

Clinical Workshop

S. G. HERSHEY, M.D., Editor

Ketamine-induced Apnea in Patients with Increased Intracranial Pressure

CHARLES H. LOCKHART, LCDR MC USNR, AND
JAMES J. JENKINS, LT MC USNR

Ketamine has been proposed as an anesthetic of unique usefulness for certain neurodiagnostic and therapeutic procedures, particularly in the pediatric age group.¹⁻³ We report two pediatric patients with evidence of increased intracranial pressure who developed apnea during induction of anesthesia with ketamine. In these same patients, when there were no signs of increased intracranial pressure, no respiratory depression was observed with the use of ketamine.

REPORT OF TWO CASES

Patient 1. A 7 pound, 8 ounce Caucasian female infant delivered by elective low forceps following a normal prenatal course had hydrocephalus and a meningocele at birth. The meningocele was repaired uneventfully during halothane anesthesia on the first day of life.

Signs of increased intracranial pressure (ICP), including increasing head circumference, irritability, poor feeding, and vomiting, developed postoperatively, necessitating ventricular taps and cerebrospinal fluid (CSF) removal for decompression of the seventh, eighth, tenth, eleventh, sixteenth and nineteenth days of life. On the twenty-first day the patient was brought to the operating room to have a ventriculo-peritoneal shunt placed. Premedication consisted of 0.1 mg of atropine given 45 minutes prior to induction. Rectal temperature was 99 F and pulse rate, 130/min. Ketamine, 50 mg im, was administered, and within three minutes spontaneous respirations decreased in frequency, then ceased. Bradycardia soon ensued. An endotracheal tube was placed and the patient ventilated with oxygen. Pulse rate, pulse volume, and ECG rhythm rapidly recovered to normal, and vital signs remained normal during the 60-minute operative procedure. One supplemental dose of 12.5 mg of ketamine was given im 30 minutes into the procedure because of movement. The patient was extubated

at the conclusion of the procedure after resumption of spontaneous respiration. Recovery from anesthesia and postoperative course were uneventful.

The patient returned to the hospital at the age of 11 months for elective lengthening of a heel cord. The ventriculo-peritoneal shunt was functioning well and no signs of increased ICP were present. Head circumference was stable. Weight was 9 pounds, 7 ounces. Premedication was atropine, 0.05 mg im. Rectal temperature was 96.6 F and pulse rate, 120/min at the time of induction of anesthesia with 45 mg of ketamine, im. No respiratory depression developed with this or subsequent supplementary doses.

Patient 2. The second patient, a 5-month-old female infant, was hydrocephalic at birth. Because of this anomaly, a ventriculo-peritoneal shunt was placed at the age of 9 days. She did well until 5 months of age, when erythema developed at the peritoneal end of the shunt. The shunt continued to function well despite obvious infection and there were no signs of increased ICP. At the time of operation for the placement of a new shunt she weighed 17 pounds. Premedication consisted of atropine, 0.1 mg im. Rectal temperature was 98.8 F and pulse rate, 140/min, at the time of induction with 100 mg of ketamine, im. This and three supplementary doses of 50 mg im at 15-minute intervals were well tolerated and no respiratory depression was encountered.

The new shunt functioned well for a week, then failed, with the patient becoming progressively more irritable, taking feedings poorly, and vomiting frequently after feeding. Head circumference increased more than 2 cm in a two-day period. Ventricular tap the day before corrective surgery drained 25 ml of fluid. Premedication consisted of 20 mg of pentobarbital and 0.1 mg of scopolamine. Pulse rate was 140/min and rectal temperature, 98.5 F, before induction of anesthesia with 75 mg of ketamine im. In the following minutes respiratory rate slowed and spontaneous ventilation ceased. Bradycardia and absent pulse soon followed. Intubation and controlled ventilation with oxygen promptly restored normal vital signs. Concentrations of halothane of less than 1 per cent were administered intermittently for

Received from the Department of Anesthesiology, Naval Hospital, Portsmouth, Virginia 23708.

maintenance of anesthesia during the 90-minute procedure. Thirty minutes passed after discontinuation of halothane before spontaneous ventilation was adequate to allow extubation. Subsequent postoperative recovery was unremarkable.

