Anesthesiology
62:287–293, 1985

Pulmonary and Systemic Hemodynamic Responses to Ketamine in Infants with Normal and Elevated Pulmonary Vascular Resistance

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Avoidance of ketamine has been recommended in children with pulmonary hypertension or with limited right ventricular reserve, despite absence of data about the effects of ketamine on pulmonary vascular resistance (PVR) in children. Ketamine has been associated with increased PVR in studies of adults; in these studies adults were spontaneously breathing through unprotected airways, despite ketamine's known effects of ventilatory depression and partial loss of airway. The authors measured pulmonary and systemic hemodynamic responses to ketamine during spontaneous ventilation in 14 intubated infants who were receiving minimal ventilatory support with an intermittent mandatory ventilation (IMV) of 4 at an $F_{I_{O_2}}$ of 0.3–0.4. No significant changes were found in cardiac index (CI), pulmonary vascular resistance index (PVRI), or systemic vascular resistance index (SVRI) in a group of seven infants with normal PVRI or in another group of seven infants with preexisting increased PVRI. Results did not differ in infants receiving diazepam sedation. The authors conclude that ketamine has little effect on baseline hemodynamics in mildly sedated infants whose airway and ventilation are maintained; in particular, PVRI is little changed by ketamine administration in ventilated infants with either normal or increased baseline PVRI. (Key words: Anesthesia: pediatric. Anesthetics, intravenous: ketamine. Hemodynamics: pulmonary vascular resistance. Lung: pulmonary vascular resistance.)

INCREASES in pulmonary vascular resistance (PVR) with ketamine have been documented in a number of studies in adults,[1–4] but PVR has not been studied in children given ketamine. Although ketamine's effect in patients with increased PVR has not been studied in any age group, avoidance of ketamine has been recommended in patients with pulmonary hypertension,[1] as well as in patients with reduced ventricular reserve.[2] Despite lack of pediatric data, there is reluctance by some anesthesiologists to use ketamine in children with pulmonary hypertension or with limited right ventricular reserve, such as children with tetralogy of Fallot. However, recent studies in both young lambs and in adult sheep have in fact shown decreases in PVR with ketamine.[5,6]

The contention that PVR in children is increased by the administration of ketamine is contradicted by clinical experience with ketamine during induction of anesthesia in small children with teralogy of Fallot and other forms of cyanotic congenital heart disease where pulmonary blood flow is limited and increases in PVR will result in increased right-to-left shunting and cyanosis. At many centers anesthesia is induced with ketamine in these children without notable clinical problems. In children with pulmonary hypertension and decreased right ventricular reserve due to large left-to-right shunts, ketamine also is used successfully for induction of anesthesia.

Although apnea, hypoxemia, and hypercapnea have been documented in patients receiving ketamine,[7,8] previous studies of ketamine's effect on PVR have used spontaneously breathing subjects. From these studies,[1–4] it is unclear whether increases in PVR are a primary effect of ketamine or are secondary to ketamine's effect on ventilation. Some of the increase in PVR documented in adults might well be secondary to hypoventilation with subsequent hypoxia and hypercarbia.

Our study was designed to evaluate ketamine's effect on PVR and other hemodynamic variables in infants with normal or increased PVR, while controlling for the effects of ketamine on the airway and on ventilation.

Methods

The study was approved by the institutional Committee on Clinical Investigation. We studied 14 children on the day following repair of their congenital heart disease. Age, weight, and diagnosis for these infants are shown in table 1. Only hemodynamically stable infants not requiring inotropic support were studied. Indwelling right and left atrial, pulmonary artery, and radial artery

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Received from the Departments of Anaesthesia and Pediatrics, The Children's Hospital, Harvard Medical School, Boston, Massachusetts 02115. Accepted for publication September 11, 1984. Supported in part by the CHMC Anesthesia Foundation, Inc and by Grant #HL07193 from the Heart, Lung, and Blood Institute, National Institutes of Health, Bethesda, Maryland. Presented in part at the American Society of Anesthesiologists Annual Meeting, October, 1984.

