

## INTRAOCULAR PRESSURE EVALUATION OF EQUINES ANESTHETIZED WITH ROMIFIDINE, TILETAMINE/ZOLAZEPAM, HALOTHANE AND VECURONIUM<sup>1</sup>

### AVALIAÇÃO DA PRESSÃO INTRA-OCULAR DE EQUÍNOS ANESTESIADOS COM ROMIFIDINA, TILETAMINA/ZOLAZEPAM, HALOTANO E VECURÔNIO

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#### SUMMARY

*The purpose of this study was to evaluate an anesthetic association with and without the use of a nondepolarizing muscle relaxant agent and its effect on intraocular pressure of horses, and also obtain an anesthetic technique free of adverse effects for ophthalmic surgeries in this specie. Sixteen horses were randomly divided in two groups of eight horses each. In group I, horses were pre-medicated with romifidine, anesthesia induced with tiletamine/zolazepam and maintained with halothane and vecuronium. Horses of group II received the same anesthetic association except for vecuronium. Intraocular pressure, arterial pressure and heart rate were evaluated in different moments during the experiment. The anesthetic association composed by romifidine, tiletamine/zolazepam and halothane with and without vecuronium did not promote statistically significant alterations in horses intraocular pressure and its use is practicable in ophthalmologic procedures.*

**Key words:** *intraocular pressure, anesthesia, horses, neuromuscular blocking agent.*

#### RESUMO

*O objetivo deste estudo foi o de avaliar uma associação anestésica com e sem a utilização de relaxante muscular não-despolarizante e seu efeito sobre a pressão intra-ocular de equínos. Também objetivou-se uma técnica anestésica sem efeitos adversos que possa ser utilizada em procedimentos e cirurgias oftálmicas nesta espécie animal. Para tanto, dezesseis equínos foram divididos aleatoriamente em dois grupos de oito animais cada. Os animais do grupo I foram pré-medicados com romifidina, induzidos com tiletamina/zolazepam e a anestesia foi mantida com halotano e vecurônio. Os animais do grupo II receberam a mesma associação anestésica, com exceção do vecurônio. No decorrer do experimento, a pressão intra-ocular, a pressão arterial e a frequência cardíaca foram avaliadas em diferentes momentos. A associação anestésica composta pela romifidina, tiletamina/zolazepam e halotano com e sem vecurônio não promoveu alterações estatisticamente significativas na pressão intra-ocular de equínos e o seu uso é exequível em procedimentos oftálmicos nesta espécie animal.*

**Palavras-chave:** *pressão intra-ocular, anestesia, equínos, bloqueador neuromuscular.*

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## INTRODUCTION

In veterinary medicine few studies were conducted about different anesthetic associations that can be used in ophthalmic surgeries and procedures in horses with the intent to minimize the changes on intraocular pressure. Specialized literature shows contradictory opinions among several authors and few studies made in veterinary medicine in concern with the use of dissociative anesthetic agents in ophthalmic procedures. This study was conducted after a review about different anesthetic associations used in ophthalmic surgery in the last few years in veterinary and human medicine. The review made by MURPHY (1985) and CUNNINGHAM & BARRY (1986) on anesthesia and intraocular pressure (IOP) pointed out several improvements made in the highly specialized field of human intraocular surgery that surfaced in recent years and also defined IOP as the pressure exerted by the contents of the eye against its containing wall (MURPHY, 1985).

Due to the development of new anesthetic agents and techniques, the anesthesiologist can improve the conditions for examination and for ophthalmic surgery. Apart from providing an immobile and uncongested field he can, by manipulating the factors at his disposal, decrease intraocular pressure and thus minimize the danger of expulsion of intraocular contents when the eye is opened (MURPHY, 1985). With the use of a nondepolarizing neuromuscular blocking agent an immovable operating camp is obtained and there is also the possibility of using fewer depressing inhalatory anesthetic agents.

It is believed that the action of romifidine on equine IOP is equal to that caused by xylazine, which means that probably romifidine causes a decrease in IOP. IOP tends to decrease after intravenous administration of xylazine (MCCLURE *et al.*, 1976; VAN DER WOERDT *et al.*, 1995) and xylazine with ketamine in equines (TRIM *et al.*, 1985).

The main problem caused by anesthesia on ophthalmic human surgery is the increase of IOP that occurs in the moment of endotracheal intubation when a depolarizing neuromuscular blocking agent is used to facilitate endotracheal intubation (WYNANDS & CROWELL, 1960; MACDIARMID & HOLLOWAY, 1976; COUCH *et al.*, 1979). Succinylcholine chloride administered to horses anesthetized with halothane in oxygen and mechanically ventilated induced slight but insignificant increases in IOP (BENSON, 1981).

