Yohimbine and Atipamezole on the Treatment of Experimentally Induced Amitraz Intoxication in Cats

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ABSTRACT

Experimental amitraz intoxication and its reversal by atipamezole and yohimbine were studied in cats. Twenty four cats were randomly divided equally into 3 groups: Group A (amitraz); Group AY (amitraz/yohimbine) and Group AA (amitraz/atipamezole). Sedation, loss of reflexes, hypothermia, bradycardia, bradyarrhythmia, hypotension, bradypnea, mydriasis, and initial transitory hyperglycemia occurred in Group A. Median intervals for sedation return, in minutes, were significantly lower in amitraz-intoxicated cats treated with either yohimbine or atipamezole. Yohimbine and atipamezole were very effective in the treatment of amitraz intoxication, although atipamezole was more effective in reversal of arrhythmias, mydriasis, and sedation induced by this acaricide in cats.

INTRODUCTION

Amitraz is a very popular acaricide and tickicide included in the formamidine pesticide group and used in veterinary medicine in many countries.[1,2] In Brazil, a recent study showed that 13.9% of intoxications in dogs were from use of pesticides on farms (39.3% organophosphorous, 35.7% carbamate insecticides, and 25.0% amitraz), and intoxication in cats were 27.6% (46.1% carbamate, 38.5% organophosphorous, and 15.4% other insecticides).[3]

Amitraz has been used to eliminate mites, lice, and ticks in cattle, swine, and dogs, but has been contraindicated for use in horses because it can cause fatal colon impaction.[2] In mammals, amitraz is a α_2-adrenergic agonist[1] and inhibits monoamine oxidase (MAO)[2] and prostaglandin synthesis.[4] Classical signs of amitraz intoxication are characterized by nervous system changes, such as sedation, loss of reflexes, and motor incoordination. Other clinical signs include bradycardia, hypotension, hypothermia, polyuria, hyperglycemia, emesis, mydriasis, and decreased intestinal transit.[1,2]

Because little information is available about this intoxication in cats,[5-7] the manufacturer has not recommended the use of amitraz in this species, despite its efficaciousness in treating feline scabies and demodicosis.[8,9] Although amitraz could be used in such treatments, lack of experimental studies for the treatment of amitraz intoxication in cats prevents such a recommendation. The α_2-adrenergic antagonists yohimbine and atipamezole are usually chosen for treatment of amitraz intoxication associated with other therapeutic procedures (dermal and gastrointestinal decontamination).[5,10]

Yohimbine is a α_2-adrenergic antagonist found in the bark of the tree *Pausinystalia yohimbe* and in the root of *Rauwolfia*.[2] It has high affinity for the α_2-adrenergic receptors α_{2A}, α_{2B}, and α_{2C}, and a low affinity for the α_{2D} receptor.[11,12] Its is also a 5-HT antagonist,[12] but in higher doses it acts as a 5-HT_{1A} agonist inhibiting sympathetic activity.[13] This α_2-adrenergic antagonist also acts indirectly in other receptors, such as GABAergics, cholinergics, dopaminergics, or serotoninergics.[14]

Atipamezole is a potent and selective α_2-adrenergic antagonist approved by the US Food and Drug Administration in 1996 for treatment to reverse sedative and analgesic effects of medetomidine in dogs.[2,15] It is considered a new generation of α_2-adrenergic antagonist due to its high selectivity of α_2-adrenergic receptors,[16] like α_{2A}, α_{2B}, and α_{2C} receptors, and a 100-times higher affinity for the α_{2D} receptor than that of yohimbine in the sheep brain.[12,17] Atipamezole has no antagonistic effect on other receptors.[2]

The objective of this study was to investigate the efficacy of yohimbine and atipamezole in the treatment of amitraz intoxication in cats.

MATERIALS AND METHODS

Experimental Animals

The experiment was approved by the Ethical Committee of FMVZ-UNESP-Botucatu (Protocol no. 47/2001). Mixed-breed adult cats (males and females) obtained from the UNOESTE cat pound were used. First, the cats were sorted by health condition and only those with normal values for the following physiological parameters were used: temperature (T), respiratory rate (RR), heart rate (HR), systolic arterial pressure (SAP), electrocardiogram (ECG), pupil diameter (PD), red (RBC) and white (WBC) blood cell count, urea, creatinine, alanine aminotransferase (ALT), and aspartate aminotransferase (AST). Blood samples were collected by jugular puncture. One day before running the experiment, the cats were socially isolated and held in individual stainless steel cages under 12:12 artificial light-dark cycle, room temperature about 25°C, and fed ad libitum.