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TABLE 1. Age, Weight, and Diagnosis of Study Patients (Mean ± SEM)

Normal PVRI			Increased PVRI		
Age (mo)	Weight (kg)	DX	Age (mo)	Weight (kg)	DX
2½	5.1	TOF	4	5.0	CAVC
22	8.6	VSD	26	12.6	TOF
8	6.5	VSD	4.5	4.4	VSDs
24	8.9	VSD	5	5.3	CAVC
3	4.7	VSD	35	13.4	VSDs
17	8.6	DORV, PS	10.5	5.9	CAVC
2	5.4	VSD	14	7.8	VSD
Mean 11 ± 4	6.8 ± 0.7		14 ± 5	7.8 ± 0.4	

TOF = tetralogy of Fallot; VSD = ventricular septal defect; CAVC = complete atrio ventricular canal; DORV = double outlet right ventricle; PS = pulmonic stenosis.

catheters were inserted during operation, along with a separate pulmonary artery thermistor. Postoperative chest x-rays and characteristic pressure tracings confirmed the position of intrathoracic catheters. Pulmonary artery saturations of less than 80% or normal indocyanine green dye studies assured the absence of residual intracardiac shunts.[9]

The infants were studied when they were judged ready for extubation. Morphine in doses of 0.1 mg/kg had been given intermittently in the postoperative period for sedation and analgesia, and this had been withheld for at least 4 h prior to the study in preparation for extubation. Diazepam in doses of 0.1 mg/kg had been given either once or twice to five of the children up to 5 h prior to the study. No other sedative medications were used.

All infants were awake and breathing spontaneously through nasotracheal tubes at the time of the study. As is our practice prior to extubation, all children had been weaned to an intermittent mandatory ventilation (IMV) rate of 4 breaths/min with an $F_{I_{O_2}}$ of 0.3–0.4. During the study, all patients were breathing at rates appropriate for age.

Baseline measurement of left and right atrial, pulmonary and systemic arterial pressures were obtained, and an arterial blood gas was drawn. Thermodilution cardiac output was determined by injecting either 1 or 3 ml of 5% dextrose solution (0° C) through the right atrial catheter. Volume of injectate depended upon the infant's weight. Thermodilution curves were examined, and three determinations of cardiac output were obtained during each measurement period. Successive cardiac output determinations done during each measurement period were generally within 5% of each other and always within 10%.

Ketamine, 2 mg/kg, was given through the right atrial catheter as a bolus and the child's respiratory pattern and rate observed. After 3 min hemodynamic measurements were repeated. These were completed by 5 min, and the child's level of responsiveness was evaluated at that time. A repeat arterial blood gas was drawn between 5 and 7 min after the ketamine was given. The children were reevaluated for level of responsiveness at 13–15 min, and hemodynamic measurements were repeated. All patients were extubated within an hour after administration of the ketamine.

From the cardiac output data, cardiac index (CI) was calculated using a nomogram to calculate body surface area for each child. Using the CI and the pressure data, systemic vascular resistance index (SVRI) and pulmonary vascular resistance index (PVRI) were calculated. Patients with a baseline PVRI greater than 3 Wood units ($mmHg \cdot l^{-1} \cdot min \cdot m^2$) were considered to have an abnormally increased PVRI. Mean data from infants with normal and with increased PVRI were analyzed separately for significant changes from baseline at 3–5 min and 13–15 min after ketamine. Additionally, hemodynamic data were analyzed separately for the group of infants receiving diazepam in the postoperative period prior to the study (five patients) and for those not receiving diazepam (nine patients). The paired *t* test was used to compare baseline data with changes after ketamine. A P value of <0.05 was considered statistically significant.

One additional patient was studied both 12 h prior to extubation and 1 h after extubation. No data from this patient were included in the analyses described above.

