Arterial Hypoxemia Caused by Intravenous Ketamine

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Ketamine given IV in a dose of 2 mg/kg caused a significant reduction in Pa_{O_2} in 7 patients spontaneously breathing with an unassisted airway. Under the same conditions, in 7 patients, ketamine (2 mg/kg IV) preceded by diazepam (0.2 mg/kg IV) also caused a reduction in Pa_{O_2} not significantly different from that caused by ketamine. In some patients, alarmingly low levels of Pa_{O_2} ($\leq$ 40 torr) were seen following ketamine administration. Based on these findings, the authors recommend that O_2 and ventilatory assistance accompany ketamine given IV for anesthesia.

SINCE its introduction into clinical anesthesia,[1,2] ketamine has geen given IV for induction and maintenance of general anesthesia without respiratory assistance and O_2 administration, in the belief that it causes neither respiratory depression nor airway obstruction from jaw relaxation.[3-5] Ketamine was even recommended as an anesthetic induction agent for patients with bronchial asthma.[6] However, no blood-gas studies or determinations of the response to CO_2 inhalation were reported to substantiate these claims.

The present study was therefore undertaken to evaluate arterial blood gases after ketamine administration.

MATERIALS AND METHODS

Patient Material.—Fourteen adult gynecology patients (ASA physical states I-II) were selected for the study. Patients gave informed consent to arterial catheterization and blood sampling. No patients were receiving any medications at the time of the study and none was pregnant. No significant differences in age, weight, or other physical characteristics were observed between the 2 groups studied. Group I (N=7) received 2 mg/kg of ketamine IV over 30 seconds; group II was given the same dose of ketamine preceded by 0.2 mg/kg of IV diazepam.

Experimental Method.—All patients received routine preoperative medication consisting of 0.15 mg/kg of diazepam and 0.007 mg/kg of atropine IM, combined with either 1.5 mg/kg of meperidine (N=4) or 0.15 mg/kg of morphine (N=8). One patient received 0.75 mg/kg of promethazine HCl with 0.75 mg/kg of meperidine and 0.008 mg/kg of atropine IM, and another patient, 0.036 mg/kg of droperidol with 0.7 μg/kg of fentanyl and 0.007 mg/kg of atropine IM.

On the patient's admission to the anesthesia study unit, a 16-gauge Teflon catheter was inserted into an antecubital vein

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and 5% dextrose in 0.2% NaCl solution was started to keep the IV path open for drug injections. A 20-gauge Riley needle was inserted into the contralateral brachial artery, and a 20-minute rest period was allowed before the baseline sampling for blood gases. In the ketamine group, 2 mg/kg of ketamine was injected IV in 50 ml IV solution over 30 seconds, and blood-gas samples were taken before and at 2, 5, and 10 minutes after injection.

In the diazepam-ketamine group, first diazepam (0.2 mg/kg) was given in 30 ml of IV fluid over 30 seconds and, after 5 minutes, 2 mg/kg of ketamine was given over 30 seconds with 50 ml of IV solution. Blood-gas samples were obtained before diazepam and at 2, 5, and 10 minutes after ketamine administration. No airway support, ventilation, or O_2 were given, with the exception of 1 patient of the ketamine group who became cyanotic after the 2-minute sample was taken.

Positional changes, skin disinfection, and stimulation were avoided during the study. No additional doses of ketamine or any other IV or inhalational anesthetic agents were given, even if the patient fully awakened from sleep during the 10-minute period after ketamine administration. Additional doses of ketamine or thiamylal and muscle relaxants for endotracheal intubation were used only after the completion of blood sampling.

Laboratory Analysis.—All heparinized blood samples were immediately studied by the Radiometer Copenhagen Astrup Blood Gas Analyzer for Pao_2, $Paco_2$, and pH. Duplicate determinations were carried out on samples with a low Pao_2 by a similar analyzer, and the low Pao_2 values were found to be accurate within 5%.

Monitoring.—ECG, pulse, and blood pressure were continuously monitored throughout the study. With the exception of 1 patient in the ketamine group, chest plethysmographic recordings were also continuously taken.

