USE OF LIDOCAINE HYDROCHLORIDE 2% INTRATHECALLY ASSOCIATED WITH PRIOR ANESTHESIA WITH THIOPENTAL AS A METHOD OF EUTHANASIA IN HORSES

UTILIZAÇÃO DE LIDOCAÍNA 2% POR VIA INTRATECAL ASSOCIADO À ANESTESIA PRÉVIA COM TIOPENTAL SÓDICO COMO MÉTODO DE EUTANÁSIA EM EQUINOS

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SUMMARY

The aim of this study was to evaluate the efficiency of intrathecal lidocaine preceded by pre-anesthesia using intravenous sodium thiopental as euthanasia protocol in horses presenting different degrees of awareness and clinical condition. Twenty two horses that were admitted to the HCV-UFPel and sent to euthanasia after clinical evaluation, were used in the study. Clinical general and specific examinations were performed to classify the horses according to their clinical condition and level of consciousness on a scale from 1 to 3. The time to cardiac arrest and other reactions during euthanasia was monitored. The moment of cardiac arrest was not influenced by clinical condition, disease or dose of sodium thiopental. It was observed that the higher the volume of intrathecal lidocaine, the shorter the time to cardiac arrest ($P<0.05$). The post-euthanasia histopathological analysis of the central nervous system indicated that this technique did not cause macro or microscopic injuries to the tissue. Thus, intrathecally lidocaine associated with sodium thiopental pre-anesthesia was effective as equine euthanasia protocol, since it promoted rapid unconsciousness with mild reactions and insensitivity, without causing injuries in the central nervous system as well.

KEY-WORDS: Lidocaine chloridrate. Equine. Euthanasia. Intrathecal.

RESUMO

O objetivo deste trabalho foi avaliar eficiência da utilização de lidocaína por via intratecal, associada à anestesia prévia com thiopental sódico endovenoso, como método de eutanásia em eqüinos com diferentes graus de consciência e condição clínica. Foi utilizada a rotina clinica do HCV-UFPel, onde foram avaliados 22 eqüinos os quais apresentavam indicação de eutanásia. Foi realizado exame clínico geral e específico, classificando a condição clínica e grau de consciência, numa escala de 1 a 3. Foi monitorado o tempo para ocorrência de parada cardíaca e a ocorrência de reações durante o período trans-eutanásia. O tempo para parada cardíaca não foi influenciado pela classificação clínica, tipo de doença ou dose do tiopental sódico. Foi observado que quanto maior o volume de lidocaína utilizada por via intratecal, menor é o tempo para parada cardíaca ($p<0,05$). A análise histopatológica do sistema nervoso central pós-eutanásia demonstrou que a técnica não causou lesões macro e microscópicas. Assim, a utilização da lidocaína via intratecal associada a pré anestesia com tiopental sódico, mostrou-se eficaz na eutanásia de eqüinos, proporcionando uma inconsciência rápida, com discretas reações e insensibilidade, além de não causar lesões ao sistema nervoso central.

PALAVRAS-CHAVE: Cloridrato de lidocaína. Equinos. Eutanásia. Intratecal.

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INTRODUCTION

As the relationship between humans and animals becomes closer, the questions linked to animal well being are also becoming more evident. In veterinary, the well being of the animal is extremely valued and methods that minimize animal suffering are routine.

When necessary, euthanasia should offer the animal a humane death, without evident pain or agony, by methods that use anesthetics in a dosage sufficient to lead to quick unconsciousness, followed by cardiac arrest and death (ANDRADE, 2002).

According to Resolution No. 714 of the Conselho Federal de Medicina Veterinária (CFMV, 2002), euthanasia may be performed by chemical or physical means.

Sodium thiopental is an anesthetic thiobarbiturate administered intravenously used in protocols for euthanasia. Barbiturates depress the central nervous system (CNS), cortex, thalamus and medulla, thereby reaching the respiratory center, as well as vasomotor and sensory areas (MASSONE, 2003). They are used to induce or complement the protocol for euthanasia due to their quick action and the fact that they do not cause excitement (OLIVEIRA et al., 2002).

