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Epidural Sufentanil/bupivacaine Combinations for Analgesia during Labor: Effect of Varying Sufentanil Doses

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The use of epidural narcotics for control of labor pain has been disappointing because of the side effects that may occur and because control of pain may be inadequate.[1,2] Epidural administration of local anesthetic solutions is usually successful in controlling pain, but can lead to undesirable side effects, including both hypotension secondary to sympathetic blockade and muscle weakness. Combining an opioid and a local anesthetic may preserve the benefits of each drug without substantially increasing, and possible even decreasing, the risk of side effects. Reports of the beneficial effects of epidural fentanyl and bupivacaine combinations in providing labor analgesia have recently been published.[3,4] Among the advantages claimed have been more rapid onset and longer duration of analgesia.

In the study reported here, the efficacy of three different doses of the new opioid drug sufentanil, combined with epidural bupivacaine, in providing labor analgesia was evaluated. Sufentanil was chosen over other opioids because of its high lipid solubility and high affinity for the μ opiate receptor. These properties may make it the drug of choice for epidural analgesia.[5,6] The aim of this study was to determine the advantages, if any, of this combination and to find the most appropriate dose of sufentanil.

MATERIALS AND METHODS

Forty healthy women in active term labor were included in the study which was approved by the Institutional Review Board. Informed consent was obtained from all patients. The subjects were ASA physical status I or II, had a single fetus with vertex presentation, and had uncomplicated pregnancies. They were randomly divided into four groups of ten.

All patients were hydrated with 1000 ml of intravenous lactated Ringer's solution prior to epidural injection. The second or third lumbar epidural interspace was located by the loss of resistance to air technique using a 17-g epidural needle. A Racz epidural catheter was advanced 3–4 cm into the epidural space. If aspiration did not yield blood or CSF, 3 ml of 1.5% lidocaine were injected as a test dose to confirm that the catheter was not in a blood vessel or in the intrathecal space. If no motor block developed within 5 min, then the contents of a 1-ml coded ampule were injected together with 7 ml of 0.25% bupivacaine. The ampules contained saline (group 1), 10 μg sufentanil (group 2), 20 μg sufentanil (group 3), or 30 μg sufentanil (group 4). Ampules were coded so that neither patient nor anesthesiologist knew which treatment the patient received. Sufentanil doses were based on judgment about probable useful range as inferred from available information.

Patients were asked to assess their pain using a visual analog pain scale[7] before drug treatment, then again 10 min and 30 min after epidural injection. The extremes of this 100 mm scale are 0 = no pain and 100 = worst pain imaginable. Duration of analgesia was defined as the time from epidural injection to the time when the patient requested an additional epidural injection for relief of pain.

Maternal pulse, blood pressure and respiratory rate were recorded at 5-min intervals for 30 min, and at 15-min intervals thereafter. Fetal heart rate was continuously monitored in all patients. Patients were observed closely for side effects, such as nausea, vomiting, pruritus, maternal hypotension (a decrease in systolic blood pressure of 20% or more below the last pre-epidural reading), and respiratory depression (a decrease in respiratory rate below 12 breaths per minute). Fetal status was assessed by Apgar scores at 1 and 5 min. Data from the four groups were examined by analysis of variance (ANOVA), of χ^2 analysis for frequency data. Where ANOVA showed that significant differences existed between groups, data were further analyzed by a Tukey test to determine which groups differed significantly from the control group. A P value of 0.01 or less was considered to be statistically significant.

RESULTS

Patients in the four treatment groups were comparable in terms of age, weight, height, and pain scores prior to epidural medication (table 1).

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TABLE 1. Patient Data

	Age*	Weight (kg)*	Height (cm)*	Parity		Initial Pain Score*
				Primiparous	Multiparous	
Group 1 (saline)	22.8 (7.1)	73.1 (7.2)	163 (10.0)	8	2	76 (17.4)
Group 2 (sufentanil 10 μg)	19.6 (2.3)	71.9 (9.9)	160 (4.2)	10	0	69 (16.8)
Group 3 (sufentanil 20 μg)	20.5 (3.4)	74.8 (10.9)	163 (6.6)	8	2	82 (9.2)
Group 4 (sufentanil 30 μg)	19.7 (4.3)	78.0 (10.0)	161 (10.0)	8	2	77 (11.7)

* Mean (SD).

Ten minutes after epidural medication there was a greater percentage reduction in pain scores in patients given sufentanil than in patients given saline (fig. 1). Reduction in pain score was significantly greater in patients given 30 μg sufentanil than it was in saline-treated patients, while pain scores in patients given 10 or 20 μg sufentanil were not significantly different from those in patients given saline. No patient given saline was completely pain free (pain score = 0) at 10 min after epidural medication, whereas seven patients given 30 μg sufentanil were pain free at this time (table 2). At 30 min after epidural medication, pain scores in the four groups were similar (fig. 1), and there were comparable numbers of pain-free patients in each group (table 2). This suggests that there was more rapid relief of pain in patients given 30 μg of sufentanil with the epidural bupivacaine, but that the ultimate quality of analgesia was not altered by the addition of sufentanil.

