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KETAMINE ANAESTHESIA IN PATIENTS WITH INTRACRANIAL PATHOLOGY

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SUMMARY

Intravenous ketamine anaesthesia induced abrupt increases in intracranial pressure levels ranging from 25 to 82 mm Hg on nine occasions in five patients with abnormal cerebrospinal fluid flow dynamics and/or other intracranial pathology. The mean gain in intracranial pressure in patients with cerebral abnormalities was 41.5 (SD 16.6) mm Hg. This is compared with a ketamine-induced mean pressure increase of 19.4 (SD 6.9) mm Hg found by other investigators in a group of neurologically normal patients. Intravenous injection of thiopentone may terminate intracranial pressure elevations caused by ketamine.

Recently we reported an intracranial pressure (ICP) increase to 75 mm Hg secondary to ketamine injection in a patient with high ICP due to cerebrospinal fluid (c.s.f.) obstruction (Wyte et al., 1972) and other investigators have noted ICP increases to 62 mm Hg in neurosurgical patients (List et al., 1972). Fitch and McDowall (1971) have shown in dogs that c.s.f. pressure elevations of this magnitude can be generated by halothane and may be associated with intracranial pressure gradients producing brain impaction at the tentorium. Ketamine (Dawson, Michenfelder and Theye, 1971; Takeshita, Okuda and Sari, 1972) resembles halothane (McDowall, 1969) in its ability to increase cerebral blood flow. For these reasons the following investigation on the effects of ketamine on intracranial tension was performed in a situation in which we were capable of terminating excessive rises in intracranial pressure.

MATERIALS AND METHODS

The response of intracranial pressure to ketamine anaesthesia was measured on eleven occasions in seven patients in the supine position. These studies were performed during neurodiagnostic procedures or anaesthetic induction prior to an operation. The intracranial pressure was measured in a lateral cerebral ventricle by a Statham transducer connected either to a ventriculostomy catheter or to a 19-gauge scalp vein needle inserted into the dome of a valveless ventriculo-atrial c.s.f. shunting device. The deadspace in both catheters was filled with saline and no c.s.f. was lost during establishment of the external drainage system. Ventriculostomy catheters were inserted under local anaesthesia, except in one child (Patient 3) who required a short halothane-nitrous oxide general anaesthetic for catheter insertion prior to ventriculography. This patient was communicative before ketamine induction. In some patients the ventriculostomy catheters were placed prior to the day of study. These were clamped 60–90 min before induction of anaesthesia to permit cannulation of the ventricle with a new shunting device. Arterial blood pressure was measured with a brachial cuff or an indwelling radial artery catheter and the respiration rate was counted. In one patient arterial blood gases were measured before induction and during the peak intracranial pressure response.

Anaesthesia was induced with ketamine (2 mg/kg i.v. or 4 mg/kg i.m.). Patients 1 and 2 had functional internal c.s.f. shunts and no clinical evidence of increased ICP prior to induction. Patients 3–7 required external c.s.f. drainage for management of raised ICP. Patient 3 was studied on three occasions, and Patient 4 received a second i.m. injection of ketamine for maintenance of anaesthesia during ventriculography.

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RESULTS

Table I summarizes the intracranial pressure, blood pressure, and respiratory rate changes observed in our seven patients. Patients 1 and 2 had normally functioning c.s.f. shunts and intracranial pressures below 10 mm Hg (normal ICP is less than 10 mm Hg; Lundberg, 1960), and in these two patients ketamine administration was followed by a small rise in pressure. Patients 3–7, with abnormal c.s.f. flow dynamics, had augmented ICP responses to ketamine. In all patients intravenous ketamine caused a peak pressure response in 2–5 min, and this response was slightly delayed when the intramuscular route was employed.

A typical intracranial pressure response to ketamine in a patient with abnormal c.s.f. flow dynamics is shown in figure 1. After ketamine 2 mg/kg and following loss of consciousness, the ICP rose from a mean of 13 to 63 mm Hg; the blood pressure increased by a mean of 5 mm Hg, and the respiratory rate decreased by 8 b.p.m. Thiopentone, given just before the peak of the ICP response, was followed by a rapid reduction in the intracranial tension to 11 mm Hg with no change in the systemic blood pressure. Also, as indicated in figure 1, manual hyperventilation with an anaesthesia bag and facepiece reduced ketamine-induced intracranial hypertension. The final ICP peak in figure 1 was associated with tracheal intubation and subsequent administration of halothane anaesthesia. This ICP increase was of the same magnitude as that induced by ketamine earlier in this patient.