The local anesthetic lidocaine chloridrate can also be used in euthanasia protocols, since it is responsible for blocking the generation and conduction of nerve impulses (ANDRADE, 2002). When used intrathecally, it blocks impulses from the cardiorespiratory centers by suppressing them, resulting in apnea and myocardial arrest. The advantage of using this drug intrathecally includes the rapid onset of sensory and motor blockage with predictable efficiency (SCHNEIDER et al., 1993).

The objective of this study was to evaluate the efficiency of using intrathecally lidocaine associated with sodium thiopental pre-anesthesia in the hospital routine as euthanasia method for horses at different stages of consciousness and clinical condition.

MATERIAL AND METHODS

The data were collected at Hospital de Clinicas Veterinárias da Universidade Federal de Pelotas (HCV-UFPel), Pelotas/RS. Twenty two male and female horses, with no defined breed (NDB), weighing an average 300 kg (70-480 kg) that were admitted to the hospital with irreversible medical condition and, therefore, euthanasia was justified, were used. These horses went through both general clinical and specific examination, and classified according to clinical standards and degree of consciousness. This information was the parameter used to evaluate efficiency of the euthanasia protocol. This study was approved by the Ethics Commission for Animal Experimentation (CEEA) of UFPel (protocol 033/07).

Attitude, awareness, heart rate (HR), capillary refill time (CRT), color of oral and eyelid mucosa, as well as body temperature (T°) of the horses were monitored in order to characterize their clinical condition. The horses were classified as follows: Grade 1, horses with no or minor changes of general clinical parameters and responding actively to external stimuli; Grade 2, horses with moderate changes of clinical parameters and responding discreetly to external stimuli; Grade 3, horses with severe changes of clinical parameters and not responsive to stimulus. Table 1 shows the parameters used to classify the horses.

The doses of intravenous sodium thiopental were calculated according to the degree of awareness of the horses and were sufficient to produce homogeneous anesthesia and to stun the horses. The horses received doses of sodium thiopental of 9, 6 and 3 mg/kg according to Grade 1, 2 or 3, respectively.

With the horse in the lateral position, the head was positioned at a 90º angle to the neck, and the foramen magnum was punctured between the occipital and the atlas, in the intrathecal space, using a 14G catheter or a 40 x 16 mm needle. The dose of lidocaine used varied according to horse weight. Horses weighing between 600 - 400 kg; 399 - 200 kg; 199 - 70 kg and below 70 kg received the following amounts: 40 mL (800 mg), 30 mL (600 mg), 20 mL (400 mg) and 10 mL (200 mg) of lidocaine, respectively. CSF (*liquor cerebrospinalis)* was withdrawn in the same amount of the lidocaine to be infused, using a 20 mL syringe.

Following euthanasia, cardiac arrest, leg movements and involuntary jerking, as well as muscle tremors were evaluated. During the procedure, three veterinary students were present as observers in order to evaluate the impact of the procedure on the people watching it.

After euthanasia, necropsy was performed in the horses at Departamento de Patologia, in the Universidade Federal of Pelotas, a portion of the spinal cord was examined histopathologically to assess any damage caused to the Central Nervous System (CNS).

The data obtained in the experiment were statistically analyzed using the computer program Statistix (2003) and the means of the studied variables were compared by Tukey test HSD ($P<0.05$) and linear regression was used to establish the relation between time to cardiac arrest and the doses of thiopental and lidocaine used .

Table 1 – Parameters used to classify the horses clinically, according to pre-euthanasia degree of awareness.

Class	CRT (sec.)	Mucous membranes	Rectal Temperature (°C)	Awareness
Grade 1	1 - 3	Rosy	37.0 – 38.5	Alert
Grade 2	4 - 5	Congested	36.0 – 40.0	Apathetic
Grade 3	> 5	Cyanotic	< 36.0	Comatose

RESULTS

Pre-anesthesia using sodium thiopental was efficient to produce chemical contention and stun the horse, which confirms the relationship between the degree of awareness and the dose necessary to induce homogeneous anesthesia and stunning. After pre-anesthesia, it was easier to proceed with intrathecal puncture and to administer lidocaine; however, this procedure requires specific training from the veterinarian.

The horses were grouped according to the diseases they presented: 22.7% (n=5) chronic metabolic changes; 31.8% (n=7) irreversible chronic diseases; 31.8% (n=7) limb fracture and 13.6% (n=3) nervous system changes. Table 2 shows sodium thiopental doses and lidocaine mean doses used in horses with different clinical diagnosis, and the mean time to cardiac arrest (P>0.05).

