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Comparison of the Anesthetic Effects of Tiletamine HCl–Zolazepam–Xylazine and Ketamine–Diazepam–Xylazine in Older Foals under Field Conditions

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ABSTRACT

The purpose of the study was to compare the drug combinations effect of xylazine–tiletamine HCl–zolazepam (XZ group) and xylazine–ketamine–diazepam (XKD group). Both drug groups were administered to six older foals, with ages ranging from 4 to 6 mth and body weight between 107 to 125 kg in a crossover design. Measured parameters were heart rate, respiratory rate, body temperature, blood glucose, systolic and diastolic blood pressure, mean arterial blood pressure and blood gas variables (pH, PaO_2, $PaCO_2$, HCO_3, TCO_2, BE, and saturated oxygen (SaO_2). All parameters were evaluated at 5 min before and 7 min after administering xylazine and were also measured at 5, 10, 15 and 20 min after the administration of the anesthetic drugs. The quality of induction and recovery, quality of mouth opening and intubation, number of attempts to regain sternal recumbency, standing position and duration of anesthetic effects were measured. There were no significant ($P > 0.4$) differences in any measured parameters of both drug groups suggesting that the xylazine – tiletamine HCl–zolazepam combination was safe for anesthetic induction in older foals.

Keywords: foal, xylazine, ketamine, diazepam, tiletamine, zolazepam, Zoletil®

INTRODUCTION

The aims of anesthesia in veterinary practice are to produce analgesia and immobilization of the patient for medical treatment or surgical procedures. In the beginning, equine practice anesthesia was focused on physical restraint for immobilization. However, equine anesthesia is associated with a higher mortality rate than in other animal species and humans (Flaherty *et al*., 1996; Staffieri and Driessen, 2007).

The Confidential Enquiry into Perioperative Equine Fatalities (Johnston *et al*., 2002) concluded that the choice of anesthetic technique had a relatively high risk mortality rate of 3% if only inhalant agents are used compared with 0.3% for the total intravenous anesthetic (TIVA) technique. Induction with injectable agents followed by maintenance with an inhalation anesthetic for prolonged anesthesia in horses can result in the perioperative mortality rate in horses under anesthesia being around 1%, while the

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mortality rates in foals aged less than 6 mth, and foals aged less than 1 mth are 1.1% and 1.5%, respectively (Johnston *et al*., 2002). One third of foal mortalities was caused by cardiac arrest, one third from fractures and myopathies, and one third from a range of causes (Marntell, 2004).

The selection of the applied anesthetic technique and anesthetic drugs to obtain easy recumbency, rapid surgical procedures without changing cardiovascular or respiratory functions while producing good muscle relaxation and avoiding movement of the horse, and smooth recovery are required (Garcia *et al*., 2002; Staffieri and Driessen, 2007).

The selection of sedatives and anesthetics for foals is difficult for the equine practitioner because of the immature physiology in neonatal foals and the smaller body size, low fat and glycogen storage in the body and the heat loss because of their high surface area relative to body weight and lack of cutaneous fat. Hypoglycemia may be a problem due to the very small energy reserves and higher metabolic rate compared with adult horses particularly in sick, premature or very young foals. Furthermore, foals may easily pass into hypoxemia, hypercapnia and acidosis resulting from the anesthetic agents, which can induce cardiovascular depression. Therefore, an understanding of anesthetic drugs and their prescription is important.