Experimental Procedure

Twenty four healthy cats were randomly divided into 3 groups (4 males and 4 females each). Cats (mean weight, 3.5 ± 0.6 kg) in Group A (amitraz, Mitrax®, Agribrands Purina, Paulínia, Brazil) were administered 1 mg amitraz/kg iv at a 1.5% concentration (by dilution of 0.6 mL of amitraz, 75 mg, in 4.4 mL of bi-distilled water). Amitraz dose and dilution were based on a model described for dogs.[15] The other 2 groups received the same concentration and dose of amitraz as group A and 60 min later (T60): Group AY (amitraz/yohimbine; yohimbine, Yobine®, VET-A-MIX, Iowa, USA) (mean weight, 3.0 ± 0.9 kg) were administered 0.1 mg yohimbine/kg iv at a 2 mg/mL concentration; and Group AA, (amitraz/atipamezole; atipamezole, Antisedan®, Pfizer, New York, USA) (mean weight, 3.2 ± 0.7 kg) were administered 0.2 mg atipamezole/kg iv as a 5 mg/mL concentration.

Values of T, RR, HR, SAP, ECG, and PD were measured at times 0, 30, 60, 120, 180, 240, and 360 min of the experiment (yohimbine and atipamezole were administered at the 60-min time point). Glucose, insulin, and cortisol were measured at 0, 60, 180, and 360 min. Levels of RBC, WBC,

urea, creatinine, ALT, and AST were measured at 24 hours before and after amitraz administration.

Specific Procedures

Systolic arterial pressure was measured by an indirect or non-invasive method, with Doppler Ultrasonic equipment (Parks Medical-841-A). Electrocardiogram of cats in right lateral recumbency was recorded using an automated electrocardiograph (Cardiotest EK51). The mean value of 5 consecutives heart beats was recorded on lead II (paper speed of 50 mm/s, 1 cm = 1 mv) for each parameter. Cardiac rhythm was evaluated by occurrence of a) sinusal; b) sinusal arrhythmia; c) sinusal bradycardia; d) 1st degree A-V block; or e) sinus arrest.[18] Pupil diameter was assessed by direct punctiform light toward the pupil. Three levels were scored: normal (1), mydriasis (2), and myosis (3). Mean interval for sedation return (MISR) was considered the time (min) necessary for the animal to recover protective pupillary, palpebral, and interdigital reflexes, and also to stand up without ataxia after the experimental drug administration. Clinical signs were evaluated at the end of the treatments and consisted of occurrence of vomiting, diarrhea, sialorrhea, diuresis, vocalization, ataxia, tremors, 3rd eyelid prolapse, and increased appetite.

Statistical Analysis

Profile analysis[19] compared means among groups and within a group (over time). Whenever normality and/or homocedasticity were not achieved, non-parametric tests were used: Friedmam for comparisons within groups, over time; and Kruskal-Wallis for comparing among groups.[20] A significance level of $P < 0.05$ was adopted.

RESULTS

Amitraz decreased temperature significantly from 60 to 360 min (Table 1). This effect was reduced by yohimbine, with temperatures returning to basal values in 260 min, and atipamezole (return to basal level from 180 min) ($P < 0.05$). Moreover, amitraz administration reduced the respiratory rate from 120 min to 360 min. However, this decreased RR was abolished in groups receiving either yohimbine or atipamezole. Heart rate was decreased by amitraz from 30 min to 360 min of observations. Yohimbine reestablished HR after 260 min, while atipamezole restored earlier (after 180 min) HR to basal values. Considering SAP, amitraz decreased this parameter, an effect reversed more by yohimbine than atipamezole.