The greater the amount of lidocaine used intrathecally, the shorter the elapsed time to cardiac arrest (P>0.05) was, as shown in Figure 1. Average time to cardiac arrest and the volume of lidocaine used are shown in Table 2. The average time to cardiac arrest was not affected by clinical diagnosis, type of disease or thiopental dose (Table 3).

In six (27.3%) of the 22 horses studied, discreet involuntary jerking and leg movement were observed in the period right before cardiac arrest, that varied between 5 and 8 seconds; however, the protocol was well accepted according to the observers. Still some horses presented a period of transitory apnea soon after thiopental was administered.

Histopathological evaluation determined there were neither macroscopic nor microscopic lesions in the portions of the CNS analyzed.

Table 2 - Average time to cardiac arrest in horses submitted to euthanasia protocol, according to the doses of lidocaine chloridrate 2%.

Volume of lidocaine	Number of horses	Average time to cardiac arrest (min.)
10 mL (200 mg)	1	6.7[ab]
20 mL (400 mg)	5	10.3[a]
30 mL (600 mg)	12	4.4[b]
40 mL (800 mg)	4	4.2[b]

Values with differed letters differ statistically (p<0.05).

Table 3 - Grade of awareness, sodium thiopental dose, mean volume of lidocaine 2% and average time to cardiac arrest in horses submitted to euthanasia protocol according to different clinical diagnosis.

Diagnosis	n	Grade of Awareness	Thiopental dose (mg/kg)	Lidocaine mean volume (mL)	Average time to cardiac arrest (min.)
Chronic metabolic changes and nervous system changes	8	3	3	30	4.4
Irreversible chronic disease	7	2	6	25	6.7
Fractures	7	1	9	27	6.1

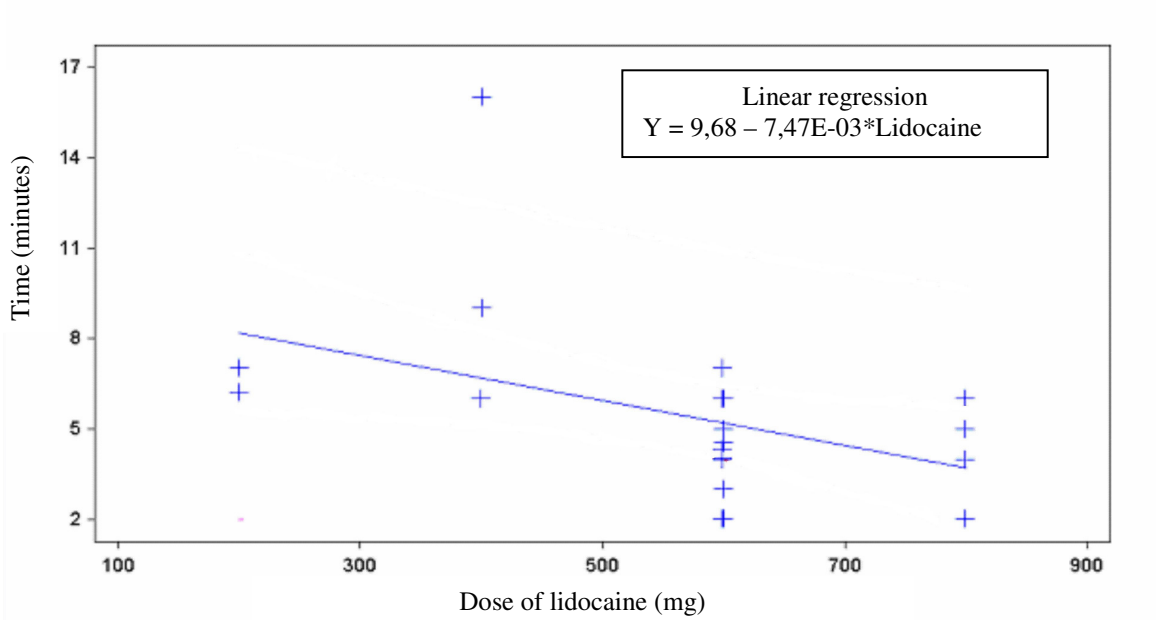

Figure 1. Relationship between the dose (mg) of lidocaine chloridrate administered intrathecally and the time (min.) to cardiac arrest for horses submitted to euthanasia.

