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Eficacia antiemética de citrato de maropitant en *Felis catus* premedicados con xilacina+tramadol o dexmedetomidina + tramadol en orquiectomías

Antiemetic efficacy of maropitant citrate in Felis catus premedicated with xylazine+tramadol or dexmedetomidine + tramadol in orchiectomies

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Palabras claves:
Citrato de maropitant, premedicación, dexmedetomidina, xilacina, tramadol, gatos, sialorrea, vómito, ayuno.

Resumen

Introducción. La casuística de pacientes felinos ha experimentado un aumento notable en la clínica veterinaria. Es importante destacar que no todos los gatos son dóciles durante su manejo médico; la mayoría tiende a mostrar comportamientos agresivos y nerviosos. Estas actitudes han llevado en ocasiones a la necesidad de sedar al paciente, ya sea para procedimientos cortos o prolongados. No obstante, en algunos casos, no se logra implementar el ayuno necesario por parte del paciente. Por consiguiente, el empleo de sedantes agonistas alfa-2 adrenérgicos en la premedicación de felinos suele conllevar la aparición de vómitos, incluso en aquellos pacientes que ha observado el ayuno recomendado, lo que en ciertas situaciones puede dar lugar a complicaciones como neumonías por aspiración, esofagitis y dificultades durante la intubación endotraqueal. **Objetivo.** El propósito fundamental de este estudio consistió en evaluar la eficacia antiemética de citrato de maropitant usado en dos protocolos de premedicación (xilacina + tramadol) y (dexmedetomidina+ tramadol) en felinos machos sometidos a cirugías de Orquiectomía. **Metodología.** Esta investigación se realizó en gatos jóvenes de 6-24 meses de edad, con un ayuno de 8 horas, con clasificación ASA I. Se tomó una muestra de 40 felinos, a todos los gatos se administró citrato de maropitant a una dosis de 1mg/kg SC, una hora antes a la premedicación, de forma posterior se dividió en 2 grupos de estudio de 20 gatos cada uno. En el grupo 1 se realizó la premedicación con (xilacina 1mg/Kg+ tramadol 2mg/kg) IM y en el grupo 2 (dexmedetomidina 10ug/Kg + tramadol 2mg/Kg) IM. **Resultados.** En este trabajo de estudio, en los resultados obtenidos, se presentaron 2 casos de Sialorrea en el primer tratamiento (10%), frente a 1 caso en el segundo (5%) (p=0,548); ningún animal se Lamió los Labios en el primer tratamiento (0%), mientras en el segundo caso, 1 animal (5%) presentó este signo (p=0,311); con respecto a la arcada, ningún animal (0%) en los dos casos manifestó este signo ($p>0,999$); sin que existan diferencias estadísticas en la suma de los signos negativos ($p>0,999$). No existió ningún caso de Emesis en los gatos jóvenes de 6-24 meses de edad tratados con maropitant (1mg/kg). **Conclusión.** El uso de citrato de maropitant SC

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controla el vómito en gatos jóvenes premedicados con alfa 2 adrenérgicos. **Área de estudio:** (medicina veterinaria, anestesia, premedicación, etc.)

Keywords:
Maropitant citrate, premedication, dexmedetomidine, xylazine, tramadol, cats, sialorrhea, vomiting, fasting.

Abstract

Introduction. The casuitry of feline patients has experienced a remarkable increase in the veterinary clinic. It is important to note that not all cats are docile during medical management; most tend to show aggressive and nervous behaviors. These attitudes have sometimes led to the need to sedate the patient, either for short or prolonged procedures. However, in some cases, it is not possible to implement the necessary fastening on the part of the patient. Consequently, the use of alpha-2 adrenergic agonist sedatives in feline premedication often leads to vomiting, even in those patients who have observed the recommended fasting, which in certain situations can lead to complications such as aspiration pneumonias, esophagitis, and difficulties during endotracheal intubation . **Objective**.The primary purpose of this study was to evaluate the antiemetic efficacy of maropitant citrate used in two premedication protocols (xylazine + tramadol) and (dexmedetomidine + tramadol) in male felines undergoing orchiectomy surgeries. **Methodology.** This investigation was performed in young cats 6-24 months of age, fasting for 8 hours, with ASA I classification. A sample of 40 felines was taken, all cats were administered maropitant citrate at a dose of 1mg/kg SC, one hour before premedication, then divided into 2 study groups of 20 cats each. Group 1 was.**Results.** In this study, in the results obtained, there were 2 cases of Sialorrhea in the first treatment (10%), compared to 1 case in the second (5%) (p=0.548); no animal licked its lips in the first treatment (0%), while in the second case, 1 animal (5%) presented this sign (p=0.311); With respect to arcade, not animal (0%) in the two cases showed this sign (p>0.999); there were no statistical differences in the sum of the negative signs (p>0.999). There was no case of Emesis in the young cats aged 6-24 months treated with maropitant (1mg/kg).**Conclusion.** The use of maropitant citrate SC controls vomiting in young cats premedicated with alpha 2 adrenergics.**Area of study:**(veterinary medicine, anesthesia, premedication, etc.).