The most popular sedative drug used in foals is benzodiazepine because of its minimal cardiovascular and respiratory side effects. Other drugs such as phenothiazine and alpha-2 adrenoceptor agonist are typically avoided in foals aged less than 6 wk and in ill foals because the administration of these drugs is associated with hypotension, bradycardia, and decreasing cardiac output effects. However, xylazine is an excellent sedative and analgesic (Aubin and Mama, 2002; Garcia *et al*., 2002) and older foals (aged 6 wk up to 6 mth) with a mature metabolic pathway and circulatory and respiratory systems can be treated similarly to an adult horse (Tranquilli and Thurmon, 1990). The most popular drug for producing short-term general anesthesia in horses is ketamine because it has less effect on cardiovascular and respiratory depression; however, this drug is a controlled drug in Thailand due to its potential for human abuse. Therefore, it is not easily obtained by the equine practitioner in Thailand. Other drugs such as propofol, thiopental and pentobarbital have effects of depression of the cardiovascular and respiratory systems (Muir 1991). Zoletil® is commercially available in Thailand as a combination of a tiletamine and a zolazepam and usually is used for producing short-term chemical restraint and induction to inhalation anesthesia in horses (Muir *et al.,* 1991; Hubbell, 1999; Staffieri and Driessen, 2007).

The aim of the present study was to compare and evaluate the physiological changes of older foals after using a ketamine-diazepam combination and Zoletil® as anesthetic induction agents.

MATERIALS AND METHODS

Animals

Six healthy thoroughbred-cross foals, five males and one female, with an age range from 4 to 6 mth (4.5 ± 0.5; mean ± SD) and weighing between 107 and 125 kg (118.3 ± 7.2; mean ± SD) were used in this study. The foals were determined healthy based on a complete physical examination, complete blood count and blood chemistry for 1 wk before the experiment. The study used foals in this age range because according to Dunlop (1994), emergency anesthesia for the repair of a ruptured bladder, patent urachus, gastrointestinal surgery and musculoskeletal repair is most commonly required for foals aged more than 6 wk (1–6 mth).

Experimental design

As a crossover design, the study was

divided into two parts. Each foal was anesthetized twice, 1 wk apart. All foals were used in a blind random design and Group 1 animals were anesthetized with tiletamine–zolazepam (1 $mg.kg^{-1}$ BW: Zoletil®, Virbac Laboratories, France) and Group 2 animals with ketamine (2.0 $mg.kg^{-1}$ BW: Calypsol, Gedeon Richter Ltd., Hungary)–diazepam (0.1 $mg.kg^{-1}$ BW: Ropam® injection, L.B.S. Laboratory Ltd., Part., Thailand). Xylazine (1 $mg.kg^{-1}$ BW: X–zine®, L.B.S. Laboratory Ltd., Part., Thailand) was used as a sedative for both groups.

Experimental procedure

All foals were anesthetized under field conditions. Before foal sedation, the mare was sedated with acepromazine maleate (0.04 $mg.kg^{-1}$ BW: Combistress, Phoenix Pharmaceuticals N.V., Antwerp, Belgium) and was separated from the foal and kept in an adjacent box. At 5 min before sedation, an indirect blood pressure monitoring cuff (IW1, Omron Healthcare CO. Ltd., Japan) was placed at the base of the foal's tail (middle coccygeal artery) to record the systolic and diastolic blood pressure. An arterial blood sample (facial arteries, transverse facial arteries, or dorsal metatarsal arteries) was collected for blood gas analysis of pH, PaO_2, $PaCO_2$, HCO_3, TCO_2, BE, SaO_2 (i - Stat® G3+ Cartridge, Portable Clinical Analyzer, Abbott Laboratories Inc., USA). HR (heart rate), RR (respiratory rate), BT (body temperature), CRT (capillary refill time) and mm (mucus membrane color) were also recorded. Five minutes after induction, all parameters were repeatedly recorded. Seven minutes after xylazine administration, an induction with XZ (xylazine/Zoletil: Group 1) or XKD (xylazine/ketamine and diazepam: Group 2) was applied. The observers were blinded to the combination of induction drugs used in each study. During induction and the recovery phase, each foal was observed without help to record induction and recovery scores (see the index in the Appendix). After induction, the foal was placed in lateral recumbency and an endotracheal tube, No.12, 15.6 mm. internal diameter cuffed, (KRUUSE, Denmark) was intubated. The ease of mouth opening and intubation were evaluated by the method of Frias *et al*. (2003) and recorded on a scale of 1 to 3 (1 = difficult, intubation after more than three attempts; 2 = moderate, intubation after two or three attempts and 3 = easy, intubation at first attempt). An 18 G, 30 mm catheter (NIPRO Corporation Limited, Thailand) was inserted into a jugular vein for collection of blood samples for blood glucose analysis and a 20 G, 25 mm catheter (NIPRO Corporation Limited, Thailand) was inserted into a facial artery or transverse facial artery and/or dorsal metatarsal artery for measurement of blood gas parameters. Observation of the color of mucous membranes, capillary refill time and ocular reflex (blink, palpebral, and corneal reflex) were also recorded. Data were recorded at 5, 10, 15, and 20 min after induction via intravenous administration. After administration of the anesthetic induction drugs, the following times were recorded: time from inducing agent injection to lateral recumbency (T*effect*), time from injection of the inducing agent to loss of swallowing reflex (T*intubation*), time from injection of the inducing agent until the swallowing reflex happened (T*swallowing*), time from injection of the inducing agent to sternal recumbency (T*sternal*), time from inducing agent injection to standing (T*standing*), time from standing to no ataxia on walking (T*locomotion*) and time from inducing agent injection to no ataxia on movement (T*recovery*). The number of attempts to sternal recumbency and standing position were recorded during the recovery period.

