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Patient-controlled Analgesia Following Cesarean Section: A Comparison with Epidural and Intramuscular Narcotics

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Epidural morphine and intravenous patient-controlled analgesia (PCA) are alternative methods to the traditional intramuscular administration of analgesics for treating postoperative pain. Yet, epidural morphine frequently produces bothersome side effects, and rarely produces life-threatening respiratory depression,[1] while PCA requires patient participation and is provided by bulky, expensive machines which could be unintentionally misprogrammed and produce narcotic overdose.[2]

Few studies compare epidural morphine and PCA, and these have usually focused on pain scores.[3-5] In this study, we compare pain scores, side effects, and patient satisfaction in women receiving epidural morphine, iv PCA, or im narcotics following cesarean section.

MATERIALS AND METHODS

The Clinical Research Practices Committee approved the protocol, and all patients gave written informed consent. We studied 60 ASA physical status 1 or 2 parturients scheduled for elective repeat cesarean section. All women had uncomplicated pregnancies, were taking no medications, and had received im narcotics following their previous cesarean section. All cesarean sections were performed between 7:30 and 11:30 A.M. Following routine epidural catheter insertion and testing with 2-chloroprocaine (2 ml followed in 5 min by 5 ml of 2% or 3% solution), we established and maintained epidural anesthesia with plain 0.5% bupivacaine in divided doses.

Immediately following delivery, each woman received 0.5 mg droperidol, iv, as prophylaxis against postoperative nausea,[6] and was assigned in a random manner to receive postoperative analgesia by one of three methods: 1) epidural morphine (5 mg preservative-free morphine in 10 ml prior to leaving the operative room, supplemented, if needed, during the first postoperative day by incremental butorphanol 1 mg, iv, or nalbuphine 10 mg, iv); 2) iv PCA morphine (5-mg dose, lockout interval 5 min in the recovery room, then 2-mg dose, lockout interval 15 min); or 3) im narcotics as ordered by the obstetricians (morphine 5–10 mg, iv, every 5–10 min as needed in the recovery room, then morphine 10–15 mg or meperidine 25–75 mg, im, every 2–4 h as needed). We excluded patients who required systemic narcotics intraoperatively for analgesia. We also excluded patients requiring >200 mg epidural bupivacaine for adequate anesthesia, based on previous experience that such patients experienced inadequate or brief analgesia from epidural morphine.

Postoperatively, parturients rated their level of pain using a five-point scale (1 = comfortable, 2 = mildly uncomfortable, 3 = very uncomfortable, 4 = in pain, and 5 = in bad pain) every 2 h while awake for 24 h following surgery. Nurses assessed sedation using a five-point scale (1 = wide awake, 2 = drowsy, 3 = dozing intermittently, 4 = mostly sleeping, and 5 = only awakens when aroused), questioned the patients for presence of nausea and pruritus, and recorded respiratory rate every 2 h for 24 h following surgery. In addition, nurses monitored respiratory rate every hour in patients receiving epidural morphine. Following the study period, each woman completed a questionnaire[7] concerning her perception of her postoperative analgesia. We also recorded age, height, weight, epidural 2-chloroprocaine and bupivacaine dose, and recovery room time, and time, dose, and indication for all medications given during the study period. We converted parenteral narcotics administered to morphine equivalents using the following potency ratios: meperidine (0.1), nalbuphine (0.8), morphine (1), and butorphanol (8).

Data are presented as means ± SEM. We used an analysis of variance followed by Neuman-Keuls test to compare the three groups for maternal demographic data and morphine consumption/24 h. We used Kruskal-Wallis analysis, Chi-Square analysis, and Fisher-Yates exact tests where appropriate to compare the groups for noncontinuous demographic data, pain and sedation scores, incidence of side effects, and frequency of responses to the questionnaire. Plots of cumulative

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TABLE 1. Patient Characteristics and Intraoperative and Recovery Room Course

Parameter	im Therapy	Patient Controlled Analgesia	Epidural Morphine
Age	28 ± 2	28.5 ± 2	29.5 ± 2
Height (cm)	162 ± 5	160 ± 5	161 ± 9
Weight (kg)	77 ± 6	75 ± 6	75 ± 5
Intraoperative			
2-Chloroprocaine (mg)	178 ± 15	190 ± 24	187 ± 16
Bupivacaine (mg)	189 ± 15	181 ± 14	181 ± 14
Recovery room			
Time (min)	105 ± 15	94 ± 12	102 ± 15
Morphine Equivalent (mg)	3.8 ± 1.1	11 ± 2.3*	1.0 ± 0.6*†
Nausea (%)	0	5	0
Pruritus (%)	10	10	30