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Introduction

Vomiting is a reflex action by which the violent expulsion of gastric contents through the mouth occurs. It is a protective reflex (poisoning, anesthetic drugs, etc.) (2). Emesis begins with triggering impulses from the abdominal viscera, the chemoreceptor trigger zone that modulates certain impulses directed to the vomiting center and the limbic system, reaching and triggering muscular contractions at the abdominal level and in the viscera that allow the expulsion of the material contained in the stomach and the proximal part of the small intestine. (15)

Traditionally, prior to general anesthesia, a solid fast of between 8-10 hours is usually prescribed with the responsible carer, to ensure complete gastric emptying and minimize the risk of regurgitation or vomiting and aspiration pneumonia. Although it is true that prolonged fasting cannot completely guarantee gastric emptying, it can cause the accumulation of gastric juice and, therefore, increase the volume of stomach contents. Under these conditions, the gastric pH is very low, which makes a potential reflux of gastric juices more harmful to the esophagus area (16).

Fasting in healthy adult patients should be 5 hours of solids and 2 hours of liquids. In pediatric patients, it should be 4 hours of solids and liquids, while in neonatal patients, solids should be a maximum of 2 hours and liquids are not recommended (11).

The most effective preventive use of antiemetics refers to those that act in an integrated manner both in the vomiting center and in the chemoreceptor trigger zone. This specific region, located in the area postrema in the floor of the fourth ventricle and outside the blood-brain barrier, performs the function of detecting toxins (or drugs) in the systemic circulation, triggering vomiting as a defense mechanism (5).

Maropitant acts as a suppressor of both centrally and peripherally mediated vomiting. It is a neurokinin-1 (NK1) receptor antagonist, and its main function is to inhibit the binding of substance P, a neuropeptide belonging to the tachykinins. Since substance P is found in significant concentrations in the nuclei that make up the emetic center, by blocking its binding in this vomiting center, maropitant shows efficacy against neural and humoral causes (both central and peripheral) of vomiting. (14).

When administered prior to anesthetic premedication, maropitant demonstrates the ability to prevent or significantly decrease the incidence of induced vomiting. In addition, its application has been noted to facilitate early initiation of food intake in patients, reducing the use of sevoflurane. This effect is attributed to its adjuvant analgesic action, especially at the visceral level (4).

Maropitant is rapidly absorbed and reaches plasma concentrations in less than 1 hour after receiving 1 mg/kg subcutaneously and achieves a bioavailability of 91% (12).

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Premedication focuses on preparing the patient for the administration of anesthetics by providing varying levels of sedation and tranquilization with various drugs. These effects allow for safer handling of the patient, especially in situations where they may be aggressive or have an unfavorable predisposition to certain procedures, such as intravenous cannulation or surgical site preparation. In veterinary medicine, sedatives are used to chemically immobilize patients prior to performing minimally invasive procedures (11). α-2 agonists have gained importance for their strong sedative effects (10).

Xylazine, an alpha 2 adrenergic agonist, is used as a sedative and analgesic in several species. In cats, it is used as an inducer of vomiting, sometimes to induce expulsion of toxins or to treat drug overdose. Its use in small animals is controversial and is generally reserved for those in good health, as it can cause arrhythmias, decrease cardiac output, and increase the risk of fatal complications associated with general anesthesia (7).