RESULTS

A significant reduction in the mean Pao_2 ($p<0.01$) and elevation in the mean $Paco_2$ ($p<0.01$) occurred 2 minutes after ketamine injection (table 1). Arterial hypoxemia persisted throughout the study, and both Pao_2 and $Paco_2$ remained abnormal

TABLE 1

Blood-Gas Changes in Patients Induced with Ketamine and Diazepam-Ketamine Combination

Patient groups	N	Before drug administration			After drug administration								
					2 minutes			5 minutes			10 minutes		
		pH, units	Pao_2, torr	$Paco_2$, torr	pH, units	Pao_2, torr	$Paco_2$, torr	pH, units	Pao_2, torr	$Paco_2$, torr	pH, units	Pao_2, torr	$Paco_2$, torr
Ketamine 2 mg/kg IV	7	7.40 ±0.02*	84.0 ±3.4	34.0 ±1.5	7.37 ±0.02	58.0† ±6.5	38.0† ±1.1	7.37 ±0.02	67.2‡ ±5.1	39.0† ±1.3	7.36 ±0.02	74.8‡ ±3.8	38.4‡ ±1.6
Ranges of values		(7.35-7.5)	(72-96)	(25-37)	(7.32-7.44)	(35-84)	(35-43)	(7.32-7.44)	(45-76)	(33-43)	(7.32-7.47)	(65-92)	(33-46)
Diazepam 0.2 mg/kg and ketamine 2 mg/kg IV	7	7.38 ±0.01	74.4 ±7.0	37.0 ±1.7	7.34 ±0.01	46.6† ±3.8	43.7‡ ±1.2	7.34 ±0.02	55.0‡ ±3.0	43.3† ±1.6	7.35 ±0.02	65.5‡ ±4.0	42.2‡ ±1.0
Ranges of values		(7.35-7.44)	(57-102)	(34-46)	(7.3-7.4)	(31-59)	(40-47)	(7.3-7.43)	(46-71)	(37-48)	(7.3-7.42)	(54-85)	(39-47)

*Standard error of the mean.

†Significant change from baseline values at $p<0.01$.

‡Significant change from baseline values at $p<0.05$.

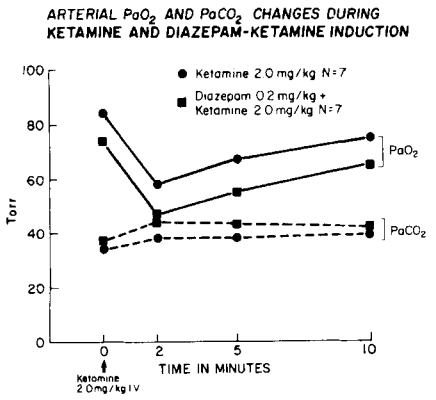

FIG. 1. Pao_2 and $Paco_2$ changes after ketamine and diazepam-ketamine administration.

even at 10 minutes after ketamine administration (fig 1). The changes from baseline values in mean Pao_2 and $Paco_2$ in the diazepam-ketamine group, with the exception of mean $Paco_2$ at 2 minutes ($p \leq 0.05$) were not significantly different from those observed in the ketamine group (table 1).

Diazepam neither antagonized nor potentiated the effect of ketamine on arterial blood gases. The changes in mean arterial pH were not statistically significant in either group. Some patients had an alarming decrease in Pao_2 (eg, from 96 to 35 torr and from 85 to 39 torr) and marked increases in $Paco_2$ (eg, from 34 to 44 torr and from 35 to 47 torr) (table 1).

A significant decrease in the respiratory rate occurred in both study groups at 3 minutes after ketamine injection (table 2). The ranges in respiratory rates in both groups indicate the varied respiratory response to ketamine. Although a few patients showed an increase in tidal volume, 50 to 60% of the patients developed apnea after ketamine injection. An example of the pattern is shown in figure 2. Pretreatment with diazepam did not alter the incidence or duration of apnea.

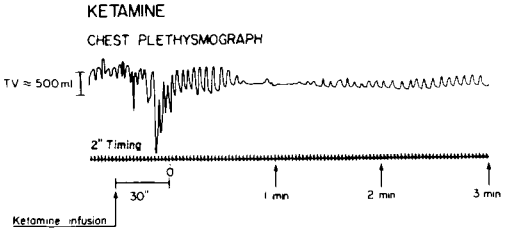

FIG 2. Typical chest-plethysmographic tracing from a patient after ketamine administration.