Results

The children uniformly became unresponsive by 3 min after administration of ketamine. Several children became apneic for brief periods during the maximal effect of ketamine at 3–5 min; the baseline ventilatory support provided by the IMV prevented deleterious hemodynamic changes until spontaneous respiration resumed. Almost all patients were responsive by the time

TABLE 2. Mean Arterial Blood Gases (Mean ± SE)

	Normal PVRI		Increased PVRI	
	Baseline	5–7 Min after Ketamine	Baseline	5–7 Min after Ketamine
*p*H	7.45 ± 0.02	7.41 ± 0.02	7.43 ± 0.01	7.43 ± 0.02
Pa_{CO_2} (mmHg)	33 ± 1	36 ± 1	38 ± 1	40 ± 1
Pa_{O_2} (mmHg)	154 ± 17	143 ± 10	128 ± 6	116 ± 10

No significant changes compared with baseline for either group.

of the second set of measurements after ketamine at 13–15 min. Mean arterial blood gases before ketamine and at 5–7 min after ketamine are shown in table 2 for the children with normal PVRI and for those with increased baseline PVRI. Small increases in Pa_{CO_2} and small decreases in *p*H and Pa_{O_2} were seen after ketamine; these changes did not achieve statistical significance.

Seven patients had an increased baseline PVRI of greater than 3 Wood units; the hemodynamic results for this group and for the other seven patients who had a normal baseline PVRI are shown in table 3. In the group with preexisting increased PVRI, mean PVRI did not change significantly after ketamine; neither did heart rate (HR), mean arterial pressure (MAP), mean pulmonary arterial pressure (MPAP), CI, or SVRI. The same was true of the seven infants with a normal baseline PVRI. The calculated PVRI showed significantly more variability in the group with increased PVRI, since baseline PVRI covered a much wider range (3–12 Wood units) compared with the group with normal PVRI.

The individual PVRI data for each child in the study are shown in figure 1. None of the children had a clinically significant increase in PVRI after ketamine.

The data for those children receiving and for those not receiving diazepam prior to the study are shown in table 4. No significant change in HR, MPAP, CI, or PVRI occurred in either group. The group receiving diazepam had a decrease in MAP at 3–5 min, which was significant; likewise, the group not receiving diazepam had a decrease in SVRI at 3–5 min, which was also significant. Both of these changes were small and not clinically noteworthy.

The one additional child studied both before extubation and then again shortly after extubation had changes in PVRI after ketamine, which are shown in figure 2. Before extubation, while the child was receiving minimal ventilatory support, the PVRI decreased slightly after ketamine as the child became unresponsive, at 3–5 min and remained below baseline at 13–15 min as the child again became responsive. After extubation, the PVRI rose by almost 300% after ketamine as the child became stridorous and unresponsive at 3–5 min.

TABLE 3. Mean Hemodynamic Findings (±SEM) for Each Group

Variable	Baseline	3–5 Min after Ketamine	13–15 Min after Ketamine
Normal PVRI (n = 7)			
HR (beats/min)	118 ± 8	123 ± 8	123 ± 8
RAP (mmHg)	9 ± 1	9 ± 1	9 ± 1
LAP (mmHg)	8 ± 1	8 ± 1	8 ± 2
MAP (mmHg)	75 ± 3	72 ± 5	74 ± 4
MPAP (mmHg)	13 ± 1	13 ± 2	13 ± 2
CI ($l \cdot min^{-1} \cdot m^{-2}$)	3.6 ± 0.4	3.8 ± 0.4	3.6 ± 4
SVRI (Wood units)*	19 ± 1	17 ± 1	19 ± 2
PVRI (Wood units)*	1.5 ± 0.4	1.5 ± 0.4	1.6 ± 0.4
Increased PVRI (n = 7)			
HR (beats/min)	114 ± 6	113 ± 5	113 ± 5
RAP (mmHg)	9 ± 1	9 ± 1	9 ± 2
LAP (mmHg)	9 ± 1	10 ± 1	9 ± 1
MAP (mmHg)	72 ± 6	69 ± 6	67 ± 6
MPAP (mmHg)	27 ± 3	29 ± 3	27 ± 4
CI ($l \cdot min^{-1} \cdot m^{-2}$)	3.4 ± 0.3	3.4 ± 0.3	3.4 ± 4
SVRI (Wood units)*	20 ± 1	18 ± 1	18 ± 2
PVRI (Wood units)*	5.6 ± 1	5.8 ± 1	5.5 ± 0.9

No significant changes compared with baseline for either group.
** $mmHg \cdot l^{-1} \cdot min \cdot m^2$.