Cardiac rhythm was affected by amitraz at 180 min after the drug administration (Table 2). This effect was not found in groups AA and AY, but heart rhythm was changed earlier in the AY group and remained unchanged in the AA group. Moreover, only AY cats showed heart rhythm different from the control group (A: 30, 60, 120, and 180 min). Some cats individually presented arrhythmias during intoxication by the amitraz (Group A), such as sinusal bradycardia, sinusal arrhythmia, and 1st A-V block.

Amitraz intoxication induced mydriasis in all the cats until 240 min. In AY cats, mydriasis persisted until T120, and in AA cats it persisted until T60 (Table 3). The MISR was drastically reduced by either yohimbine or atipamezole, both administered during amitraz intoxication (Table 4).

Regarding blood variables, amitraz increased glucose levels in all groups (Table 5), but this effect was shortened by AY treatment, where cats had reestablished basal glucose levels by 360 min. Cats receiving atipamezole reestablished these levels earlier, at 180 min. Considering insulin levels, the 3 groups showed a similar profile compared with the respective basal levels: insulin level increased, then decreased, and then increased again. However, the increased values at 180 min were lower in both yohimbine and atipamezole groups respective to the control amitraz group. Basal plasma cortisol levels were increased in AY and AA groups compared with the A group, and a significant decrease of cortisol occurred in all groups at 60 min. While amitraz (Group A) decreased cortisol at 30 and

Table 1. Means (± SD; n = 8) of T, RR, HR, and SAP From Cats Treated With Either Amitraz (A), Amitraz + Yohimbine (AY), or Amitraz + Atipamezole (AA).

Parameters	Group	Time (min)						
		0	30	60	120	180	260	360
T	A	38.5 ± 0.7 Aa	38.0 ± 0.8 Aa	37.5 ± 0.6 Ab	36.6 ± 0.7 Ab	36.5 ± 1.3 Ab	36.8 ± 1.7 Ab	36.7 ± 1.4 Ab
	AY	38.4 ± 0.3 Aa	38.1 ± 0.6 Aa	37.6 ± 0.2 Bb	37.2 ± 0.2 Bb	37.8 ± 0.2 Bb	38.0 ± 0.3 Ba	38.1 ± 0.4 Ba
	AA	38.7 ± 0.3 Aa	38.5 ± 0.7 Aa	38.0 ± 0.6 Cb	37.8 ± 0.8 Bb	38.2 ± 0.3 Ba	38.3 ± 0.3 Ba	38.3 ± 0.3 Ba
RR	A	54.1 ± 14.9 Aa	53.5 ± 15.4 Aa	50.5 ± 13.8 Aa	42.6 ± 13.2 Ab	36.1 ± 8.8 Ab	36.0 ± 12.6 Ab	32.5 ± 8.9 Ab
	AY	56.4 ± 9.7 Aa	55.3 ± 11.1 Aa	54.8 ± 18.4 Aa	62.5 ± 13.8 Ba	60.0 ± 17.9 Ba	53.8 ± 17.0 Ba	49.5 ± 11.9 Ba
	AA	57.8 ± 8.3 Aa	55.5 ± 12.4 Aa	51.3 ± 11.6 Aa	52.0 ± 14.7 Ba	50.5 ± 11.5 Ca	52.3 ± 11.4 Ba	50.5 ± 12.6 Ba
HR	A	212.5 ± 18.3 Aa	135.0 ± 32.1 Ab	132.5 ± 32.8 Ab	147.5 ± 44.0 Ac	150.0 ± 47.5 Ab	165.5 ± 60.2 Ab	172.5 ± 51.2 Ab
	AY	200.0 ± 32. Aa	120.0 ± 44.1 Bb	110.0 ± 40.0 Bb	152.5 ± 30.1 Bc	170.0 ± 26.2 Bc	182.5 ± 24.9 Ba	195.0 ± 31.6 Ba
	AA	202.5 ± 24.9 Aa	132.5 ± 21.2 Ab	135.0 ± 35.1 Ab	187.5 ± 14.9 Cc	195.0 ± 20.7 Ca	200.0 ± 23.9 Ca	205.0 ± 29.8 Ba
SAP	A	171.3 ± 33.3 Aa	133.8 ± 27.4 Ab	137.5 ± 27.3 Ab	142.5 ± 27.3 Ab	133.8 ± 19.3 Ac	135.0 ± 24.5 Ac	140.0 ± 18.0 Ab
	AY	168.8 ± 34.0 Aa	141.3 ± 25.3 Ab	121.3 ± 21.0 Bb	160.0 ± 37.4 Ba	161.3 ± 21.0 Ba	141.3 ± 25.9 Ab	146.3 ± 27.2 Ab
	AA	176.3 ± 20.3 Aa	148.8 ± 12.5 Ab	142.5 ± 20.5 Ab	165.0 ± 31.6 Ba	157.5 ± 35.8 Bc	153.8 ± 25.0 Ab	145.0 ± 19.3 Ab

