Evaluation of a Xylazine-Ketamine Hydrochloride Combination in the Cat

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ABSTRACT

Cardiopulmonary function was assessed in healthy cats given a xylazine-ketamine hydrochloride combination intramuscularly. Cardiac output, heart rate, stroke volume and cardiac index were significantly decreased. Systolic, diastolic and mean arterial blood pressure were also significantly decreased. Systemic vascular resistance and central venous pressure were significantly increased. Blood gas values remained stable. In conclusion, significant cardiovascular depression was noted in normal cats given the xylazine-ketamine combination at the dosages listed.

Key words: Cat, cardiopulmonary function, xylazine-ketamine.

RÉSUMÉ

Cette expérience consistait à évaluer la fonction cardio-pulmonaire, chez des chats sains auxquels on avait administré une infection intramusculaire d'un mélange de xylazine et de chlorhydrate de kétamine. Les auteurs constatèrent une baisse appréciable du débit cardiaque, de la fréquence cardiaque, du débit systolique et de l'index cardiaque. Les pressions sanguines systolique, diastolique et artérielle moyenne affichèrent aussi une baisse significative, tandis que la résistance vasculaire systémique et la pression veineuse centrale manifestèrent une élévation appréciable. Les valeurs des gaz sanguins demeurèrent stables. En conclusion, on enregistra une dépression cardio-vasculaire appréciable, chez les chats sains auxquels on avait injecté un mélange de xylazine et de kétamine, aux doses prescrites.

Mots clés: chat, fonction cardio-pulmonaire, xylazine-kétamine.

INTRODUCTION

Anesthetics used alone and in combination provide an efficient and relatively safe means for surgical or medical procedures that might not be possible otherwise. The xylazine-(Rompun, Bayvet, Mississauga, Ontario)-ketamine hydrochloride (Ketaset, rogar/STB, Montreal, Quebec) combination is one such example.

Xylazine is a sympatholytic, sympathomimetic and parasympathomimetic agent (1). It is associated with a rapid onset, good to excellent sedation of one to two hours duration, excellent analgesia of 15 to 30 minutes duration and a smooth recovery (3,4). The analgesia and sedation are due to central nervous system depression and the muscle relaxation is due to the central inhibition of intraneural transmission (5). After an intravenous or intramuscular injection, there is a brief elevation in arterial blood pressure reflecting the drug's alpha stimulatory effect and an increase in cardiac contractility independent of heart rate. This is followed by a more pronounced fall in arterial blood pressure due to a fall in aortic blood flow reflecting the depression of the sympathetic nerve system and the heart rate (1,4). Stroke volume and pulse pressure are not significantly altered (6). Although there is a fall in the respiratory rate, the tidal volume is increased and a stable arterial pH and blood gas tension are maintained (1). A significant incidence of second degree heart block after intravenous injection has been noted in the cat and the horse (2,7). Emesis is frequently observed one to five minutes after injection at any dose level (3,5). The drug is metabolized in the liver. Any unchanged drug is eliminated in the urine (8).

Ketamine hydrochloride is a dissociative anesthetic with central sympathomimetic and parasympatholytic activity (9). Used alone it tends to cause hypertonus, poor muscle relaxation and persistent pain reflex responses. The muscle twitching and rigidity and convulsive seizures are centrally mediated (10). Evaluating the level of consciousness is difficult. Although ketamine produces a dose dependent depression of cardiac function in isolated studies, increased heart rates, cardiac output and left ventricular pressure indices have been demonstrated in studies in man (11).

The combination of xylazine-ketamine has been used and evaluated in the horse, dog and cat (4,7,8,13,14).

In the dog the pressor effects, hyperptyalism and extensor rigidity of ketamine are offset by the effects of xylazine (13). In most horses second degree heart block initially caused by xylazine disappeared shortly following the administration of ketamine (7). Cardiac output, arterial blood pressure, pulmonary arterial and central venous pressure were not significantly altered. It was concluded that the drug combination is safe and effective in the horse (4). In the cat, however, this drug combination has been associated with a large number of anesthetic deaths (15).

However, it has been stated by other investigators that the xylazine-ketamine combination provides a safe and pleasant narcosis with minimal side effects other than vomition (8,16).

The purpose of this project was to

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study the effects of a xylazine-ketamine combination on indices of cardiopulmonary function in healthy cats.

MATERIALS AND METHODS

Ten healthy, mature cats of either sex and mixed breed were used. They were judged as having a normal cardiovascular system on the basis of history, physical examination, chest radiography and electrocardiography. Suitable cats were anesthetized one day prior to the study for placement of the thermodilution (Edwards Laboratories, Santa Ana, California) and arterial pressure (Tectronics, Beaverton, Oregon) catheters (17). The anesthetic used was halothane (Ayerst Laboratories, Montreal, Quebec). Cats were maintained in a light surgical plane of anesthesia.

