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Comparison of four chemical restraint protocols in pacas

Comparação de quatro protocolos de contenção farmacológica em pacas

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ABSTRACT

Discussions about different anesthetic techniques designed for wild rodents, particularly neotropical species, are scarce in the literature. However, chemical restraint is required for management and medical procedures in these animals, due to their susceptibility to stress and their behavioral characteristics. This research evaluated quality and duration of chemical restraint of pacas (Cuniculus paca) using low doses of ketamine in association with xylazine (Group 1), xylazine and midazolam (Group 2), butorphanol and midazolam (Group 3), and azaperone and midazolam (Group 4). All doses were calculated by interspecific allometric scaling. In Group 1, recovery was disturbed and the moment of incapacity of manipulation occurred early. In Groups 2, 3 and 4, the duration of chemical restraint was higher. The best chemical restraint quality occurred in Group 2 (ketamine, xylazine and midazolam). Midazolam provided an extremely calm recovery, and afforded animals' manipulation for prolonged time, even and after return of normal ambulation.

Keywords: Anesthesia; Rodents; Wild animals; Zoological medicine.

RESUMO

A literatura é escassa em informações sobre técnicas anestésicas empregadas em roedores selvagens, particularmente as espécies neotropicais. Entretanto, a contenção farmacológica é necessária para o manejo e para a realização de procedimentos médicos nesses animais, em função de suas características comportamentais e sua suscetibilidade ao estresse. Neste estudo avaliou-se a qualidade e a duração da contenção farmacológica de pacas (Cuniculus paca), com o uso de doses baixas de cetamina em associação a xilazina (Grupo 1), xilazina e midazolam (Grupo 2), butorfanol e midazolam (Grupo 3), e azaprone e midazolam (Grupo 4). As doses foram calculadas por meio de extrapolação alométrica interespecífica. No Grupo 1, a recuperação foi inadequada e o momento da incapacidade de manipulação foi prematuro. Nos Grupos 2, 3 e 4, a duração da contenção farmacológica foi mais longa. Contenção de melhor qualidade ocorreu no Grupo 2 (cetamina, xilazina e midazolam). O midazolam propiciou recuperação extremamente suave, e possibilitou a manipulação dos animais por tempo prolongado, mesmo após o retorno à ambulação normal.

Palavras-chaves: Anestesia; Roedores; Animais selvagens Animais de zoológico.

INTRODUCTION

Chemical restraint is essential for handling and for accomplishing medical procedures in wild rodents (PACHALY *et al*., 2001; PACHALY *et al*., 2014; MONSALVE-BURITICA, ROJANO-BOLAÑO, CARRASCAL-VELÁSQUEZ, 2013). However, currently there is no broad review on anesthetic techniques for wild rodents and for neotropical species the literature is even scarcer. The lack of studies on chemical restraint of large wild rodents leads to the use of inadequate drugs and dosage protocols. Therefore, it is necessary to seek new anesthetic protocols that aim at a better anesthetic quality, decreasing risks for personnel and patients (PACHALY *et al*., 2014). Therefore, many investigators working with large wild rodents have to cope with extremely long periods of anesthetic recovery, associated to high mortality rate. It is practically

common sense that the ideal chemical restraint protocol for large wild rodents should be safe, have a short induction time, a wide safety margin, produce minimal long-term effects, require a small volume (facilitating remote delivery), and be completely reversible (PACHALY *et al*., 2001). Currently, unfortunately, no drug alone meets all these criteria. However, several drug combinations may be useful for chemical restraint of wild rodents. Authors suggested exploring, for this specific purpose, dissociative anesthetics, alpha$_2$adrenoceptor agonists, opioids, benzodiazepines and neuroleptics (phenothiazines and butyrophenones) (PACHALY, 2000). Nevertheless, no comparison of the use of these different drug class combinations for chemical restraint of large wild rodents has been published before.

The use of ketamine HCl, a dissociative anesthetic, is reported as causing catalepsy (HEITZ; BENCE, 2013). However, its association to acetylpromazine maleate made possible reduction of ketamine dose and promoted adequate immobilization and analgesia for handling proceduresin pacas (PACHALY; WERNER, 1998). The association of alometrically scaled doses of ketamine HCl and the alpha$_2$ adrenoceptor agonist xylazine HCl was described in another neotropical rodents, the agouti (*Dasyprocta azarae*) (PACHALY *et al*., 2014) and the red acouchi (*Myoprocta acouchy*) (PACHALY; KOPROSKI; LANGE, 2009), promoting an efficient and safe chemical restraint. Beside, association of ketamine HCl and xylazine HCl was used in the capybara with dose calculated by body weight (MONSALVE-BURITICA, ROJANO-BOLAÑO, CARRASCAL-VELÁSQUEZ, 2013).

