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Intensive Analgesia Reduces Postoperative Myocardial Ischemia? I

To the Editor:—An article by Mangano *et al.*[1] demonstrates that the incidence of severe ischemic episodes is decreased in patients who receive intravenous sufentanil for postoperative pain control. Overall outcome, however, was not improved. The incidence of myocardial infarction and left ventricular failure was not statistically different from one group to another.

To demonstrate clearly that any treatment would decrease the incidence of adverse outcome, a large study is needed. For example, patients undergoing peripheral vascular surgery have a 40% incidence of postoperative ischemia, and 30% of those develop a bad outcome (death, myocardial infarction, or death).[2–4] If a therapy is to reduce the incidence of complications from 30 to 20%, approximately 3,000 patients would be required to demonstrate that aggressive therapy is useful (power of 0.80 for a 33% reduction in complications). Thus, unless a multicenter study enrolling a significant number of patients is planned, definitive conclusions will be difficult to draw.

The incidence of postoperative ischemia may be closely related to the activation of the neuroendocrine response. In fact plasma norepinephrine and renin levels are higher during episodes of silent ischemia.[5] In healthy humans, the coronary vessels dilate due to endothelium-derived relaxing factor and prostacyclin produced in response to acetylcholine and norepinephrine. When atherosclerosis is present, this stimuli will result in coronary vasoconstriction.[6] Moreover, postoperative hypercoagulability is experienced by patients with atherosclerotic disease.[7] This vasoocclusive phenomenon acting synergistically with a high adrenergic tone may be responsible for the high incidence of postoperative myocardial ischemia and bad outcome in patients with coronary artery disease.

We suggest that postoperative epidural analgesia using a local anesthetic and opioid in low doses may be associated with a better outcome in this high-risk population.[8,9] Moreover, a short-acting β blocker and/or calcium-channel blocker, when indicated, may further reduce the incidence of ischemia associated with supply–demand or spasm.[10,11]

The use of intravenous opioids, on the other hand, not only provide inferior analgesia when compared with epidural opioids but are also unable to suppress hemodynamic and hormonal responses even when high doses are used.[12] Since no improvement in cardiac outcome could be derived from postoperative infusions of sufentanil, based on these data, one must evaluate the effects of these infusions (cost, intubation time, complications, *etc.*) with the potential benefits (improved clinical outcome).

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Intensive Analgesia Reduces Postoperative Myocardial Ischemia? II

To the Editor:—I read with interest the recent article by Mangano and the Study of Perioperative Ischemia Research Group.[1] Their data reveal that patients who receive a continuous infusion of sufentanil after cardiac surgery have "less severe" ECG changes in the postbypass and intensive care unit time periods when compared to patients who receive intermittent intravenous injections of morphine for pain relief. From these data, the authors conclude that "the severity of ischemic episodes can be diminished following myocardial revascularization by use of prolonged intensive analgesia." Such a conclusion, while intuitively appealing, is not the only way to interpret the data.

The design of this study significantly limits any conclusions that can reasonably be drawn from its results. The two groups differ in many ways other than the degree of analgesia.

The groups received two different drugs (morphine or sufentanil). The patients in the morphine group also received significantly more midazolam. Thus, the differences in ischemia between the groups may come from a proischemic effect of morphine, not an antiischemic effect of sufentanil. The additional midazolam, alone, or in combination with the morphine, could have incited more ischemia in that group.

The intraoperative management of the groups was different. The morphine group received up to 2 mg/kg of morphine while on bypass. The sufentanil group received a bolus and infusion of sufentanil. Morphine, in these doses, has considerable hemodynamic effects. In contrast, sufentanil is well known for promoting "hemodynamic stability." Thus, differences in the intraoperative management of these two groups could be responsible for the reported results.

In the intensive care unit, the drugs were given by different protocols. In one group, the patients received intermittent injections of opioid "as needed for pain." The other group, in contrast, received a constant infusion of opioid. These different methods of drug administration could have influenced the study outcome.

The authors suggest that the less severe ischemia in the sufentanil group resulted from "intensive analgesia." However, they offer no data to show that the patients in the sufentanil group indeed had less pain than those in the morphine group. Admittedly, this is a difficult task when dealing with patients in whom the trachea is intubated, but I think the point is important.

Lastly, the investigation was in no way blinded. Nurses and physicians caring for the patients in the operating room and intensive care unit were most likely aware of the study. Even if they did not know the authors' hypothesis, they could have guessed it or derived one of their own. Either event might have produced subtle changes in the manner in which they responded to clinical events.

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In Reply:—We appreciate the comments of de Leon-Casasola and Lema. Regarding their suggestion that a larger study is needed, we agree and have so stated in the third limitation cited in the Discussion section. The intent of this study was to investigate the differential effects of the techniques on the incidence and severity of perioperative myocardial ischemia. As such, the 100 patients studied provide adequate power. To differentiate the effects on myocardial infarction and cardiac death, a much larger study is needed both because of a lower incidence