

multate in body fat. The metabolites of nitroglycerin are glycerol dinitrate and nitrite, both water soluble and excretable in urine.<sup>2</sup> However, with decreased urine production both metabolites would remain in the body for a longer period of time. This may explain the high level of methemoglobin found despite discontinuation of the nitroglycerin almost 16 hours earlier.

This patient's clinical condition seemed to respond and improve with the treatment of the methemoglobinemia with methylene blue. Methylene blue is 3,9-bisdimethylaminophenazothionium chloride. In low concentrations, the reduced form of methylene blue speeds the conversion of methemoglobin to hemoglobin, and the NADP-dependent methemoglobin reductase can regenerate reduced methylene blue from oxidized methylene blue.<sup>3,8</sup> The increase in O<sub>2</sub> transport associated with the increase in functional hemoglobin following treatment with methylene blue may have been responsible for the improvement in the patient's clinical condition.

In conclusion, we present a case of methemoglobinemia complicating the postoperative period of a patient following cardiac surgery who was exposed to iv nitroglycerin therapy. The methemoglobinemia occurred in

association with respiratory distress secondary to pulmonary congestion. Whether the methemoglobinemia was a causal factor in the generation of the respiratory distress is unknown; however, treatment of the methemoglobinemia seemed to enhance recovery.

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### Clinical Advantages of Fentanyl Given Epidurally for Postoperative Analgesia

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The analgesic effect of epidurally administered narcotics is well documented.<sup>1-4</sup> The various possible mechanisms of action include systemic absorption, medullary fixation, and cephalad diffusion via the cerebral spinal fluid. These factors may be a determining factor in the relative importance of side effects, in particular, respiratory depression.<sup>5</sup> The action of fentanyl given epidurally is rapid, intense, and of short duration.<sup>6,7</sup> However,

the role played by systemic absorption on the respiratory effect from this analgesic technique, is unknown. The present study was designed to examine the analgesic effects, plasma concentrations, and ventilatory consequences of an injection of the same dose of fentanyl given epidurally or intramuscularly in random sequence and in the same subjects for postoperative pain relief.

#### MATERIALS AND METHODS

This study was conducted with the informed consent of 11 patients who had undergone an abdominal or thoracic surgery. In these subjects, the indication for analgesia was determined by the presence of pulmonary disease sufficient to require intense and rapid respiratory physiotherapy. All patients were anesthetized with flunitrazepam, fentanyl, and pancuronium iv. All patients had radial artery and epidural catheters inserted, the latter at the end of surgical intervention. The day after

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surgery, 5 of the 11 subjects were chosen randomly to receive an epidural injection of 200  $\mu$ g of fentanyl diluted in 10 ml of saline. This was followed, at least 3 h later, by an im injection of the same dose of fentanyl. The remaining six patients underwent the same procedure but in the inverse order, *i.e.*, the im injection preceded the epidural injection.

**Variables:** Respiratory rate,  $\text{PaO}_2$  and  $\text{PaCO}_2$ , forced vital capacity, and pain score were determined before the injection and then at 10, 20, 30, 60, 120, and 180 min after injection. In six patients, arterial blood was obtained for the determination of plasma fentanyl concentrations before the injection and then at 1, 3, 5, 10, 20, 30, 60, 120, and 180 min after injection. Respiratory rate as well as  $\text{PaO}_2$  and  $\text{PaCO}_2$  were measured without any sensory stimulation. The forced vital capacity was measured with a frandripen oral volumeter, and the highest value over three trials was used for analysis. Analgesic effects were evaluated by the visual scale method (8) (scored from 0 to 10) in two situations, first, with the subject breathing normally, and secondly, during exertion at a level analogous to that achieved during a respiratory physiotherapy session.

Plasma concentrations of fentanyl were determined by radioimmunoassay. Each heparinized plasma sample was centrifuged and frozen until assay. This method, with a sensitivity of 0.15 ng/ml, is affected little by the presence of fentanyl's metabolites.<sup>9</sup>

Results were analysed using the nonparametric Wilcoxon test for the pain scores and analysis of variance for the other variables. Results are expressed as means  $\pm$  SEM.

## RESULTS

At a dose of 200  $\mu$ g, fentanyl was more effective when given epidurally than im regardless of the sequence of administration; this was the case whether the pain was spontaneous or was provoked by coughing (fig. 1). This difference in analgesic effectiveness between the two techniques was significant from the 10th minute to the first hour for spontaneous pain and from the 10th minute to the second hour for provoked pain. This difference ceased to be significant, however, between 2 and 3 h after injection.

Respiratory rate decreased an average of 25% from the 20th min to the second hour following epidural injection of fentanyl (fig. 1). The lowest respiratory rate was 9 breaths  $\cdot$  min<sup>-1</sup>, which returned to its baseline value at the third hour. No significant variations in respiratory rate were recorded after the im injection, even when it followed the epidural injection.