Reference values: 38.1-39.2°C (T); 20-50 mov/min (RR); 120-240 bpm (HR); 120-170 mmHg (SAP).[37]
Upper-case letters compare groups at a same time (Kruskal-Wallis test).
Lower-case letters compare times within each group (Friedman test).
Same letters indicate no significant difference ($P > 0.05$).
The α_2-adrenegic antagonists were administrated at T60 in the AY and AA groups.

Table 2. Medians (quartiles P25;P75) of Heart Rhythm Over Time After Amitraz Intoxication and Treatments in Cats.

Groups	Time (min)						
	0	**30**	**60**	**120**	**180**	**240**	360
A	1 (1;1) Aa	1 (1;3) Aa	1 (1;3) Aa	1 (1;4) Aa	2 (1;4) Bb	1 (1;3) Aa	1 (1;3) Aa
AY	1 (1;1) Aa	3 (1;4) Bb	3 (2;4) (Bb)	2 (1;4) (Bb)	1 (1;4) (Aa)	1 (1;3) (Aa)	1 (1;4) (Aa)
AA	1 (1;1) Aa	1 (1;4) Aa	1 (1;4) (Aa)	1 (1;1) (Aa)	1 (1;1) (Aa)	1 (1;1) (Aa)	1 (1;1) (Aa)

Medians represent heart rhythms: sinusal (1). sinusal arrhythmia (2). sinusal bradycardia (3). 1st degree A-V block (4). and sinus arrest (5). Normal rhythm: sinusal.[18]
Data from 8 cats each group.
Upper-case letters compare groups at a same time (Kruskal-Wallis test).
Lower-case letters compare times within each group (Friedman test).
Same letters indicate no significant difference ($P > 0.05$).
The α_2-adrenegic antagonists were administrated at T60 in the AY and AA groups.

Table 3. Medians (quartiles P25;P75) of PD Over Time After Amitraz Intoxication and Treatments in Cats.

Groups	Time (min)						
	0	30	60	120	180	240	360
A	1.0 (1.0;1.0) Aa	2.0 (2.0;2.0) Ab	2.0 (1.0;2.0) Ab	2.0 (1.0;2.0) Ab	2.0 (1.0;2.0) Ab	2.0 (1.0;2.0) Ab	1.5 (1.0;2.0) Aa
AY	1.0 (1.0;1.0) Aa	2.0 (2.0;2.0) Bb	2.0 (1.0;2.0) Bb	2.0 (2.0;2.0) Bb	1.5 (1.0;2.0) Ba	1.0 (1.0;2.0) Aa	1.0 (1.0;2.0) Aa
AA	1.0 (1.0;1.0) Aa	2.0 (2.0;2.0) Bb	2.0 (2.0;2.0) Bb	1.5 (1.0;2.0) Aa	1.0 (1.0;1.0) Aa	1.0 (1.0;1.0) Aa	1.0 (1.0;1.0) Aa

PD was quantified as normal (1), mydriasis (2) or myosis (3).
Data from 8 cats each group.
Upper-case letters compare groups at a same time (Kruskal-Wallis test).
Lower-case letters compare times within each group (Friedman test).
Same letters indicate no significant difference ($P > 0.05$).
The α_2-adrenegic antagonists were administrated at T60 in the AY and AA groups.

Table 4. Mean (± SD; n = 8) of MISR in Minutes After Amitraz Intoxication and Treatments in Cats.

Groups	MISR (min)
A	175.0 ± 70.7
AY	10.1 ± 4.5*
AA	5.4 ± 2.6*

*Indicates statistical difference from the amitraz group, but similar to each other (Kruskal-Wallis test; $P > 0.05$).