Dexmedetomidine, an alpha-2 agonist, is used as a preanesthetic, sedative and analgesic in dogs and cats. Its use as a premedicant not only provides excellent muscle relaxation, but also contributes to the hypnotic state, thus reducing the requirements for inducing anesthetics. Therefore, it decreases the amount of drug needed to induce unconsciousness (3). This evolved α2 adrenergic agonist contains exclusively the dextroenantiomer of medetomidine, being pharmacologically pure and allowing effective doses to be reduced by approximately 50%. In addition, it can be administered by continuous infusion. In human medicine, it is the only α2 adrenergic agonist used to generate sedation in critical patients and as an adjuvant in anesthesia and analgesia (5).

Alpha-2 adrenergic agonists, xylazine, act as a central vomiting inducer in cats by irritating the trigger chemoreceptor zone due to its lower selectivity. On the other hand, dexmedetomidine, when used as a premedication in cats, can cause vomiting, retching, pale mucous membranes and a decrease in body temperature (1).

This group of drugs induces vomiting by activating central alpha-2 receptors, but this effect varies by species. Xylazine usually causes vomiting in cats in the majority of cases, while in dogs it only occurs in 10-20%. Dexmedetomidine, on the other hand, has an incidence of vomiting of 10% in dogs and 50% in cats, depending on the dose and route of administration (9).

Methodology

For this research study we worked with 40 cats from6-24 months old with ASA I classification, clinically healthy, according to the American Society of Anesthesiology, who underwent orchiectomy surgeries at the Pets Home Veterinary Clinic, located on Los Shyris and Imbabura Avenue, in the city of Ambato, province of Tungurahua, Ecuador.

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All cats were fasted for 8 hours and were administered Maropitant Citrate at a dose of 1 mg/kg subcutaneously (SC) one hour before premedication. Cats for premedication were randomly grouped into two groups of 20 patients each. The treatments administered were: T1 (xylazine 1 mg/kg + tramadol 2 mg/kg) and T2 (dexmedetomidine 10 ug/kg + tramadol 2 mg/kg), drugs that were administered intramuscularly (IM).

Figure 1. *T1 premedication with (xylazine 1 mg/kg + tramadol 2 mg/kg) after waiting one hour after*

applying maropitant citrate

Figure 2. *T2 premedication with (dexmedetomidine 10ug/Kg + tramadol 2mg/Kg) after waiting one hour after applying maropitant citrate.*

The vomiting assessment was carried out during the 15 minutes after administration of the premedication protocol, using (Table 1) the phases of vomiting: nausea (salivation, lip licking), gagging, presence of vomiting and/or absence of vomiting) and observation. In this way, the information that helped us determine which treatment had a better antiemetic response was collected.

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Table 1.*Phases of vomiting*

Nausea		Arcades	Vomit
Sialorrhea	Licking lips	Contraction of diaphragmatic and abdominal muscles.	Expulsion of gastric contents.

Fountain:(Flores, M. 2016)

For the analysis of the data obtained,A Chi2 test adapted to the number of cases studied (n) was performed to define the association between the study variables, the frequencies of each case were contrasted. By using theSPSS program (Statistical Package for the Social Sciences) and R software.

Results

Application of maropitant citrate (1 mg/kg) SC, one hour before premedication with xylazine 1 mg/kg + tramadol (2mg/kg) anddexmedetomidine (10ug/kg)+ tramadol (2mg/kg) was evaluated by the frequency of each case in cats (Table 2.), which had similar mean ages (p=0.710). There were 2 cases of Sialorrhea in the first treatment (10%), compared to 1 case in the second (5%) (p=0.548); no animal Licked its Lips in the Nausea phase, in the first treatment (0%), while in the second case, 1 animal (5%) presented this sign (p=0.311); regarding Retching, no animal (0%) in the two cases showed this sign (p>0.999); there are no statistical differences in the sum of the negative signs(p>0.999). There were no cases of emesis in young cats aged 6-24 months treated with Maropitant (1 mg/kg), one hour before premedication.

Table 2. Frequency of Negative Signs and Emetic Response to Maropitant Citrate.

