

was considered normal in 355 (46%) and moderately impaired in 409 (54%) patients. The mean number of grafts performed was 3.6 (range 1–6). There were no intraoperative deaths. There were seven in-hospital deaths, a mortality of 0.91%. Four patients died in the early postoperative period. All had profound myocardial depression with or without intractable arrhythmias despite well-functioning grafts on reopening of the chest. Within 16 days after the surgery three patients died as a result of: 1) poor left ventricular function not helped by intraaortic balloon pump and inotropes; 2) bilateral *Pseudomonas pneumonia* and septicemia; and 3) late hemorrhage from a graft.

Twenty-three (3.0%) patients showed S-T changes on ECG over a period of more than 30 min intraoperatively, and overall myocardial damage was detected in 30 (3.9%) patients.

Our retrospective mortality and perioperative infarction data correspond closely with those presented by Bashein *et al.* and both compare favorably with the mortality rate reported by the Coronary Artery Surgery Study.<sup>2</sup>

We agree with the authors that in this group of patients, despite sometimes extensive coronary disease (judged by

the number of grafts placed) but with relatively healthy left ventricular function, pulmonary artery pressure measured perioperatively offers very little, if any, advantage over central venous pressure monitoring. To be used, it should offer real benefit to the patient, which does not appear to be the case for this group of patients. In addition, its potential for complications should always be considered.

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### Potency of Sufentanil

*To the Editor:*—Goldberg and colleagues recently reported a case of chest wall rigidity in the recovery room following sufentanil, which had been administered several hours earlier.<sup>1</sup> They provided a thoughtful case report and an excellent brief review of the poorly understood problem of narcotic-induced chest-wall rigidity. We believe the authors raised several important issues not directly addressed in their article. Specifically:

1. What should the dose of sufentanil be when combined with a muscle relaxant and ½ MAC of an inhalational agent?

2. Does the manufacturer's literature adequately describe sufentanil dosing?

3. Should we anticipate that chest wall rigidity will occur frequently after sufentanil is used in an appropriately administered, balanced anesthetic?

We therefore reviewed the available dosing information for this agent when used during balanced anesthesia for noncardiac operations. To estimate drug requirements for loading and maintenance doses requires that we know the volume of distribution and clearance of the drug, and the blood concentration required for the desired effect.<sup>2</sup>

Loading Dose

$$= \text{Target Concentration} \times \text{Volume of Distribution}$$

Maintenance Dose

$$= \text{Target Concentration} \times \text{Clearance}$$

Sufentanil's volume of distribution and clearance are approximately 3 l/kg and 12 ml · kg<sup>-1</sup> · min<sup>-1</sup>, respectively.<sup>3</sup> The potency of sufentanil is considered to be 5–10 times that of fentanyl.<sup>3–5</sup> In the absence of specific data defining effective serum concentrations for sufentanil, we extended the data of McClain and Hug and Murphy and Hug for fentanyl<sup>6,7</sup> and applied them to sufentanil dosing as outlined subsequently. The results have been used with reasonable clinical success, in the sense that patients emerge from balanced anesthesia comfortable, with respiratory rates in excess of 12 breaths/min and do not require naloxone for sustained normal ventilation and recovery.

These data indicate that a fentanyl serum concentration of 2.0 µg/l should be effective in balanced anesthesia, without causing excessive postoperative respiratory depression (ventilation relatively normal in pain-free vol-

unteers at  $1.5 \mu\text{g}/\text{l}^6$ ). For sufentanil, the target range becomes 0.2 to  $0.4 \mu\text{g}/\text{l}$ , using potency ratios of 10 and 5, respectively. The loading and maintenance doses for sufentanil during balanced anesthesia may thus be approximated:

