor blockade did not differ significantly between groups.

Duration

The duration of complete analgesia was 33.7 ± 30.8 minutes in the control group (fig. 1). All patients in the control group reported a pain score greater than 0 during surgery following delivery of the infant. The addition of 2 μg or 5 μg of fentanyl caused a slight but insignificant increase in the duration of complete analgesia to 81.5 ± 57.9 and 73.2 ± 24.6 min, respectively. However, with the addition of 6.25 μg of fentanyl, complete analgesia was significantly increased to 130 ± 30 min. Increasing the dose of fentanyl above 6.25 μg did not further increase the duration of complete pain relief.

The duration of effective analgesia was 71.8 ± 43.2 min in the control group (fig. 2). Effective analgesia was increased to 85 ± 56.8 min (NS) with the addition of 2.5 μg of fentanyl and 114.7 ± 64.7 min (NS) with 5 μg of fentanyl. The increase in effective analgesia with the addition of 6.25 μg of fentanyl to 192 ± 74.9 min was significant ($P < 0.05$). Increasing the dose of fentanyl above 6.25 μg of fentanyl did not increase the duration of effective analgesia. Six patients (67%) in the control groups received intraoperative opioids, usually when the uterus was replaced into the abdominal cavity. Three patients (50%) in the 2.5 μg fentanyl group and two patients (25%) in the 5 μg fentanyl group received intraoperative opioids. None of the other patients required intraoperative opioids.

Side Effects

Respiratory depression as defined as a respiratory rate of less than 10 breaths/min was not observed in any patient. Euphoria or dysphoria was not observed in any patient. There were no differences in the incidence of chest tightness, somnolence, or shivering (table 3) with Fisher's exact test or the Scheffe F-test. Furthermore, with the Scheffe F-test, there were no differences in the incidence of nausea and pruritus. However, with Fisher's exact test, the incidence of nausea was increased in the 6.25 μg fentanyl group with a P value of 0.035. Caution should be used in interpreting P values because some of the values may be spurious due to multiple comparisons. Droperidol was administered to treat nausea in one patient in the control group, in two patients in the 6.25 μg fentanyl group, in two patients in the 12.5 μg fentanyl group, and in three patients in the 37.5 μg fentanyl group. The incidence of pruritus was significantly increased in the 25

TABLE 2. Onset and Regression of Sensory Blockade and Onset and Resolution of Motor Blockade

Fentanyl dose (μg)	0	2.5	5	6.25	12.5	25	37	50
No. of patients	9	6	8	7	7	6	7	5
Onset time to T4 (min)	4.571 ± 2.76	3.333 ± 1.155	6.5 ± 2.517	2.57 ± 1.512	4.222 ± 2.108	3.5 ± 1	5.333 ± 2.733	4 ± 1.633
Number of segments regressed in 60 min	2.5 ± 2.588	2 ± 2	1.333 ± 1.155	1.571 ± 1.902	0.75 ± 1.389	0.667 ± 1.155	1.167 ± 0.983	0.2 ± 0.447*
Number of segments regressed in 90 min	7.2 ± 3.271	4.5 ± 2.121	7.667 ± 2.517	4.143 ± 3.237	3.714 ± 2.138*	3.333 ± 3.055	2.5 ± 0.577*	2.6 ± 3.286*
Number of segments regressed in 120 min	9 ± 3.651	7 ± 1	8.5 ± 2.121	7.286 ± 4.855	5.4 ± 2.811	4.25 ± 2.63	5.75 ± 1.258	4.4 ± 3.578
Onset to complete motor block (min)	4 ± 2	6 ± 3.464	6.75 ± 6.185	5.429 ± 2.225	4.571 ± 1.512	7.2 ± 2.683	5.5 ± 3.0	7.0 ± 3.83
Time to complete resolution of motor blockade (min)	126 ± 32.863	180 ± 0	170 ± 75.498	180 ± 69.282	130 ± 40.988	156 ± 77.46	150 ± 77.46	126 ± 32.84

Values are mean ± SD.

* Significantly different from control.

μg fentanyl group ($P = 0.01$) and 50 μg fentanyl group ($P = 0.02$). Five patients experienced pruritus requiring treatment with iv naloxone. These patients had received 2.5, 6.25, or 37.5 μg fentanyl. No increase in the pain score was observed following the naloxone.