Neuromuscular blocking agents are also used to promote centralization of the eye during surgery. In regard to the nondepolarizing agents, it is said that they do not increase the IOP significantly. According to POLARZ *et al.* (1995), vecuronium preceded by thiopentone and alfentanil decreases IOP, and concluded that it can be given when increases in humans IOP have to be avoided.

In spite of the mention made by some authors that the use of the dissociative agent ketamine cause an increase of IOP (COUCH *et al.*, 1979; FRAGEN & HAUCH, 1981; CALLA *et al.*, 1987; MIRAKHUR *et al.*, 1988), it is said that it can be used safely for pediatric ophthalmic examinations (YOSHIKAWA & MURAI, 1971; PEULER *et al.*, 1975).

Although there is knowledge about the isolated effects of dissociative agents and it is known that in human beings it can cause no significant increase on IOP, the effect of the administration of a combination of drugs including a dissociative anesthetic drug in animals is not yet known.

In a study made by WATCHA *et al.* (1990) with children anesthetized with halothane and nitrous oxide, was concluded that IOP after induction remains constant over time and is not affected by end-tidal halothane concentrations up to 1.0% but is affected by tracheal intubation. In human patients with a low normal pre-operative IOP tended to show a rise in IOP during halothane anesthesia, and those with a high normal pre-operative IOP tended to show a fall (VAN DEN BERG *et al.*, 1995).

The objective of this study was to evaluate the IOP of horses anesthetized with the association of romifidine, tiletamine/zolazepam and halothane with and without vecuronium.

## MATERIAL AND METHODS

### Animals

Sixteen horses of different breeds and ages, weighing between 300 and 500kg referred to the University of São Paulo Veterinary Hospital were used. The horses underwent both clinical and ophthalmic examinations to rule out diseases that could interfere in IOP values. They were randomly assigned into two groups of eight horses each.

### Anesthesia

Group 1: Romifidine<sup>a</sup> (0.08mg/kg) was administered by intravenous route (IV) as the pre-anesthetic medication. After 15 minutes a combination of tiletamine/zolazepam<sup>b</sup> (2.00mg/kg, IV) were administered. The animals gradually collapsed into a

dog-sitting position and could be easily positioned in lateral recumbency. Endotracheal intubation was performed since the swallowing reflex was absent in all horses. Anesthesia was maintained on a closed circle system of a large animal anesthetic machine (Model 2800, Mallard Medical, Irvine, California) with halothane<sup>c</sup> in 100% oxygen. Halothane concentration was enough to maintain the horses on a stable surgical anesthetic plane. Abolition of spontaneous ventilation was accomplished by the administration of vecuronium<sup>d</sup> (0.1mg/kg, IV). Once apnea was established controlled ventilation was started. Tidal volume (12ml/kg), respiratory rate (10breaths/min.) and I:E relation (1:2) were settled in the ventilation machine (Rachel, Model 2800, Mallard Medical, Irvine, California). At the end of the surgical procedure, in all animals the respiratory rate at the ventilator was gradually decreased. The intent was to increase the partial carbon dioxide pressure in order to promote stimulation of the respiratory center by the chemoreceptors. There was no necessity of the administration of neostigmine to reverse the neuromuscular blockade caused by vecuronium, because of its short acting time. In fact, after weaning the animals were able to maintain a normal tidal volume, which reinforced the no need of pharmacological antagonism.

Group 2: The same anesthetic protocol used in Group 1 was used in this group except for vecuronium, which was not administered. Controlled ventilation was not required.

#### Assays

The parameters of: intraocular pressure, systolic and diastolic arterial pressure (SAP and DAP) and heart rate (HR) were evaluated at the moments M0 (before the pre-anesthetic medication), M1 (5 minutes after the pre-anesthetic medication), M2 (1 minute after induction), M3 (immediately after endotracheal intubation), M4 (15 minutes after the beginning of the inhalatory anesthesia), M5 (one minute after neuromuscular blockade) and M6 (three minutes after neuromuscular blockade). The IOP was measured with an applanation tonometer (TONOPEN, Biorad, California) after topical anesthesia with proximetacaine<sup>e</sup>. Three measurements were taken for each moment probe. Arterial pressure was evaluated by indirect measurement using an aneroid manometer and mitt placed over the base of the animal tail and the auscultation of the bruits by the alignment of the extremity of a ultrasonic stethoscope (Imbracrios, São Paulo, SP) with gel over the coccigeal artery. Heart rate on non-anesthetized horses was measured with the auscultation of heart beats with the stethoscope over

the cardiac area. Once the animal was anesthetized, heart rate was obtained with an oscilloscope (Ecafix, São Paulo, SP).