Values expressed as mean ± SEM.
* $P < 0.05$ *vs.* im group.
† $P < 0.01$ *vs.* PCA group.

morphine use were constructed using a first order regression analysis. Pairwise testing was done only if group distributions differed significantly. In accordance with previous studies of postoperative analgesia,[7,8] we eliminated from analysis pain and sedation scores from 10:00 P.M. to 6:00 A.M. We considered $P < .05$ significant.

RESULTS

The groups did not differ in demographic data, and differed in intraoperative and recovery room course only in the larger dose of narcotic in patients receiving PCA (table 1). No patient had a respiratory rate of <10/minute.

Cumulative morphine use is shown in figure 1. Although hourly morphine consumption remained constant in the PCA and im groups, the interpatient variability was large (range 0.6–5.2 mg/hour in the PCA group, 0.75–3.5 mg/hour in the im group). The groups differed in total (systemic + epidural) narcotic use: PCA (62 ± 5 mg) > im (48 ± 4 mg) > epidural morphine (23 ± 5 mg; morphine equivalents/24 h, $P < .001$; all groups differ from each other). Forty per cent of patients in the epidural morphine group required parenteral narcotics within 12 h of surgery, and 50% required parenteral narcotics within 24 h of surgery.

Patients in the im group were more likely than those in the PCA or epidural morphine groups to report being very uncomfortable or in pain (fig. 2, upper panel). Nurses assessed patients in the PCA group to be more sedated than those in the im or epidural morphine groups (fig. 2, lower panel). Although the incidence of nausea did not differ among groups, epidural morphine caused more pruritus than PCA or im therapy ($P < .01$; table 2).

Although patients in both the PCA and epidural morphine groups preferred their therapy over the narcotic administered following their first cesarean section, only those receiving epidural morphine perceived better pain relief than those in the im group (table 3). Patient perception of sedation or effect of analgesic medication on activity did not differ among groups.

Decreased pain scores correlated with patient satisfaction within the entire study population ($P < .001$). However, the relationship differed among groups. For example, among women who reported the highest satisfaction, pain scores were significantly higher in the PCA group than in the epidural morphine group ($P < .01$).

DISCUSSION

Although most authors report that PCA produces better pain relief than im therapy,[7–9] patients using

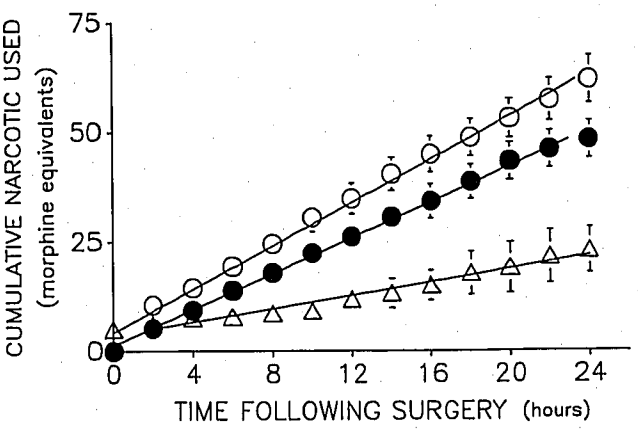

FIG. 1. Cumulative narcotic administered (including initial 5 mg epidural morphine) for the first 24 h following cesarean section in the PCA (○), im (●), and epidural morphine (△) groups. N = 20 in each group. Values expressed as mean ± SEM, plots constructed by first order linear regression.

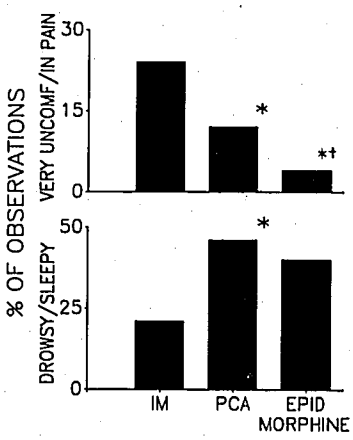

FIG. 2. The % observations (excluding those between 10:00 P.M. and 6:00 A.M.) in which patients reported being very uncomfortable or in pain (upper panel) or were assessed by the nurse to be drowsy or sleeping (lower panel). N = 20 in each group. *$P < 0.05$ *vs.* im group. †$P < 0.05$ *vs.* PCA group.

