HIGHLIGHTS

Plasma Concentration of Fentanyl, with 70% Nitrous Oxide, to Prevent Movement at Skin Incision

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BY defining the therapeutic plasma concentration of a drug, it becomes possible to design dosing schemes to achieve these target therapeutic levels and examine how altered physiologic states change this therapeutic plasma concentration requirement. To define therapeutic plasma concentrations for anesthetic drugs, it is frequently necessary to examine the relationship between defined clinical stimuli and equilibrated, steady-state plasma concentrations that allow or prevent clinical responses to the stimuli.

In this paper, Glass and colleagues (page 842) have defined that, in the presence of 70% nitrous oxide, the therapeutic plasma concentration of fentanyl (Cp50, or plasma concentration that has a 50% probability of no clinical response) for prevention of somatic movement to the noxious stimuli of skin incision is 3.26 ng/ml and that the Cp50 for the prevention of systemic increases of catecholamines from the skin incision is 4.17 ng/ml.

The investigators utilized a computer-driven infusion pump to achieve constant plasma fentanyl concentrations and then waited the appropriate period of time to allow the CNS to equilibrate. Fentanyl has a moderately long half time of plasma:CNS equilibration of 6–7 min. Translating the fentanyl Cp50 for prevention of purposeful movement into clinical context, fentanyl plasma concentrations of 15–20 ng/ml without nitrous oxide are required to prevent movement. Fentanyl plasma concentrations of 0.5–2 ng/ml are needed to provide adequate pain relief without excessive ventilatory depression. The data presented by Glass *et al.* in this paper provide us with new information on the intraoperative concentrations of fentanyl needed for adequate clinical anesthesia.

Intrathecal Sufentanil for Labor Analgesia: Effects of Added Epinephrine

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INTRASPINAL opioid administration offered the early promise of profound intrapartum analgesia without sympathectomy or motor blockade. Clinical studies soon noted problems with the intrathecal or epidural administration of opioids alone during labor. However, anesthesiologists have identified two applications of intraspinal opioid administration during labor. First, the combination of opioid with local anesthetic allows a reduction in the epidural dose of local anesthetic and provides effective analgesia with little motor blockade. Second, a combined spinal–epidural technique seems useful in some patients. With this technique, the anesthesiologist first injects a small dose of opioid intrathecally. At the same time, an epidural catheter is placed, and local anesthetic (with or without opioid) is injected epidurally when the intrathecal opioid analgesia subsides.

The latter technique has become more attractive with the availability of new spinal needles that result in a low incidence of postdural puncture headache. The combined spinal–epidural technique facilitates early involvement of the anesthesiologist in the obstetric patient's care. The side effects of systemic opioids are avoided, and the patient retains the ability to ambulate during early labor.

In this issue of ANESTHESIOLOGY, Camann *et al.* (page 870) assessed the effects of adding 0.2 mg epinephrine to 10 μg intrathecal sufentanil during labor. The addition of 0.2 mg epinephrine did not improve the quality or prolong the duration of intrathecal sufentanil

analgesia during labor. Epinephrine significantly increased the incidence of nausea, but it decreased both the incidence and severity of pruritus. The authors do not recommend the addition of epinephrine to sufentanil when providing analgesia during labor.

Although the results seem clear, questions remain. First, it is unclear whether the authors' conclusions apply to the addition of epinephrine to smaller doses of sufentanil. Is it possible that the addition of epinephrine to a smaller dose of sufentanil might result in analgesia of similar quality and duration to that observed in the present study, but with fewer side effects and less risk of respiratory depression? Second, what is the risk of respiratory depression in patients who deliver shortly after intrathecal administration of sufentanil? These patients are not subjected to the ongoing stimulus of painful labor, and they may not receive close surveillance. Third, the authors did not discuss technical problems. Surprisingly, it is not always possible to perform dural puncture successfully by introducing a spinal needle through the epidural needle. Fourth, it is unclear whether a combined spinal–epidural technique affects obstetric outcome (*e.g.*, progress of labor, method of delivery).