



## Postoperative Analgesia following Thoracotomy

### Danger of Delayed Respiratory Depression\*

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Narcotic anesthesia is commonly used for patients with depressed myocardial function. Post-thoracotomy analgesia is increasingly provided by epidural narcotic analgesia. Combination of the two techniques may have resulted in respiratory depression and death in a 66-year-old ischemic heart disease patient following thoracotomy.

Fentanyl in high doses (50 to 150  $\mu\text{g}/\text{kg}$ ) is a recently established useful anesthetic technique for patients with depressed cardiac function.<sup>1</sup> Epidural narcotics to provide long-lasting postoperative analgesia also are increasingly popular.<sup>2</sup> The major side effect limiting epidural narcotic use is delayed respiratory depression, which occurs most often with concomitant parenteral narcotic use.<sup>3</sup> The result of combining high-dose fentanyl anesthesia and postoperative epidural narcotic analgesia has not been reported previously.

#### CASE REPORT

A 66-year-old, 79 kg man with a history of two prior myocardial infarctions and a 20 percent ejection fraction was scheduled for thoracotomy to evaluate a right lower lobe pulmonary nodule. The patient was not considered a suitable candidate for preoperative coronary revascularization. Maintenance oral medication therapy included nifedipine, 20 mg tid, isosorbide dinitrate, 40 mg qid, and dipyridamole, 25 mg tid. Forced expiratory volume in 1 sec (FEV<sub>1</sub>) was 2.86 L (3.47 L predicted) and forced vital capacity (FVC) was 4.03 L (5.09 L predicted).

The patient received anesthetic premedication with nifedipine, 20 mg, isosorbide dinitrate, 40 mg, diazepam 10 mg PO, and morphine 10 mg IM. Systemic and pulmonary arterial catheters and peripheral venous cannulae were inserted and electrocardiographic monitoring initiated prior to induction of anesthesia. Fentanyl, 30  $\mu\text{g}/\text{kg}$ , and pancuronium, 0.1 mg/kg, were administered intravenously while the patient was ventilated with oxygen (FIO<sub>2</sub> 1.0). Additional fentanyl followed through intravenous infusion (total dose, 90  $\mu\text{g}/\text{kg}$  during the three hour procedure). A lumbar epidural catheter (L2-3) was inserted following completion of the uneventful operation.

In the intensive care unit, the patient's ventilation was managed with a volume-cycled ventilator (FIO<sub>2</sub> 0.4, tidal volume 12 ml/kg, IMV rate 6 breaths/min). Diazepam, 10 mg, was administered intravenously for sedation and nitroglycerine, 1  $\mu\text{g}/\text{kg}/\text{min}$  was infused. Prior to discontinuation of mechanical ventilation, correct epidural catheter placement was verified by segmental analgesia obtained with 5 ml of 0.5 percent bupivacaine solution. Four mg of

morphine diluted in 8 ml of saline solution was injected and ventilatory weaning begun. The patient was extubated 22 hours after arrival in the intensive care unit postoperatively.

One hour after extubation (three hours following the initial epidural morphine injection) the patient was alert but complained of incisional pain. Additional morphine, 4 mg in 8 ml of saline solution, was injected through the epidural catheter, followed by relief of pain one hour later (Fig 1). Two hours after the second epidural morphine injection he was alert and able to suction his mouth. One hour later, however, he was obtunded, but maintained a respiratory rate of 16 breaths/min. Naloxone, 80  $\mu\text{g}$ , was administered intravenously. Three minutes later the patient was able to follow commands but developed acute pulmonary edema. The nitroglycerine infusion was increased to 2  $\mu\text{g}/\text{kg}/\text{min}$ . Following tracheal intubation, ventricular tachycardia and cardiorespiratory arrest occurred. He was resuscitated but died from multiorgan failure ten days later.

	TLV 8am	OLV 9am	ADMIT 11am	POD1 7am	POD1 10am	POD1 12pm	POD1 1pm
	INTRAOP		INTENSIVE CARE UNIT				
Resp rate	8	8	8	14	12	16	cpr
IMV rate	8	8	8	4	extubated		cpr
FIO <sub>2</sub>	1.0	1.0	0.4	0.4	0.4	0.3	1.0
pH	7.46	7.44	7.44	7.40	7.38	7.35	7.19
PaO <sub>2</sub>	410	220	150	125	123	75	51
PaCO <sub>2</sub>	32	32	31	38	41	46	59
HCO <sub>3</sub>	21	20	20	23	24	25	22
HR	85	82	96	82	87	99	CARDIORESPIRATORY ARREST
BP	$\frac{122}{70}$	$\frac{126}{67}$	$\frac{102}{50}$	$\frac{102}{52}$	$\frac{116}{60}$	$\frac{126}{60}$	
PAOP	23	18	15	16	14	21	
PAP	$\frac{45}{25}$	$\frac{37}{19}$	$\frac{27}{19}$	$\frac{40}{29}$	$\frac{34}{16}$	$\frac{42}{22}$	
CO	6.0	4.1	5.4	5.6	5.1	6.8	
Drug Rx	①		②	③	③		