PCA appear to tolerate some mild and non-distressing pain. Patient expectation of some mild pain as normal postoperatively and attempts to balance analgesia with side effects may explain the patient's failure to self-medicate to complete relief.[10] In this study, PCA produced better pain relief than im therapy, although both groups tolerated some pain and used only a small portion of the maximum prescribed narcotic.

An advantage stated for PCA is the avoidance of wide swings in plasma morphine concentration inherent in im dosing, thereby maintaining steady morphine concentration despite perioperative changes in morphine pharmacokinetics.[11] This may be a disadvantage at night, when plasma morphine concentrations decrease below analgesic levels more rapidly than following im dosing, leading to patient awakening with pain and interference with sleep. However, patients using PCA in this study did not complain of being awakened at night in pain, and were more satisfied with their therapy than the im group. A separate analysis of data taken between 10:00 P.M. and 6:00 A.M. revealed that patients in the PCA group were awake and reported pain at night only 4% of the time, less than during the day (12%) and less than the im group (15%; $P < .01$).

Epidural morphine produces more profound analgesia than iv PCA or im therapy,[4,5] but this analgesia is of variable duration. Although epidural 2-chloroprocaine may affect the duration of subsequent morphine,§ we used 2-chloroprocaine for catheter testing only, and our findings agree with others using bupivacaine only[12] that approximately 35% of women receiving 5 mg epidural morphine following cesarean section require systemic narcotics within 12 h, and 50% require systemic narcotics within 24 h, of surgery. Unfortunately, physicians may prescribe inadequate amounts of parenteral narcotics to patients receiving epidural morphine because of the concern that systemic narcotics at this time may increase the chance of respiratory depression.

In addition to analgesic efficacy, the choice of analgesic therapy should be based, in part, upon patient preference and incidence and nature of side effects. Although others have reported patient preference for PCA rather than im therapy,[7,8] this is the first report comparing patient satisfaction following PCA and epidural morphine. The importance of including an im control group is underscored by the apparent placebo response in this study—55% of patients receiving im therapy preferred this therapy to their previous im therapy. We anticipated, but did not find, that more effective pain relief provided by epidural morphine would enhance patient satisfaction. Possible explanations for the enthusiasm for PCA, despite less complete analgesia, include immediate accessibility of analgesia, and ability to titrate analgesia and side effects. In this regard, analgesic efficacy and patient satisfaction with PCA vary with the incidence of side effects produced by the administered drug.[13] We chose to use PCA morphine because of high patient satisfaction and low incidence of side effects with this drug.[13]

Narcotics, regardless of route of administration, can produce pruritus, nausea, sedation, and respiratory depression. Bothersome pruritus requiring treatment occurs in 40–45% of women receiving epidural morphine after cesarean section.[4,12] In contrast, only 5% of those receiving PCA or im therapy in this study experienced treatable pruritus. Nausea is reported to be either more common[1] or equally common[4,5] following epidural morphine than im or PCA therapy. In this study, the increased incidence of nausea in the epidural morphine group did not reach statistical significance ($P = .06$), perhaps due to the small sample size. In contrast to previous reports,[7,8] we observed more sedation, not less, in patients receiving PCA than epidural morphine or im therapy. Although this likely reflected the larger dose of narcotic in the PCA group, most authors report similar narcotic dose and sedation between PCA and im

TABLE 2. Side Effects

Parameter	im Therapy	Patient Controlled Analgesia	Epidural Morphine
Nausea			
Experiencing Nausea	25	30	50
Requiring Treatment	10	5	30
Pruritus			
Experiencing Pruritus	35	60	85*
Requiring Treatment	5	5	40*†

Values expressed as percent of patients.
* $P < 0.01$ *vs.* im group.
† $P < 0.05$ *vs.* PCA group.

§ Kotelko DM, Thigpen JW, Shnider SM, Foutz SE, Rosen MA, Hughes SC: Postoperative epidural morphine analgesia after various local anesthetics (abstract). ANESTHESIOLOGY 59:A413, 1983

TABLE 3. Patient Response to Questionnaire

Parameter	im Therapy	Patient Controlled Analgesia	Epidural Morphine
Analgesia—quality overall			
Comfortable	25	40	65*
Mildly uncomfortable	55	60	30*
Very uncomfortable	10	0	0
In pain	10	0	5
Satisfaction—compared to previous cesarean section			
Much prefer current therapy	25	90†	65*
Prefer current therapy	30	10	30
Don't care	30	0*	0*
Prefer prn im therapy	15	0	5

Values expressed as percent of responses. No differences between PCA and epidural morphine groups.