Statistical analysis

Parameters measured for the study were blood gas analysis values (pH, PaO_2, $PaCO_2$, HCO_3, TCO_2, BE, SaO_2), blood pressure (systolic, diastolic and mean arterial blood pressure: MAP),

HR, RR, BT and blood glucose. Data were analyzed for normality, and were compared using a paired sample t–test. Nonparametric variables measured for the study included the differences between times, number of attempts to sternal recumbency, number of attempts standing position, and scores for the quality of induction, recovery, and mouth opening and intubation. Data were analyzed for normality and compared based on Wilcoxon scores (rank sums). Differences were considered significant at the 5% level ($P < 0.05$).

RESULTS

Cardiovascular and respiratory effects

The effects of XZ and XKD on the cardiovascular and respiratory systems are presented in Table 1 and blood glucose and blood gas analyses are presented in Table 2. No statistically significant differences were seen between the XZ group and XKD group in the parameters associated with the cardiovascular and respiratory systems and blood glucose and blood gases. Xylazine caused bradycardia within 7 min after intravenous administration; however 5 min after induction, HR in both groups was slightly increased but remained slower than that of the base line. RR was decreased at 5 min after xylazine intravenous administration and decreased during the first 5 min after induction in both groups and remained lower than that of the base line until 20 min after induction. Body temperature slightly increased from the base line at 7 min after xylazine injection and decreased at 5, 10, 15 and 20 min after induction in both groups but was still in the normal range.

Systolic and diastolic blood pressures tended to increase from the base line at 7 min after xylazine injection and were still increasing at 5 min after induction before slightly deceasing in both groups. Analysis of the blood gas parameters ($PaCO_2$, PaO_2, BE, pH, HCO_3, TCO_2, SaO_2 and blood glucose) showed no significant differences between groups ($P > 0.4$). However, hypoxemia and decreased SaO2 were found in both groups.

Quality of anesthesia

Both groups revealed a good quality of induction but the quality of recovery varied from poor to excellent and two foals in the XKD group required five attempts to achieve sternal recumbency (Table 3).

Duration of anesthetic effects

Analysis of the time from induction to recovery showed no difference between groups. The mean time (± SD) duration of the T*effect* or to knockdown was less than 1 min in the XZ group and 1.2 ± 0.4 min the XKD group (Table 4). The time from induction to loss of the swallowing reflex and intubation to sternal and standing position in the XZ group was faster than in the XKD group. The time from induction to swallowing reflex, the time from standing to no evidence of ataxia on walking and the time from induction to no evidence of ataxia on locomotion in the XZ group were longer than for the XKD group.