60 min, then returning to basal level (180 min), cats treated with both yohimbine and atipamezole decreased cortisol level at 30 min but increased it at 60 and 180 min.

The other investigated parameters (RBC, WBC, urea, creatinine, ALT, and AST) were not affected by either group or time conditions. The other clinical signs investigated are shown in Table 6.

Table 5. Effects of Yohimbine and Atipamezole on Amitraz-Intoxicated Cats on Glucose, Insulin, and Cortisol Values.

Parameters	Group	Time (min)			
		0	60	180	360
Glucose (mg/dL)	A	85.8 ± 23.3 Aa	167.6 ± 52.9 Ab	136.7 ± 42.0 Ab	103.7 ± 23.7 Ab
	AY	76.1 ± 15.3 Aa	174.7 ± 47.8 Bb	112.7 ± 35.7 Bb	88.6 ± 18.9 Aa
	AA	76.7 ± 20.8 Aa	154.7 ± 36.8 Cb	95.7 ± 24.7 Ca	82.0 ± 16.4 Aa
Insulin (µU/mL)	A	0.81 ± 0.58 Aa	0.30 ± 0.28 Ab	1.04 ± 1.19 Ac	0.30 ± 0.21 Ab
	AY	0.71 ± 0.70 Aa	0.29 ± 0.13 Ab	0.90 ± 0.88 Bc	0.35 ± 0.34 Ab
	AA	0.62 ± 0.60 Aa	0.24 ± 0.09 Ab	0.81 ± 0.67 Bc	0.47 ± 0.49 Ab
Cortisol (µg/mL)	A	2.90 ± 1.55 Aa	1.80 ± 1.89 Ab	2.49 ± 1.26 Ab	2.91 ± 1.26 Aa
	AY	1.16 ± 0.60 Ba	0.74 ± 0.34 Bb	1.73 ± 1.58 Bc	1.90 ± 1.49 Bc
	AA	1.53 ± 1.30 Ba	0.96 ± 0.36 Bb	2.43 ± 1.38 Cc	2.01 ± 0.81 Bc

Means ± SD; n = 8.
Referent values: glucose (73-134 mg/dL) insulin (0-18 U/mL) and cortisol (0.33-2.57 g/mL).[38]
Upper-case letters compare groups at each time (Kruskal-Wallis test).
Lower-case letters compare times within each group (Friedman test).
Same letters indicate no significant difference ($P > 0.05$).
The α_2-adrenegic antagonists were administrated at T60 in the AY and AA groups.

Table 6. Number (and percentage) of Cats Showing Clinical Signs After Intoxication With Amitraz (A), and Treatments With Yohimbine (AY) or Atipamezole (AA).

Groups	Vomit	Diarrhea	Sialorrhea	Diuresis	Vocalization	Ataxia	Tremors	3rd Eyelid Prolapse	Increased Appetite
A	5 (62.5%)	0 (0%)	4 (50.0%)	2 (25.0%)	2 (25.0%)	5 (62.5%)	0 (0%)	0 (0%)	4 (50.0%)
AY	7 (87.5%)	2 (25.0%)	2 (25.0%)	2 (25.0%)	1 (12.5%)	1 (12.5%)	1 (12.5%)	0 (0%)	0 (0%)
AA	6 (75.0%)	1 (12.5%)	3 (37.5%)	1 (12.5%)	1 (12.5%)	1 (12.5%)	1 (12.5%)	0 (0%)	0 (0%)

Data from 8 cats each group.
The α_2-adrenegic antagonists were administrated at T60 in the AY and AA groups.