Twenty-four–Hour Postoperative Parenteral Opioid Dose

The total cumulative doses of parenteral opioid received by the patients in the first 24 h were recorded. The patients received morphine, meperidine, or hydromorphone in the postdelivery period on an "as needed" schedule. The choice of opioid was made by the obstetrician. For comparison of patients, all opioid analgesic drugs were converted to "morphine equivalents" using the following equivalencies: 100 mg meperidine = 10 mg morphine sulfate; 1 mg hydromorphone = 7 mg morphine sulfate®. The results are shown in figure 3. No statistically significant reduction of 24-h opioid dosage was seen with the addition of fentanyl.

Neonatal Effects

There were no significant differences in umbilical vein or artery blood gases between groups. All blood gases were within normal limits. Apgar scores at 1 min were 7 or better in all infants except one. A 1-min Apgar score of 5 was present in one infant whose mother received 12.5 μg fentanyl. However, this mother was hypotensive (80/50) for 3–5 min prior to delivery despite treatment with ephedrine and iv fluid. This low Apgar score probably reflects a reduction in uterine perfusion despite normal umbilical cord gases because there was no meconium staining and the delivery was atraumatic with a uterine incision to delivery interval of 1 min. This infant had a 5-min Apgar score of 9. All infants had 5-min Apgar scores of 8 or better.

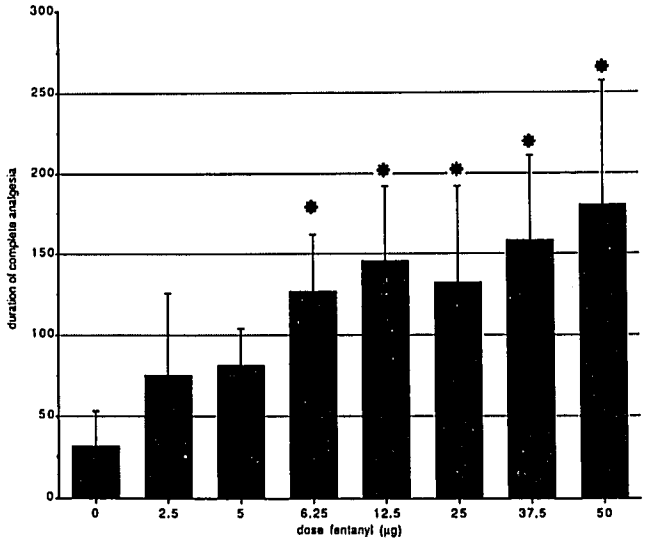

FIG. 1. Duration of complete analgesia (pain score equals 0) with increasing doses of subarachnoid fentanyl. There was a significant increase ($P < 0.05$) in the duration of complete analgesia with the ≥6.25 μg doses of fentanyl compared with control.

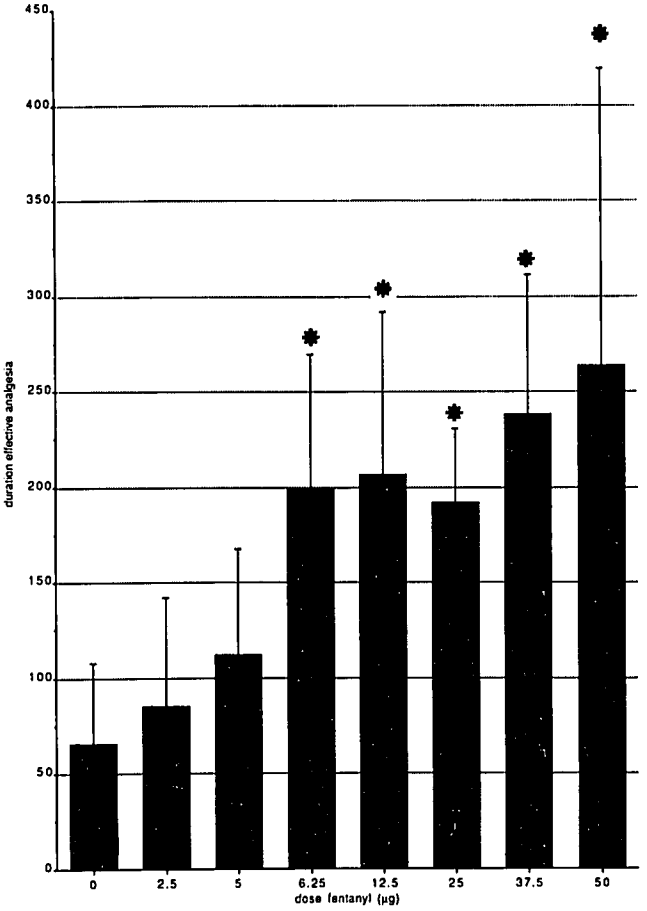

FIG. 2. Duration of effective analgesia (time to first narcotic) with increasing doses of subarachnoid fentanyl. There was a significant increase ($P < 0.05$) in the duration of effective analgesia with the ≥6.25 μg doses of fentanyl compared with control.

