

## Cardiovascular and Respiratory Effects of Romifidine and/or Xylazine in Ketamine Anaesthesia in Dog: An Experimental Study

Mohammad Reza Emami<sup>\*1</sup> DVSc  
Mohammad Reza Sedighi<sup>1</sup> DVSc  
Shamsedin Sarhaddi<sup>2</sup> DVM

<sup>1</sup>Department of Clinical Sciences, Faculty of Veterinary Medicine,  
Ferdowsi University of Meshad, Meshad, Iran.

<sup>2</sup>Private Veterinary Practitioner, Meshad, Iran.

---

### Abstract

**Objective:** To compare romifidine and xylazine premedication in ketamine anesthesia of the dog.

**Design:** Experimental design.

**Animals:** Fifteen cross-breed dogs.

**Procedures:** Animals randomly allocated into three groups of five. Group G1 premedicated by xylazine 1 mg/kg, G2 romifidine 40 µg/kg and G3 romifidine 80 µg/kg intramuscularly. All animals premedicated with atropine 0.02 mg/kg subcutaneously ten minutes before induction of anesthesia. Anesthesia was induced by 15 mg/kg ketamine IM. Heart rate, respiratory rate, mean arterial blood pressure and electrocardiac activity beside quality of anesthesia were evaluated.

**Results:** No significant differences were found between three groups around all recorded parameters.

**Conclusions and Clinical relevance:** Usage of different doses of romifidine in canine species is possible without any unexpected outcome, 80 µg/kg of romifidine make better onset of anesthesia.

**Key Words:** Romifidin, Xylazin, Ketamine, anesthesia, dog

---

### \*Corresponding Author:

Mohammad Reza Emami  
Department of Clinical Sciences, Faculty of Veterinary Medicine,  
Ferdowsi University of Meshad, Meshad, Iran.  
Email address: [emami@um.ac.ir](mailto:emami@um.ac.ir)

## Introduction

Romifidine is a potent and selective  $\alpha_2$ -adrenoreceptor agonist that is approved for use in horses in Europe, Australia, New Zealand and Canada, and for use in dogs in Europe. It has been shown to be a reliable sedative and analgesic agent in dogs after intravenous<sup>1</sup>, intramuscular<sup>2</sup> and subcutaneous administration<sup>3</sup>. Xylazine premedication in healthy dogs has been associated with an increase in mortality rate compared with other pre-anesthetic regimes<sup>4,5</sup>.

The cardiovascular effects of  $\alpha_2$ -adrenoreceptor agonists have been generally described as dose dependent with the duration of effect clearly prolonged at higher doses<sup>6</sup>. Low doses of romifidine (5  $\mu$ g/ kg) appeared to have less pronounced cardiovascular effects than low doses of medetomidine, despite similar levels of sedation<sup>7</sup>. Anticholinergic premedication has also been recommended with  $\alpha_2$ -agonists to prevent bradyarrhythmias and, potentially, the reduction in cardiac output produced by these agents<sup>8</sup>.

Dysrhythmias characterized by heart block, premature ventricular depolarizations and tachycardia have been noted with anticholinergic and  $\alpha_2$ -agonist combinations, especially if the anticholinergic is administered concurrently rather than prior to the  $\alpha_2$ -agonist<sup>9,10</sup>.

This current study was designed to evaluate the electrocardiographic and circulatory effects of two different doses of romifidine in compare to xylazine as preanesthetic agents in ketamine anesthesia of dogs.

## Materials and Methods

The study was conducted in 15 healthy dogs (cross breed). The dogs were anaesthetized for an experimental skin healing procedure. The dogs were housed indoors at ambient temperature, fed meat and rice. Prior to anesthesia and surgery, food was withheld for 12 hours but the animals had free access to water.

Baseline cardiovascular, pulmonary and analgesia measurements were obtained in conscious dogs prior to injection of any drugs. Animals were allocated in three groups of five (G1, G2 and G3). G1, G2 and G3 were weighing 26.8 $\pm$ 8.19, 25.9 $\pm$ 6.63 and 25.8 $\pm$ 6.05 kg (mean  $\pm$  SD) respectively. All dogs received atropine sulfate (Atropine, Pasture Inst., Iran) (0.02 mg/ kg IM). G1, G2 and G3 dogs premedicated with romifidine HCl (Sedivet®, Boehringer Ingleheim, Swiss) (40  $\mu$ g/ kg IM), romifidine (80  $\mu$ g/ kg IM) and xylazine HCl (Rumpon®, Bayer, Germany) (1 mg/ kg IM) respectively. Anesthesia was induced with ketamine HCl (Ketalar®, Pantex, Holland) (15 mg/ kg IM) ten minutes after preanesthesia. Heart rate (HR), respiratory rate (RR), indirect mean arterial blood pressure (MBP) (KBM-115, Japan), ECG (Fukudadenshi Card Max, Japan) and extent of analgesia were measured immediately before and during minutes 15, 30, 45 and 60 after induction. Remaining in lateral decubency, absence of reaction to skin cutting and suturing and negative response to ear pinching were used as the most important measures for depth of anesthesia.