DISCUSSION

After administration of xylazine, all foals had bradycardia and a depressed respiratory system. Body temperature was slightly increased from the base line because xylazine is an alpha-2 adrenoceptor agonist. The mechanism of action of xylazine is the activation of central alpha-2 receptors. The alpha-2 receptors are located both presynaptic and postsynaptic in the peripheral and central nervous system. The presynaptic alpha-2 receptors actions generally have an inhibitory effect on the releasing of transmitters from the synaptic nerve endings, that is, on norepinephrine, dopamine, serotonin, acetylcholine (Benson and Thurmon, 1990; Aubin and Mama, 2002) and also induce sympathetic blockage as well as vagal

Table 1 Cardiovascular and respiratory parameters (mean ± SD) during anesthetic administration in older foals.

	Group	Time 0	After xylazine	After anesthetic drug administration			
				5 min	10 min	15 min	20 min
Heart rate	XZ	58.0 ± 12.0	44.0 ± 8.0	48.0 ± 7.0	45.0 ± 10.0	48.0 ± 8.0#	50.0 ± 9.0#
(bpm)	XKD	48.0 ± 7.0	43.0 ± 6.0	48.0 ± 7.0	46.0 ± 5.0*	43.0 ± 11.0*	56.0 ± 9.0*
Respiratory rate	XZ	27.0 ± 5.0	22.0 ± 4.0	12.0 ± 5.0	16.0 ± 11.0	18.0 ± 5.0#	21.0 ± 3.0#
(bpm)	XKD	33.0 ± 8.0	19.0 ± 2.0	17.0 ± .0	15.0 ± 6.0*	20.0 ± 5.0*	24.0 ± 8.0*
Temperature	XZ	38.0 ± 0.3	38.2 ± 0.3	38.1 ± 0.3	37.8 ± 0.6	37.4 ± 0.5#	37.6 ± 0.4#
(ºC)	XKD	38.1 ± 0.4	38.4 ± 0.4	38.3 ± 0.5	37.9 ± 0.5*	37.9 ± 0.4*	37.8 ± 0.3*
MAP	XZ	65.0 ± 4.4	78.6 ± 21.1	83.2 ± 11.5	75.2 ± 14.6	71.5 ± 10.1#	68.1 ± 15.0#
(mmHg)	XKD	73.3 ± 19.8	88.9 ± 25.2	86.3 ± 15.3	78.9 ± 16.4*	71.1 ± 17.9*	80.8 ± 24.1*
Systolic BP	XZ	91.3 ± 5.0	111.2 ± 22.8	114.2 ± 11.5	104.5 ± 15.6	104.8 ± 11.5#	94.2 ± 18.9#
(mmHg)	XKD	95.8 ± 14.5	109.8 ± 22.4	115.3 ± 17.5	109.6 ± 19.6*	101.6 ± 23.1*	103.6 ± 20.7*
Diastolic BP	XZ	51.0 ± 4.3	62.3 ± 21.5	67.7 ± 11.7	60.5 ± 14.3	54.8 ± 9.8#	55.0 ± 13.3#
(mmHg)	XKD	62.7 ± 22.9	78.3 ± 27.0	71.8 ± 15.3	63.6 ± 15.5*	55.8 ± 15.9*	69.4 ± 26.4*

BP = Blood pressure; XZ = xylazine–Zoletil®; XKD = xylazine–ketamine–diazepam.

n = 6 unless labeled otherwise; * = number of foals equals 3; # = number of foals equals 4.

Table 2 Blood gas analysis of pH, partial pressure of O_2 (PaO_2), partial pressure of CO_2 ($PaCO_2$), HCO_3, total CO_2 (TCO_2), Base excess (BE), Saturated O_2 (SaO_2) and blood glucose concentration (Data are expressed as a mean ± SD).