TABLE 2
Respiratory Rate Changes in Patients Induced with Ketamine and Diazepam-Ketamine Combination

Patient groups	N	Mean respiratory rates per minutes*					
		Before ketamine administration	After ketamine administration				
			1 minute	2 minutes	3 minutes	4 minutes	5 minutes
Ketamine 2 mg/kg IV	6	19.0 ± 3.92†	13.0 ± 4.17	11.0 ± 6.42	14.0 ± 2.61‡	17.0 ± 4.82	20.0 ± 5.23
Ranges of values		(15-24)	(7-18)	(0-20)	(11-18)	(10-21)	(12-24)
Diazepam 0.2 mg/kg IV and ketamine 2 mg/kg IV	7	19.0 ± 3.16	12.0 ± 5.97‡	12.0 ± 5.37‡	13.0 ± 2.55‡	14.0 ± 2.2‡	14.0 ± 2.08‡
Ranges of values		(15-24)	(3-20)	(5-18)	(8-16)	(11-16)	(12-16)§

*Respiratory rates derived from chest plethysmographic tracings.
†Standard deviation.
‡Significant change from baseline values at $p \leq 0.05$.
§N = 4.

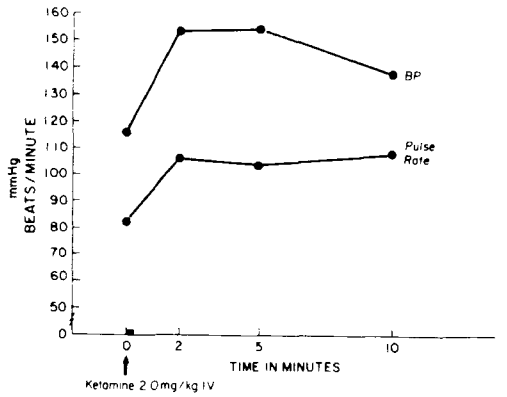

FIG 3. Blood pressure and pulse rate changes following IV ketamine administration.

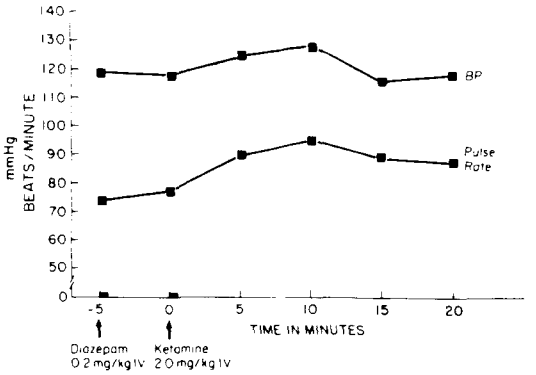

FIG 4. Blood pressure and pulse rate changes following diazepam-ketamine administration.

Arterial blood pressure and pulse rate were elevated in the ketamine group (fig 3). Diazepam reduced these effects of ketamine (fig 4). No arrhythmias or airway obstruction were observed in any patient. Analysis of circulatory effects will be presented in a later publication.

DISCUSSION

Despite reports on the lack of respiratory depressant effect of ketamine[7-9] and its recommendation as an induction agent for patients with airway and respiratory problems,[2,4,6] marked arterial hypoxemia was observed in our studies. The concomitant increase in $Paco_2$ makes it likely that ketamine directly depresses the respiratory center. Indeed, several patients became apneic for more than 30 seconds following ketamine administration.

Regardless of the exact mechanism of the arterial hypoxemia induced by ketamine, it must be promptly corrected, since it results in severe oxyhemoglobin desaturation (eg, 98 to 67% and 95 to 71%) in some patients. If this alarming result is allowed to persist, even briefly, in patients with anemia and/or with reduced cardiopulmonary reserve, it may result in morbidity or mortality.

Therefore, we recommend adequate ventilatory assistance and O_2 administration during induction of anesthesia either with ketamine or diazepam-ketamine combination. Arterial blood gases, catecholamines, O_2 uptake, and CO_2 response, especially in patients with abnormal cardiopulmonary reserve, should be studied further to elucidate the mechanism of arterial hypoxemia following ketamine administration in man.

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