Conventionally, doses of drugs are calculated and expressed as amount by unit of body weight (milligrams per kilogram) in wild animals (CASTILLO *et al*., 2012; ROBERT *et al*., 2012; BAKKER *et al*., 2013; ERDMANN *et al*., 2013; CAMPAGNOL *et al*., 2014; LESCANO *et al*., 2014), including rodents (MONSALVE-BURITICA; ROJANO-BOLAÑO; CARRASCAL-VELÁSQUEZ, 2013).

The allometric scaling method, however, calculates and expresses doses as amount for energy consumed by a given animal under basal metabolism (milligrams per kilocalorie). The purpose of allometric scaling in veterinary medicine is to extrapolate doses of drugs between animals of different sizes and/or taxa, facilitating the use of data obtained in a "model animal" (animal for which the drug was developed) for the treatment of a "target animal" (wild or domestic patient) (PACHALY, 2006).

This study has evaluated quality and duration of chemical restraint obtained in pacas by the use of a protocol constituted by low doses of ketamine HCl and xylazine HCl, and compared it to three different drug associations: ketamine, xylazine and a benzodiazepine, midazolam; ketamine, midazolam and an opioid, butorphanol, and ketamine, midazolam and a butyrophenone, azaperone.

MATERIAL AND METHODS

Animals

Twenty-four adult pacas (*Cuniculus paca* Linnaeus, 1766 – Rodentia : Mammalia) were used in this investigation, being 11 males and 13 females, coming from the Wild Animal Triage Center of the Brazilian Environment and Natural Resources Institute – IBAMA, in Tijucas do Sul, Paraná, Brazil. These animals were rescued from illegal traffic and required chemical restraint for physical examination and biological samples collection, being divided into four groups for the research purpose.

Groups 1, 2 and 4 were formed by three males and three females each, weighing respectively 6.4kg to 8.0kg (7.35 ± 0.63kg), 5.38kg to 8.01kg (7.1 ± 0.83kg), and 4.50kg to 10.0kg (7.0 ± 1.8kg). Group 3 had two males and four females, weighing between 6.31kg and 8.35kg (7.52 ± 0.71kg). All individuals were considered healthy after clinical, hematological and parasitological evaluations.

Drugs

The drugs used were ketamine[1] HCl, xylazine[2] HCl, midazolam[3], butorphanol[4], and azaperone[5] and animals from each group was chemically restrained with one of the four studied protocols. Group 1 received the association of ketamine HCl and xylazine HCl), Group 2 received ketamine HCl, xylazine HCl and midazolam), Group 3 received ketamine HCl, butorphanol tartrate and midazolam), and Group 4 received ketamine HCl, azaperone and midazolam).

Interspecific allometric scaling

Interespecific allometric scaling method was used to calculate all drug doses. The domestic dog (*Canis familiaris*), with a standard weight of 10.0kg, was used as model animal to calculate most of the drugs and the following initial doses for this species were used on the calculation: ketamine HCl – 11.0 mg/kg, xylazine HCl – 1.1 mg/kg, butorphanol tartrate – 0.5 mg/kg and midazolam – 0.5 mg/kg. The model animal and the dose model for azaperone were a 100.0 kg domestic swine (*Sus scrofa*) and 2.0 mg/kg, respectively.

The general method of calculation for interspecific allometric scaling of drug doses of drugs begins with the calculation of the basal metabolic rates (BMR) of the “model animal” and the “target animal”. After this, the total dose indicated for the “model animal” (in miligrams) is

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[1]Francotar, Virbac Saúde Animal, São Paulo, SP, Brazil.
[2]Virbaxyl, Virbac Saude Animal, São Paulo, SP, Brazil.
[3]Dormonid, Produtos Roche Químicos e Farmacêuticos, Rio de Janeiro, RJ, Brazil.
[4]Torbugesic, Fort Dodge Saúde Animal, Campinas, SP, Brazil.
[5]Destress, Biofarm Química e Farmacêutica, Jaboticabal, SP, Brazil.

divided by its BMR and the result is multiplied by the BMR of the "target animal". This final result is already the total dose (in miligrams) for the "target animal" (PACHALY, 2006).