	Group	Time 0	After xylazine	After anesthetic drugs administration			
				5 min	10 min	15 min	20 min
pH	XZ	7.47 ± 0.02	7.44 ± 0.02	7.41 ± 0.04†	7.43 ± 0.03	7.40 ± 0.02†	7.42 ± 0.02†
	XKD	7.48 ± 0.03	7.45 ± 0.02	7.42 ± 0.04†	7.43 ± 0.05#	7.45 ± 0.03†	7.44 ± 0.04†
PaO_2(mmHg)	XZ	91.2 ± 9.8	85.0 ± 8.3	60.4 ± 11.8†	66.0 ± 11.9	65.6 ± 11.2†	73.8 ± 27.1†
	XKD	78.2 ± 24.0	85.8 ± 8.9	69.6 ± 14.5†	62.0 ± 14.2#	55.0 ± 11.7†	49.2 ± 13.0†
$PaCO_2$(mmHg)	XZ	38.3 ± 3.2	40.1 ± 1.9	44.1 ± 3.7†	41.8 ± 4.0	42.8 ± 2.6†	42.1 ± 3.1†
	XKD	36.9 ± 3.7	37.2 ± 3.4	41.6 ± 4.2†	41.5 ± 5.1#	37.8 ± 5.6†	38.4 ± 5.1†
HCO_3(mmol.L^{-1})	XZ	27.8 ± 2.2	27.5 ± 1.9	27.7 ± 1.9†	27.3 ± 2.1	26.9 ± 1.9†	27.2 ± 1.9†
	XKD	26.7 ± 3.2	25.9 ± 2.7	26.8 ± 2.8†	27.2 ± 3.1#	25.8 ± 3.6†	25.9 ± 3.3†
TCO_2(mmol.L^{-1})	XZ	29.0 ± 2.4	28.5 ± 1.9	29.0 ± 1.9†	28.7 ± 2.1	28.2 ± 1.9†	28.4 ± 1.9†
	XKD	28.0 ± 3.5	27.0 ± 2.8	27.2 ± 3.2†	28.3 ± 2.9#	26.8 ± 3.8†	27.0 ± 3.4†
BE(mmol.L^{-1})	XZ	4.2 ± 2.3	3.3 ± 2.2	3.0 ± 2.4†	2.8 ± 2.4	2.2 ± 2.2†	2.8 ± 2.3†
	XKD	3.8 ± 2.6	2.0 ± 2.8	2.4 ± 2.9†	2.3 ± 3.8#	2.0 ± 3.4†	2.0 ± 3.5†
SaO_2(%)	XZ	97.5 ± 0.8	96.7 ± 1.2	88.8 ± 7.7†	92.2 ± 5.6	92.0 ± 4.1†	91.4 ± 9.6†
	XKD	97.3 ± 0.8	96.5 ± 0.8	93.4 ± 4.9†	90.0 ± 7.7#	89.2 ± 6.6†	85.0 ± 10.0†
Glucose(mg.mL^{-1})	XZ	77.6 ± 7.1	74.9 ± 5.2	82.8 ± 7.95	88.7 ± 6.7	84.6 ± 6.3	87.2 ± 8.3
	XKD	72.4 ± 13.6	69.7 ± 9.9	77.3 ± 12.4	83.0 ± 11.9	84.1 ± 8.6	79.2 ± 2.5

XZ = xylazine–Zoletil®; XKD = xylazine–ketamine–diazepam.

n = 6 unless labeled otherwise; † = number of foals equals 5; # = number of foals equals 4.

stimulation involving baroreceptor activation, peripheral vasoconstriction, bradycardia, sinu-arterial arrest and first and second degree artrioventricular blocks (Aubin and Mama, 2002; Garcia *et al*., 2002; Frias *et al*., 2003; Marntell, 2004). The aforementioned mechanism of xylazine could cause bradycardia, arrhythmia and decreased blood pressure; however, the mean arterial pressure could not drop below 60 mmHg (Tranquilli and Thurmon, 1990; Frias *et al*., 2003). A decrease in cardiac output and initial hypertension followed by prolonged hypotension and increased pulmonary pressure were reported; however, the body temperature was reduced (Vaala, 1985; Tranquilli and Thurmon, 1990; Hubbell, 1999; Aubin and Mama, 2002; Marntell, 2004). The muscle hypertonicity and excitement is normally associated with dissociative drugs, with ketamine, being often used to induce anesthesia (Aubin and Mama, 2002). The Colorado State University studied eight foals using a xylazine dose of 0.3 $mg.kg^{-1}$ by intravenous administration and found a decrease in the heart rate and cardiac output as well as a reduction in oxygen tissue perfusion in the foals (Dunlop, 1994).

