Title: CENTRAL NERVOUS SYSTEM AND CARDIOVASCULAR EFFECTS AND INTERACTION BETWEEN LIDOCAINE AND CHRONIC VERAPAMIL THERAPY IN AWAKE CATS

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INTRODUCTION: The concomitant acute administration of calcium channel blockers and local anesthetics have been examined by several authors.(1,2) These studies may not be applicable to patients receiving calcium channel blocker on a chronic basis. The aim of this study was to examine if chronic administration of calcium channel blockers alter central nervous system toxicity or cardiovascular toxicity of local anesthetics.

METHODS: Sixteen cats were divided into two groups. Group 1 (N=8) served as a control group. Group 2 (N=8) received verapamil 4 mg/kg/day in three divided doses during the day over a period of at least two weeks. The investigators were blinded to which group the cat belonged until the entire protocol was completed. The animals were anesthetized in a halothane/nitrous oxide/oxygen chamber. Scalp EEG electrodes, EKG, and rectal temperature proves were applied to the cat. Both the femoral vein and artery were cannulated by cut-down. The animal was placed in a "cat restraining bag" and allowed to wake up. Thirty minutes after the cat was fully conscious, an infusion of lidocaine 2 mg/kg/min was started. The cats were allowed the spontaneously breath oxygen by mask when they became unconscious from the lidocaine infusion. When both clinical seizures and eliptiform burst were noted on the EEG the cat received vecuronium 0.2 mg/kg and promptly intubated. Mechanical ventilation and the lidocaine infusion continued until cardiac arrest occurred. Cardiac arrest was defined as a flat arterial trace for longer than 15 seconds. Arterial samples for lidocaine levels and arterial blood gases were drawn during the awake state, at the onset of seizures, and when cardiac arrest occurred. Sodium bicarbonate was administered for correction of any base deficit throughout the experiment. A student's T-test was used to examine the difference between the two groups. A $p < 0.05$ was considered statistically significant.

RESULTS: There was no statistical difference between the two groups regarding weight, ages, sex, or resting MAP. Arterial blood gases and body temperatures remained within normal limits during each experiment. Clinical seizures occurred at the same time the high voltage eliptiform burst were noted on the EEG. Intubation of all cats was easily performed within 30 seconds after the onset of seizures. Table 1 shows that there was no statistical difference in the amount of lidocaine, plasma level of lidocaine or time to produce seizures between the two groups. As shown in Table 2, there was no statistical difference in the amount of lidocaine, plasma level of lidocaine, or time to produce cardiac arrest between the two groups of cat. Also, Table 2 shows that the time to produce a 25% decrease in MAP pressure was similar in both groups.

DISCUSSION: Verapamil possesses local anesthetic properties.(3) Despite the fact that local anesthetics central-nervous-system toxicity are additive, (4) our study would indicate that verapamil may be relative void of central nervous system toxicity. One study has advised caution with the concomitant acute administration of both intravenous verapamil and lidocaine.(1) Another study demonstrated an increased mortality with acute overdose of verapamil and lidocaine when compared to acute overdoses of either drug alone.(2) Our study did not show any difference between the two groups to produce a 25% decrease in MAP or cardiac arrest. In conclusion, the authors have demonstrated that the central nervous system toxicity of lidocaine is unaltered by chronic verapamil therapy in cats. Also, this data of this study support that a major regional anesthetic with lidocaine is safe in patients who receive chronic verapamil therapy.

REFERENCES

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TABLE 1:This data indicates the differences between the two groups at the time of seizures

	Group One	Group Two
Dose of Lidocaine (Mg/Kg)	50.8 +/- 17.8	49.9 +/- 21.7
Time to Seizure (Min)	25.4 +/- 4.5	25.0 +/- 10.9
Lidocaine Plasma Level (MCG/ML)	28.2 +/- 6.6	31.0 +/- 11.3

TABLE 2: The time to produce a 25% decrease in MAP and cardiac arrest in the two groups is shown in this table. Also, the amount and plasma level of lidocaine to produce cardiac arrest is depicted

	Group One	Group Two
Resting MAP (torr)	123 +/- 7	118 +/- 14
Time to 25% drop in MAP (Min)	27.2 +/- 2.4	32.8 +/- 6.9
Time to Cardiac Arrest (Min)	71.0 +/- 45	78.1 +/- 44.9
Dose of Lidocaine (MG/KG)	142 +/- 91	156 +/- 89
Plasma level of lidocaine (MCG/ML)	144 +/- 96	155 +/- 105