There were no differences between groups in ENNS. These evaluations included the infant's state of wakefulness, muscle tone, reflex responses (rooting, sucking, and Moro reflex), and responses to light, sound, and limb flexion. Decrement responses following light, sound, and limb flexion were also similar for all groups.

Discussion

The results indicate that the addition of ≥6.25 μg fentanyl to hyperbaric bupivacaine for spinal anesthesia in parturients undergoing elective repeat cesarean delivery improves intraoperative as well as immediate postoperative analgesia with no adverse effects on the mother or neonate. Although there were minor changes in the du-

TABLE 3. Incidence of Side Effects

Fentanyl dose (μg)	0	2.5	5.0	6.25	12.5	25	37.5	50
No. of patients	9	6	8	7	8	6	7	5
Chest tightness	1	0	1	1	0	0	0	0
Nausea	1	2	2	5*	2	0	3	1
Somnolence	1	1	1	3	0	2	1	3
Shivering	3	3	4	2	2	2	1	1
Pruritus	1	1	3	4	3	5*	4	4*

Values are number of patients experiencing side effects.
* Significant difference ($P < 0.05$) using Fishers exact test. There were no differences using the Scheffe F-test.

ration of sensory blockade as evaluated by the number of segments over which anesthesia had regressed at 60 and 90 min, by 120 min there were no differences among groups. In retrospect, two-segment regressions of sensory blockade may have provided a more sensitive evaluation.

We chose to evaluate fentanyl due to the extensive research that has been completed with epidural fentanyl for both labor and vaginal delivery as well as cesarean delivery.[5–8] Fentanyl is a lipophilic molecule similar to meperidine, which is more readily eliminated from the CSF than hydrophilic drugs, such as morphine.[12,13] However, drugs that are lipophilic have a potential disadvantage of a short duration of action. Epidurally administered fentanyl in doses of 50–100 μg has been shown to provide postoperative analgesia of 3–4 h duration.[5] This was similar to our duration of effective analgesia following ≥6.25 μg doses of subarachnoid fentanyl. In contrast, morphine provides approximately 24 h of postoperative pain relief following epidural and subarachnoid administration.[1,2,14,15] The advantage of prolonged pain relief must be weighed against the potential for late respiratory depression. This complication is well recognized with epidural and intrathecal morphine administration.[16,17] Although pregnant women are thought to be at less risk for delayed respiratory depression due to their young age and hyperstimulation of their respiratory centers, this complication has been seen with epidural and intrathecal morphine.[18];‡‡ Although many centers are able to monitor their patients following epidural and intrathecal morphine in a recovery room or on the postpartum units, this is not possible in our institution. Thus, we have not administered intrathecal or epidural morphine on a routine basis and have relied on short-acting opioids with conventional intramuscular injections or patient-controlled analgesia for postoperative pain control.

There are several other potential adverse effects from intrathecal opioid administration.[16,17] Although urinary retention has been reported with intrathecal opioids, we were unable to evaluate this because all of our patients routinely have a Foley catheter for 24 h.

The incidence of nausea is increased in patients given epidural or intrathecal morphine.[1,15] No increased incidence has been reported with epidural fentanyl.[5] In this study the incidence of nausea was increased in only the group receiving 6.25 μg of fentanyl using Fisher's exact test but not with the Scheff's F-test. However, the small number of patients in each group may have precluded the opportunity to obtain statistically significant increases of nausea in each of the fentanyl groups.

Pruritus is another frequent complication of subarachnoid and epidural opioid administration. Although we observed a significant increase in the overall incidence of pruritus in the 25 μg and 50 μg fentanyl groups with the Fisher's exact test, the incidence of treated pruritus was not dose-related. Again, this may reflect the small numbers of patients in each group.

With the use of any drug in the subarachnoid space, the potential for neurotoxicity must be considered. Animal studies have demonstrated the safety of fentanyl in this regard.[19,20] In our experience with epidural fentanyl, there has been no evidence of neurotoxicity. None of the patients in this study experienced any neurologic complications.