The stridor cleared quickly, without requiring intervention, as the child awoke. By 13–15 min after ketamine, the PVRI had returned to baseline. No further studies

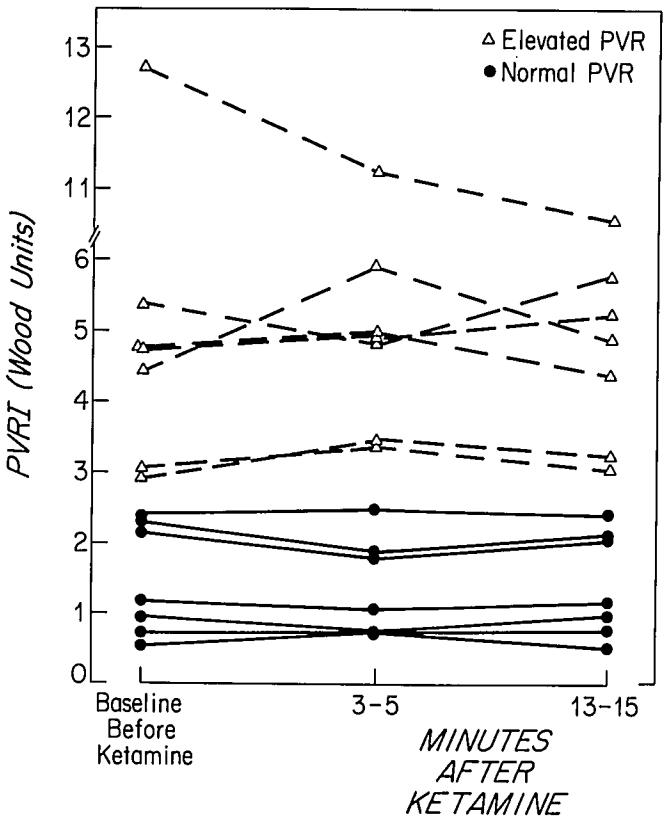

FIG. 1. Individual PVRI data in Wood units ($mmHg \cdot l^{-1} \cdot min \cdot m^2$) in 14 infants with normal or elevated PVRI breathing spontaneously at an IMV of 4 through nasotracheal tubes.

TABLE 4. Mean Hemodynamic Findings (±SEM) in Infants with and without Diazepam

Variable	Baseline	3–5 Min after Ketamine	13–15 Min after Ketamine
Diazepam (n = 5)			
HR (beats/min)	109 ± 9	105 ± 7	107 ± 8
MAP (mmHg)	73 ± 8	69 ± 7*	72 ± 9
MPAP (mmHg)	20 ± 2	21 ± 3	21 ± 2
CI ($l \cdot min^{-1} \cdot m^{-2}$)	3.9 ± 0.5	3.9 ± 0.6	3.8 ± 0.6
SVRI (Wood units)	17 ± 1	16 ± 1	18 ± 2
PVRI (Wood units)	3.2 ± 0.6	3.7 ± 0.8	3.5 ± 0.7
No diazepam (n = 9)			
HR (beats/min)	120 ± 6	125 ± 5	124 ± 5
MAP (mmHg)	75 ± 3	71 ± 5	70 ± 4
MPAP (mmHg)	20 ± 4	21 ± 4	20 ± 4
CI ($l \cdot min^{-1} \cdot m^{-2}$)	3.3 ± 0.3	3.5 ± 0.2	3.3 ± 2
SVRI (Wood units)	21 ± 1	18 ± 1*	19 ± 2
PVRI (Wood units)	3.8 ± 1.3	3.6 ± 1.2	3.5 ± 1.1

* $P < .05$ compared with baseline.

of ketamine were done in extubated children for ethical reasons. The data from this child are not included in the results reported above.