Chemical restraint

The body weight of each animal was determined by weighing the animals inside a metallic restraint cage with a previously known weight. Based on the weight, doses for each association of drugs were calculated and administered intramuscularly. Table 1 shows dose values used in this research, obtained through interspecific allometric scaling.

Table 1 – Variation of doses of ketamine HCl, xylazine HCl, butorphanol tartrate, azaperone and midazolam, expressed in mg/kg, after the interspecific allometric scaling for pacas (*Cuniculus paca*).

Weight (kg)	Ketamine HCl	XylazineHCl	Butorphanol tartrate	Azaperone	Midazolam
4.5	13.430	1.22	0.610	4.342	0.610
5.0	13.081	1.189	0.594	4.229	0.594
5.5	12.773	1.161	0.580	4.129	0.580
6.0	12.498	1.136	0.568	4.041	0.568
6.5	12.250	1.113	0.556	3.960	0.556
7.0	12.025	1.093	0.546	3.888	0.546
7.5	11.820	1.074	0.537	3.821	0.537
8.0	11.631	1.057	0.528	3.760	0.528
8.5	11.456	1.041	0.520	3.704	0.520
9.0	11.293	1.026	0.513	3.651	0.513
9.5	11.141	1.012	0.506	3.602	0.506
10.0	11.000	1.000	0.500	3.556	0.500

The moment of the injection was considered "time zero", when a chronometer was initiated. All subsequent moments of analyses were referred as "minutes post-injection" (MPI). Each animal was kept under observation in the restraint cage, from which it was removed after reduction on intensity of defensive behavior. Then the animals were laid on the ground, outside the cage in lateral recumbence.

The moment when each animal lost its capacity of spontaneously assuming ventral recumbence was marked as the loss of the righting reflex (RR). After loss of RR, the animals were weighed again to confirm the previous weight. Following this, the animals were transferred to a table and laid in right lateral recumbence, for physical examination and initial anesthetic examination.

Physical and anesthetic examination

The physical examination was constituted by visual inspection of skin and oral cavity, abdominal palpation, cardiac and pulmonary auscultation, rectal temperature measurement, and

pulse oxymetry[6].At 5, 10, 20, 30, 40 and 50 MPI data referring to rectal temperature, cardiac frequency, respiratory frequency, blood oxygen saturation and anesthetic examination were evaluated and registered.

Evaluation of anesthetic quality was based on the following parameters: muscle relaxation, nociception, and behavior during physical examination and other medical procedures (PACHALY *et al*., 2014).

Nociception was tested periodically, at the above mentioned MPI, through evaluation of the response to compression of certain parts of animals' bodywith a hemostatic forceps. The compressed areas were an ear, an interdigital membrane and a digit of a thoracic and a pelvic limband the skin of the abdominal region, all on the opposite side to that one that received the injection. The reaction to venipuncture of a lateral saphenous vein for blood collection, at 15 MPI, and to the process of marking the animals by incisionsmade withscissors, on either one or both ears, at 20 MPI, was also evaluated. This marking method is based on the "ear notching system" currently used in pigs, and described for neotropical rodents by LANGE (1998).

In order to produce data for comparison the quality of the tested protocols, the concepts "excellent", "good" and "unsatisfactory" were attributed to analgesia, muscle relaxation and anesthetic depth, as proposed by PACHALY *et al*. (2014).

Analgesia was considered excellent when no reaction to painful stimuli was observed, good when the animal showed mild pain reaction with slight head and limb shaking, and unsatisfactory if the animal showed moderate pain reaction, with head and limb shaking and obvious response to the nociceptive tests.

Muscle relaxation was considered excellent when a total loss of muscle tonus was observed, without tremors and/or rigidity, good when a moderate maintenance of the muscle tone was observed, with slight tremors and/or rigidity, and unsatisfactory if the animal presented seizures or catalepsy.

Finally, the quality of the chemical restraint was considered excellent when the animal presented total muscle relaxation, unconsciousness and immobility during the medical procedures. It was good when the animal presented excellent or good muscle relaxation and moderate reaction to handling, with slight voluntary movement, being medical procedures possible without physical restraint. If the animal showed unsatisfactory muscle relaxation or great resistance to handling, with voluntary movements and impossibility of performing medical procedures without physical restraint, the quality of the chemical restraint was considered unsatisfactory.