Pharmacological Parameter	Age of patients	Sialorrhea	Licking Lips	Arcade	Negative Signs	Emesis
Maropitant (1mg/Kg) –Xylazine 1mg/kg + Tramadol (*2mg/Kg)*	11.55a (+/-4.49)	2/20 (10%)a	0/20 (0%)a	0/20 (0%)a	2/20 (10%)a	0/20 (0%)a

Table 2. Frequency of Negative Signs and Emetic Response to Maropitant Citrate. (continued)

Pharmacological Parameter	Age of patients	Sialorrhea	Licking Lips	Arcade	Negative Signs	Emesis
Maropitant (1mg/Kg) -Dexmedetomidine (*10ug/kg)*+ Tramadol (*2mg/Kg)*	11.55a (+/-4.49)	1/20 (5%)a	1/20 (5%)a	0/20 (0%)a	2/20 (10%)a	0/20 (0%)a
p-value	*0.710*	*0.548*	*0.311*	*>0.999*	*>0.999*	*>0.999*

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The two protocols were contrasted between treatments (Figure 3). The frequency of negative signs of the vomiting phases: Nausea (Sialorrhea, Lip Licking), Gagging and Emesis are observed according to each color. The Treatmentof Maropitant Citrate (1mg/kg) SC, one hour before premedication withXylazine(1mg/kg)+ Tramadol (2mg/Kg); did not present Emesis (20/20), Gagging (20/20) or the sign of Licking the Lips (20/20) compared to cases that did not present Sialorrhea (18/20). The Treatment ofMaropitant citrate (1 mg/kg) SC, one hour before premedication with Dexmedetomidine (10ug/kg)+ Tramadol (2mg/Kg). There was no emesis (20/20) or nausea (20/20), there were also animals that did not present the sign of lip licking (19/20) or sialorrhea (19/20).

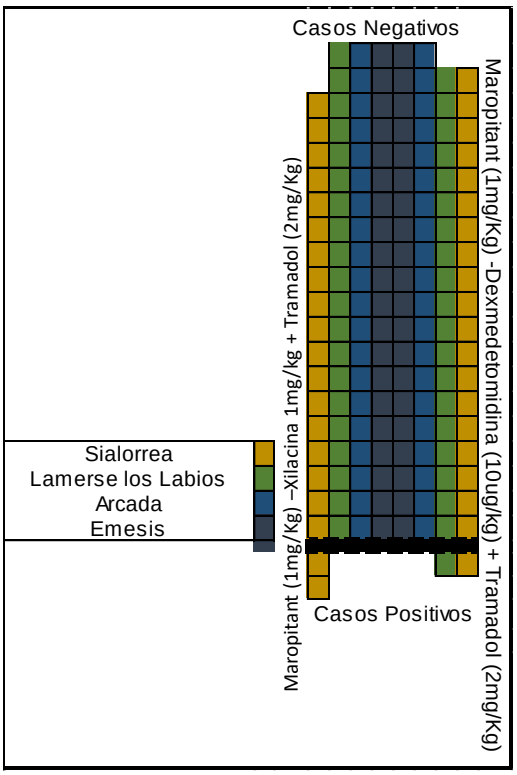

Figure 3.*Contrast of Negative versus Positive Cases of Negative Signs and Emetic Response of Maropitant Citrate versus the 2 premedication protocols.*

Discussion

The results obtained in this study were compared with those found in several literature reviews. Subcutaneous administration of maropitant citrate (1 mg/kg) one hour before the two premedication protocols resulted in 0% cases of vomiting and 10% signs of nausea, compared with other investigations that used ondansetron and buprenorphine at different doses and times as antiemetics, and other control groups with different doses of dexmedetomidine, xylazine and acepromazine as anesthetics, as well as various doses of tramadol and morphine as analgesics (see Table 3).

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Control treatments using 0.9% NaCl showed a range of 15% to 59% of vomiting cases and 25% to 56% of nausea signs. On the other hand, the inappropriate use of maropitant showed no effect, since 50% of vomiting cases and 70% of nausea signs were observed. The inappropriate use of ondansetron (0.22 mg/kg) induced 67% of vomiting cases and 67% of nausea signs, while as a premedication it presented 33% of vomiting cases and 33% of nausea signs.

Administration of buprenorphine at 0.1 mg/kg and 0.2 mg/kg as dexmedetomidine premedication did not cause vomiting (0%) as long as the dose did not exceed 20 µg/kg. However, it is important to note that, in this case, signs of nausea were observed in a range of 21% to 29% when the dose was 0.2 mg/kg and reached 50% of signs when the dose was 0.1 mg/kg.

The use of dexmedetomidine at 25 µg/kg, without analgesia or the use of an antiemetic, can cause up to 71% of cases of vomiting. Similarly, the exclusive use of xylazine at 0.5 mg/kg can generate up to 92% of cases of vomiting, despite the use of an analgesic in the procedure.