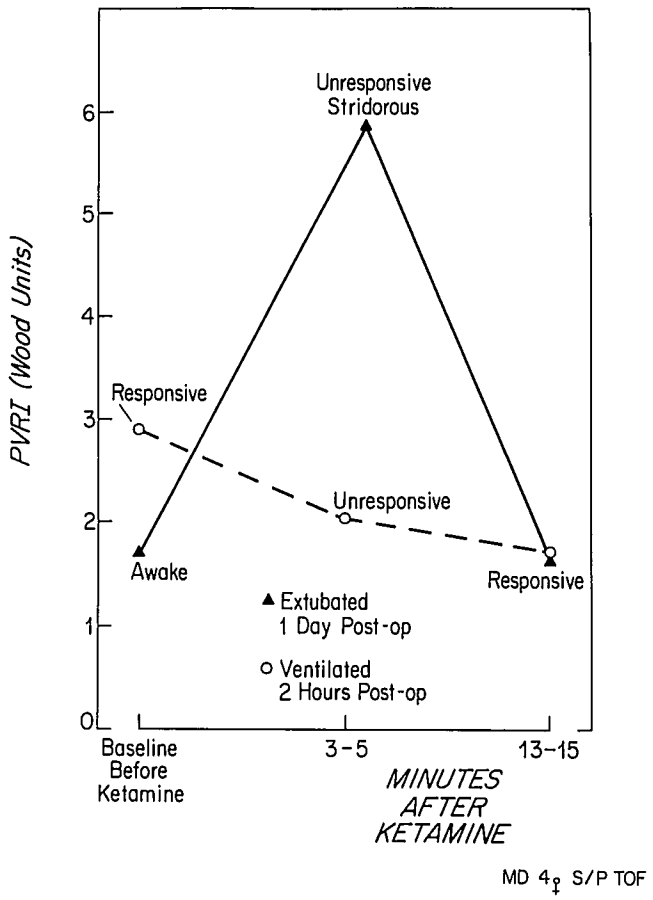

FIG. 2. PVRI in Wood units ($mmHg \cdot l^{-1} \cdot min \cdot m^2$) from one patient 12 h before and shortly after extubation.

Discussion

Measurements of PVRI, SVRI, and cardiac index after ketamine in children have not been reported previously, despite extensive use of ketamine in children undergoing cardiac catheterization.[10–12] One of these studies reported no increase in pulmonary arterial pressure after ketamine in 28 children who received droperidol premedication, whereas pulmonary arterial pressure increased in two children not receiving droperidol.[11] No actual data were presented in this report. Another study showed a small increase in pulmonary artery pressure after ketamine compared with heavy sedation alone, but the increase was statistically insignificant due to great variability in the pulmonary arterial pressure data after ketamine.[12] The third study documented increases in heart rate and systemic arterial pressure after intramuscular ketamine was given, but pulmonary artery pressures were not measured.[10]

In contrast, the children in our study did not show pressor and heart rate responses to ketamine. Furthermore, there was no change in PVRI or MPAP with ketamine in our study, in contrast to reports of increased PVR in the studies of adults summarized in table 5. An increase in PVRI occurred only in the one child in our study whose airway and ventilation were not supported. The differences between our findings and those of other investigators might be explained by use of sedative agents, catecholamine depletion, age differences, or ketamine's effects on ventilation.

Droperidol, midazolam, and diazepam all have attenuated the pressor responses following ketamine in adults.[13–15] Droperidol blocked increases in pulmonary artery pressure in children in the study of Gassner *et al.*[11] In our study, the infants were sedated only mildly, primarily with morphine; results in infants given diazepam up to 5 h before the study were not substantially different from the other infants. While mild sedation with morphine may have had some influence on our results, morphine has not been shown to blunt responses to ketamine. Certainly the large increase in PVRI with ketamine after extubation was not blocked in the child in Figure 2, whose morphine regimen and study time relative to operation were identical to the other children in our study.