[6]Pulse oximeter, model 1001, JG Moriya, São Paulo, SP, Brazil.

Duration of the restraint

The duration of the restraint was established by checking three parameters: a) initial awakening, represented by the initial occurrence of conscious reactions to sound and/or touch stimuli; b) return to RR; c) return to normal ambulation.

When manipulation without risks became impossible or after return of RR, each animal was transferred to a transport box, remaining inside it until complete anesthetic recovery.

Statistical analysis

The values of loss and return to RR, initial awakening and normal ambulation were analyzed with ANOVA for non-paired data and *post-hoc* tests.

Ethical committee

The study was approved by the Ethics in Animal Research Committee of the UNIPAR (register number 17553/2010).

RESULTS AND DISCUSSION

Table 2 shows the moments of occurrence loss of RR, initial awakening, return of RR, and return to normal ambulation in the four groups of pacas. Table 3 presents the results of evaluation of analgesia, muscle relaxation and quality of chemical restraint, and Table 4 shows data referring to cardiac and respiratory frequencies checked at 5, 10, 20 e 50 minutes after induction of the anesthesia. Finally, Table 5 presents data referring to temperature and oxygen saturation checked at 5, 10, 20 e 50 minutes after induction of the anesthesia.

Table 2 – Moment of the occurrence of loss of the righting reflex (RR), initial awakening, return of RR and return to normal ambulation in pacas (*Cuniculus paca*) anesthetized with the association of ketamine HCl and xylazine HCl (Group 1); ketamine HCl, xylazine HCl and midazolam (Group 2); ketamine HCl, butorphanol tartrate and midazolam (Group 3), and ketamine HCl, azaperone and midazolam (Group 4).

	Loss of RR (in minutes)	Initial awakening (in minutes)	Return of RR (in minutes)	Normal ambulation (in minutes)
Group1	5.67 (2.25)^{a}	21.50 (7.12)^{a}	22.67 (7.55)^{a}	50.50 (15.42)^{a}
Group2	3.33 (1.03)^{a}	51.00 (8.07)^{b}	57.33 (9.89)^{b}	153.50 (18.77)^{c}
Group3	3.67 (2.42)^{a}	46.83 (17.35)^{b}	61.67 (21.86)^{b}	105.00(29.17)^{b}
Group4	6.42 (2.48)^{a}	42.67 (21.76)^{ab}	55.17 (19.29)^{b}	120.00 (25.17)^{bc}

Note: different letters (a, b, c) correspond to statistically different values ($p<.0,05$).

Table 3 – Evaluation of analgesia, muscle relaxation and quality of chemical restraint in pacas (*Cuniculus paca*) anesthetized with the association of ketamine HCl and xylazine HCl (Group 1); ketamine HCl, xylazine HCl and midazolam (Group 2); ketamine HCl, butorphanol tartrate and midazolam (Group 3), and ketamine HCl, azaperone and midazolam (Group 4).

Group	Muscle relaxation %			Analgesia %			Quality of restraint %		
	Excellent	Good	Unsatisfactory	Excellent	Good	Unsatisfactory	Excellent	Good	Unsatisfactory
1	0.0	0.0	100.0	0.0	0.0	100	0.0	0.0	100.0
2	100.0	0.0	0.0	0.0	100.0	0	100.0	0.0	0.0
3	33.3	66.7	0.0	0.0	33.3	66.7	0.0	83.3	16.7
4	0.0	100.0	0.0	0.0	0.0	100	0.0	100.0	0.0

Table 4 – Data referring to cardiac and respiratory frequencies in pacas (*Cuniculus paca*), checked at 5, 10, 20 e 50 minutes after the induction of the anesthesia with the association of ketamine HCl and xylazine HCl (Group 1); ketamine HCl, xylazine HCl and midazolam (Group 2); ketamine HCl, butorphanol tartrate and midazolam (Group 3), and ketamine HCl, azaperone and midazolam (Group 4).

	Cardiac frequency in beats per minute				Respiratory frequency in movements per minute			
MPI*	Group 1	Group 2	Group 3	Group4	Group1	Group2	Group3	Group4
5		150±22	172±19			74 ±9	61±10	
10	119±09	140±28	169±18	152±25	119 ±11	75 ±10	58±11	61±03
20	120±09	142±13	166±24	151±33	116 ±07	71 ±4	57±15	57±09
50		138 ±9	188±20	159±27		75 ±10	64±14	55±11

Note: the empty cells indicate impossibility to check the determined parameters, due to the impossibility of handling the individuals safely.
*Minutes post-injection.