A *t*-test for independent samples was used to determine whether the two main effects, time and treatment, were significant for the variables HR, RR, MBP. A *p*-value of 0.05 or less was considered significant. Results are presented as mean  $\pm$  standard deviation unless stated otherwise. Analyses were carried out using the Windows statistical package Sigmastat (Jandel scientific).

## Results

A stable depth of anaesthesia was achieved with all three preanesthetic agents. Table 1 details the parameters which were measured during anaesthesia. Baseline values did not vary significantly among groups for all variables measured and were within the expected range for conscious clinically normal dogs<sup>11</sup>.

There was some obvious increase in HR in all animals during experiment, however, significant differences among treatment comparisons were not observed at any time point.

All animal developed hypertension from 10 to 60 minutes in compare to baseline, although no significant differences were noted among treatment comparisons at any time point.

ECG showed arrhythmias, including second-degree atrioventricular (AV) heart block, were noted in a dog in G1 at 5 minutes as well as in a dog in G2. Second-degree AV heart block was recorded in two dogs in G3 15 minutes after anesthesia. No evidence of first-degree and third-degree AV heart block was detected.

Recorded RRs showed a significant difference between G1 and G2 and between G1 and G3 at time 0, beginning of experiment ( $p<0.05$ ). All groups showed decreases in respiratory rate from 5 to 55 minutes.

Onset of analgesia was from 12 minutes (average time) in G1, from 14 minutes in G2 and from 9 minutes in G3. Analgesia was complete till 60 minute (end of experiment) in all groups.

Duration of anesthesia (min),  $71.60\pm 3.07$  for **G1**,  $80.00\pm 6.20$  for **G2** and  $84.00\pm 6.20$  for **G3**, didn't differ significantly among three groups ( $p<0.05$ ).

**Table 1: Measured parameters in groups under study (Mean±SD)**

Group	Parameter	Time (min)				
		0	15	30	45	60
<b>G1</b>	HR	90.40±	137.40±	128.80±	110.80±	107.20±
	(Beat/Min)	1.60	11.93	15.56	7.41	4.60
	MAP	109.20±	168.90±	146.30±	154.30±	141.80±
	(mmHg)	9.54	6.73	10.35	9.46	9.21
	RR	30.80±	18.40±	15.00±	15.40±	16.40±
(Beat/Min)	4.02	3.41	1.64	2.49	2.82	
<b>G2</b>	HR	89.40±	139.20±	132.40±	115.40±	112.80±
	(Beat/Min)	9.40	10.20	8.49	10.28	8.42
	MAP	109.90±	143.20±	158.30±	134.90±	163.10±
	(mmHg)	4.56	10.60	3.10	31.05	2.07
	RR	49.40±	26.60±	16.40±	15.40±	16.00±
(Beat/Min)	4.33	7.63	1.50	1.16	1.22	
<b>G3</b>	HR	87.20±	166.40±	149.20±	134.00±	119.00±
	(Beat/Min)	9.30	30.68	3.04	12.23	9.80
	MA	107.80±	146.60±	168.40±	167.20±	156.00±
	P(mmHg)	3.90	5.93	5.11	6.86	11.7
	RR	55.40±	14.20±	13.60±	13.00±	12.20±
(Beat/Min)	7.93	1.82	0.81	1.78	1.52	

## Discussion

The main clinical cardiovascular changes produced by romifidine or xylazine in this study included bradycardia and associated bradyarrhythmias, increase of heart rate after ketamine induction in all groups and an overall increase in MAP. These effects are consistent with another study of romifidine<sup>7</sup> and other  $\alpha_2$ -agonists<sup>6</sup>.

Changes in cardiovascular value have been reported after atropine/xylazine/ketamine anesthesia<sup>6</sup>, romifidine/propofol/halothane<sup>12</sup> as well as romifidine/ketamine<sup>13</sup> in dogs. All mentioned investigations have been showed that use of xylazine and/or romifidine result in bradycardia and associated bradyarrhythmias and administration of ketamine increase and correct heart rate<sup>14,15</sup>.