As summarized in table 5, the ketamine studies that reported increases in PVR had used diazepam and droperidol premedication and still found increased PVR with ketamine.[1–4] In the two clinical studies in adults where no increase in PVR was demonstrated, *no* premedication was given to explain the lack of increase in PVR.[13,16] Thus, it seems unlikely that our results can be explained solely by sedation. In any case, the amount

TABLE 5. Studies of PVRI with Ketamine

Author	Patients	Dose (mg/kg)	Ventilation	Significant ABG Δs	PVR	Premedication	Comments
Tween *et al.*, 1972[4]	12 adults Cardiac cath	2.0	Spontaneous room air	*p*H↓	↑44%	Diazepam	Upper airway obstruction in 3 100% O_2 given to 2
Gooding *et al.*, 1977[1]	16 adults Skin grafts	2.2	Spontaneous room air	Pa_{CO_2}↑ *p*H?	↑40%	Diazepam	—
Tarmow *et al.*, 1979[3]	6 adults CABG	1.5	Spontaneous room air	*p*H↓ Pa_{O_2}↓ (60 mmHg) Pa_{CO_2}↑ (47 mmHg)	↑100%	Promethazine demoral	—
Spotoft *et al.*, 1979[2]	6 adults Valve replacement	2	Spontaneous 100% O_2	—	↑>100%	Diazepam	Assisted ventilation only after respiratory depression
Waxman *et al.*, 1980[25]	12 adults Critically ill	1 (mean)	Spontaneous 100% O_2	—	↔	None	—
Balfours *et al.*, 1983[13]	8 adults peripheral vascular disease	2	Assisted with 25% O_2	—	↔	None	—

of sedation given in our study was no more than the premedication routinely given to children who will receive ketamine in the operating room, so that our results are relevant to the clinical situation.

Ketamine reportedly causes central sympathomimetic stimulation,[17] inhibition of neuronal reuptake of norepinephrine,[18] activation of the pituitary–adrenal axis,[19] and thus increased levels of circulating catecholamines,[20] thereby explaining some of ketamine's pressor effects. Catecholamine depletion, due to the outpouring of catecholamines with cardiopulmonary bypass and hypothermia,[21] might be invoked to explain our findings in children. However, our studies were performed the day after operation in children who did not require pressor support. When physically stimulated by removal of chest tubes immediately after the study, our patients were able to markedly increase heart rate, systemic arterial, and pulmonary arterial pressures, suggesting that catecholamine-mediated reflexes were intact and that the infants were not heavily sedated, even after the ketamine had been given previously.

Age differences might explain the discrepancies with studies in adults. However, infants with congenital heart disease given ketamine would be expected to have greater changes in PVR than adults, since infants have increased reactivity of their pulmonary arterial tree.[22] Increased muscularity of infant pulmonary arteries is present on the basis of age,[23] as well as on the basis of cardiac disease processes.[24] Pulmonary vascular obstructive disease with a high, fixed PVR occurs in children older than the infants we studied. Infants with increased PVR have more muscular and reactive pulmonary vasculature and might have especially marked increases in PVR with ketamine. These considerations often have led to avoidance of ketamine in infants with increased PVR.

The differences between our results and those from previous studies might be resolved by considering ketamine's effects on the airway and on ventilation,[7,8] since the well-documented effects of hypoxia, hypercapnea, and acidosis in increasing PVR are especially marked in the young.[25] Coppel and Dundee's study[10] of ketamine use in children reported that Pa_{O_2} decreased and Pa_{CO_2} increased significantly when heart rate and arterial pressure first increased; at least two of 40 children in that study developed severe apnea or stridor with ketamine. Faithfull and Haider's study[12] of ketamine in children undergoing cardiac catheterization reported a 20% incidence of upper airway obstruction alone. The large variability in their pulmonary arterial pressure data suggests that those children with upper airway obstruction had large increases in pulmonary arterial pressure. Stanley and associates[8] reported significant increases in Pa_{CO_2} (mean of 50 mmHg) and decreases in *p*H (mean of 7.29) in one of several groups of children receiving ketamine anesthesia for cardiac catheterization. Similar, but insignificant, changes occurred in our infants, who tended to increase their Pa_{CO_2} and decrease their Pa_{O_2}, despite airway support and minimal IMV with O_2. Several of our patients became briefly apneic. Without a protected airway and ventilatory support, the changes in arterial blood gases might well have become both statistically and clinically significant.