Table 5 – Data referring to the temperature and oxygen saturation in pacas (*Cuniculus paca*), checked at 5, 10, 20 e 50 minutes after the induction of the anesthesia with the association of ketamine HCl and xylazine HCl (Group 1); ketamine HCl, xylazine HCl and midazolam (Group 2); ketamine HCl, butorphanol tartrate and midazolam (Group 3), and ketamine HCl, azaperone and midazolam (Group 4).

	Temperature in ºC				SpO_2 (%)			
MPI	Group 1	Group 2	Group 3	Group 4	Group 1	Group 2	Group 3	Group 4
5		37.6±0.3	39.0±1.3			89±6	84±7	
10	36.6±0.8	37.2±0.6	38.7±1.0	35.9±1.5		89±4	82±7	94±3
20	36.7±0.8	37.0±0.6	38.0±1.3	35.5±1.4		87±4	85±6	88±9
50		36.4±0.8	38.0±1.4	34.3±1.6		90±4	85±7	90±3

Note: the empty cells indicate impossibility to check the determined parameters, due to the impossibility of handling the individuals safely.
*Minutes post-injection.

No great dose variation occurred with ketamine HCl, xylazine HCl, midazolam and butorphanol tartrate, when compared to the model animal (dog), due to similarity between weights of model and studied species (Table 1). By the same reason, this variation was observed in the dose of azaperone.

Table 2 illustrates the lack of statistical difference, among the four groups, in the loss of RR, applying Bonferroni test. It also illustrates that the loss of RR in Group 4 was slower when compared to Groups 2 and 3, according to Fisher test. This moment represents the initial possibility of handling the animals andall values were very fast.

Initial awakening, return of RR and return to normal ambulation were much faster in Group 1 (Table 2). Additionally, all animals from Groups 2, 3 and 4 showed an extremely smooth anesthetic recovery. It was possible to handle these animals even after return of RR (Table 2).

The animals in which only ketamine HCl and xylazine HCl were used (Group 1) had a troubled anesthetic recovery, characterized by early impossibility of being handled. The values obtained in this group for return of RR, initial awakening and normal ambulation were similar that reported by other authors who used a much higher dose of ketamine HCl (25.0 mg/kg) associated with acetylpromazine maleate and atropine sulfate (PACHALY and WERNER, 1998). In spite of smoothness in recovery, those authors reported discreet psychomotor excitement and incapability of handling, before return to normal ambulation, similar to what was observed in Group 1, in our study.

Dissociative anesthetics, such as ketamine HCl, are the most popular class of anesthetics used for chemical restraint of wild animals from various taxonomic categories (PACHALY; WERNER, 1998; CASTILLO *et al*., 2012; ROBERT *et al*., 2012; BAKKER *et al*., 2013; ERDMANN *et al*., 2013; MONSALVE-BURITICA; ROJANO-BOLAÑO; CARRASCAL-VELÁSQUEZ, 2013; CAMPAGNOL *et al*., 2014; LESCANO *et al*., 2014; PACHALY *et al*., 2014). However, they do not produce muscle relaxation, and may induce catatonia, tonic-clonic seizures, and maniac behavior (PACHALY, 2000). Moreover, they commonly promote a disturbed anesthetic recovery. By other hand, xylazine HCl promotes muscle relaxation, which can avoid occurrence of these undesirable effects (PACHALY, 2000; ERDMANN *et al*., 2013). Despite the fact that xylazine avoided any sign of catatonia or seizure activity, it was possible to observe psychomotor excitement during anesthetic recovery of animals from Group 1. In that animals the quality of analgesia, muscle relaxation and chemical restraint (Table 3) were considered unsatisfactory, and this was attributed to the use of lower ketamine doses than previously reported for pacas and other rodents, using the same drug protocol (PACHALY and WERNER, 1998; PACHALY; KOPROSKI; LANGE, 2009).

