

## Blood-pressure and Pulse-rate Responses to Ketamine during General Anesthesia

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Because of its speed of onset and cardiovascular stimulating properties, ketamine has gained popularity as an induction agent.<sup>1</sup> For these reasons it has also been used as a supplement to inhalation anesthesia. However, while ketamine has been shown to increase pulse rate, arterial blood pressure, and cardiac output in unanesthetized patients,<sup>2-4</sup> its effects on cardiovascular functions during general anesthesia have not been evaluated. This study was conducted to determine the effects of a single intravenous dose of ketamine on blood pressure and pulse rate during general inhalation anesthesia in man.

### METHODS

Subjects of the study were 120 patients, A.S.A. Class I or II (ages 13-72 years), scheduled for a variety of elective intra-abdominal operations. All patients were premedicated with atropine (0.05-0.1 mg/kg) and diazepam (1 mg/10 kg). The patients were arbitrarily divided into three groups of 40 each, depending upon the anesthetic management. In Groups I and II anesthesia was induced with sodium thiopental (3-5 mg/kg), followed by succinylcholine (1.5 mg/kg) to facilitate tracheal intubation. In Group I, anesthesia was maintained with halothane (0.5-1.5 per cent) and nitrous oxide (60 per cent), and in Group II, with nitrous oxide (60 per cent) and Innovar (4-14 ml, iv), or morphine (15-40 mg). Both groups of patients were paralyzed with *d*-tubocurarine (12-36 mg) after induction and anesthesia was maintained with a semiclosed circle absorption system using 5 l/min of fresh gases. Respiration was controlled at volumes of 8-12 ml/kg and rates of 10-16 breaths/min with a volume-limited

ventilator to maintain PaCO<sub>2</sub> values between 35 and 40 torr as determined from radial-artery blood samples obtained at 15-minute intervals. The patients in Group III were not anesthetized, paralyzed, or intubated, and served as controls.

Systolic and diastolic blood pressures were directly recorded from percutaneously implanted radial-artery catheters or auscultated indirectly via standard Riva Rocci blood pressure cuffs. Apical pulse rates were obtained from esophageal or chest-wall stethoscopes. Control, pre-ketamine, pulse rate and systolic and diastolic blood pressure values were recorded after Group III patients had been placed on the operating room table and in Groups I and II after the abdominal peritoneal cavity was opened, when the surgical stimulus was stable. Two mg/kg of ketamine were then rapidly given intravenously. Blood pressures and pulse rates were measured every minute for the next 10 minutes and the mean changes during this interval were calculated and recorded.

### RESULTS

Pre-ketamine systolic and diastolic blood pressures and pulse rates were similar in the three groups (table I). Ketamine resulted in mean systolic and diastolic blood pressures that were significantly decreased in Group I ( $P < .01$ ), increased in group III ( $P < .001$ ) and unchanged in Group II. The changes in blood pressures in Groups I and III were usually present within 3 minutes of ketamine administration. In Group I blood pressures were maximally decreased between the fourth and seventh minutes and almost always back to normal by the tenth minute. Group III patients had elevations in blood pressures that were maximal by the second minute and remained elevated throughout the period of observation. Mean pulse rate was significantly increased in Group III ( $P < .001$ ) but not significantly changed in Groups I and II.

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TABLE 1. Mean Blood Pressures and Pulse Rates before and after Ketamine

	Systolic Blood Pressure (mm Hg)		Diastolic Blood Pressure (mm Hg)		Pulse Rate (Beats/Min)	
	Initial	After Ketamine	Initial	After Ketamine	Initial	After Ketamine
Group I	112	99†	71	64‡	88	82
Group II	113	116	72	77	91	89
Group III	106	141*	74	98*	86	107*

\*  $P < .001$ , Student's *t* test.

†  $P < .01$ , Student's *t* test.

### DISCUSSION

Dowdy and Kaya<sup>5</sup> and Traber *et al.*<sup>6</sup> have reported that ketamine has significant direct negative inotropic effects on the heart. Traber *et al.*<sup>7-9</sup> demonstrated that the hypertension and tachycardia from ketamine could be completely blocked by epidural anesthesia, ganglionic blockade with hexamethonium, or a combination of vagal and alpha-adrenergic blockade with atropine and phentolamine. On the basis of these findings, Traber suggested that the cardiovascular stimulating properties of ketamine are primarily the result of central sympathetic stimulation and parasympathetic inhibition. Chodoff<sup>10</sup> came to the same conclusion after showing that ketamine was without effects on pulse rate and central venous and arterial blood pressures in a patient with complete interruption of his spinal cord at C 7-8 and a pharmacologic vagotomy.

Our findings in this study are consistent with those of the above authors. They demonstrate that general anesthetics also inhibit the pressor response and positive chronotropic effects of ketamine and imply that the autonomic stimulating properties of ketamine depend upon an intact, nondepressed central nervous system. Furthermore, they indicate that the administration of ketamine during anesthesia with agents that are sympatholytic, *e.g.*, halothane, uncovers the direct negative inotropic effects of ketamine and can result in significant hypotension. On occasion this hypotension is severe enough (> 40 mm Hg) to necessitate the use of a vasopressor. Finally,

our results suggest that when used as a supplement during general anesthesia, ketamine should be administered with the same caution as any potent anesthetic with myocardial depressant properties.

### REFERENCES

- McDonald JS, Mateo CV, Reed EC: Modified nitrous oxide or ketamine hydrochloride for cesarean section. *Anesth Analg (Cleve)* 51: 975-983, 1972
- McCarthy DA, Chen G, Kaump DH, et al: General anesthetic and other pharmacological properties of 2-(0-chlorophenyl)-2-methylamino cyclohexanone HCl (CI-581). *J New Drugs* 5:21-33, 1965
- Virtue RW, Alanix JM, Mori M, et al: An anesthetic agent: 2-ortho-chlorophenyl-2-methylamino cyclohexanone HCl (CI-581). *ANESTHESIOLOGY* 28:823-833, 1967
- Tweed WA, Minuck M, Myrmin D: Circulatory responses to ketamine anesthesia. *ANESTHESIOLOGY* 37:613-619, 1972
- Dowdy EG, Kaya K: Studies of the mechanism of cardiovascular response to CI-581. *ANESTHESIOLOGY* 29:931-943, 1968
- Traber DL, Wilson RD, Priano LL: Differentiation of the cardiovascular effects of CI-581. *Anesth Analg (Cleve)* 47:769-777, 1968
- Traber DL, Wilson RD: Involvement of the sympathetic nervous system in the pressor response to ketamine. *Anesth Analg (Cleve)* 48:248-252, 1969
- Traber DL, Wilson RD, Priano LL: Blockade of the hypertensive response to ketamine. *Anesth Analg (Cleve)* 49:420-426, 1970
- Traber DL, Wilson RD, Priano LL: The effect of alpha-adrenergic blockade on the cardiopulmonary response to ketamine. *Anesth Analg (Cleve)* 50:737-742, 1971
- Chodoff P: Evidence for central adrenergic action of ketamine. *Anesth Analg (Cleve)* 51:247-250, 1972