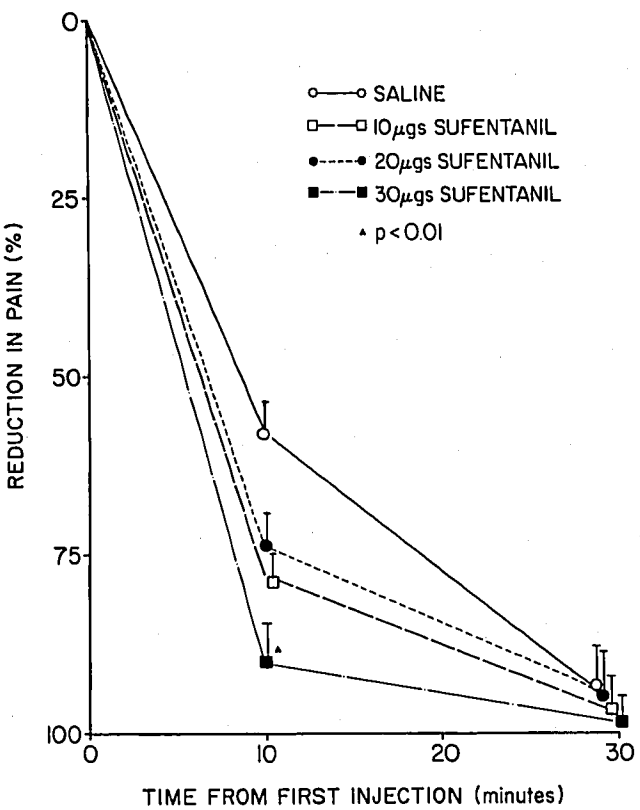

FIG. 1. Percentage reduction in pain score at 10 and 30 min after epidural medication. There is a significantly greater reduction in pain score at 10 min in group 4 (30 μg sufentanil) than in group 1 (saline) $P < 0.01$.

Duration of analgesia was increased by sufentanil. This increase was statistically significant for patients given 20 or 30 μg of sufentanil ($P < 0.01$). Duration of analgesia in patients given 20 μg epidural sufentanil was 137 min, compared to 90 min in saline treated patients. Patients who were given 30 μg sufentanil had an average duration of analgesia of 144 min, which was not significantly longer than that obtained with 20 μg sufentanil (table 2).

Fetal condition at birth was good in all cases. There were no differences in birthweight or 1- and 5-min Apgar scores between neonates in the four groups

TABLE 2. Development and Duration of Analgesia

	Saline	Sufentanil		
		10 μg	20 μg	30 μg
Number of patients pain free at 10 min	0	3	4	7
Number of patients pain free at 30 min	8	8	8	9
Minutes of analgesia ± SD	90 ± 16	114 ± 19	137 ± 20*	144 ± 17*

* $P < 0.05$; significantly different from saline.

(table 3). There were few maternal side effects. Two patients (one in group 2, and one in group 4) had transient mild pruritus involving the legs and abdomen which did not require treatment. One patient in group 1 had a brief period of hypotension after bupivacaine injection, which quickly responded to rapid intravenous fluid infusion. No other side effects were apparent; in particular, no changes in respiratory rates or level of arousal were noted.

TABLE 3. Fetal Status at Birth

	Number of Neonates with Apgar Scores of 7 or More		
	At 1 Min	At 5 Min	Birthweight (kg)*
Group 1 (n = 10) (saline)	9	10	3.32 (0.75)
Group 2 (n = 10) (sufentanil 10 μg)	9	10	3.41 (0.38)
Group 3 (n = 10) (sufentanil 20 μg)	9	10	3.48 (0.24)
Group 4 (n = 10) (sufentanil 30 μg)	9	10	3.53 (0.49)

* Mean (SD).

DISCUSSION

As opposed to other similar studies in which fentanyl was used,[3,4,9,10] this study evaluated sufentanil because of its potential advantages over fentanyl. For instance, sufentanil is more lipid-soluble than fentanyl, and thus penetrates the spinal cord well, leaving low drug levels in the cerebrospinal fluid (CSF). Because of this, sufentanil should have even lower potential to cause delayed respiratory depression, an effect which is thought to be due to rostral migration of hydrophilic drugs in the CSF to the respiratory center in the medulla.[8] Sufentanil also has a higher affinity for the μ opioid receptor than does fentanyl and, therefore, possibly a longer duration of action.[6] It is possible that the higher affinity of sufentanil for the μ receptor may be offset by rapid "washin" and "washout" related to its lipid solubility. This apparently is not so, as evidenced by the prolonged analgesia reported here.