DISCUSSION

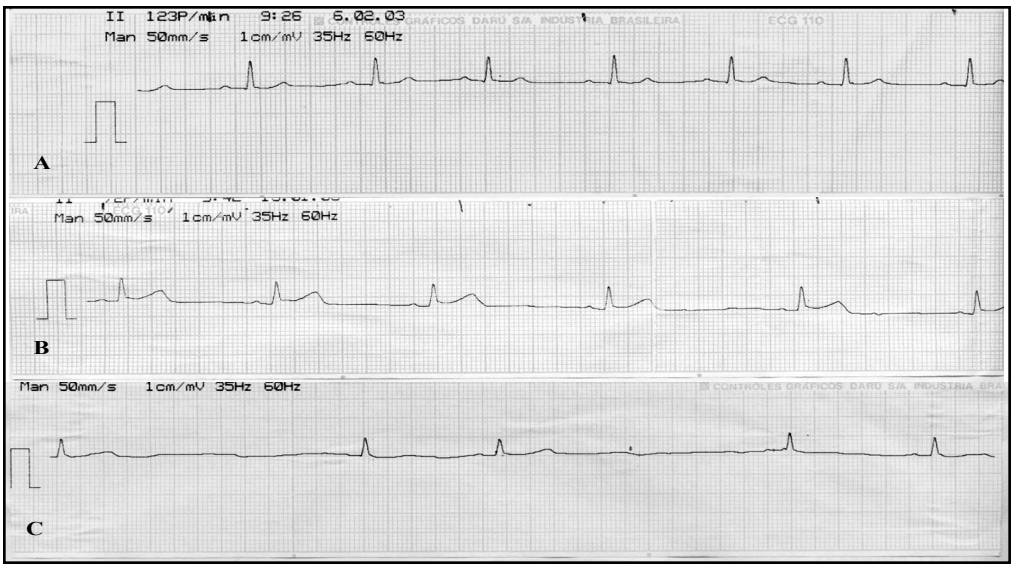
Amitraz induced hypothermia in cats, an effect that was restored effectively by yohimbine and atipamezole. Amitraz α-agonist action decreases body temperature, as also reported for other α-agonists, xylazine and detomidine.[1,2] Alpha-adrenergic agonists are known to affect the thermoregulation center at the hypothalamus.[21]

Contention and handling are stressors that induce the typical stress response of increased adrenocortical hormones.[22,23] This effect explains the slightly increased mean RR basal values in the 3 groups investigated.

Amitraz has been shown to depress respiratory rate by central action,[24] probably by inhibition of respiratory neurons located in the ventral portion of the brain.[25] High concentration of α_2-adrenergic agonists can reduce both sensitivity of the breathing center to increased PCO_2 and tidal volume, thus accentuating breathing depression.[26] The present study showed that this effect of amitraz on breathing was reversed by using treatments with either yohimbine or atipamezole.

Amitraz-induced bradycardia and hypotension are mainly a result of reducing sympathetic tonus by activation of central

Figure 1. Examples of arrhythmias of cats in Group AY: (A) sinusal bradycardia of the cat n.1 in T30; (B) 1st A-V block of the cat n.4 in T60; (C) sinus arrest of the cat n.7 in T60. Electrocardiograms from lead II (paper speed = 50 mm/sec. 1 cm = 1 mv).



pre-synaptic α_2-receptors.[27] The α_2-adrenergic antagonists used in this study reverted this effect of amitraz on HR.

Reported arrhythmias caused by α_2-adrenergic agonists are sinusal bradycardia, 1st or 2nd degree A-V block, and, rarely, complete 3rd degree A-V block with escape pulsations, probably by reducing CNS sympathetic tonus and increasing parasympathetic activity.[16,26] Amitraz induced sinusal bradycardia, 1st degree A-V block, and sinus arrest (Figures 1 and 2). After yohimbine administration, some animals still presented some arrhythmias (eg, sinusal arrhythmia), sinusal bradycardia, and 1st degree A-V block; However, atipamezole administration induced no arrhythmia until the end of the experiment, thus corroborating that this treatment is more effective than yohimbine for treating arrhythmias induced by amitraz intoxication. As far as we know, this is the first report of this effect.

Mydriasis induced by amitraz is a dose-dependent phenomenon, which is mediated by post-synaptic α_2-adrenoceptors.[27] Although both atipamezole and yohimbine restored the amitraz-induced mydriasis, atipamezole induced an earlier effect (120 min) than did yohimbine (180 min).