* $P < 0.05$ *vs.* im group.
† $P < 0.001$ *vs.* im group.

treatments.[4–9] Alternatively, since the nurses who assessed sedation were not necessarily the same for all patients, the difference we observed could conceivably have been from unequal assessment among groups.

The incidence of delayed severe respiratory depression following 5 mg epidural morphine after cesarean section is 1–2:1000,[14] and most authors recommend monitoring of respiration for 24 h following injection. Although mild respiratory depression probably follows PCA and im techniques,[3] severe respiratory depression with PCA has been reported only in association with human error (incorrect programming,[2] accidental nurse-administered bolus dose,[2] subcutaneous infiltration of iv while not using the required Y-connector,[15] use of large dose of slow onset drug[16]) or hemorrhagic hypovolemia.[11] Otherwise, patients safely titrate their own analgesics, do not overmedicate themselves, and have safely used up to 108 mg/hour morphine.[17] Although we observed no respiratory depression in this study, we monitored only respiratory rate, and it is possible that more sensitive methods (apnea monitor, continuous pulse oximetry, CO_2 response) may have detected respiratory depression.

In summary, compared with prn im narcotics following cesarean section, epidural morphine, and PCA provide better analgesia and patient satisfaction. PCA produces the most sedation, while epidural morphine produces the most pruritus, and frequently requires systemic narcotic supplementation in the first postoperative day. PCA is an excellent alternative to epidural morphine and, compared to im narcotics, enhances patient satisfaction.

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Epidural Sufentanil for Postoperative Analgesia after Cesarean Section

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The greater lipid solubility of sufentanil when compared to morphine[1] is likely to result in a more rapid onset of analgesia when used as an epidural agent. In addition, sufentanil has a higher affinity for opiate receptor sites,[2] which may provide a prolonged duration of analgesia. High lipid solubility of sufentanil may result in rapid clearance of sufentanil from cerebrospinal fluid and allow for less cephalad spread. Cephalad spread of spinal opioids has been associated with the occurrence of side effects, such as pruritus, nausea, and respiratory depression;[3] sufentanil may result in fewer and less severe side effects than morphine when administered epidurally to provide analgesia. This prospective study was undertaken to evaluate the efficacy, dose response, and side effects of sufentanil when administered as a postoperative epidural analgesic for cesarean section and to compare these results with epidural administration of morphine sulfate (5.0 mg), commonly used at our institution.

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MATERIALS AND METHODS

With approval from the University of California, San Francisco Committee on Human Research and informed consent from each patient, 40 healthy women undergoing cesarean section with epidural anesthesia were studied. Major complications during pregnancy, major organ diseases, or a history of drug abuse excluded a patient from study. However, patients with lesser medical problems or complications of pregnancy, such as gestational diabetes, mild preeclampsia, cephalopelvic disproportion, or premature rupture of membranes were included.

Patients were given no preoperative medication except an antacid. Epidural anesthesia was provided with 2% lidocaine and epinephrine (1:200,000) administered through a catheter inserted at the L2-3 or L3-4 interspace. Diazepam, not exceeding 7.5 mg iv, and/or fentanyl, not exceeding 100 μg iv, were used during the cesarean procedure to supplement anesthesia. The epidural catheters were left in place following surgery.

When patients first requested pain relief during recovery, they were randomly assigned to one of four groups that received either sufentanil (30, 45, or 60 μg) or morphine sulfate (5.0 mg) through the indwelling epidural catheters. Each group consisted of 10 patients. Each dose of epidural opioid (morphine or sufentanil) was prepared in advance by a pharmacist (CJ) in a 10-ml volume of sterile preservative-free normal saline and packaged in single-administration glass ampules with coded labels. The codes were assigned by and known only to the pharmacist. Neither the investigator nor the patient knew which opioid the patient had received.

The intensity of pain was assessed by each patient using a visual linear analog scale[4] immediately before epidural administration of opioid, and, thereafter, at 15, 30, 45, and 60 min, followed by every half hour for the next 2 h, then every hour for 9 h. Blood pressure, pulse, and respiratory rates in each patient were mea-