Intravenous injection of thiopentone can reverse ketamine-induced intracranial hypertension (fig. 1). This action of thiopentone is rapid, usually requiring less than 1 min to reduce the ICP to near pre-

TABLE I. *Mean intracranial pressure (ICP), blood pressure (BP) and respiratory rates (R) before and after ketamine anaesthesia.*

	Pre-ketamine			Post-ketamine			Change			
Pt.	ICP (mm Hg)	BP (mm Hg)	R (b.p.m.)	ICP (mm Hg)	BP (mm Hg)	R (b.p.m.)	ΔICP (mm Hg)	ΔBP (mm Hg)	ΔR (b.p.m.)	CPP (mm Hg)
1	2	90*	12	7	90	6	+ 5	0	− 6	83
2	3	110	8	4	125	14	+ 1	+ 8	+ 6	121
3a	22	90	12	72	112	15	+50	+22	+ 3	40
b	13	110	20	63	115	12	+50	+ 5	− 8	52
c	10	95	16	43	100	20	+33	+ 5	+ 4	57
4a	16†	—	—	46	—	—	+30	—	—	—
b	10	—	13	70	—	32	+60	—	+19	—
c	30	—	20	82‡	—	17	+52	—	− 3	—
5	15	76	15	75	40	17	+60	+14	+ 2	15
6	13	75	21	25	75	24	+12	0	+ 3	50
7	21	102	20	48	115	30	+27	+13	+10§	67

Patients 1 and 2 had functional ventriculo-atrial c.s.f. shunts and no signs of increased ICP. Patients 3 through 7 had acute shunt obstruction or required an external ventriculostomy to prevent a high ICP. The change in the above variables is noted in the third column and cerebral perfusion pressures (CPP = mean BP minus the ICP) during the peak in ICP after ketamine are shown in the last column to the right.

* Systolic † Lumbar puncture (supine) ‡ Repeat i.m. dose

§ Arterial P_{CO_2}; pre- 37.5 mm Hg; post- 33.5 mm Hg; P_{O_2} > 100 mm Hg

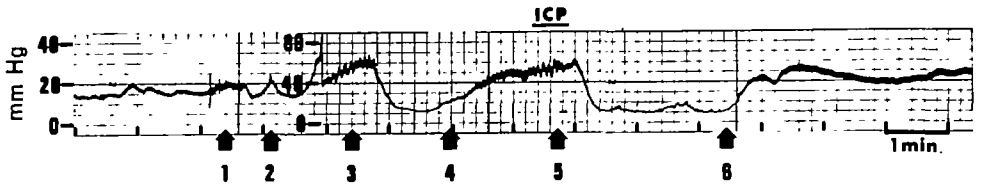

FIG. 1. Intracranial pressure (ICP) changes following intravenous injection of ketamine and subsequent administration of halothane anaesthesia. Numbered arrows indicate events as follows: (1) ketamine i.v., BP 140/80 mm Hg, resp. 20 b.p.m.; (2) sigh, then unresponsive; (3) thiopentone 100 mg, BP 130/100 mm Hg; (4) BP 140/90 mm Hg, resp. 12 b.p.m.; (5) controlled hyperventilation with 100% oxygen; (6) tracheal intubation preceded by suxamethonium 80 mg and followed by 1.5% halothane and 50% nitrous oxide in oxygen. Pressures are in mm Hg and the time scale marked in minutes. Note scale change between arrows 2 and 3.

induction levels. However, ICP reduction with thiopentone is transient and subsequent hyperventilation may be required to maintain the reduced ICP. Table II shows the effect of thiopentone in reducing the intracranial pressure rise caused by ketamine. Thiopentone 100 mg was given four times to our patients, and in these instances the ICP decreased on average by 51 mm Hg and the mean blood pressure by 5 mm Hg, with little change in respiration rate. In the absence of a subsequent dose of thiopentone, the pressure elevation caused by ketamine gradually dissipates to preanaesthetic levels over 15–20 min, at which time the patient becomes responsive.