DISCUSSION

The euthanasia protocol studied proved to be an efficient technique in the hospital routine, and met the standards required by Resolution no. 714, from 2002, by Conselho Federal de Medicina Veterinária.

The use of thiopental as anesthetic in doses depending on the degree of horse awareness allowed a desirable unconsciousness state to be reached, thus giving the horse a humane death, without suffering, since action was quick and did not cause excitement. This can be justified by the drug characteristics, such as high lipid solubility and great availability of the drug in the blood, since 72 to 86% of the drug binds to plasma proteins causing hypoproteinemia and thus increasing the availability of free drug. Still, the degree of protein biding is directly related to arterial pH, low pH produces less protein biding and therefore more active barbiturate will be available to induce general anesthesia. As a result, metabolic acidosis, uremia and hypoalbuminemia all increase the availability of the drug in the CNS, causing greater depression and prolonged action (ANDRADE, 2002). This could be observed in this study, where horses with chronic metabolic changes required lower levels of thiopental compared to horses euthanized for having fractures. As described by Gonzalez & Silva (2006) albumin concentration is affected by liver function, availability of dietary protein, electrolyte balance and protein loss due to some disease.

Transitory apnea observed in some horses can be attributed to sodium thiopental use, which has been already described by Boelter & Magalhaes (1987) and justified by the fact that this drug causes bulbar depression.

Horses classified as Grade 1 needed greater doses of thiopental compared to Grades 2 and 3. Animals clinically compromised that displayed low awareness, needed lower doses of the barbiturate to become unconscious (ANDRADE, 2002, GONZÁLEZ & SILVA, 2006).

Following the use of thiopental, manipulation of the intrathecal space was facilitated. The local anesthetic lidocaine intrathecally administered diffuses through the dura mater, cerebrospinal fluid and spinal cord, as described by Johnson (2000) and Rocha et al. (2002), who observed vascular absorption of the drug and the binding with protein receptors located in the sodium channels of the nervous membrane present in the bone marrow and brain.

Intrathecal lidocaine has the advantage of rapid onset of motor and sensory blockage, with predictable efficiency (SCHNEIDER et al., 1993). However, lidocaine, when administered in the cerebrospinal fluid produces neurotoxicity, whose effects are dose, concentration and time dependent (KROIN et al., 1986). A fact that can justify the results obtained in this

study, which demonstrated that the greater the amount of lidocaine used intrathecally, the shorter is the time to cardiac arrest.

The doses of lidocaine used were based on the concept described by Getty (1986), who suggested a positive correlation between bone marrow diameter and horse size. Therefore, lidocaine volumes varied from 10 to 40 mL according to each weight class. However, in this study, time elapsed to cardiac arrest was proportional to the volume of lidocaine injected.

Time elapsed to cardiac arrest can also be influenced by the levels of calcium in the liquor. According to Rocha et al. (2002), lidocaine binds to protein receptors located in the sodium channel of the nervous membrane. Compounds that have greater affinity bind more tightly to receptor sites, remain for longer time and have longer conduction blockage. Some authors believe that the effect on the flow of sodium is mediated via calcium interaction-local anesthetic (ROCHA et al., 2002). Increasing or decreasing the concentration of calcium ions across the nerve can enhance or antagonize the analgesia, respectively, suggesting a competition between local anesthetic and membrane bound calcium (STOETTING, 1987). Thus, a relationship between serum calcium levels and time to animal death is possible, but this hypothesis needs further investigation.

Behavioral reactions of horses observed during the protocol may be related to CNS stimulation by the needle (JOHNSON, 2000). Such information was not confirmed during this study, since the needle did not penetrate the bone marrow according to necropsy results. The thiopental dose may have also induced the patient into Stage II of Guedel for too long, called excitement or delirium phase, resulting in increased muscle tone and episodes of excitement due to inhibition of reticulo-spinal pathways or by the paradoxical release of an excitatory neurotransmitter (BOELTER & MAGALHÃES, 1987).