The  $\text{PaCO}_2$  tended to increase from 10 to 30 min after the epidural injection; however, these changes

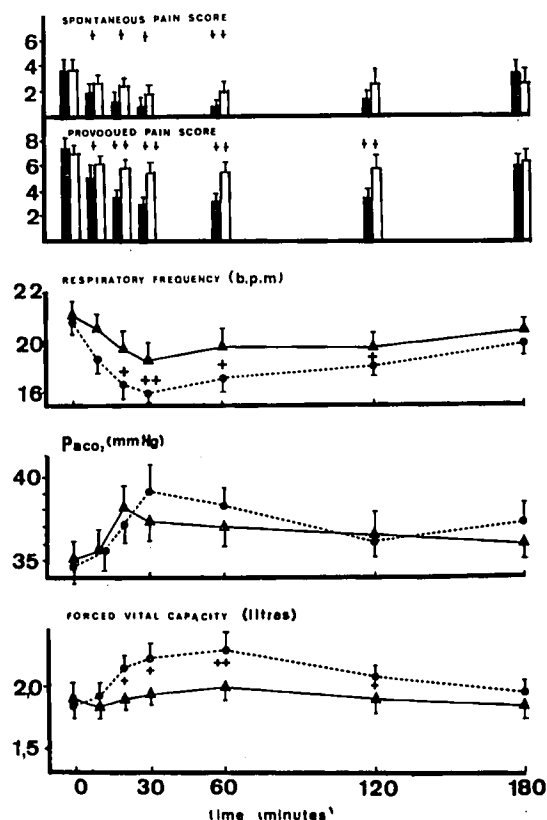


FIG. 1. Spontaneous and provoked pain scores, respiratory frequency,  $\text{PaCO}_2$ , and forced vital capacity in patients who had received 200  $\mu$ g fentanyl epidurally (filled columns and circles) or im (open columns and filled triangles), mean  $\pm$  SEM. + =  $P$  < 0.05. ++ =  $P$  < 0.01.

were not significant. When the preinjection values of  $\text{PaCO}_2$  were greater or equal to 38 mmHg (three cases), the variation in  $\text{PaCO}_2$  never was greater than 7.5 mmHg. When, in contrast, preinjection  $\text{PaCO}_2$  was less than or equal to 32 mmHg (eight cases), the increase could be greater than 7.5 mmHg (the maximum was 12 mmHg), which coincided with the reduction in respiratory rate.

After the im injection of fentanyl, the variations in  $\text{PaCO}_2$  followed a similar curve, though the maximum amplitude was smaller (3.2 mmHg).

The forced vital capacity increased significantly from 20 min after epidural injection to reach a maximum at the first hour (+22%). This variable was unchanged, however, by the im injections.

Assay results following epidural and im injection are displayed in figure 2. Baseline values are not zero but correspond to the sensitivity limits of the assay method. The average of the peaks following epidural injection occurs earlier but is smaller than that following im injection ( $0.67 \pm 0.05$  ng/ml at 5 min, against  $1.2 \pm 0.29$  at 20 min). Plasma levels fell rapidly, and by 30 min they were  $0.573 \pm 0.093$  for epidural and  $0.975$

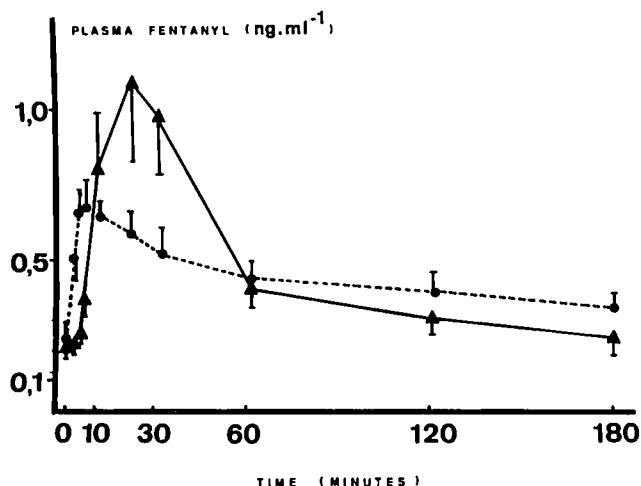


FIG. 2. Mean immunoreactive plasma fentanyl levels after 200  $\mu$ g of the drug were injected epidurally (filled circles) or intramuscularly (filled triangles). Vertical lines, representing SEM, are drawn in one direction only for clarity of presentation.

$\pm 0.19$  ng/ml for im injections. By the third hour, plasma levels were only  $0.34 \pm 0.05$  ng/ml and  $0.29 \pm 0.05$  ng/ml, respectively.

Somnolence and miosis were observed in all patients after both the im and epidural injection. After epidural injection, only transitory pruritus was noted in two subjects. Nausea and vomiting were seen in two other patients.

#### DISCUSSION

Our study of fentanyl given epidurally at a dose of 200  $\mu$ g confirmed previously reported rapidity of analgesic action.<sup>4,6,7</sup> The intensity of this action also has been assessed by the quality of the analgesic effect obtained during the exertion of coughing. The increase in the forced vital capacity noted after epidural injection is, in fact, further confirmation of this effect. Satisfactory respiratory physiotherapy was possible in all patients. Although the dose adopted by us was twice that used by other authors,<sup>6</sup> the duration of analgesia from provoked pain appeared to be limited to about 2 h. The analgesic scores remained acceptable, however, for 3 h, when only spontaneous pain was evaluated. After the im injections, analgesia was less intense and, although it appeared to be sufficient to counteract spontaneous pain, it did not allow forced vital capacity to increase sufficiently for effective respiratory physiotherapy.