TABLE II. *Change in the mean ICP and BP and R due to administration of thiopentone 100 mg given at the peak ICP due to ketamine.*

Patient	ΔICP (mm Hg)	ΔBP (mm Hg)	ΔR (b.p.m.)
3*	−57	0	+1
3*	−64	−12	0
5	−65	− 4	0
7	−18	− 5	0

The arterial P_{CO_2} in Patient 7 was 36 mm Hg after thiopentone. Abbreviations as in table I.

* Patient 3 was studied on two separate occasions.

Arterial blood-gas analysis in patient 7 revealed a preinduction Pco_2 of 37.5 mm Hg and a slight decrease to 33.5 mm Hg during a peak ICP of 27 mm Hg. The arterial Po_2 remained above 100 mm Hg during the entire anaesthetic course.

DISCUSSION

Within 5 min of intravenous administration ketamine causes a 62% (Takeshita et al., 1972) to 80% (Dawson, Michenfelder and Theye, 1971) increase in cerebral blood flow which returns to normal ranges within 20 min. The pattern and time course of the c.s.f. pressure changes in our patients and those of other observers parallels these cerebral blood flow alterations (Gardner, Olson and Lichtiger, 1971; List et al., 1972). The acute and reversible ICP changes in patients given ketamine are probably directly related to changes in cerebral blood flow and associated alterations in intracranial blood volume (Risberg, Lundberg and Ingvar, 1969). Jennett and his co-workers (1969) noted similar increases in ICP associated with the administration of certain volatile anaesthetic agents.

Hypoxia and hypercarbia can also lead to reversible increases in ICP, and since no attempt was made to control ventilation in our study this remains a possible source for the ICP rise in our patients. We noted an increase in ICP after ketamine without changes in arterial Po_2 or Pco_2 in the one patient in whom blood gases were measured. List and associates (1972), in work performed concurrently with ours, noted similar ICP increases in several patients without alteration in blood-gas status. Wilson, Fotias and Dillon (1969) found no significant changes in Pa_{CO_2} or Pa_{O_2} in an extensive study of neurologically abnormal patients given ketamine for neurodiagnostic procedures. Increases in cerebral venous pressure probably did not occur since no signs of increased central venous pressure such as distended neck veins or facial congestion were noted and jugular venous obstruction was carefully avoided. The increase in ICP after ketamine was much greater than the rise in systemic arterial pressures, further suggesting a primary intracranial cause for the acutely elevated intracranial tension.

In the absence of lesions obstructing the subarachnoid space, c.s.f. pressures are freely transmitted throughout the craniospinal axis (Langfitt, 1968). This permits a comparison of c.s.f. pressures measured by Gardner, Olsen and Lichtiger (1971) in the lumbar subarachnoid space of normal volunteers with the intraventricular pressures obtained in our study. The different ICP response between patients with normal and abnormal c.s.f. pathways given ketamine is shown in figure 2. A similar differential response exists between patients with and without intracranial space-occupying lesions given certain volatile anaesthetic agents (Jennett et al., 1969). It has been suggested that ICP pressure changes related to cerebral oedema, tumour mass or increases in brain blood volume may be attenuated by displacement of c.s.f. from within the relatively closed cranial cavity into the more distensible spinal subarachnoid space (Langfitt, 1968). Variable loss of this ICP buffering mechanism could explain the differential ICP response to ketamine between neurologically normal patients (Gardner, Olson and Lightiger, 1971) and our patients with intracranial lesions. Also, abnormal cerebrovascular responses to ketamine cannot be excluded.

Apart from the marked difference in the mean net rise between the groups ("normals" 19.4 ± 6.9 mm Hg, abnormals 41.5 ± 16.6 mm Hg [SD]), figure 2 reveals a tendency toward a greater scatter in the preanaesthetic intracranial pressures in the abnormal patients. Additionally, the figure demonstrates that some "abnormals" with the lowest