Table 3 Number of foals at each score level and the mean score (1–5 level, see Appendix) of the quality (for induction, recovery, mouth opening and intubation) and number of attempts (to sternal recumbency and standing position). (n=6).

Score level / mean	XZ group						XKD group					
	1	2	3	4	5	mean	1	2	3	4	5	mean
Quality												
Induction	0	0	2	4	0	3.7	0	0	1	5	0	3.8
Recovery	1	1	1	2	1	3.2	0	1	1	2	2	3.8
Mouth opening and intubation	0	4	2	0	0	2.3	2	2	2	0	0	2.0
Number of attempts												
Sternal recumbency	5	1	0	0	0	1.2	2	1	1	0	2	2.8
Standing position	1	5	0	0	0	1.8	3	3	0	0	0	1.5

XZ = xylazine–Zoletil®; XKD = xylazine–ketamine–diazepam.

Table 4 Duration of time parameters (mean ± SD) : T*effect* , T*intubation*, T*swallowing*, T*sternal*, T*standing*, T*locomotion* and T*recovery* in six foals pre-medicated with xylazine (1.1 $mg.kg^{-1}$) and anesthetized with Zoletil®(1 $mg.kg^{-1}$) or diazepam (0.1 $mg.kg^{-1}$) and ketamine (2 $mg.kg^{-1}$).

Time (min)	XZ group	XKD group
T*effect*	1.0 ± 0.0	1.2 ± 0.4
T*intubation*	1.0 ± 0.5	2.0 ± 0.9
T*swallowing*	21.2 ± 7.6	19.2 ± 7.1
T*sternal*	24.2 ± 7.1	24.8 ± 8.6
T*standing*	25.2 ± 7.1	26.3 ± 9.0
T*locomotion*	17.3 ± 6.4	15.8 ± 6.2
T*recovery*	42.3 ± 10.5	42.2 ± 8.4

XZ = xylazine–Zoletil®; XKD = xylazine–ketamine–diazepam.

In the present study, during induction anesthesia by Zoletil® or ketamine and diazepam, there was no statistically significant difference in any of the variables because the basic pharmacology of tiletamine is similar to ketamine. Zolazepam is a benzodiazepine tranquilizer having a central muscle relaxant effect and anticonvulsant activity similar to diazepam. The tiletamine effects on the cardiovascular system are an increase in the heart rate and cardiac output, a decrease in arterial blood pressure, systemic vascular resistance and myocardial contractility, but there is no effect on the central venous and pulmonary vascular pressure (Benson and Thurmon, 1990). The group XZ administration induced hypoventilation resulting in increased $PaCO_2$, decreased PaO_2 and decreased arterial pH. This was similar to a previous report in horses by Hubbell *et al*. (1989). The tiletamine has a longer duration of action, a greater analgesic effect and more muscle relaxation than ketamine (Benson and Thurmon, 1990; Aubin and Mama, 2002; Marntell *et al*., 2006; Staffieri and Driessen, 2007). The mouth opening and intubation or jaw tone relaxation remained quite relaxed and easy, which was similar to a previous report (Short *et al*., 1989). The quality of the anesthesia induction using xylazine for sedation was smooth with excellent muscle relaxation which was the same as a previous report (Matthews *et al.,* 1991a,b). Benson and Thurmon (1990) reported that normally, a horse remained in lateral recumbency for an average of 45 min after finishing anesthesia or assumed the horse roll to sternal recumbency after 30 to 39 min and stood up within 32 to 45 min, and the duration of anesthesia was related to the dose of Zoletil®.

