Clinical Workshop

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Failure to Produce Analgesia with Ketamine in Two Patients with Cortical Disease

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Ketamine has received much attention as the sole anesthetic for minor surgical procedures in children.1–3 Two cases describing the failure of recommended doses of ketamine to produce adequate analgesia have been reported recently.4,5 The cases reported here confirm this experience.

REPORT OF TWO CASES

Patient 1. A 5-day-old, 3-kg infant was brought to the operating room for revision of incision following removal of an intracranial teratoma. Normal in other respects, the infant had undergone craniectomy during uncomplicated halothane anesthesia on the third day of life. His head appeared slightly microcephalic, but he was without other obvious defects. Atropine, 0.15 mg, was given intramuscularly for premedication and induction was attempted with ketamine, 10 mg/kg, im. Adequate analgesia was not obtained. Even after five additional increments of ketamine, 1 mg/kg, given iv in a 15-minute period, the infant continued to phonate and make purposeful movements. To complete the procedure the infant was restrained and infiltrated with local anesthetic was used.

Patient 2. A 2½-year-old, 15-kg child was scheduled for open brain biopsy. After normal growth and development to the age of 1 year, she had developed ataxia and further central nervous system development had ceased. Skull x-rays, lumbar puncture and laboratory studies disclosed no abnormalities. Electroencephalographic study showed "sharp activity over the fronto-central region," and the pneumoencephalogram revealed cortical atrophy without evidence of a mass lesion. The presumptive diagnosis was diffuse cerebral degenerative disease.

Thirty minutes after premedication with atropine, 0.2 mg, im, induction of anesthesia was attempted with ketamine, 1 mg/kg, given iv. The child continued to respond vigorously to stimuli despite numerous increments of 1 mg/kg ketamine, iv. Preparation of the skin, after 37 minutes and a total of 90 mg of ketamine (6 mg/kg), was accompanied by marked agitation and purposeful motion. An additional 30 mg of ketamine iv, succinylcholine, 50 mg, iv (followed by 20 mg three minutes later), and xylcaine, 4 per cent, applied topically were administered to facilitate endotracheal intubation. An additional 39 mg of ketamine was given, iv; the child became quiescent and breathed spontaneously in a regular pattern without coughing or breath-holding. Xylcaine (10 ml of 0.25 per cent solution with 1:400,000 epinephrine) was injected into the scalp. The child responded vigorously to the injection and to the placement of a single marking suture. In the next 12 minutes, an additional 45 mg of ketamine was given. Incision of the skin resulted in marked agitation and purposeful motion. A total of 210 mg (14 mg/kg) of ketamine had been administered intravenously in 78 minutes without achievement of adequate analgesia despite local infiltration of the incision. Nitrous oxide (3.5 I/min) with oxygen (1.5 I/min) was then administered with a Mapleson D non-breathing system, and the operation was performed without incident.

Gross examination of the brain revealed atrophic convolutions and a thick "jello-like" arachnoid. The procedure lasted an hour, and the trachea was extubated before the patient was taken to the recovery room. After 75 minutes in the recovery room, the patient appeared to have recovered her preoperative level of central nervous system func-
tion, and she was discharged to the floor. Results of the brain biopsy showed diffuse astrocytosis with severe, widespread cortical nerve cell damage.

**DISCUSSION**

The dose of ketamine recommended for induction of anesthesia in infants and children is 1–2 mg/kg iv or 10 mg/kg im. This has proven successful for a number of clinical needs, including neurosurgical diagnostic procedures. The mechanism of action of ketamine is thought to involve blockade of afferent impulses in the diencephalon and associated areas of the cortex, with relative sparing of the brain-stem reticular formation. Ascending impulses are prevented from integration at a cortical level. The selective effect of ketamine on the neocortex, with delta-wave electroencephalographic activity elicited in the somatosensory and association areas along with theta-like activity in the frontal cortex, has led to its characterization as a dissociative anesthetic agent. Accordingly, it is reasonable to expect that analgesic potency may be related to cerebral function and development.

The failure of ketamine to produce analgesia in Drury's case of massive craniocerebral trauma was attributed to cerebral contusion that produced interruption of cortical function with alternation and/or derangement at the site of pharmacologic action. In the case described by Morgan, failure to achieve analgesia was attributed to microcephaly with absence of cerebral development. The two cases presented here resemble the two cases reported previously. The first case represents congenital absence of appropriate cerebral development and, therefore, is similar to Morgan's report. The second case represents acquired cerebral cortical derangement with cortical cell dysfunction, analogous to the acquired deficit in the case reported by Drury. Failure to achieve adequate analgesia was not reported in two series presenting results of ketamine anesthesia for pediatric diagnostic neuroradiology (a total of 301 anesthetics). Existing reports of the failure of ketamine to produce satisfactory operating conditions predominantly refer to unobtunded reflexes (often visceral pain) and muscular rigidity or non-purposeful motion, rather than to failure to provide analgesia. Recent evidence also shows that subdissociative doses of ketamine can supply analgesia when cortical function is intact. It is reasonable, therefore, to hypothesize that intact cortical function is necessary if analgesia is to be produced by ketamine. The addition of these two cases to those reported previously supplies evidence to support a hypothesis that, since the site of action of ketamine lies in the higher cortical areas, ketamine should not always be expected to produce adequate analgesia in patients with congenital or acquired cortical disease.

**REFERENCES**