The reactions observed in some horses subjected to the protocol may also be related to the fact that toxicity of lidocaine administered in the CSF is directly related to the rate of absorption and tissue injury. The toxic effects of lidocaine when applied at concentrations of 2.5% to 5% include: convulsions, leg movements, excitement and stunning (HODGSON et. al., 1999).

The use of intrathecal lidocaine may cause changes in perineural permeability, edema in the fascicular nerve and increased pressure in the cerebrospinal fluid, contributing to the dysfunction of the nervous fiber and, eventually causing neurotoxic damage, although the mechanisms that lead to such neuronal lesions are not completely known (MYERS et al., 1986). However, *post morten* examination did not show macroscopic or microscopic lesions after the drug was administered intrathecally, and did not interfere with the evaluation of the changes in the CNS; however, further investigation with a larger number of animals is required.

This study showed that intrathecal administration is effective, since the amount of the drug was reduced, especially when compared with other parenteral routes, thereby improving the cost-benefit ratio of the protocol and minimizing side reactions as well.

CONCLUSIONS

The use of intrathecal lidocaine associated with sodium thiopental pre-anesthesia was an effective euthanasia protocol for horses in the hospital routine. The euthanasia protocol has provided rapid unconsciousness, with mild reactions and insensitivity, and caused no injury to the central nervous system.

REFERENCES

ANDRADE, S. F. **Manual de Terapêutica Veterinária**. 2° ed. São Paulo: Roca, 2002, 365-376p.

BOELTER, R.; MAGALHÂES, H.M. **Elementos de Terapêutica Veterinária**. 2.ed. Porto Alegre: Sulina, 1987, 164 p.

CONSELHO FEDERAL DE MEDICINA VETERINÁRIA. RESOLUÇÃO 714, de 20 de JUNHO de 2002. Disponível em: www.cfmv.com.br. Acessado em 01 de setembro de 2007.

GETTY, R. **Anatomia dos Animais Domésticos**. 5.ed. Rio de Janeiro, Guanabara Koogan, 1986, 2048 p.

GONZÁLEZ, F. H. D., SILVA, S. C. **Introdução a bioquímica clinica veterinária**. 2.ed. Porto Alegre: UFRGS, 2006, 260 p.

HODGSON, P. S., NEAL, J. M., POLLOCK, J. E., LIU, S. S. The Neurotoxicity of Drugs Given Intrathecally (Spinal). **Anesthesia & Analgesia**, v. 88, p. 797, 1999.

JOHNSON, M. E. Potential neurotoxicity of spinal anesthesia with lidocaine**. Mayo Clinic Proceedings**, v. 75, p. 921-32, 2000.

KROIN, J. S., PENN, R. D., LEVY, F. E., KERNS, J. M. Effect of repetitive lidocaine infusion on peripheral nerve. **Experimental Neurology**, v. 94, p. 166-173, 1986.

MASSONE, M. **Anestesiologia Veterinária: farmacologia e técnicas**. 5.ed. Rio de Janeiro, Guanabara Koogan, 2008, 571 p.

MYERS, R. R., KALICHMAN, M. W., REISNER, L. S.; POWELL, H. C. Neurotoxicity of local anesthetics: altered perineural permeability, edema, and nerve fiber injury. **Anesthesia & Analgesia**, v. 64, p. 29-35, 1986.

OLIVEIRA, H. P., ALVES, G. E. S., REZENDE, C. M. F. **Eutanásia em Medicina Veterinária**. Escola de Veterinária UFMG. Minas Gerais. 2002. Disponível em: http://www.ufmg.br/coep/eutanasia.pdf. Acesso em 27 de janeiro de 2008.

ROCHA, A. P. C., LEMONICA, L. BARROS, G. A. M. Uso de medicação por via subaracnóidea no

tratamento da dor crônica. **Revista Brasileira de Anestesiologia**, v. 52, p. 628-643, 2002.

SCHNEIDER, M., ETTLIN, T., KAUFMANN, M. Transient neurologic toxicity after hyperbaric subarachnoid anesthesia with 5% lidocaine. **Anesthesia & Analgesia**, v. 76, p. 1154-1157, 1993.

STOETTING, R. K. **Local Anesthetic**. 2. ed, London: Lippincott Company, 1987, p. 148-168.