

the source of air because in each case the burr hole had been made some time before the detection of air in the right atrium. The burr hole as the source of air was considered after we were relatively certain that the source was not the suboccipital incision or the tumor mass. Other sources of air, such as the pin holes from the skeletal fixation device used to stabilize the head, could have been considered. In the first operation, the burr hole was considered a likely source when air entrainment stopped after the burr hole was closed. In the second operation, the burr hole was suspected when the bulk of the air entrainment stopped after closure of the burr hole, with only a small amount of air aspirated after the doppler sounds changed with surgical manipulation of the tumor bed. Jackson⁹ recently challenged the need for right atrial catheters by concluding that effective treatment can be instituted without such catheters. Our cases illustrate the value of the right atrial catheter for aspirating air. Since the source of air was not immediately identified and the quantity was large, the ability to aspirate the air from the right atrium may have prevented a catastrophe.

The entry of air from the burr holes may have been delayed because 1) the bone wax and wet saline cotton plug seal may have failed after a certain period of time, 2) opening the suboccipital area may have provided a bellows-like pump, allowing air entrainment from veins where previously there had been none, or 3) changing intracranial blood volume, cerebrospinal

fluid volume, and brain water volume may allow the brain to shift in a more caudad direction and, in the process, hold open the dural veins, which had previously been closed.

We believe these cases illustrate the need to suspect all of the potential sources of air, including burr holes performed for ventriculostomies. They also emphasize the value of a right atrial catheter for aspiration of air, which, in the case of the second patient, was therapeutic as well as diagnostic.

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Fentanyl-associated Delirium in Man

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Berryhill *et al.*¹ recently reported a case in which a patient experienced a dramatic stimulatory effect after the intravenous administration of morphine sulfate. We recently observed a patient who showed hyperexcitability after intravenous administration of fentanyl.

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REPORT OF A CASE

A 23-year-old, 65-kg man was scheduled for arthrodesis of the index finger of his left hand. Medical history included two previous orthopedic procedures for stabilization of this same digit, performed with local anesthesia. He was taking no medication and denied drug abuse. Preoperative laboratory data were normal.

The patient received no medication preoperatively. A digital nerve blockade was performed with lidocaine, 1 per cent. The patient appeared apprehensive, for which diazepam, 5 mg, iv, was given. Because this was ineffective, fentanyl, 0.1 mg, iv, was given. He then became increasingly agitated, and was unaffected by an additional dose of diazepam, 5 mg, iv. Because this agitation interfered with the operation, thiopental, 250 mg, iv, was given to induce general anesthesia, which was then maintained with nitrous oxide, 70 per cent, for the duration of the surgical procedure. The operation and anesthesia lasted 15 min and proceeded without further difficulty.

On recovery from anesthesia, the patient was confused and combative. He was quickly transferred to the recovery room, where six persons were needed to restrain him. Efforts to calm the patient by talking and by reassurance were totally ineffective. Physostigmine, 2.0 mg, iv, had no effect. Naloxone, 0.1 mg, iv, was given 5 min later, and within 30 sec he became markedly less restless. Several minutes later, although he still appeared confused, he was calm, conversant, and did not need restraint. Serum electrolytes and blood glucose values were normal.

The next day, the patient revealed that he had become combative and uncontrollable a year previously when undergoing a similar procedure on the same finger with local anesthesia. Review of that anesthetic record (from another hospital) indicated that his combativeness had seemed to follow the intravenous administration of Innovar® at the start of the surgical procedure.

DISCUSSION

Delirium following anesthesia, frequently a result of pre- or intraoperative cholinergic drug administration, can be treated with physostigmine. We gave physostigmine, 2.0 mg, iv, because of the possibility that physostigmine will reverse the sedative effect of diazepam.² When physostigmine had no effect, we administered naloxone, on the chance that the delirium had been induced by fentanyl and could be reversed by a narcotic antagonist. The transition from uncontrollable excitation to calm was almost immediate.

The mechanism responsible for hyperexcitability after morphine administration is uncertain. Berryhill

*et al.*¹ outlined the evidence from studies in animals and man to suggest three different possible mechanisms for morphine-induced hyperexcitability: 1) the response may be mediated via central dopaminergic pathways and would be blocked by a dopaminergic inhibitor such as a butyrophenone or a central nervous system catecholamine depletor such as reserpine; 2) endogenous opiate receptors may be involved, and naloxone would be expected to block the response; 3) morphine may have an effect on receptors not responsive to beta-endorphin and not blocked by specific opiate antagonists such as naloxone.

The second mechanism may have been important in the case of our patient, because his delirium was immediately reversed by naloxone. Although stimulation of dopaminergic pathways could have occurred, and would have been reversed by a specific dopaminergic antagonist, the history of a similar episode of delirium after receiving Innovar® suggests that droperidol had not been effective in blocking the response previously.

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Pharmacokinetics of High-dose Thiopental Used in Cerebral Resuscitation

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Administration of large doses of barbiturates has been utilized for various brain injuries: anoxic encephalopathy,¹ Reye's syndrome,² and head trauma.³ During initial clinical trials of large doses of thiopental,

we found an alteration in the kinetics of elimination. Thiopental elimination changed from first-order (rate of elimination and elimination half-life are constant regardless of plasma concentration) to nonlinear or Michaelis-Menten elimination (rate of elimination varies with the plasma concentration). This resulted in a decrease of the rate of elimination and an increase in the apparent elimination half-life as the plasma concentration increased.

METHOD

Five patients who sustained neurologic evidence of severe cerebral ischemia secondary to cardiac arrest or closed head injury were studied. The protocol has received approval of the Stanford Committee on Human Research, and informed consent was obtained from an available relative. Concurrent intensive

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