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Epidural Alfentanil: Is It Volume- or Concentration-dependent?

To the Editor:—I read with interest the article by Camu and Debucquoy¹ concerning alfentanil infusion for postoperative pain. However, the comparison of intravenous and epidural infusions is difficult, in that only the total dose delivered and not the alfentanil concentrations were mentioned. Because alfentanil is a very lipophilic agent, its effects in the epidural space would be highly volume-dependent. The effects of an $18\text{-}\mu\text{g}\cdot\text{kg}^{-1}\cdot\text{h}^{-1}$ infusion or a $10\text{-}\mu\text{g}/\text{kg}$ bolus would be vastly different depending upon the concentration of the infusate. This is what separates the overall effects of epidural infusion of the more highly lipophilic agents, such as alfentanil, fentanyl, and sufentanil, from the more hydrophilic agents, such as morphine. The results of any study concerning the epidural use of these highly lipophilic agents would be vastly different depending on whether the agent was given as a highly concentrated infusate or as a less concentrated infusate that would receptor-bind over a larger area. Perhaps if the concentration of the alfentanil infusion was cited, this study could be interpreted in a more realistic light.

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In Reply:—The letter by Camp refers to one of the fascinating aspects of epidural opioid analgesia, the relation among amount of drug, volume of diluent, and intensity of analgesia. In our study we used the commercially available drug form of alfentanil with a concentration of $0.5\text{ mg}\cdot\text{ml}^{-1}$. The loading dose ($15\text{ }\mu\text{g}\cdot\text{kg}^{-1}$) was administered in a total volume of 10 ml saline. During continuous infusion of alfentanil, the drug was not diluted. As such, the heaviest patient in this epidural group (74 kg) received $1.33\text{ mg}\cdot\text{h}^{-1}$ of alfentanil, or $2.66\text{ ml}\cdot\text{h}^{-1}$ of infusate volume. The concentrations and volumes of alfentanil given to the epidural and intravenous groups of patients were absolutely identical.

Previous reports indicate that a 10-ml volume of injectate provided significantly shorter onset time and longer duration of analgesia with epidural fentanyl.¹ Such data are at present not available for alfentanil, and their extrapolation to alfentanil may be unwarranted because of the different receptor binding kinetics of alfentanil. However, this volume of injectate is currently used in our department for any opioid given epidurally. The present data apply to concentrated infusates of alfentanil supplementing a high-volume low-concentration epidural injection of alfentanil. Camp suggests that less concentrated infusates would provide better analgesia because of the larger spread of the lipophilic opioids, thus allowing receptor binding over a larger area. We do not believe that the higher concentration of alfentanil (undiluted) given as continuous infusion affected the degree of analgesia obtained, because the visual analog scores between the epidural and intravenous groups were not different after 15 min until 20 h of infusion.

However, the design of our study does not allow the separation of volume- and concentration-related aspects of epidural opioid action. Whether the high-volume low-concentration theory applies to continuous infusion of epidural opioids remains undocumented. Once an-

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algia is established following an epidural loading dose, maintaining this analgesia appears to require only small doses of opioid in small volumes, as shown by epidural patient-controlled analgesia techniques. For example, epidural fentanyl boli of $15\text{ }\mu\text{g}$ (2 ml) delivered by patient-controlled analgesia were reported to provide effective analgesia with a total fentanyl dose one-third that needed by a continuous infusion regimen using diluted fentanyl ($10\text{ }\mu\text{g}\cdot\text{ml}^{-1}$ fentanyl, infusion rate $0.1\text{ ml}\cdot\text{kg}^{-1}\cdot\text{h}^{-1}$).² Thus, for maintaining analgesia the role of volume of injectate appears less relevant than the concentration of the epidurally given opioid.

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