Ketamine affords excellent cardiovascular stability and maintenance of airway reflexes and adequate spontaneous ventilation, thus permitting rapid changes in body position and positioning of the head unencumbered by anesthetic apparatus. Particularly in pediatric patients, radiologic procedures such as pneumoencephalography, carotid arteriography, and cerebral ventriculography can be performed with favorable conditions for both radiologist and anesthesiologist. Similar benefits might be gained in neurosurgical procedures such as ventriculo-peritoneal or ventriculo-jugular shunts. Many of these patients, however, may have evidence of increased intracranial pressure. Severe, acutely increased ICP in infants may cause apnea.⁴ Ketamine has been shown to cause increased CSF pressure, and presumably ICP, in humans by Gardner *et al.*⁵ Dawson *et al.*,⁶ in work with animals, and Takeshita *et al.*,⁷ studying human subjects, have shown increased cerebral blood flow with ketamine, perhaps accounting for this increased ICP.

It is postulated that in the two cases presented, pre-existing symptomatic increased ICP coupled with the added effect of ketamine on ICP caused respiratory depression and apnea. This would seem to be corroborated by the ob-

ervation that both patients, when there was no evidence of symptomatic increased ICP, tolerated ketamine anesthesia without difficulty.

In selecting ketamine for certain procedures, clinicians should be alerted to its possible deleterious effect when used in the presence of increased ICP.

REFERENCES

1. Corssen G, Groves EH, Gomez S, et al: Ketamine, its place in anesthesia for neurosurgical diagnostic procedures. *Anesth Analg (Cleve)* 48:181-188, 1969
2. Wilson GH, Nicholas A, Fotias MO, et al: Ketamine, a new anesthetic for use in pediatric neurooentgenologic procedures. *Am J Roentgenol* 106:434-439, 1969
3. Tjaden RJ, Ethier R, Gilbert MB, et al: Use of Ketalar for pediatric pneumoencephalography. *J Can Assoc Radiol* 20:155-156, 1969
4. Clark DD: Increased Intracranial Pressure, Pediatrics. Ninth Edition. Edited by WE Nelson, VC Vaughan, RJ McKay. Philadelphia, W. B. Saunders, 1969, p 1283
5. Gardner AE, Olson BE, Lichtigen M: Cerebrospinal-fluid pressure during dissociative anesthesia with ketamine. *ANESTHESIOLOGY* 35: 226-228, 1971
6. Dawson B, Michenfelder JD, Theye RA: Effects of ketamine on canine cerebral blood flow and metabolism: Modification by prior administration of thiopental. *Anesth Analg (Cleve)* 50:443-447, 1971
7. Takeshita H, Okuda Y, Sari A: The effects of ketamine on cerebral circulation and metabolism in man. *ANESTHESIOLOGY* 36:69-75, 1972

Impurities in ¹⁴C-labeled Halothane

J. R. TRUDELL, Ph.D., E. WATSON, M.S., E. N. COHEN, M.D.

Analyses of commercially available ¹⁴C-halothane by combined radio gas chromatography-mass spectrometry occasionally have indicated the presence of significant amounts of impurities. On the other hand, a sample of labeled halothane (1-¹⁴C-2-bromo-2-chloro-1,1,1-trifluoroethane) recently purchased from a major manufacturer was supplied to us with the ra-

diocromatogram in figure 1, indicating radio-purity of more than 99 per cent.^{*} Subsequent metabolic studies with this ¹⁴C-halothane sample *in vivo* revealed compounds which were unlikely metabolites, but which were likely precursors or side-reaction products of halothane synthesis. Radio gas chromatography in our laboratory of the original batch of ¹⁴C-

Received from the Department of Anesthesia, School of Medicine, Stanford University, Palo Alto, California 94305. Supported by N.I.H. Program Project Grant GM-12527.

* Although the explanation for such chromatographic purity is not clear, it is possible that column temperatures and geometry were below maximal operating efficiency levels.