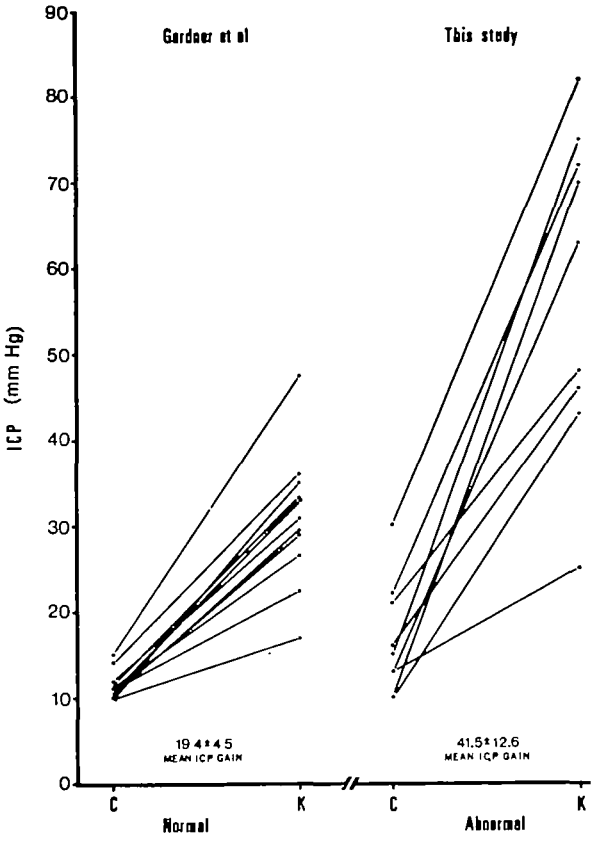

FIG. 2. Comparison of control (C) and post-ketamine (K) intracranial pressures (ICP) in a group of normal patients (data from lumbar c.s.f. pressure measurements of Gardner, Olson and Lichtiger, (1971)) with a group of patients in this study with intracranial pathology. The mean ICP gain for each group with its 95% confidence limits is indicated below the graphed pressure responses. Pressure is in mm Hg. (Data from Gardner, Olson and Lichtiger reproduced by permission of authors and the editor of *Anesthesiology*.)

initial intracranial pressure levels developed the greatest increases after ketamine. The scatter in their initial pressures as well as the net ICP gain may be explained by a variable state of intracranial spatial compensation, as discussed above. In patients 1 and 2, with functioning surgically placed ventriculo-atrial c.s.f. shunts, the pressure increase was approximately 15 mm Hg less than that found by Gardner, Olsen and Lichtiger in the lumbar c.s.f. space in volunteers given ketamine. A functional c.s.f. shunt may possibly provide a lower resistance conduit for c.s.f. egress and ICP dissipation than exists in the normal subarachnoid space.

Most general anaesthetics depress cerebral metabolic rates and may thereby offer some protection to the brain during ischaemic-hypoxic episodes, although the latter effect remains controversial. No evidence for a reduction in cerebral metabolic rate was found in recent studies in dogs (CMR increased) (Dawson, Michenfelder and Theye, 1971) or in humans (CMR unchanged) (Takeshita, Okuda and Sari, 1972) during ketamine anaesthesia and normocarbia. As demonstrated in our study, ketamine can reduce cerebral perfusion pressure (CPP) below the critical cerebral blood flow autoregulatory limit of 60 to 30 mm Hg (Langfitt, 1969; Heilbrun, Balslev and Boysen, 1972). CPP reductions of this magnitude due to increased ICP have been associated with biochemical evidence of cerebral hypoxia (Zwetnow, 1970). Therefore, intracranial hypertension caused by ketamine may potentially be more hazardous metabolically than increased ICP due to volatile anaesthetic agents which decrease oxygen uptake.

Thiopentone decreases cerebral blood flow and metabolism in man (Pierce et al., 1962). Pretreatment with thiopentone blocked both the cerebral blood flow and metabolic responses to ketamine in dogs (Dawson, Michenfelder and Theye, 1971). After ketamine caused an abrupt gain in ICP in our patients, the administration of thiopentone (100–200 mg) led to a rapid and marked reduction in intracranial tension. A similar response to thiopentone has been observed in patients given halothane (Shapiro, Wyte and Galindo, unpublished observations). The duration of the thiopentone-induced decrease in ICP is transient, lasting only 1–2 min. The effect of thiopentone in reversing intracranial hypertension caused by ketamine is presumptive evidence for the existence of a thiopentone-ketamine antagonism in the cerebral circulation of man.