$$\begin{aligned} \text{Load} &= (0.2 \text{ to } 0.4 \mu\text{g}/\text{l}) \\ &\quad \times 3.0 \text{ l}/\text{kg} = 0.6 \text{ to } 1.2 \mu\text{g}/\text{kg} \\ &\quad (\text{vs. } 6\text{--}8 \mu\text{g}/\text{kg} \text{ for fentanyl}) \\ &= 45\text{--}90 \mu\text{g} \text{ in a } 75\text{-kg patient} \end{aligned}$$

$$\begin{aligned} \text{Maintenance Dose} &= (0.2 \text{ to } 0.4 \mu\text{g}/\text{l}) \\ &\quad \times 0.012 \text{ l} \cdot \text{kg}^{-1} \cdot \text{min}^{-1} \times 60 \text{ min}/\text{h} \\ &= 0.15 \text{ to } 0.3 \mu\text{g} \cdot \text{kg}^{-1} \cdot \text{h}^{-1} \text{ (approximately)} \\ &\quad (\text{vs. } 1.5 \mu\text{g} \cdot \text{kg}^{-1} \cdot \text{h}^{-1} \text{ for fentanyl}) \\ &= 11\text{--}22 \mu\text{g}/\text{h} \text{ in a } 75\text{-kg patient.} \end{aligned}$$

Maintenance dosing should begin approximately 3 alpha half-lives after induction (30–45 min for sufentanil). The case reported lasted 2.5 h and involved a 75-kg, 43-yr-old man in good general health. The previous calculations suggest that this patient should have received an induction dose plus 2 h of maintenance sufentanil: 67–134  $\mu\text{g}$  compared with the 300- $\mu\text{g}$  administered.<sup>1</sup>

Flacke *et al.*<sup>8</sup> have recently reported the sufentanil dose required in 17 patients randomly allocated to receive this narcotic administered in 10  $\mu\text{g}$  increments in conjunction with 60–67% nitrous oxide and oxygen. On average, these patients received 1.3  $\mu\text{g}/\text{kg}$  for induction and  $0.35 \mu\text{g} \cdot \text{kg}^{-1} \cdot \text{h}^{-1}$  thereafter, numbers remarkably similar to the upper limits estimated previously. The fact that 41% of their patients required naloxone for reversal of narcotic-induced respiratory depression at the end of the case suggests that the smaller doses calculated previously may be a better starting point for anticipating patient requirements.

During the operation reported by Goldberg *et al.*,<sup>1</sup> the patient received 300  $\mu\text{g}$  of sufentanil (the equivalent of 1.5–3.0 mg [30–60 ml] of fentanyl), 2.5 to five times the anticipated need for the anesthetic regimen chosen. To our consternation (and education), when we turned to the drug company's literature on the subject, we found that 2–8  $\mu\text{g}/\text{kg}$  was recommended as an analgesic dose for "more complicated major surgical procedures," which would provide "relatively rapid recovery." In our experience this is an excessively simplistic dosing recommendation, as it ignores case duration (*vs.* the bigness of the operation) and does not separate loading (induction) from maintenance doses. It is a recommendation that should get patients into clinical problems, as the cited case report indicates.

We have found sufentanil to be an excellent "tb syringe" drug for use in general anesthesia and postoperative pain management. Our clinical experience suggests that mild to moderate chest-wall rigidity is frequently encountered during induction with fentanyl or sufentanil, presumably due to high serum concentrations and the rapid achievement of peak effect.<sup>1,9</sup> By contrast, during emergence or when small increments of drug (0.03–0.06  $\mu\text{g}/\text{kg}$  of sufentanil) are given, the phenomenon is not encountered separately from respiratory depression. We believe that the present case report represents a substantial sufentanil overdosage. The case report and the literature cited therein suggest that narcotic-induced chest-wall rigidity will be rarely encountered postoperatively when appropriate induction and maintenance doses of the drugs are applied during general anesthesia.

Pharmacokinetic and pharmacodynamic concepts can be simplified and usefully applied to guide clinical dosing regimens. For several new and potent agents, the application of these concepts is essential for proper drug administration and patient safety.

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