Comparison of the plasma levels of fentanyl, which were greater after the im injection than after epidural injection, with the analgesic effects, which were more intense epidurally, suggests that systemic absorption is not the essential mechanism of analgesic action. These results obtained with fentanyl are in close agreement with those previously reported for morphine<sup>5</sup> and me-

peridine.<sup>10</sup> Epidural injection of fentanyl induced a significant reduction in respiratory rate and a trend for  $\text{PaCO}_2$  to increase that was not significant. The mechanism proposed for this effect has involved either vascular absorption or a diffusion in the cerebrospinal fluid (CSF) toward the respiratory centers. The later hypothesis is supported by a larger decrease in respiratory rate with a lower plasma concentration of fentanyl following an epidural injection than after an injection of the same dose of fentanyl im. Furthermore, the plasma fentanyl concentration required for respiratory depression (1–2 ng/ml)<sup>13</sup> is above those found in our study following epidural injection.

In our study, the decreases in respiratory rate did not induce hypercapnia and were closely linked to the analgesic effects. These facts can be explained by a specific medullary drug-receptor interaction<sup>15</sup> related to the liposolubility of fentanyl molecule,<sup>5,14</sup> which could reduce the amount of fentanyl available for cephalad transfer in the CSF,<sup>14,15</sup> thus minimizing the risk of central respiratory depression.<sup>14</sup>

In conclusion, when given epidurally at the dose of 200  $\mu$ g, fentanyl provides a rapid analgesia that remains optimum during 2 h, despite the intensity of pain stimulation related to postoperative respiratory physiotherapy in thoracic or abdominal surgery.

The effectiveness of its analgesic action cannot be explained by its systemic absorption, which seems to be negligible. Although of short duration, this technique seems also reliable in regard to the risk of immediate and above all delayed respiratory depression.

These characteristics of fentanyl given epidurally probably are related to its physicochemical and pharmacokinetic properties.

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## The Use of a Stylet in Blind Nasotracheal Intubation

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Blind nasotracheal intubation is a technique to establish an airway in patients in whom it is either desirable to have a nasotracheal tube or in whom it is difficult to visualize the larynx.<sup>1</sup> When this approach is unsuccessful, various techniques can be used to facilitate nasotracheal intubation, including the use of a flexible fiberoptic bronchoscope, special endotracheal tubes, and various other appliances.<sup>2,3</sup> The lack of appropriate-sized fiberoptic bronchoscopes and other suggested equipment precludes those methods in small children. We developed a technique proven to be useful in several conditions, such as Goldenhars syndrome, cherubism, fractured cervical vertebrae, rheumatoid arthritis, and in other conditions precluding adequate visualization of the cords. The age range for using this technique is from three years through adult.

A diagrammatic representation of the problem in unsuccessful intubation is depicted in figure 1. The problem is that the tip of the nasotracheal tube will not advance anteriorly into the larynx and trachea but courses posteriorly into the esophagus. The solution is to direct the tip of the tube more anteriorly and this clinical report addresses this problem.

### METHOD

When the anatomic problem is recognized preoperatively either by history or by physical examination, then preparations for the technique to be described should

be done before the induction of anesthesia. The preliminary formation of the stylet is very important. The tip of the stylet needs to extend to within 2-3 mm of the end of the nasotracheal tube but not beyond. The middle section of the stylet must have a gentle bend to follow the course of the nasopharynx and then a short, sharper angle at the tip to achieve the anterior angulation required. After the stylet has been tested for both length and angle of the tip, it then is removed, lubricated, and placed in a readily accessible location. The technique involves the passage of the nasotracheal tube into the proper position first and then the insertion of the stylet into the tube. The proper position of the tube is similar to figure 1, but the tube should be withdrawn a short distance under the epiglottis and positioned so that maximum breath sounds are heard. Placement of the stylet in the nasotracheal tube first and then attempting intubation is not recommended, since the nasotracheal tube becomes quite rigid. This increased rigidity requires excessive pressure for advancement, which may cause a host of undesired results, including, but not limited to, bleeding, the creation of a false passage, and laceration of adenoid tissue.

The stylet then is passed down the nasotracheal tube. The amount of force required to pass the stylet should not exceed the amount of force to pass the nasotracheal tube. If it does, the stylet needs to be reformed so that it will pass more easily. The stylet is advanced to the appropriate length that was measured in the preparation of the stylet, and breath sounds are monitored carefully. The position of the tube and stylet now should be as in figure 2. The tube and stylet can be advanced forward gently for a short distance, until breath sounds are maximal, and then the nasotracheal tube is slipped off of the stylet into the larynx and trachea as in figure 3. If the stylet is pulled out of the nasotracheal tube, the

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