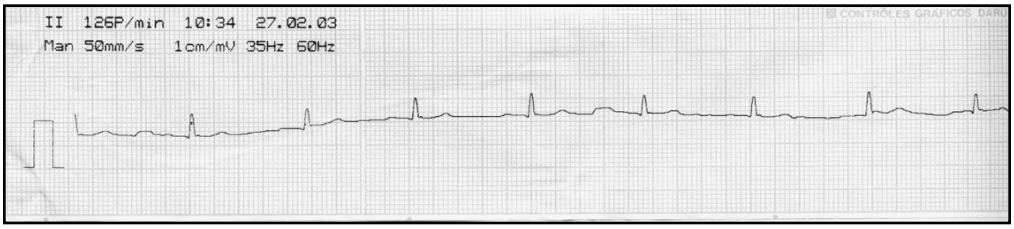
Amitraz has been shown to induce a high degree of sedation by activation of the central pre-synaptic α_2-receptor.[21] Although cats treated with atipamezole and yohimbine showed no different mean time for sedation return, atipamezole abolished sedation faster than yohimbine.

Hyperglycemia and hypoinsulinemia induced by amitraz and its active metabolite, BTS 27271, derive from inhibition of insulin secretion a mechanism mediated by α_2-adrenergic receptors, mainly the α_{2D} located within the pancreatic islets,[28-30] possibly by inhibition of adenyl cyclase mediated by G PTX-sensitive proteins.[30] Both yohimbine and atipamezole were very effective in restoring the amitraz-induced hyperglycemia. This result agrees with Andrade et al,[5] who successfully abolished hyperglycemia in 2 cats intoxicated accidentally with amitraz by administering this α_2-adrenergic antagonist.

The increased plasma cortisol level detected in the cats from the amitraz group at the beginning of the experiment (0 min) may be a consequence of handling stress.[31] Considering that handling was similar among groups, the Group A cats may be more susceptible to stress. Cortisol, insulin, and glucose concentrations are changed in stressed animals.[32] The decreased cortisol level after amitraz administration in Group A may be due to amitraz-induced CNS depression by stimulation of α_2-adrenergic central receptors, resulting in decrease of sympathetic efflux of CNS, of catecholamines, and of other stress-related substances.[31,32] On the other hand, yohimbine and atipamezole increased plasma cortisol, an α_2-adrenergic antagonistic effect.

Despite the effects of amitraz described above, RBC, WBC, urea, creatinine, ALT, and AST were not affected by amitraz administration. This has also been reported in amitraz intoxication in other animals, for example, humans,[33] horses,[34] and mice.[35] Treatment by yohimbine and atipamezole also did not affect these parameters.

Figure 2. 1st A-V block of the cat n.3 in T60 of Group AA. Electrocardiograms from lead II (paper speed = 50 mm/sec. 1 cm = 1 mv).



Amitraz inhibits the antidiuretic hormone and thus may increase diuresis.[2] This drug also stimulates chemically the vagal nucleus of the postrema area, thus inducing vomiting and sialorrhea.[25] Moreover, vocalization and sialorrhea are common in stressed animals.[31,32]

Amitraz depresses the CNS by stimulation of α_2-adrenergic receptors and provokes sedation and ataxia.[21] In the present study, no cat presented 3rd eyelid prolapse, contrary to the report by Andrade and Sakate.[15] At the end of the experiment, appetite was increased in half of the cats, a result also reported in mice.[36] Moreover, appetite in cats treated with either of the α_2-adrenergic antagonists was unchanged during the experiment.

Summing up the effects of amitraz intoxication in cats, by iv route, the main effects detected here were: sedation, loss of reflexes, hypothermia, bradycardia, bradyarrhythmia, hypotension, bradypnea, mydriasis, vomiting, and in some cases diuresis, increased appetite, sialorrhea and vocalization. Bradyarrhythmias consisted of sinusal bradycardia, 1st degree A-V block, and sinus arrest. Hematological alterations were hyperglycemia and transitory hypoinsulinemia, and transitory decrease of plasma cortisol levels; no changes occurred in RBC, WBC, urea, creatinine, ALT, or AST.

This study showed that yohimbine and atipamezole were effective in treating amitraz intoxication. However, arrhythmias, mydriasis, and sedation induced by this acaricide were more effectively reversed by atipamezole, probably due by the higher affinity of atipamezole for α_2-adrenergic receptors.

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