The Zsigmund *et al.* study[7] of ventilation in adults breathing room air showed significant decreases in Pa_{O_2} and increases in Pa_{CO_2} 2–5 min after ketamine

administration when peak increases in heart rate and blood pressure occurred. Over half of these patients became apneic, and two of 14 patients had Pa_{O_2} below 40 mmHg during the same time period. These authors recommended that O_2 and ventilatory assistance accompany intravenous ketamine.

In the studies of PVR with ketamine in adults (table 5), similar changes in ventilation have contaminated the results. Tweed *et al.*,[4] Gooding *et al.*,[1] and Tarnow *et al.*[3] all showed increased PVR in adults spontaneously breathing room air. Increases in arterial Pa_{CO_2}, decreases in *p*H, or in Pa_{O_2} occurred in all these studies when the increases in PVR were measured; in none of the studies were these findings commented upon. In the only study where ventilation was closely observed, upper airway obstruction developed in 25% of the adults.[4] Only Spotoft *et al.*[2] showed an increase in PVR without significant changes in arterial blood gases. While their patients were breathing 100% O_2, respirations were assisted only *after* respiratory depression developed when effects on PVR already may have occurred.

In contrast to the above studies documenting increases in PVR, Balfors and colleagues[13] did not find any increase in PVR after ketamine in the unpremedicated adults in their study whose ventilation was assisted with the use of supplemental oxygen. Ketamine has less marked effects on airway and ventilation at lower doses[17]; Waxman and colleagues[16] found no statistically significant changes in PVR after ketamine dose of 1 mg/kg in a group of 12 critically ill adult patients who also were given supplemental 100% oxygen.

These previous studies, together with our results, generally support the hypothesis that the effects of ketamine on PVR partially may be due to the effects of ketamine on ventilation. We think that adequate ventilation is very important in preventing changes in PVR after administration of ketamine. The lack of heart rate and pressor responses in our patients suggests that airway obstruction and hypoventilation may play some role in other sympathomimetic effects of ketamine, in addition to elevating PVR. In support of this suggestion, animal studies have shown that acute hypoxemia, hypercapnia, and respiratory acidosis result in increases in adrenergic activity and circulating catecholamines.[26,27]

We conclude from our study that hemodynamics, especially PVRI, are little changed by ketamine in mildly sedated infants with congenital heart disease regardless of baseline PVRI, as long as the airway and ventilation are supported. Our results, in combination with previous work, suggest that partial airway obstruction and hypoventilation may be responsible in part for the increases in PVR previously reported after ketamine and even may contribute to other sympathomimetic effects seen after administration of ketamine.