Heart rates were slightly less in the high-dose romifidine group (G3) than the low-dose group (G2) and xylazine group (G1), although the difference was not significant. Therefore, in our study, the magnitude of bradycardia did not appear to be dose and drug related. However, lower doses of romifidine (5 and 10  $\mu\text{g kg}^{-1}$ ) did induce less severe bradycardia<sup>7</sup>.

Recorded MAP showed no significant differences among treatment comparisons at any time point. In contrast, the increase in arterial blood pressure appeared to be dose and drug related. Lesser changes in MAP were noted with G2 compared with greater increases with G3. Lower doses of romifidine may be associated with more predominant central nervous system effects, whereas higher doses probably cause a more pronounced stimulation of peripheral adrenoreceptors and vasoconstriction<sup>16,7</sup>. Hypotension, defined as MAP < 80 mm Hg, did not develop in any dogs, in contrast to studies with xylazine<sup>17</sup>. This may be associated with an insufficient measurement period in our study. Strong maintenance of MAP with newer  $\alpha_2$ -agonists may be due to a more specific peripheral  $\alpha_2$ -adrenoreceptor affinity, which may predominate over the centrally mediated hypotensive effects, especially at higher doses<sup>18,16</sup>.

Second degree AV heart block has been seen in this study is consistent with effects noted by others and isn't uncommon consequent of administration of  $\alpha_2$ -agonists<sup>19,6,14</sup>.

Decrease in respiratory rate after administration of romifidine and/or xylazine from 5 to 60 minutes in all groups with a similar pattern are consequent step of CNS depressant effect of  $\alpha_2$ -agonists. This respiratory rate alteration is consistent with medetomidine sedation in dogs<sup>20,21</sup> and romifidine sedation in dogs<sup>22</sup>; however there is not any significant difference between three groups at any time point when xylazine and/or different doses of romifidine have affected.

In spite of the result in this study, Kerr noted priority of romifidine to xylazine in lengthening of anesthesia in horse<sup>15</sup>. This result may be a consequent of use of combination of romifidine and diazepam or a specific effect of romifidine in horse.

These positive effects need to be balanced against the marked increase in blood pressure produced by the mentioned dose of these drugs, with the realization that the high HR and MBP may well affect myocardial oxygen supply.

Overall, usage of different doses of romifidine in canine species is possible without any unexpected outcome and we suggest premedication with 80  $\mu\text{g/ kg}$  of romifidine make better onset of anesthesia.