The results of this study show that it is possible to increase the duration of analgesia by adding sufentanil to 0.25% epidural bupivacaine solutions. The addition of 20 μg of sufentanil increases the duration of analgesia by over 50%. As a result, fewer injections are required during labor, and there is a reduction in total bupivacaine dose. There was also significantly more rapid relief of pain with the sufentanil-bupivacaine combination when sufentanil 30 μg was given, as compared to when saline was given. Similarly, more rapid onset of analgesia with bupivacaine-fentanyl combinations, as compared with plain bupivacaine solutions, has been reported.[3,4] The optimum fentanyl dose, namely, 50 μg, increased duration of analgesia from 88 min with 0.25% bupivacaine alone to 108 min with fentanyl added.[9] This contrasts with the much greater increase in duration of analgesia achieved with sufentanil 20 μg.

The benefits to the mother of adding sufentanil to bupivacaine were not offset by any obvious adverse effects on the fetus. However, subtle neurobehavioral effects might have gone undetected, as detailed neurobehavioral testing was not done.

Although adding sufentanil to bupivacaine speeded the onset of analgesia and prolonged it, the quality of analgesia was no better than that achieved with 0.25% bupivacaine alone. Previous studies using fentanyl added to 0.125% bupivacaine have shown improved analgesia, as compared to that achieved with 0.125% bupivacaine alone. This raises the possibility that equally favorable results with reduced risks of side effects could be obtained by using sufentanil with a lower concentration of bupivacaine.

In conclusion, the addition of 20–30 μg of sufentanil to 0.25% epidural bupivacaine solutions increases duration of analgesia, and sufentanil 30 μg produces more rapid relief of pain. These advantages were obtained without any increase in side effects other than a low incidence of pruritus (7% in this study). The sufentanil/bupivacaine combination offers increased duration of analgesia as compared to fentanyl/bupivacaine, and is worthy of further investigation to determine its safety in providing analgesia in labor.

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Hemodynamic Changes during Total Knee Replacement Surgery with Total Condylar Prosthesis

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Total knee replacement surgery with cemented Guepar prosthesis may induce complications such as hypotension, cardiac arrest, and fat embolism.[1–3] This prosthesis induces increases in pulmonary arterial pressure and pulmonary vascular resistance which were not observed when it was inserted without cement.[4,5] Total knee replacement surgery with total condylar prosthesis should avoid the above complications.[6] However, relevant hemodynamic data are not available. We sought to obtain hemodynamic data during total knee replacement surgery performed with a total condylar prosthesis inserted with or without the use of cement, inserted either during or after release of the tourniquet.

MATERIALS AND METHODS

Twenty-nine patients with no history or objective evidence of cardiopulmonary disease were studied after informed consent and approval by our Institutional Ethical Committee. All the patients were ASA Physical Status I or II. The patients were randomly divided into three groups. Group I consisted of six patients who underwent knee replacement without the use of bone cement (Freeman prosthesis). Groups II and III consisted of ten and 13 patients, respectively, who underwent knee replacement surgery with use of bone cement inserted after and before release of the tourniquet, respectively. The three groups were similar in respect to sex ratio and age (table 1). All patients were subjected to similar anesthetic techniques. Premedication consisted of hydroxyzine 100 mg po. Induction of anesthesia was performed with fentanyl 15 μg/kg iv, and endotracheal intubation facilitated by iv pancuronium 0.1 mg/kg. Anesthesia was maintained using controlled ventilation with N_2O 50% in oxygen and fentanyl 10 $\mu g \cdot kg^{-1} \cdot hr^{-1}$iv. The limb was exsanguinated with an Esmarch bandage, and the pneumatic cuff was inflated to 500 mmHg. Intravascular volume was maintained with saline and red packed blood cells to maintain pulmonary artery wedge pressure (PWP) between 10 and 15 mmHg, and hematocrit between 30 and 40%. Central venous pressure (CVP), PWP, and pulmonary arterial pressure (PAP) were measured using a flow-directed triple-lumen pulmonary artery catheter, which was inserted *via* the internal jugular vein. Mean arterial pressure (MAP) was measured through a radial artery catheter. Heart rate (HR) was determined from a standard ECG lead. Cardiac output (CO) was measured in triplicate by the thermal dilution method with a computer (Edwards). Derived variables were:

Cardiac index (CI) = CO/body surface area

$(l/min/m^2)$

Systemic vascular resistance (SVR)

$= (MAP\text{-}CVP)/CI\ (mmHg/l/min/m^2)$

Pulmonary vascular resistance (PVR)

$= (PAP\text{-}PWP)/CI\ (mmHg/l/min/m^2)$

The quantities of the monomeric methylmethacrylate in expired gases sampled during 5 min were measured

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