The final consideration is the effect of subarachnoid fentanyl on the neonate. Epidural fentanyl has an excellent safety record in this regard. There has been only one report of neonatal respiratory depression following maternal administration of epidural fentanyl. Carrie *et al.* administered 150–200 μg epidural fentanyl, often in repeated doses, as the sole analgesic during labor.[21] One infant experienced respiratory depression requiring oxygen, intubation, and naloxone. Unfortunately, the total dose of fentanyl and the drug injection to delivery interval were not reported. This infant had an umbilical arterial fentanyl concentration of 0.25 ng/ml. Other infants had similar fentanyl levels and had no evidence of respiratory

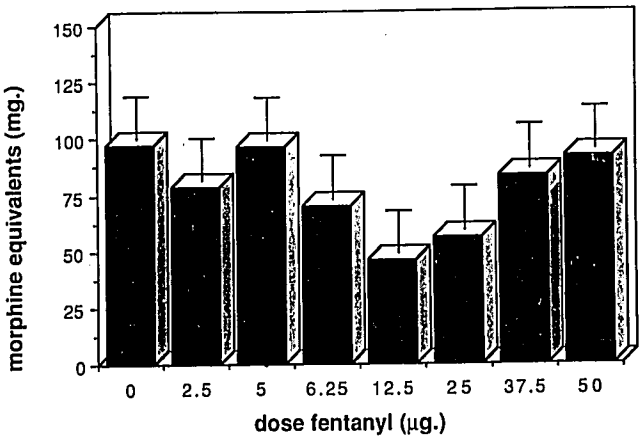

FIG. 3. The amount of opioids received by the patients in the 24 h following increasing doses of subarachnoid fentanyl. The actual opioids used have been converted to equivalent doses of morphine. There were no differences from control.

depression. Both Youngstrom *et al.*§§ and Skerman *et al.*¶¶ failed to detect umbilical venous fentanyl levels following epidural fentanyl administered as a single bolus or continuous infusion. Neither of these groups found neonatal depression as evidenced by normal Apgar scores and umbilical cord blood gases. Neurobehavior examinations of neonates whose mothers have received epidural fentanyl have also shown no evidence of depression.[7,8,22] In this study of subarachnoid fentanyl, Apgar scores and umbilical cord blood gas analysis were within normal limits. ENNS scores were similar in all groups. A potential advantage of subarachnoid fentanyl is the much lower effective dose, 6.25 μg, compared with 50–100 μg of fentanyl administered epidurally. Thus, the neonate is exposed to much lower concentrations of opioid. This is similar to the lower maternal and fetal local anesthetic blood levels with subarachnoid compared with epidural administration.[23,24]

In summary, 6.25–50 μg fentanyl provided improved perioperative analgesia without affecting the onset of sensory and onset or duration of motor anesthesia with hyperbaric bupivacaine. The optimum dose of fentanyl was 6.25 μg because higher doses did not increase the duration of analgesia.

§§ Youngstrom P, Eastwood D, Patel H, Bhatia R, Cowan R, Sutheimer C: Epidural fentanyl and bupivacaine in labor: Double-blind study (abstract). ANESTHESIOLOGY 61:A414, 1984

¶¶ Skerman JH, Thompson BA, Goldstein MT, Jacobs MA, Gupta A, Blass NH: Combined continuous epidural fentanyl and bupivacaine in labor: A randomized study (abstract). ANESTHESIOLOGY 64:A450, 1985

