In this issue of the Journal of Neurosurgery, Morad et al present the results of a clinical trial using patient-controlled analgesia (PCA) for postoperative pain management in patients who underwent supratentorial intracranial surgery. The PCA group was matched with another group receiving conventional nurse-administered as needed (PRN) pain control. Fentanyl was the opiate used in both groups. The results demonstrate a significantly greater (almost doubled) opiate consumption in the PCA group, with an associated improvement in pain scores. No complications were observed.

These are very exciting data because they demonstrate the feasibility, with relatively simple interventions, of decreasing postoperative pain in this patient population. As the same research group demonstrated in another recent article, moderate to severe pain is very common in these patients, in part because clinicians are particularly concerned about the side effects of opiates in this population. It is understandable therefore that the success of their current trial prompted the authors to "... encourage others to endeavor to improve the quality of pain relief in this patient population by instituting intravenous PCA..."

However, one question was not really answered in this study: is it safe? The authors appropriately note that their trial was not powered to address the safety issue, and that based on their sample size even a fairly substantial incidence (5% or so) of significant adverse events could have been missed. Intravenous PCA-related complications in other settings have been sufficiently common that additional monitoring is currently recommended when the technique is used in certain populations. It is worthwhile considering this issue in some detail so that PCA can be used safely from the start when used in neurosurgical patients.

Life-threatening respiratory depression is a significant and underappreciated risk when PCA-administered opiates are used in the postoperative period. The reported incidence depends on the definition of respiratory depression. This is commonly diagnosed by low respiratory rate (generally < 10 bpm [breaths per minute]), low oxygen saturation (< 90%), or elevated carbon dioxide pressures (≥ 50 mm Hg), but others add the need for an opiate antagonist to the definition. One study of pooled data from > 20,000 patients reported an incidence, based on these criteria, of 1.2% (6922 patients), 11.5% (707 patients), 1.3% (301 patients), and 1.9% (4691 patients), respectively. Respiratory depression can occur at any time throughout the hospital stay, but it seems to be most common between 2 and 31 hours after initiation of PCA therapy. The number of PCA-related deaths has been estimated at ~500 in the history of the use of this device (~22 million PCA uses). Although there is a low and unpredictable incidence of life-threatening opiate-induced respiratory depression even in the young and healthy, some patients are at greater risk. These include the elderly, patients with concurrent cardiorespiratory or CNS disorders, those with obstructive sleep apnea, those receiving sedatives (especially benzodiazepines), and those receiving supplemental oxygen. It is worth noting that after craniotomy most patients will have one or more of these risk factors: in the early postoperative period they will have CNS dysfunction and a decreased level of consciousness; their breathing will be affected (by the primary process, the surgery, or lingering anesthetic effects); and many will receive supplemental oxygen. Therefore, the postoperative craniotomy patient is at increased risk for PCA-related adverse events. To make matters worse, the most reliable clinical sign of significant respiratory depression—decreased level of consciousness—is often not a useful monitor in these patients.

Intravenous PCA safety concerns led the Anesthesia Patient Safety Foundation to convene a meeting on this topic. The primary recommendation resulting from this effort was that oxygenation and ventilation should be monitored continuously in high-risk patients receiving PCA. Pulse oximetry monitors oxygenation and is an effective method of detecting hypoventilation if the patient is breathing room air. However, if the patient is breathing supplemental oxygen, oxygenation may be preserved in the presence of opiate-induced hypoventilation, impending apnea, and carbon dioxide narcosis. Respiratory rate as a measure of ventilation has significant limitations as it may or may not decrease with respiratory depression, and significant hypercapnia can occur despite a normal respiratory rate. Continuous carbon dioxide monitoring, therefore, as a true measure of ventilation, appears to be the best approach. Two recent studies have evaluated the validity and sensitivity of transcutaneous carbon dioxide measurement devices in patients receiving PCA. Both of these studies demonstrated hypercapnia in patients receiving PCA morphine and supplemental oxygen.
Both showed these changes to occur in the presence of “normal” respiratory rates (> 10 bpm) and oxygen saturation (> 94%) values. Transcutaneous carbon dioxide measurements increased 13.5 and 10.5 mm Hg in the 2 studies. The device that recorded oxygen saturation and transcutaneous carbon dioxide in these studies successfully recorded data for 98% of the time it was applied to patients. A reliable process of linking the monitoring system to summon a competent health care professional to the patient’s bedside is critical. Newer, “smart” PCA pump devices that incorporate dose-checking technology can be linked directly to oxygen saturation and transcutaneous carbon dioxide monitoring.

As demonstrated by Morad et al., PCA offers much promise for the postoperative care of patients who have undergone craniotomy. However, we should realize that this is a population at increased risk for PCA-related opiate-induced respiratory depression, and in addition a population that will tolerate respiratory depression very poorly. Hence, we believe that this technology should not be used in these patients unless current recommendations for monitoring them are followed. It seems unwise to rely on intermittent assessment of respiratory rate in neurosurgical patients in the intensive care unit at the same time that this approach is being abandoned as insufficiently safe in routine postoperative patients. If PCA is to be used safely in the neurosurgical population, we should do it right from the start and continuously monitor oxygen saturation and carbon dioxide tension. In addition, a larger scale study (which could be observational) of postcraniotomy patients receiving PCA, powered to detect adverse events and using these current monitoring recommendations, should demonstrate safety before the approach can be recommended for general use.

Response

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We thank Drs. Vorenkamp and Durieux for providing a clinical context for our study and the editor of the Journal of Neurosurgery for the opportunity to respond to their editorial.

We agree with Drs. Vorenkamp and Durieux that the guiding principle of medical practice is to do no harm (primum non nocere). We also agree that it is incumbent on us as clinicians and investigators to recognize and safely treat pain. However, we disagree with the implication by Drs. Vorenkamp and Durieux that PCA use, per se, will lead to respiratory depression and is, therefore, unsafe. Opioids, regardless of their method of administration, can lead to respiratory depression in any patient population. These issues were highlighted at the Anesthesia Patient Safety Foundation Workshop on the dangers of postoperative opioids to which Drs. Vorenkamp and Durieux refer. One of the conclusions of this workshop was that the number of opioid-induced critical events could be reduced by enhanced respiratory monitoring for patients receiving perioperative opioids by any route, particularly for patients deemed to be at higher risk. The workshop also emphasized the benefits of multimodal analgesic regimens for reasons we elucidate further on.

As indicated by the data cited by Drs. Vorenkamp and Durieux and that in other studies, PCA opioid administration is quite safe and may, in fact, be considerably safer than other methods of parenteral opioid administration. When PCA opioid administration is compared with conventional opioid administration, it provides better analgesia, fewer pulmonary complications, and greater patient satisfaction. However, this impression of safety could lead to its inappropriate use. Morbid obesity, obstructive sleep apnea, concomitant use of drugs with a sedative effect, simultaneous use of continuous background opioid infusions in addition to bolus doses, and surrogate demand dosing (PCA by proxy) are of particular concern.

Several factors may confer additional safety with PCA use for patients undergoing major craniotomy. First, at least for the multimodal analgesic regimen used in our protocol, opioid use was modest. Second, because of the concern for preserving the neurological examination, sedative drugs are rarely administered perioperatively, although some anxiolytics such as promethazine (Phenergan), often administered to counter the nausea associated with posterior fossa surgery, can have a profound sedative effect. Third, patients undergoing intracranial surgery often recover from surgery in a setting with more frequent evaluation by skilled nurses and with continuous physiological monitoring, particularly pulse oximetry. Finally, in contrast to patients who have undergone other types of surgery, those who have under-

References