- ① FENTANYL 90  $\mu\text{g}/\text{kg}$
- ② DIAZEPAM 10 mg/first 12 hours in ICU
- ③ EPIDURAL MORPHINE 4 mg

FIGURE 1. Summary of perioperative cardiorespiratory measurements and drug therapy. TLV = two lung ventilation; OLV = one lung ventilation; POD1 = postoperative day 1; IMV = intermittent mandatory ventilation; CPR = cardiopulmonary resuscitation; HR = heart rate in beats/min; BP = systemic blood pressure in mm Hg; PAOP = pulmonary artery occlusion pressure in mm Hg; PAP = pulmonary artery pressure in mm Hg; CO = cardiac output in liters/min; HCO<sub>3</sub> = bicarbonate concentration; PaO<sub>2</sub> and PaCO<sub>2</sub> in mm Hg.

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## DISCUSSION

Administration of high doses of fentanyl was described by Stanley and colleagues<sup>1</sup> and Lunn et al<sup>4</sup> as a complete anesthetic method for patients undergoing mitral valve replacement or coronary artery revascularization. It also is utilized for patients with depressed cardiac function undergoing noncardiac operations.<sup>5</sup> Ventilator weaning generally follows the morning after surgery.<sup>6</sup> Biphasic respiratory depression has been noted,<sup>7</sup> but is not observed with the high dose technique if ventilatory weaning occurs the morning after operation.<sup>6</sup>

A 50 percent decrease in carbon dioxide responsiveness occurs when plasma fentanyl concentrations are 1.5 to 3.0 ng/ml. Administration of fentanyl, 50 to 75 µg/kg, produced an average plasma level of 1.6 ng/ml at extubation the following morning, while larger doses of 100 µg/kg resulted in a value of 3.3 ng/ml.<sup>9</sup> Patients over 60 years of age have a decreased clearance of fentanyl and higher levels may result.<sup>10</sup>

Postoperative epidural morphine analgesia was used successfully in 6,000 Swedish patients.<sup>11</sup> Severe respiratory depression requiring reversal with naloxone was reported in 0.33 percent of patients.<sup>11</sup> The risk of delayed respiratory depression increased with age for patients over 70 years old. Of the 22 patients who received naloxone, only two experienced ventilatory depression more than six hours after administration of parenteral narcotics.

The lumbar epidural approach to post-thoracotomy analgesia with narcotics is effective.<sup>12</sup> Maintenance of pulmonary function (measured by FEV<sub>1</sub>) after thoracotomy or upper abdominal procedures is better maintained by administering morphine epidurally rather than intravenously.<sup>13</sup> Thoracic analgesia results from rostral spread in the cerebrospinal fluid (CSF) of the poorly lipid-soluble morphine. This same mechanism contributes to late respiratory depression. Bromage et al<sup>14</sup> demonstrated that morphine injected into the lumbar epidural space reaches the brainstem and fourth ventricle within six hours.

This patient had an uneventful perioperative course until obtundation and respiratory depression (PaCO<sub>2</sub> 59 mm Hg, despite significantly increased minute ventilation) occurred three hours after a second injection of epidural morphine. Plasma fentanyl concentration, though unmeasured, probably was between 1.5 and 3.5 ng/ml.<sup>9</sup> This, coupled with peaking CSF values of morphine in the elderly patient,<sup>11</sup> make respiratory depression more likely. Diazepam potentiation was possible, though unlikely. Ventilatory depression was not detected by the respiratory rate alarm, since respiratory frequency was maintained (Fig 1). The pattern of respiratory depression following epidural narcotic administration may be different from that following parenteral narcotic use. Frequency is unchanged but minute ventilation decreases.<sup>3,15</sup> Obtundation was reversed by naloxone therapy, but this drug may have contributed to the subsequent ventricular dysrhythmia<sup>16</sup> and pulmonary edema.<sup>17</sup> A primary myocardial ischemic event could not be ruled out.

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## Control of Hypertension with Nifedipine in the Setting of Aortic Dissection\*

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We report a 61-year-old man with dissection of the descending aorta and hypertension in whom medical management with beta-blocking antihypertensives was precluded by a history of asthma. The calcium channel blocker nifedipine was successfully employed in this setting and the rationale for its use is discussed.

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