## References

1. England GCW, Flack TE, Hollingworth E. Sedative effects of romifidine in the dog. *J Small Anim Pract* 1996;37:19–25

2. Lemke KA. Sedative effects of intramuscular administration of a low dose of romifidine in dogs. *Am J Vet Res* 1999;60:162–168.
3. England GCW, Thompson S. The influence of route of administration upon the sedative effect of romifidine in dogs. *J Vet Anaes* 1997;24:21–23
4. Clarke KW, Hall LW. A survey of anaesthesia in small animal practice: AVA/BSAVA report. *J Ass Vet Anaes* 1990;17:4–10.
5. Dyson D, Maxie MG, Schnurr D. Morbidity and mortality associated with anesthetic management in small animal veterinary practice in Ontario. *J Am Anim Hosp Assoc* 1998;34:325–335.
6. Klide AM, Calderwood HW, Soma LR. Cardiopulmonary effect of xylazine in dogs. *Am J Vet Res* 1975;36:931-935.
7. Pypendop BH, Verstegen JP. Cardiovascular effects of romifidine in dogs. *Am J Vet Res* 2001;62:490–495.
8. Mirakhur RK. Anticholinergic drugs and anaesthesia. *Can J Anaes* 1988;35:443–447.
9. Alibhai HIK, Clarke KW, Lee YH, et al. Cardiopulmonary effects of combinations of medetomidine hydrochloride and atropine sulphate in dogs. *Vet Rec* 1996;138:11–13.
10. Short CE. Effects of anticholinergic treatment on the cardiac and respiratory systems in dogs sedated with medetomidine. *Vet Rec* 1991;129:310–313.
11. Haskins SC. Monitoring the anesthetized patient. In: Thurmon JC, Tranquilli WJ, Benson GJ, eds. *Lumb and Jones' Veterinary Anesthesia*. 3<sup>rd</sup> ed. Baltimore: Williams & Wilkinson, 1996;418–419.
12. Marjorie EG, Booth NH. Tranquilizers, alpha2 agonist and related agents. In: Adams H, ed. *Veterinary pharmacology and therapeutics*. 7<sup>th</sup> ed. Iowa: Iowa State University Press, 1995;346-347.
13. Gomez VR. Romifidine /ketamine in dog: A clinical trail, in: *Proceedings*. 6<sup>th</sup> international congress of veterinary anesthesiology 1997;163.
14. Diamond MJ, Young LE, Bartram DH, et al. Clinical evaluation of romifidine/ketamine/halothane anesthesia in horses. *Vet Rec* 1993;132:572-575.
15. Kerr C, McDonnell W, Young SA. Comparison of romifidine and xylazine when used with diazepam/ketamine for short duration anesthesia in horses, in: *Proceedings*. 5<sup>th</sup> international congress of veterinary anesthesia 1994;131.
16. Hall LW, Clarke KW. Principles of sedation, analgesia and premedication. In: *Veterinary Anaesthesia*. 9<sup>th</sup> ed. London: Bailliere Tindall, 1991;52–64.
17. Haskins SC, Patz JD, Farver TB. Xylazine and xylazine ketamine in dogs. *Am J Vet Res* 1986;47:636–641.
18. Savola JM. Cardiovascular actions of medetomidine and their reversal by atipamezole. *Acta Vet Scand Suppl* 1989;85:39–47.
19. Myasa MN, Sagenge E. Clinical effect of azaperon/metomidate, as compare to propionylpromazine/xylazine/metomidate or xylazine/ketamine combinations in anesthesia of dogs. *J Vet Med* 1986;36:225-229.
20. England GC, Clarke KW. The use of medetomidine/fentanyl combinations in dogs. *Acta Vet Scand Suppl* 1989;85:179–186.
21. Pettifer GR, Dyson DH. Comparison of medetomidine and fentanyl-droperidol in dogs: sedation, analgesia, arterial blood gases and lactate levels. *Can J Vet Res* 1993;57:99–105.
22. Lemke KA. Electrocardiographic and cardiopulmonary effects of intramuscular administration of glycopyrrolate and romifidine in conscious Beagle dogs. *Vet Anaesth Analg* 2000;28:1–13.

## مطالعه تجربی تأثیرات قلبی-عروقی و تنفسی رامیفیدین و/یا زایلازین در بیهوشی با کتامین در سگ

دکتر محمد رضا امامی<sup>۱</sup>، دکتر محمد رضا صدیقی<sup>۱</sup>، دکتر شمس الدین سرحدی<sup>۲</sup>

<sup>۱</sup>گروه علوم درمانگاهی، دانشکده دامپزشکی دانشگاه فردوسی مشهد، مشهد، ایران.  
<sup>۲</sup>دامپزشک بخش خصوصی، مشهد، مشهد، ایران.

**هدف:** بررسی تأثیر دو دوز درمانی رامیفیدین بر دستگاه قلبی-عروقی و تنفسی در مقایسه با زایلازین در بیهوشی با کتامین.  
**طرح:** مطالعه تجربی.

**حیوانات:** پانزده قلابه سگ.

**روش کار:** در این مطالعه به منظور بررسی تأثیر دو دوز رامیفیدین (G2) ۴۰ µg/Kg IM و (G3) ۸۰ µg/Kg IM بر دستگاه های قلبی-عروقی و تنفسی و کیفیت بیهوشی متعاقب استفاده از آن در مقام مقایسه با زایلازین (G1) ۱ mg/Kg IM در سگ در بیهوشی با کتامین ۱۵ mg/Kg IM، پانزده قلابه سگ به سه گروه مساوی تقسیم گردیدند و بر اساس یک مطالعه کور یکی از رژیم های دارویی گفته شده در هر گروه استفاده گردید. تعداد ضربان قلب، تعداد تنفس، متوسط فشار خون سرخرگی و فعالیت الکتریکی قلب و همچنین کیفیت بیهوشی مورد ارزیابی قرار گرفت.

**نتایج:** آنالیز اطلاعات به دست آمده نشان داد که سه رژیم دارویی در هیچ کدام از فاکتورهای اندازه گیری شده اختلاف معنی داری ( $p < 0.05$ ) را با یکدیگر نشان ندادند.

**نتیجه گیری:** می توان گفت که استفاده از دوزهای مختلف رامیفیدین به عنوان پیش بیهوشی در سگ بدون اثرات غیر قابل انتظار می باشد و شروع بیدردی بهتری با رامیفیدین با دوز ۸۰ میلی گرم به ازای هر کیلوگرم وزن بدن خواهیم داشت.  
**کلید واژگان:** رامیفیدین، زایلازین، کتامین، بیهوشی، سگ