Anesthetized cats were prepared for pulmonary artery catheterization by a cut down and exposure of the left jugular vein. An introducer was used to facilitate the introduction of a 4-French Edslab pediatric thermodilution catheter into the pulmonary artery from the right ventricle. The introducer was initially made straight with a flexible metal probe to ease its introduction into the jugular vein and right heart. This metal probe was then replaced by the thermodilution catheter. Fluoroscopic examination facilitated the positioning of the introducer and thermodilution catheter and pressure recordings confirmed the presence of the thermodilution catheter in the pulmonary artery. A similar procedure without the use of the introducer was used for placing an injectate catheter via the right jugular vein into the right atrium (17). This provided two mixing chambers for the injectate solution before the change in blood temperature was recorded in the pulmonary artery. The catheters were sutured in this position and the skin wound closed. The neck was bandaged and the cats were allowed to recover. Twenty-four hours later the thermodilution catheter was connected to an Edwards laboratory cardiac output computer (Edwards Laboratories, Santa Ana, California). Two millilitres of room temperature, 5% dextrose was used as the injectate. The cardiac output was subsequently displayed by digital readout. Heart rate and electrocardiographic changes were recorded (Burdick EK-5A, Milton, Wisconsin). Respiratory rate was monitored visually.

The xylazine-ketamine combination was mixed and given intramuscularly at 1.0 mg/kg and 10 mg/kg respectively. Cardiac output, stroke volume, heart rate, systolic, diastolic and mean blood pressure were monitored prior to the injection of the drug combination and then at 5, 10, 15, 30, 45, 60, 90, 120 and 150 minutes thereafter. Arterial blood gases were also measured at these time intervals. Systemic vascular resistance was calculated using the formula

$$\text{systemic vascular resistance} = \frac{\text{mean arterial pressure} \times 80}{\text{cardiac output}}$$

in dynes-sec cm^{-5} (18). Stroke volume was calculated by dividing the cardiac output by the heart rate.

All data was statistically analyzed using a paired t-test between the parameters before the anesthetic combination was given and these same parameters at the time intervals listed. The purpose of this study was to determine if a significant change ($p < 0.05$) occurred in the parameter being studied while under the influence of the xylazine-ketamine combination.

RESULTS

Cardiac output (liters/minute) decreased significantly five minutes following xylazine-ketamine administration (Table I). It remained significantly decreased throughout the 150 minute test period. The heart rate (beats/minute) had also significantly decreased at the five minute mark and remained decreased throughout the 150 minute test (Table I). Stroke volume (mL/beat) was significantly decreased five minutes after the anesthetic combination was given and remained decreased for 60 minutes (Table I). A significant decrease in cardiac index (L/min/kg) was apparent from the five minute to the 150 minute test time. Although the time at which the maximal depression occurred varied, a significant depression was evident in all the above parameters five minutes into the study period.

In Table II systolic and mean arterial blood pressure (mmHg) were significantly decreased at the five minute interval and remained decreased throughout the 150 minute test period. Diastolic blood pressure was significantly decreased from the ten minute test period to the end of the study (Table II).

Systemic vascular resistance was calculated at each test time. A significant increase occurred at the five minute period and remained increased over a 90 minute period.

Central venous pressure was significantly increased ten minutes following xylazine-ketamine administration and remained increased over a 60 minute period (Table II).

Arterial blood p02, pC02 and pH did not change significantly during the 120 minutes the samples were analyzed (Table III).

TABLE I. Parameters of Cardiac Function of Cats Anesthetized with Xylazine-Ketamine

Parameter/ Time (min)	Cardiac Output (L/minute)		Heart Rate (beats/minute)		Stroke Volume (mL/beat)		Cardiac Index (L/min/kg)	
	Mean	Variance	Mean	Variance	Mean	Variance	Mean	Variance
Pretest	0.914	0.099	223	979.1	4.09	1.939	0.196	0.003
5	0.543	0.091	187	580.1	2.83	0.605	0.116	0.001
10	0.491	0.470	154	92.1	2.94	1.198	0.103	0.001
15	0.449	0.024	154	508.5	2.96	1.045	0.099	0.001
30	0.420	0.026	145	704.9	2.91	0.938	0.090	0.001
45	0.417	0.016	133	346.5	3.18	1.048	0.090	0.0004
60	0.418	0.016	129	359.4	3.29	1.023	0.091	0.001
90	0.416	0.017	120	440.0	3.50	1.199	0.090	0.001
120	0.456	0.024	140	1185.0	3.38	1.388	0.098	0.001
150	0.509	0.020	156	2317.0	3.49	1.417	0.113	0.001

TABLE II. Arterial Blood Pressure, Central Venous Blood Pressure and Systemic Vascular Resistance of Cats Anesthetized With Xylazine-Ketamine