Repetition of a dose of ketamine in dogs, 1 hour after an initial dose, induced changes in cerebral blood flow and metabolism of a magnitude similar to that observed after the first dose (Dawson, Michenfelder and Theye, 1971). This suggests that recurrent episodes of intracranial hypertension related to maintenance doses of ketamine can occur. In our study a repeat intramuscular dose, approximately 25 min after an induction dose in Patient 4, was associated with a second ICP elevation to over 70 mm Hg. At the time ventriculography was being performed, however, the ICP just prior to the second ketamine dose was near control levels. By contrast, maintenance of halothane anaesthesia is associated with a slow decline in ICP (McDowall, 1969).

We feel that the risk of acute and perhaps repetitive episodes of intracranial hypertension

associated with the induction and maintenance of ketamine anaesthesia is high in patients with intracranial pathology. Clinically this situation may be manifest not only in neurological patients but also in recently traumatized children with possible head injuries undergoing minor orthopaedic procedures with ketamine as the anaesthetic. List and coworkers (1972) feel that monitoring of ICP through an external ventriculostomy provides the conditions necessary for the safe conduct of ketamine anaesthesia in neurosurgical patients since c.s.f. may be withdrawn to control intracranial pressure. We caution that expansion of the brain during ketamine may collapse the ventricles and interfere with effective removal of cerebrospinal fluid. Further, external ventriculostomy catheters in our experience are quite liable to become occluded with debris suspended in the cerebrospinal fluid. When fluid removal for control of increased intracranial pressure caused by ketamine is not possible, thiopentone may be given to provide rapid, although transient, reduction of intracranial hypertension.

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ANESTHESIE A LA KETAMINE CHEZ DES PATIENTS AVEC PATHOLOGIE INTRACRANIENNE

SOMMAIRE

L'anesthésie intraveineuse à la kétamine causa des augmentations subites des taux de pression intracranienne de 25 à 82 mm Hg à neuf reprises chez cinq patients avec dynamique anormale du flux du liquide céphalorachidien et/ou autre pathologie intracranienne. L'augmentation moyenne de la pression intracranienne chez les patients avec des anomalies cérébrales était de 41,5 (SD 16,6) mm Hg. Ceci est comparé avec l'augmentation moyenne de la pression de 19,4 (SD 6,9) mm Hg, suscitée par kétamine, que d'autres auteurs ont observée dans un groupe de patients neurologiquement normaux. L'injection intraveineuse de thiopentone peut arrêter l'élévation de la pression intracranienne causée par kétamine.

KETAMIN-NARKOSE BEI PATIENTEN MIT INTRACRANIELLEN PROZESSEN

ZUSAMMENFASSUNG

Die intravenöse Ketaminnarkose führte bei 5 Patienten mit abnormen Liquorabflussverhältnissen und/oder intracraniellen Prozessen insgesamt neun mal zu einem intracraniellen Druckanstieg mit Werten zwischen 25 und 88 mm Hg. Der mittlere intracranielle Druckanstieg betrug bei Patienten mit cerebralen Anomalien 41,5 (SD 16.6) mm Hg. Diese Befunde werden verglichen mit einem durch Ketamin ausgelösten mittleren Druckanstieg von 19,4 (SD 6.9) mm Hg, wie er von anderen Untersuchern bei neurologisch unauffälligen Patienten gefunden worden ist. Durch intravenöse Gaben von Thiopentone können die durch Ketamin verursachten intracraniellen Druckanstiege beendet werden.

ANESTESIA POR CETAMINA EN PACIENTES CON LESIONES INTRACRANEALES

RESUMEN

La anestesia intravenosa por cetamina indujo incrementos súbitos en la presión intracraneal de 25 hasta 82 mm Hg en nueve ocasiones en cinco pacientes con una dinámica anormal del flujo del líquido cefalorraquídeo y/u otras lesiones intracraneales. El aumento medio en la presión intracraneal en pacientes con anormalidades cerebrales fue de 41,5 (SD 16,6) mm Hg. Esto es comparado con el incremento medio de la presión de 19,4 mm Hg (SD 6,9) inducido por cetamina que fue encontrado por otros investigadores en un grupo de pacientes neurológicamente normales. La inyección intravenosa de tiopentona pudiera terminar las elevaciones de la presión intracraneal causadas por cetamina.