Ketamine inhibits gamma–aminobutyric acid (GABA), and also may block serotonin, norepinephrin and dopamine in the central nervous system (CNS) by interfering and interacting with several central-acting neurotransmitters. It can cause increasing concentrations of serotonin and dopamine in the brain, producing excitement and increased motor activity in horses and probably poor muscle relaxation or retention of muscle tonus during the induction phase (Muir, 1991; Staffieri and Driessen, 2007). Due to the poor muscle relaxation effect of ketamine, it is rather difficult to open the horse's mouth for intubation. Therefore, relaxation of the jaw muscle is required. (Staffieri and Driessen, 2007). Ketamine stimulates sympathomimatic effects on the cardiovascular system including increased heart rate, myocardial contraction, cardiac output, mean arterial pressure, pulmonary artery pressure and central venous pressure (Benson and Thurmon, 1990). Ketamine is also a sympathetic stimulation drug and counteracts some of the vagotonic effects of the alpha-2 adrenoceptor. Ketamine also has a minimal effect on respiratory depression, inducing an apneutic respiratory pattern with mild hypoventilation characterized by hypoxemia and mild hypercapnia when the horse breathes room air (Benson and Thurmon, 1990; Bettschart-Wolfensberger and Larenza, 2007). Diazepam, a member of benzodiazepine drug group, is a central acting muscle relaxant. Benzodiazepine is most commonly used in veterinary practice for seizures. The diazepam administration is always combined with dissociative anesthetics and sedative analgesics to improve the quality of anesthesia as well as to enhance muscle relaxation by reducing the degree of tonic–clonic twitching. However the analgesic and duration of action are often not increased for short–term anesthesia (Benson and Thurmon, 1990; Muir *et al.,* 1991; Marntell, 2004; Staffieri and Driessen, 2007). The mechanism of action of diazepam is depression at the subcortical levels (primarily limbic, thalamic and hypothalamic) of the CNS. Benzodiazepine-specific receptor sites are located within the CNS; these receptors potentiate the action of GABA activity which is generally an inhibitory neurotransmitter of the brain, thus producing anxiolytic, sedative, skeletal muscle relaxant and anticonvulsant effects (Bettschart-

Wolfensberger and Larenza, 2007). The diazepam effects of producing good muscle relaxation most probably originate from the CNS although some of this action is attributable to direct activity at the neuromuscular junctions (Hubbell, 1999). Garcia *et al.* (2002) concluded that the use of anxiolytics in foals produced very good sedation and muscle relaxation.

CONCLUSION

This study showed no significant differences in all parameters between the XZ and XKD groups. All drug combinations produced relatively safe anesthesia of varying duration in all six foals. Therefore, it was concluded that Zoletil® has similar effects to a combination of ketamine and diazepam and could be used as a safe field anesthetic drug for induction in foals aged 4–6 mth.

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LITERATURE CITED

Aubin, M.L. and K. Mama. 2002. Field anesthetic techniques for use in horses. **Compendium** 24(5): 411–417.

Benson, G.J. and J.C. Thurmon. 1990. Intravenous anesthesia. **Vet. Clin. North Am. Equine Pract.** 6(3): 513–528.

Bettschart-Wolfensberger, R. and M.P. Larenza. 2007. Balanced anesthesia in the equine. **Clin. Tech. Equine Pract.** 6: 104–110.

Dunlop, C.I. 1994. Anesthesia and sedation of foals. **Vet. Clin. North Am. Equine Pract.** 10: 67–85.

Flaherty, D., A. Nolan and J. Reid. 1996. Complications during recovery from anesthesia in the equine patient. **Eq. Vet. Educ.** 8: 17–22.

Frias, A.F.G., F. Mársico, I.A. Gómez de Segora, P.R.L. Nascimento, A.Jr. Nascimento, J.H.N. Soares and N.R. Almosny. 2003. Evaluation of different doses of propofol in xylazine pre-medicated horses. **Vet. Anaesth. Analg.** 30: 193–201.

García, A.A., H. Sumano and E. Núñez. 2002. Pharmacologic basis of short term intravenous general anestesia in the equine. **Vet. México.** 33(3): 309–333.