The data presented in (Table 3.) indicate that it is crucial to consider not only the dose, but also the application time of the premedication, the anesthetic and the analgesic to be used (Hay Kraus, 2017). In this context, maropitant (1 mg/kg) emerges as the antiemetic with the best results, surpassing or equaling those obtained with buprenorphine (0.2 mg/kg). In the specific case of this investigation, the use of tramadol (2 mg/kg) as an analgesic, low doses of xylazine (1 mg/kg) and reduced doses of dexmedetomidine (10 µg/kg) surpassed the use of morphine (0.5 mg/kg) in positive results.

Table 3. Literature Review of Negative Signs and Emetic Response to Premedication with Maropitant Versus Other Doses, Products, Anesthetics and Analgesics.

Drug Previous	Anesthesia/Analgesia	Author	n	Vomit	Signs of Nausea
-Maropitant (1mg/kg)	Xylazine (1mg/kg)+ Tramadol (2mg/Kg)	Own authorship	20	0%	10%
-Maropitant (1mg/kg)	Dexmedetomidine (10ug/kg) + Tramadol (2mg/Kg)		20	0%	10%
-NaCl 0.9%	Dexmedetomidine (20ug/kg) + Morphine (0.5mg/Kg)	Martin et al., (2015)	20	40%	40%
	Maropitant (1mg/Kg)+Morphine (0.5mg/kg)+Acepromazine (0.05g/kg)(dogs)		20	50%	70%
-Maropitant (1mg/kg)	Dexmedetomidine (20ug/kg)	Martin et al., (2016)	32	3%	34%
			34	59%	56%

-NaCl 0.9%	Dexmedetomidine (10ug/kg)				
-Maropitant (1mg/kg)	Dexmedetomidine (20ug/kg) + Morphine (0.5mg/Kg)		20	4%	8%
-Maropitant (1mg/kg)	Acepromazine (0.05g/kg)+ Morphine (0.5mg/kg)(dogs)	Lorrenzutti et al., (2016)	20	55%	70%
-NaCl 0.9%	Dexmedetomidine (10ug/kg) (dogs)		20	15%	25%
-Buthorphanol (0.2 mg/kg)	Dexmedetomidine (25ug/kg)		14	71%	71%
	Dexmedetomidine (20ug/kg)		14	0%	29%
-Buthorphanol (0.1 mg/kg)	Dexmedetomidine (20ug/kg)	Papastefanau, et al., (2015)	14	0%	50%
-Buthorphanol (0.2 mg/kg)	Dexmedetomidine (25ug/kg)		14	7%	21%
	Dexmedetomidine (40ug/kg)+Buprenorphine (20ug/kg)		28	78%	82%
	Ondansetron (0.22mg/kg)+Dexmedetomidine (40ug/kg)+Buprenorphine (20ug/kg)	Santos, et al., (2015)	31	67%	67%
-Ondansetron (0.22 mg/kg)	Dexmedetomidine (40ug/kg)+Buprenorphine (20ug/kg)		30	33%	33%

Table 3. Literature Review of Negative Signs and Emetic Response to Premedication with Maropitant Versus Other Doses, Products, Anesthetics and Analgesics. *(continuation)*

Drug Previous	Anesthesia/Analgesia	Author	n	Vomit	Signs of Nausea
	Xylazine (0.5mg/kg)+Tramadol (2mg/kg)	Paredes Carvajal, et al., (2022)	6	92%	≥92%
	Xylazine (0.5mg/kg)+Buprenorphine (0.03mg/kg)		6		

Conclusions

- Maropitant citrate stands out as an antiemetic of choice in young cats, used in two premedication protocols: (xylazine 1 mg/kg + tramadol 2 mg/kg) and (dexmedetomidine 10 µg/kg + tramadol 2 mg/kg), with administration by

intramuscular (IM) route. In this study, maropitant citrate was administered at a dose of 1 mg/kg subcutaneously (SC) one hour before premedication.

- It was concluded that this drug acts effectively by inhibiting the incidence of vomiting in cats that have undergone an 8-hour fast. This finding suggests that maropitant citrate is appropriate for use in all patients requiring management or surgical procedures. This choice ensures the absence of inconveniences during endotracheal intubation, since emesis that could interfere with anesthesia is avoided.

Conflict of interest

The authors declare that there is no possible conflict of interest.

Authors' contribution statement

The article must be accompanied by a note, which expresses the contribution of each author to the study carried out.

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