The significant rise in the time of chemical restraint, when midazolam was associated to ketamine and xylazine (Group 2), shows the capability of this benzodiazepine to potentiate the effects of the previous association, especially ketamine (BARKAN *et al*., 2014). The excellent

quality of chemical restraint observed in Group 2 produced the required anesthetic effects for performance of most of medical routine and management procedures. However, analgesia in this group was considered only good, restricting the use of this protocol in painful surgical procedures. Increase on drug doses or association of regional block techniques would probably facilitate the performance of such procedures. The anxiolytic property of midazolam (MIAO *et al*., 2014) allowed manipulation of the pacas, even after return to normal ambulation, which considerably decreases the risk of traumatic accidents to animals and personnel.

The use of butorphanol and azaperone associated with ketamine and midazolam in Groups 3 and 4, respectively, did not caused any significant change in duration of chemical restraint. In these groups, it was also observed a faster return to normal ambulation, after return of RR.

When the association of midazolam, ketamine and butorphanol tartrate (Group 3) was used, muscle relaxation and quality of chemical restraint were good, in most of the individuals, restricting its use to some medical and management situations. Moreover, 66.7% of the pacas from this group presented unsatisfactory analgesia, which disqualified this protocol even for simple surgical procedures.

In all animals from Group 4, which received the association of midazolam, ketamine and azaperone, muscle relaxation and quality of restraint were considered good, making such association suitable for medical and management procedures with some restrictions, once analgesia was considered unsatisfactory, disqualifying it for surgical procedures. The association of azaperone with ketamine and midazolam made handling all the pacas from this group possible until 120 minutes after return to normal ambulation, without any risk to animals and personnel. Azaperone has been employed for handling procedures in wild animals, associated to benzodiazepines, decreasing excitement, anxiety and other effects caused by capture and transport (WOLFE; MILLER, 2016). For prolonged non-painful procedures such as travelling, azaperone provides longer period of comfort and possibility of post-anesthetic handling (VILANI, 2002).

No substantial differences were observed in physiological parameters between studied groups (Tables 4 and 5) and between these groups and those reported by other authors who anesthetized pacas in Brazil (PACHALY; WERNER, 1998). It is worth highlighting, however, the low values observed for blood oxygen saturation, which may indicate the need of maintaining airway patency and oxygen supply during procedures under this protocol.

Some parameters were not checked (Tables 4 and 5) due to the impossibility of handling the individuals safely. In Group 1, the measurement of the blood oxygen saturation through the attachment of the pulse oxymeter's sensor probe to the tongue of the patients was not possible in any moment. In the other groups, it was possible to check this parameter even after return to normal ambulation, proving the smooth anesthetic recovery.

In comparison to other groups, rectal temperature was lower in Group 4, because these animals accidentally got wet during capture, before chemical restraint.

Other controversial point is the fact that the animals from the groups that received xylazine HCl, especially Group 1, showed the lowest values for cardiac frequency. Such fact hinders the increment in drug dose without association with an anticholinergic agent (PACHALY *et al*., 2014).

The interspecific allometric scaling method proved to be safe and affective to extrapolate drug doses between different animal species, corroborating data published by others authors (PACHALY; KOPROSKI; LANGE, 2009; OSILHEIRE-JUNIOR *et al*., 2012; POLEZE *et al*., 2014; CIANCA *et al*., 2014; PACHALY *et al*., 2014; PINHEIRO *et al*., 2014; ANDO *et al*., 2015).

CONCLUSION

The association of ketamine HCl, xylazine HCl and midazolam, using doses calculated by interspecific allometric scaling, based on doses designed for the domestic dog, was highly efficient for chemical restraint of Cuniculus paca. This protocol provided efficient muscle relaxation and good analgesia, making feasible medical and handling procedures.

Excluding midazolam from the association with ketamine and xylazine, with the same proposed doses, the quality of the chemical restraint worsens.

The association of butorphanol or azaperone with ketamine and midazolam was efficient for restraining Cuniculus paca, considering the good quality of chemical restraint itself as well as muscle relaxation. Nevertheless the combination produced insufficient analgesia. This factor would certainly limit the use of both protocols only for simpler and painless procedures.

Midazolam provided an extremely smooth and calm anesthetic recovery, making handling of the animals possible for a prolonged period, longer than the required time to return to the normal ambulation.

The interspecific allometric scaling method is commonly used to rationally extrapolate drug doses between different animal species. It is based on comparison of basal metabolism of the species to be anesthetized with the basal metabolism and the previously determined dosefor a selected domestic animal or even human being, and improves safety of the anesthetic procedures performed in this study.

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