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The Effect of Ketamine on the Renin-Angiotensin System

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Ketamine, in clinical doses, usually increases blood pressure and heart rate. The exact mechanism is unknown, but central autonomic stimulation appears to regulate the peripheral as well as the cardiac effects.¹ Tanaka *et al.*² suggested that renin may play a role in the peripheral effects of ketamine in rats. To test this hypothesis in man, we undertook the following study.

METHOD

Ten healthy patients, ASA status I, 20-40 years of age, were premedicated with atropine, 0.5 mg, intramuscularly, one hour prior to surgery. Two peripheral venous catheters were inserted and control measurements of blood pressure, heart rate, and respiratory rate and a plasma renin sample were obtained. The patients were

slowly given ketamine, 2 mg/kg, intravenously, and were allowed to breathe room air. The operating room was quiet, and 5 and 15 minutes after the initial dose of ketamine, measurements were repeated. The renin samples were assayed by the radioimmunoassay method of Harber *et al.*³

RESULTS

In all patients, blood pressure and heart rate increased 5 and 15 minutes after the initial ketamine injection ($P < .001$) (table 1). In marked contrast, however, renin values did not increase and were not statistically different from the control. In fact, high baseline renin values in Patients 9 and 10 returned to normal range following administration of ketamine.

DISCUSSION

Ketamine has been shown to produce moderate to marked increases of both systolic and diastolic blood pressures.⁴ Dowdy and Kaya found the carotid baroreceptor was altered by ketamine and was responsible for the pressor component of a biphasic pressure response in anesthetized dogs,⁵ whereas Virtue and associates suggested that increased release of endogenous catecholamines may be responsible for the blood pressure

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TABLE 1. Renin-Ketamine Data

	Heart Rate (Beats/Min)	Mean Blood Pressure (torr)	Renin (ng ml ⁻¹ hr ⁻¹)
Control			
Patient 1	100	96.7	0.80
Patient 2	75	91.7	0.61
Patient 3	54	83.3	0.64
Patient 4	72	99.3	0.16
Patient 5	66	83.3	1.28
Patient 6	78	96.6	0.56
Patient 7	60	96.6	0.14
Patient 8	72	95.0	0.39
Patient 9	78	73.3	5.81
Patient 10	60	84.0	3.80
Mean	71.50	89.99	1.42
SD	12.95	8.50	1.87
SE	4.09	2.68	0.59
5 minutes after ketamine, 2 mg/kg			
Patient 1	170	111.7	0.59
Patient 2	100	116.7	0.22
Patient 3	84	116.7	0.60
Patient 4	120	117.3	0.28
Patient 5	144	103.3	0.19
Patient 6	108	113.3	0.30
Patient 7	96	133.3	0.13
Patient 8	120	120.0	0.31
Patient 9	132	110.0	0.53
Patient 10	96	112.0	0.84
Mean	117.0*	115.43*	0.39
SD	26.08	7.84	0.23
SE	8.25	2.48	0.07
15 minutes after ketamine, 2 mg/kg			
Patient 1	170	110.0	1.21
Patient 2	100	98.3	0.06
Patient 3	120	120.0	4.66
Patient 4	108	106.7	0.84
Patient 5	120	96.7	1.42
Patient 6	90	116.7	0.20
Patient 7	84	123.3	0.14
Patient 8	120	106.7	0.62
Patient 9	120	100.0	0.90
Patient 10	90	103.3	0.78
Mean	112.2*	108.16*	1.08
SD	24.89	9.24	1.33
SE	7.84	2.92	0.42

* $P < 0.001$ compared with control value, t test for paired data.

increase.⁶ Traber *et al.*⁷ and Kaplan *et al.*⁸ have shown that both alpha- and beta-adrenergic blockers are able to partially or completely modify the pressor response to ketamine.

Renin is a proteolytic enzyme devoid of vasoactive properties. It acts upon the circulating alpha-2-globulin, angiotensinogen, to yield the decapeptide fragment angioten-

sin I. Angiotensin I is then converted to the potent vasopressor, angiotensin II, by the action of the converting enzyme in the lung that splits off the two terminal amino acids of angiotensin I. Angiotensin II is the most potent vasopressor known. Since renin is released under a variety of stimuli including adrenergic stimulation,⁹ it seemed possible that renin could be released by ketamine and

play an important role in blood pressure regulation, since it does so in normal man¹⁰ as well as in various disease states.¹¹ However, our study clearly shows that renin is not responsible for the hypertension seen when ketamine is administered.

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Lymphocyte Transformation during Operations with Spinal Anesthesia

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Cellular immunity as tested by *in-vitro* techniques is depressed postoperatively. Both lymphocyte transformation and the incorporation of radioactively labeled thymidine into DNA with phytohemagglutinin (PHA) stimulation have been shown to be impaired following surgical operations.^{1,2} Since general anesthesia was

used in previous studies, this study was undertaken to determine whether operations in conjunction with spinal anesthesia also affect lymphocyte responsiveness to PHA.

PATIENTS AND METHODS

Seven patients were selected for this study. All underwent elective operations, their ages and surgical procedures being listed in table 1. For spinal anesthesia, tetracaine, 8-10 mg, was instilled. Patient 6 had two transurethral resections of his prostate, separated by a three-month interval. Results from both operations are reported, but only the values from the second operation are included in the statistical analysis, since at the time of the first operation, ³H-thymidine incorporation studies were not being done. Premedica-

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