Hubbell, J.A., R.M. Bednarski and W.W. Muir. 1989. Xylazine and tiletamine– zolazepam anesthesia in horses. **Am. J. Vet. Res.** 50(5): 737–742.

Hubbell, J.A.E. 1999. Options of field anesthesia in the horse. **Proceedings of the Annual Convention of the AAEP.** 45: pp.120–121.

Johnston, G.M., J.K. Eastment, J.L.N. Wood and P.M. Tayler. 2002. Confidential enquiry of postoperative equine fatalities (CEPEF): Mortality results of Phase 1 and 2. **Vet. Anaesth. Analg.** 29: 159–170.

Mama, K.R., E.P. Steffey and P.J. Pascoe. 1996. Evaluation of propofol for general anesthesia in pre-medicated horses. **Am. J. Vet. Res.** 57: 512–516.

Marntell, S. 2004. **Sedation and Dissociative Anesthesia in the Horse.** PhD thesis, Swedish University of Agricultural Sciences. Uppsala. 45 pp.

Marntell, S., G. Nyman and P. Funkquist. 2006. Dissociative anaesthesia during field and hospital Conditions for castration of colts. **ACTA Vet. Scand.** 47(1): 1–11.

Matthews, N.S., N.S. Dollars, D.B. Young and R.V. Shawley. 1991a. Prolongation of xylazine/ketamine induced recumbency time with temazepam in horses. **Equine Vet. J.** 23(1): 8–10.

Matthews, N.S., S.M. Hartsfield, J.L. Cornick, J.D. Williams and A. Beaslay. 1991b. A comparison of injectable anesthetic combinations in horses. **Vet. Surg.** 20(4): 268–273.

Muir, W.W. 1991. Intravenous anesthetics and anesthetic techniques in horses, pp 281–309. *In* W.W. Muir and J.A.E. Hubbell, (eds.). **Equine Anesthesia.** Monitoring and Emergency Therapy. St. Louis, MO, USA.

Muir, W.W., J.A.E. Hubbell and A.A. Gabel. 1991. Overview of equine chemical restraint, pp 1–6. *In* W.W. Muir and J.A.E. Hubbell, (eds.). **Equine Anesthesia.** Monitoring and Emergency Therapy. St. Louis, USA.

Short, C.E., C.H. Tracy and E. Sanders. 1989. Investigating xylazine's utility when used with Telazol® in equine anesthesia. **Veterinary Medicine** 84: 228–133.

Staffieri, F. and B. Driessen. 2007. Field anesthesia in the equine. **Clin. Tech. Equine. Pract.** 6: 111–119.

Tranquilli, W.J. and J.C. Thurmon. 1990. Management of anesthesia in the foal. **Vet. Clin. North Am. Equine Pract.** 6: 651–663.

Vaala, W.E. 1985. Aspects of pharmacology in the neonatal foal. **The Vet. Cli. of North Am.** 1(1): 51–75.

Appendix

Quality of induction anesthetic and recovery score (Mama *et al*., 1996).

Score	Induction	Recovery
5 (excellent)	Very smooth induction, quiet and instant lie down and lateral recumbency, good muscle relaxation no twitching after induction of drugs	Excellent; smooth to stand with minimal or no ataxia, one attempt to stand
4 (good)	Smooth induction instant lie down and lateral recumbency but head or limb twitching and movement after induction of drugs	Good; one attempt to stand, mild ataxia
3 (fairly good)	A slightly delay in time to lie down and lateral recumbency, not good muscle relaxation with muscle spasm or rigidity or limbs movement	Calm recovery; but more than one attempt to stand (2 to 3 attempts)
2 (fair)	Increased muscular activity, movement with mild signs of excitement prior, attempts to stand or any other situation during the transition from standing to lateral recumbency	Excited; several attempts to stand considerable ataxia present with or without minor injury (wound laceration)
1 (poor)	Failed to recumbency, poor muscle relaxation does not become recumbent or assumes recumbency briefly	Bad recovery; several weak attempts to stand with high risk of fatal injury