Parameter/ Time (min)	Systolic Arterial Blood Pressure (mmHg)		Diastolic Arterial Blood Pressure (mmHg)		Mean Arterial Blood Pressure (mmHg)		Systemic Vascular Resistance (dynes-sec. cm^{-5})		Central Venous Pressure (mmH_2O)	
	Mean	Variance	Mean	Variance	Mean	Variance	Mean	Variance	Mean	Variance
Pretest	128.7	900.0	91.9	416.3	104.2	515.3	9810	108400	0.4	0.933
5	100.6	764.5	74.2	555.9	82.7	618.7	13800	599100	1.0	1.250
10	90.1	924.8	64.9	454.5	74.3	525.6	13240	197200	3.57	7.333
15	86.9	671.7	63.4	339.6	71.2	422.2	12690	153500	3.7	9.122
30	84.5	612.9	63.9	337.3	68.8	314.6	13670	127600	3.4	5.156
45	82.0	428.0	59.7	203.6	67.4	258.5	12830	45600	2.6	4.044
60	81.3	434.2	57.4	168.7	65.9	215.2	12450	52100	3.0	6.889
90	80.0	409.6	58.2	180.4	65.8	234.0	12800	127400	1.9	4.544
120	82.4	380.7	61.0	234.4	68.2	268.4	12380	111700	1.5	4.944
150	92.9	339.2	70.6	308.0	77.9	308.8	13060	290200	0.9	0.989

DISCUSSION

Contrary to previous reports attesting to the safety of a xylazine-ketamine preparation for anesthesia in cats, this experiment demonstrated significant effects of this drug combination on all parameters measured except those of blood gas analysis at a dosage of 1.0 mg/kg xylazine and 10 mg/kg ketamine (8,12,14) (Fig. 1). Previous investigators have used xylazine at a dosage of 0.5 mg/kg and ketamine hydrochloride at a dosage of 20 mg/kg (14). In another experiment, dosages of 6 mg/cat xylazine and 50 mg/kg ketamine hydrochloride were used (8). No deleterious changes were evident in the heart rate, respiratory rate or arterial blood gas values even in cats presented to surgery with pyometra, foreign bodies, intestinal invagination, abdominal tumors or urolithiasis (14). The degree to which these cats were compromised prior to the administration of the xylazine-ketamine is not discussed. Cardiovascular function was not investigated in these experiments either (8,14).

Cardiac output was significantly decreased by the xylazine-ketamine combination. The decrease was evident five minutes after the anesthetic combination was administered and remained significantly decreased throughout the 150 minute test period. It has been stated that the decreased cardiac output is caused by a decrease in aortic blood flow secondary to a xylazine induced depression of the sympathetic nervous system and a decrease in the heart rate (1,2,5). Cardiac output is a product of stroke volume and heart rate (18) both of which were significantly decreased throughout the experimental period. Previous investigators have shown that stroke volume in dogs was not significantly altered with xylazine (6). Stroke volume was, however, significantly decreased in this experiment. Stroke volume is dependent on pre-