References

1. Rosen MA, Hughes SC, Shnider SM, Abboud TK, Norton M, Dailey PA, Justins VD: Epidural morphine for the relief of postoperative pain after cesarean delivery. Anesth Analg 62:666–672, 1983
2. Youngstrom PC, Cowan RI, Sutheimer C, Eastwood DW, Yu JCM: Pain relief and plasma concentrations from epidural and intramuscular morphine in postcesarean patients. ANESTHESIOLOGY 57:404–409, 1982
3. Rosen MA, Dailey PA, Hughes SC, Leicht CH, Shnider SM, Jackson CE, Baker BW, Cheek DB, O'Connor DE: Epidural sufentanil for postoperative analgesia after cesarean section. ANESTHESIOLOGY 68:448–454, 1988
4. Chestnut DH, Choi WW, Isbell TJ: Epidural hydromorphine for postcesarean analgesia. Obstet Gynecol 68:65–69, 1986
5. Naulty JS, Datta S, Ostheimer GW, Johnson MD, Burger GA: Epidural fentanyl for postcesarean delivery pain management. ANESTHESIOLOGY 63:694–698, 1985
6. Gaffud MP, Bansal P, Lawton C, Velasquez N, William A: Surgical analgesia for cesarean delivery with epidural bupivacaine and fentanyl. ANESTHESIOLOGY 65:331–338, 1986
7. Preston PG, Rosen MA, Hughes SC, Geosten B, Ross BK, Daniels D, Shnider SM, Dailey PA: Epidural anesthesia with fentanyl and lidocaine for cesarean section: Maternal effects and neonatal outcome. ANESTHESIOLOGY 68:938–943, 1988
8. Cohen SE, Tan S, Albright GA, Halpern J: Epidural fentanyl/bupivacaine mixtures for obstetric analgesia. ANESTHESIOLOGY 67:403–407, 1987
9. Negra I, Gueneron J, Ecoffey C, Penon C, Gross J, Levron J, Samii K: Ventilatory response to carbon dioxide after intramuscular and epidural fentanyl. Anesth Analg 66:707–710, 1987
10. Abboud TK, Moore M, Zhu J, Murakawa K, Minehart M, Longhitano M, Terrasi J, Klepper ID, Choi Y, Kimball S, Chu G: Epidural butorphanol or morphine for the relief of post-cesarean section pain: Ventilatory responses to carbon dioxide. Anesth Analg 66:887–893, 1987
11. Scanlon JW, Brown WV, Weiss JB, Alper MH: Neurobehavior responses of newborn infants after maternal epidural anesthesia. ANESTHESIOLOGY 40:121–128, 1974
12. Sjostrom S, Jamsen A, Persson MP, Hartvig P: Pharmacokinetics of intrathecal morphine and meperidine in humans. ANESTHESIOLOGY 67:889–895, 1987
13. Cousins MJ, Mather LE: Intrathecal and epidural administration of opioids. ANESTHESIOLOGY 61:271–310, 1984
14. Abboud TK, Dror A, Mosaad P, Zhu J, Mantilla M, Swart F, Gangolly J, Silao P, Maker A, Moore J, Davis H, Lee J: Minidose intrathecal morphine for the relief of post-cesarean section pain: Safety, efficacy and ventilatory responses to carbon dioxide. Anesth Analg 67:137–143, 1988
15. Abouleish E, Rawal N, Fallon K, Hernandez D: Combined intrathecal morphine and bupivacaine for cesarean section. Anesth Analg 67:370–374, 1988
16. Gustafsson LL, Schildt B, Jacobsen KJ: Adverse effects of extradural and intrathecal opiates: Reports of a nationwide survey in Sweden. Br J Anaesth 54:479–486, 1982
17. Rawal N, Arner LL, Gustafsson LL, Allvin R: Present stage of extradural and intrathecal opioid analgesia in Sweden. Br J Anaesth 59:791–799, 1987
18. Abouleish E: Apnoia associated with the intrathecal administration of morphine in obstetrics. Br J Anaesth 60:592–594, 1988
19. Yaksh TL, Nouihed RY, Durant PA: Studies of the pharmacology and pathology of intrathecally administered 4-anilinopiperidine analogues and morphine in the rat and cat. ANESTHESIOLOGY 64:54–66, 1986
20. Gissen AJ, Gugino LD, Datta S, Miller J, Covino BG: Effects of fentanyl and sufentanil on peripheral mammalian nerves. Anesth Analg 66:1272–1276, 1987
21. Carrie LES, O'Sullivan GM, Seegobin R: Epidural fentanyl in labor. Anaesthesia 36:965–969, 1988
22. Capogna G, Cellano D, McGannon P, Richardson G, Kennedy RL: Neonatal neurobehavior effects following maternal administration of epidural fentanyl during labor (abstract). ANESTHESIOLOGY 67:A461, 1987
23. Kuhnert BR, Zuspan KJ, Kuhnert PM, Syracuse CD, Brown DE: Bupivacaine disposition in mother, fetus, and neonate after spinal anesthesia for cesarean section. Anesth Analg 66:407–412, 1987
24. Kuhnert BR, Philipson EH, Pimental R, Kuhnert PM, Zuspan KJ, Syracuse CD: Lidocaine disposition in mother, fetus, and neonate after spinal anesthesia. Anesth Analg 65:139–144, 1986