#### Statistical methods

The results were compared statistically by parametric tests, with the ANOVA test (variance analysis) followed by the Tukey's test, for the comparison of different moments of observation of a same group, and the test of t-Student for the comparison of different moments of IOP observation within the two groups;  $p < 0.05$  was considered significant.

## RESULTS

The administration of romifidine, as well as the maintenance with halothane caused a significant decrease of heart rate. In Group I, a decrease of HR was observed 5 minutes after the romifidine administration which returned to its normal value after induction, also a decrease of HR was observed 3 minutes after the vecuronium administration. In Group II, a decrease of HR was verified 5 minutes after the pre-anesthetic medication (Tables 1 and 2).

During inhalation anesthesia, a significant decrease of arterial blood pressure was verified in both groups. The administration of romifidine and the induction with tiletamine/zolazepam caused a initial increase of blood pressure (Tables 1 and 2).

No statistically significant alteration occurred on IOP values in Groups I and II (Tables 1 and 2), and also when comparing the moments within the Groups.

## DISCUSSION

It is believed that xylazine, an  $\alpha$ -2 agonist pre-anesthetic agent, cause a decrease of horses IOP, what means that probably romifidine would have the same effect. In equines, IOP decreases after intravenous administration of xylazine (MCCLURE *et al.*, 1976; VAN DER WOERDT *et al.*, 1995) and xylazine with ketamine (TRIM *et al.*, 1985). In this study romifidine administration did not cause any significant alteration of IOP.

Almost all anesthetic agents commonly used for humans anesthetic induction decreases IOP, for example, thiopental, propofol and etomidate, with the probable exception of ketamine (COUCH *et al.*, 1979; FRAGEN & HAUCH, 1981; CALLA *et al.*, 1987; MIRAKHUR *et al.*, 1988). Ketamine presents undesirable characteristics when used for anesthetic

Table 1 - Heart rate (HR), systolic arterial pressure (SAP), diastolic arterial pressure (DAP) and intraocular pressure (IOP) in 8 horses treated with romifidine, tiletamine/zolazepam, halothane and vecuronium (Group 1) in different moments of evaluation. Results are expressed in means and standard deviations (SD).

PARAMETERS	MOMENTS						
	M0	M1	M2	M3	M4	M5	M6
HR (beats/min)	38.6 ±15.5 (a,b)	28.5 ±9.3 (a)	39.8 ±8.3 (a)	31.2 ±5.4 (a)	32.6 ±4.7 (a)	32.1 ±5.2 (b)	28.6 ±6.5 (a,c)
SAP (mmHg)	118.2 ±25.7 (a,b)	137.1 ±35.5 (a)	148.1 ±30.0 (a)	150.0 ±35.9 (a)	94.5 ±16.3 (b)	90.1 ±18.4 (a,b)	93.1 ±21.9 (a,b)
DAP (mmHg)	77.2 ±18.1 (a,c)	97.7 24.9 (a,b)	118.1 ±32.7 (b)	116.6 ±32.9 (b)	59.9 ±15.9 (c)	57.6 ±15.6 (c)	60.0 ±15.1 (c)
IOP (mmHg)	21.7 ±5.1 (a)	19.5 ±4.6 (a)	20.9 ±6.7 (a)	19.0 ±4.1 (a)	19.9 ±5.2 (a)	17.1 ±4.0 (a)	15.1 ±4.4 (a)

a, b, c: non coincident letters present statistically significant values with  $p < 0.05$  in a same parameter. The results were compared with ANOVA test followed by Tukey's test.

induction in ophthalmic surgery in humans, but it is commonly used as an anesthetic agent for pediatric ophthalmic examinations (YOSHIKAWA & MURAI, 1971; PEULER *et al.*, 1975). Indeed, according to PEULER *et al.* (1975), there is a reduction in IOP after ketamine. The IOP reduction occurs 2 minutes after the administration of ketamine and normal values are obtained 2 minutes after the initial reduction. In the present study it was verified that the association tiletamine/zolazepam did not cause a significant increase of horses IOP.

The increase of IOP that is frequently verified during difficult orotracheal intubation in humans and/or when succinylcholine is administered is one of the problems that must be avoided during

anesthesia for ophthalmic surgeries.