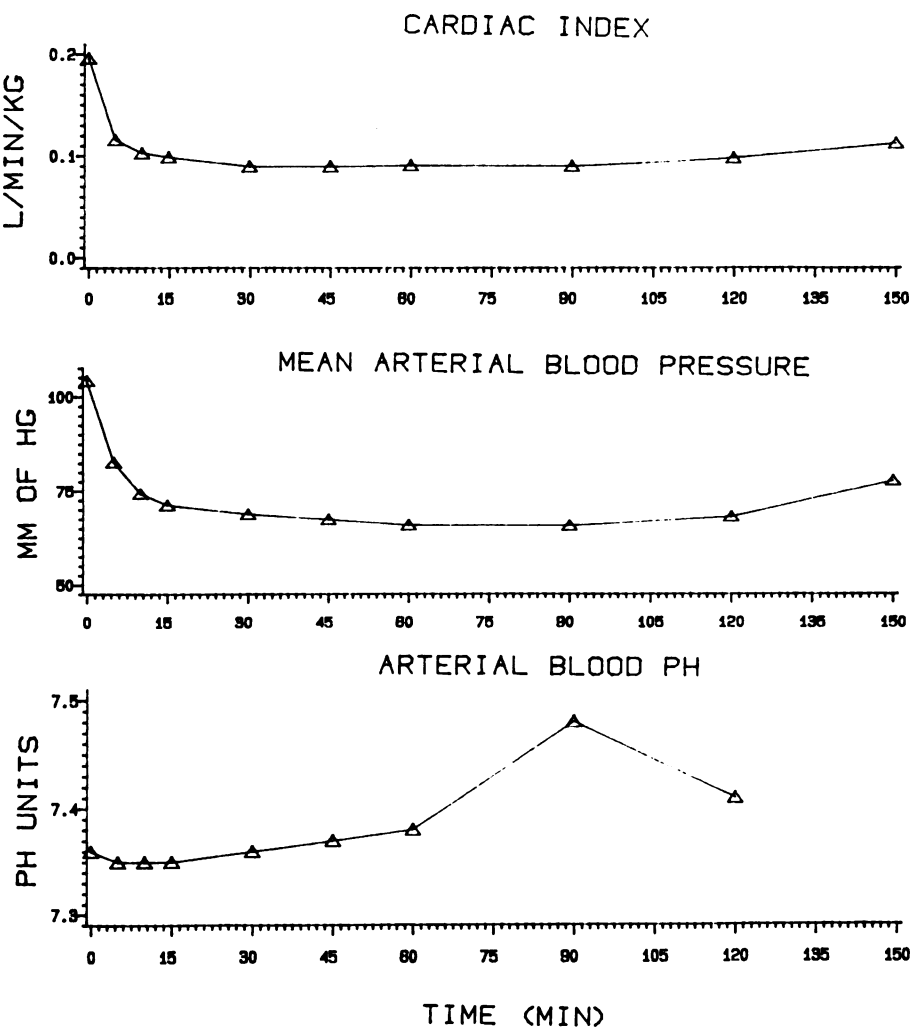

Fig. 1. Parameters of cardiopulmonary function versus time in cats anesthetized with xylazine-ketamine.

TABLE III. Arterial Blood Gas Values of Cats Anesthetized With Xylazine-Ketamine

Parameter	Arterial Blood pH		Arterial Blood pO2 (mmHg)		Arterial Blood pCO2 (mmHg)	
Time/min	Mean	Variance	Mean	Variance	Mean	Variance
Pretest	7.36	0.001	103.4	223.8	27.0	7.27
5	7.35	0.001	98.2	148.5	27.6	26.27
10	7.35	0.001	99.3	299.1	27.1	49.79
15	7.35	0.001	94.8	199.8	29.7	36.55
30	7.36	0.001	95.9	203.8	29.4	17.14
45	7.37	0.003	96.2	96.71	29.2	22.56
60	7.38	0.003	94.5	114.6	30.1	23.24
90	7.48	0.002	98.3	285.0	27.0	24.78
120	7.41	0.002	98.6	196.9	26.0	33.48

load, afterload and contractility. Central venous pressure as an indication of preload was significantly increased in this study and systemic vascular resistance was significantly increased. Contractility was not assessed in this study, but xylazine has been shown to cause a dose dependent decrease in contractility (1). Therefore, the decreased stroke volume noted here was a reflection of increased afterload, decreased myocardial contractility or both (18).

The systolic, diastolic and mean arterial blood pressure were significantly decreased through the 150 minute test period. Xylazine causes a fall in blood pressure due to its central sympatholytic activity (1,4,6). Ketamine hydrochloride causes an increase in heart rate, blood pressure and cardiac output (4,9,11,13). Therefore, the depressor effects of xylazine were not offset by the pressor effects of ketamine. This is in contrast to other investigators who studied the use of this drug combination in dogs and horses (4,7,13). Since arterial blood pressure is a function of the cardiac output, blood volume and the systemic vascular resistance and since the systemic vascular resistance increased in this experiment without an apparent change in blood volume, it can be assumed the fall in blood pressure was primarily a reflection of the decreased cardiac output. An increase in systemic vascular resistance can be expected to accompany a decrease in cardiac output in order to maintain a stable blood pressure, but in this experiment, the increase in systemic vascular resistance was not sufficient to maintain pretest blood pressure values.

Central venous pressure (CVP) increased. An increase in central venous pressure or right atrial pressure is usually accompanied by an increase in heart rate (20). This was not noted. In fact, the heart rate decreased. Possibly the sympatholytic effect of the xylazine negated an increase in the heart rate that may have otherwise occurred.

Blood gas values remained stable throughout the experiment. This is in agreement with previous investigators (8).

This experiment has demonstrated significant depression of cardiovascular function in the normal cat. Careful consideration of this anesthetic combination would have to be given in a cat with evidence of cardiovascular dysfunction. It may be argued that the depressant effects of this drug combination in this study were primarily a reflection of or a cumulative effect of the halothane anesthetic used 24 hours prior to the xylazine-ketamine administration. Halothane has been shown to have a direct, dose dependent depressive effect on cardiovascular function evidenced by a decrease in cardiac output, arterial blood pressure, peripheral resistance and myocardial contractility (19). Surgical trauma and the presence of intravascular catheters may also have had a depressant effect on cardiovascular function. Pretest values of cardiac function, however, were normal on the day of the experiment (17). It is therefore, believed that the values obtained truly represent the effects of a xylazine-ketamine combination at the dosages used and that the halothane anesthesia was not a factor on the day of the experiment.

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