References

1. Gooding JM, Dimick AR, Tavakoli M, Corssen G: A physiologic analysis of cardiopulmonary responses to ketamine anesthesia in noncardiac patients. Anesth Analg 56:813–816, 1977
2. Spotoft H, Korshin JD, Sorensen MB, Skovsted P: The cardiovascular effects of ketamine used for induction of anesthesia in patients with valvular heart disease. Can Anaesth Soc J 26:463–467, 1979
3. Tarnow J, Hess W, Schmidt D, Eberlein HJ: Narkoseeinleitung bei Patienten mit koronarer Herzkrankheit: Flunitrazepam, Diazepam, Ketamin, Fentanyl. Anaesthesist 28:9–19, 1979
4. Tweed WA, Minuck M, Mymin D: Circulatory responses to ketamine anesthesia. ANESTHESIOLOGY 37:613–619, 1972
5. Hanowell ST, Zwischenberger JB, Siwek LG, Jones M, Kim YD, Macnamara TE: The effect of ketamine in the lamb with left to right shunt (abstract). ANESTHESIOLOGY 55:A15, 1981
6. Bodai BI, Harms BA, Nottingham PB, Zaiss C, Delming RH: The effect of ketamine on endotoxin-induced lung injury. Anesth Analg 62:398–493, 1983
7. Zsigmond EK, Matuski A, Kothary SP, Jallad M: Arterial hypoxemia caused by intravenous ketamine. Anesth Analg 55:311–314, 1976
8. Stanley V, Hunt J, Willis KW, Stephen CR: Cardiovascular and respiratory function with CI-581. Anesth Analg 47:760–768, 1969
9. Lang P, Chipman CW, Siden H, Williams RG, Norwood WI, Castaneda AR: Early assessment of hemodynamic status after repair of tetralogy of Fallot: A comparison of 24 hour (intensive care unit) and 1 year postoperative data in 98 patients. Am J Cardiol 50:795–799, 1982
10. Coppel DL, Dundee JW: Ketamine anaesthesia for cardiac catheterization. Anaesthesia 27:25–31, 1972
11. Gassner S, Cohen M, Aygen M, Levy E, Ventura E, Shashdi J: The effect of ketamine on pulmonary artery pressure. Anaesthesia 29:141–146, 1974
12. Faithfull NS, Haider R: Ketamine for cardiac catheterization: an evaluation of its use in children. Anaesthesia 26:318–323, 1971
13. Balfors E, Haggmark S, Nyhman H, Rydvall A, Reiz S: Droperidol inhibits the effects of intravenous ketamine on central hemodynamics and myocardial oxygen consumption in patients with generalized atherosclerotic disease. Anesth Analg 62:193–197, 1983
14. White PF: Comparative evaluation of intravenous agents for rapid sequence induction-thiopental, ketamine, and midazolam. ANESTHESIOLOGY 57:279–284, 1982
15. Jackson APF, Dhadphale PR, Callagan ML: Haemodynamic studies during induction of anaesthesia for open heart surgery using diazepam and ketamine. Br J Anaesth 50:375–377, 1978
16. Waxman K, Shoemaker WC, Lippman M: Cardiovascular effects of anesthetic induction with ketamine. Anesth Analg 59:355–358, 1980
17. White PF, Way WL, Trevor AJ: Ketamine–its pharmacology and therapeutic uses. ANESTHESIOLOGY 56:119–136, 1982
18. Byrne AJ, Tomlinson DR, Healy TEJ: Ketamine and sympathetic mechanisms in cardiac and smooth muscle. Acta Anaesthesiol Scand 26:479–484, 1982

19. Oyama T, Matsumoto F, Kudo T: Effects of ketamine on adrenocortical function in man. Anesth Analg 49:697–700, 1970
20. Lundy PM, Colhoun EH, Gowdey CW: Pressor responses of ketamine and circulating biogenic amines. Nature 241:80–82, 1974
21. Philbin DM, Levine FH, Kono K, Coggins CH, Moss J, Slater EE, Buckley MJJ: Attenuation of the stress response to cardiopulmonary bypass by the addition of pulsatile flow. Circulation 64:808, 1981
22. James LS, Rowe RD: The pattern of response of pulmonary and systemic arterial pressures in newborn and older infants to short periods of hypoxia. J Pediatr 51:5, 1957
23. Hislop A, Reid L: Pulmonary arterial development during childhood: Branching pattern and structure. Thorax 28:129, 1973
24. Hoffman JIE, Rudolph AM, Heyman MA: Pulmonary vascular disease with congenital heart lesions: pathologic features and causes. Circulation 64:873–877, 1981
25. Rudolph AM, Yuan S: Response of pulmonary circulation to hypoxia and H^+ ion changes. J Clin Invest 45:399–405, 1966
26. Rose CE, Althaus JA, Kaiser DL, Miller ED, Carey RM: Acute hypoxemia and hypercapnea: Increases in plasma catecholamines in conscious dogs. Am J Physiol 245:H924–H929, 1983
27. Steinhart CR, Permutt S, Gurtner GH, Traystman RJ: Beta-adrenergic activity and cardiovascular response to severe respiratory acidosis. Am J Physiol 244:H46–H54, 1983d