Endotracheal intubation was easily performed in all horses after induction with tiletamine/zolazepam and no alterations on IOP immediately after endotracheal intubation were observed.

In human patients with spontaneous respiration halothane reduces IOP (MAGORA & COLLINS, 1961; MEHTA, 1962; TAMMISTO *et al.*, 1975). Apparently all volatile agents causes a decrease of IOP that is dose dependent, but factors like  $\text{PaCO}_2$  and posture may be an important factor that could change IOP in patients with spontaneous ventilation (MURPHY, 1985; CUNNINGHAM & BARRY, 1986). No statistically significant decrease of horses IOP values obtained 15 minutes after the beginning of the inhalatory anesthesia was observed in both groups.

Administration of vecuronium during steady state anesthesia was associated with a significant decrease on human IOP (MIRAKHUR *et al.*, 1987). This experiment showed that vecuronium associated with tiletamine/zolazepam and halothane did not cause a statistically significant alteration of horses IOP.

In both groups a decrease of heart rate was observed after romifidine administration what is in agreement with the results obtained by GÓMEZ-VILLAMANDOS (1995). There was a decrease of HR after the neuromuscular blockade. There was an increase of HR after the pre-anesthetic medication when the values were compared to those obtained after the induction and after the endotracheal intubation.

Continuous doses of halothane causes myocardial depression and vasodilatation that will provoke decrease of blood pressures (MILLER, 1989). A significant decrease of systolic and diastolic pressures was verified in this experiment after halothane administration when compared with the earlier moments. IOP was not directly affected by the

Table 2 - Heart rate (HR), systolic arterial pressure (SAP), diastolic arterial pressure (DAP) and intraocular pressure (IOP) in 8 horses treated with romifidine, tiletamine/zolazepam and halothane (Group 2) in different moments of evaluation. Results are expressed in means and standard deviations (SD).

PARAMETERS	MOMENTS				
	M0	M1	M2	M3	M4
HR (beats/min)	46.2	30.0	35.5	34.5	35.5
	±21.4	±7.1	±9.7	±8.5	±6.2
	(a)	(b)	(a,b)	(a,b)	(a,b)
SAP (mmHg)	145.7	153.5	166.2	165.7	116.5
	±26.1	±28.8	±20.8	±19.2	±23.8
	(a)	(a)	(a)	(a)	(b)
DAP (mmHg)	110.0	119.4	132.0	126.2	89.2
	±32.9	±28.1	±18.9	±20.1	±21.9
	(a,b)	(a)	(a)	(a)	(b)
IOP (mmHg)	20.9	20.0	26.4	27.1	19.5
	±5.4	±7.5	±10.7	±11.6	±9.8
	(a)	(a)	(a)	(a)	(a)

a, b, c: non coincident letters present statistically significant values with  $p < 0.05$  in a same parameter. The results were compared with ANOVA test followed by Tukey's test.

changes in arterial blood pressure, what confirms the results obtained by DEAR *et al.* (1987) in a study made in young children.

Vecuronium is a good neuromuscular blocking agent because it does not act in the autonomic ganglia and is almost all eliminated in bile, it also does not alter arterial pressure (MUIR *et al.*, 1995), being suitable for ophthalmic procedures. In the present study it was verified that its administration was not associated with changes of systolic and diastolic arterial pressures.

Although, the induction with tiletamine/zolazepam caused an increase of heart rate and systolic and diastolic arterial pressure, it did not alter equines IOP.

It can be concluded with the present study that romifidine can be safely used in the pre-anesthetic

medication of equines being submitted to ophthalmic procedures or surgeries once it caused a decrease of the IOP. Tiletamine/zolazepam association used for induction preceded by romifidine did not statistically alter equines IOP as well as endotracheal intubation did not promote sympathetic stimulation that would increase IOP. Halothane showed to be a good anesthetic agent for ophthalmic surgeries once it did not alter the equines IOP, vecuronium preceded by tiletamine/zolazepam and halothane did not alter equines IOP and it can be used to immobilize and centralize the ocular globe during the surgical procedure.

## SOURCES AND MANUFACTURES

- a - Sedivet©, Boehringer de Angeli, Itapeberica da Serra, SP.
- b - Zoletil©, Virbac do Brasil, São Paulo, SP.
- c - Halotano©, Cristália - Produtos Químicos Farmacêuticos Ltda, Itaparica, SP.
- d - Norcuron©, Akso Ltda., Divisão Organon Teknika, São Paulo, SP.
- e - Anestalcon© 0,5%, Alcon Laboratórios do Brasil Ltda, São Paulo, SP.

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