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T Karata Baykurt, H Erdogan, K Ural, S Erdogan

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Comparing the Antiemetic Effects of Maropitant and Ondansetron in Cats with Acute Vomiting in Clinical Practice

T. BaykurtKaratas, H. Erdogan, K. Ural, S. Erdogan*

Department of Internal Medicine, Faculty of Veterinary Medicine, Aydın Adnan Menderes University, Aydın, Türkiye

ABSTRACT: The objective of this study is to evaluate and compare the clinical efficacy of maropitant and ondansetron in cats presented with acute vomiting within the first 24 hours after a single subcutaneous administration.In total 40 cats with vomiting were enrolledandrandomly allocated to receive single subcutaneous dose of either 1 mg/kg/day maropitant (n=20) or 0.4 mg/kg/day ondansetron (n=20). All cats were evaluated and scored (visual analog scale and numerical rating scale) for vomiting/nauseaand appetite/activity andwere assessed for pain at 0 min, 30 min, 4 h, and 24 h after administration.No statistically significant difference was observed between the maropitant and ondansetron groups in terms of visual analogue scale and numerical rating scale for vomiting/nausea, appetite/activity, and pain scores throughout the 24-hour observation period (p> 0.05).A significant decrease (p< 0.05) was observed in the visual analog score and numerical rating scale for vomiting/nausea and inpain score after the antiemetic usecompared to the pre-medication period in both groups. Activity and appetite score increased (p< 0.05) whitin groupsat the end of the observation period. This research shows that in our study population both ondansetronandmaropitant effectively controlled vomiting and nausea of various causes in cats within the first 24hafter a single injection. Furthermore, clinicalscoring forpredicting vomiting and nausea in cats could be a valuable tool for selecting antiemetic drugs.

Keyword: antiemetic; nausea; cat; clinical scale; vomiting.

Correspondence author:
Erdogan S.
Department of Internal Medicine, Faculty of veterinary Medicine, Aydın Adnan Menderes University, Aydın, Türkiye, songul.toplu@adu.edu.tr

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INTRODUCTION

In cats, vomiting is a common symptom that occurs when emetic stimuli exceed the threshold required to activate the vomiting reflex (Trepanier, 2010). Nausea is a gradual sensation with a dynamic threshold influenced by various factors and usually precedes vomiting (Stern et al., 2011).

The management of vomiting and nausea often requires a pharmacological multimodal approach to manage the underlying disease process and minimize unpleasant sensation (Batchelor et al., 2013). Antiemetics used to control vomiting with blocking vomiting pathways at various points that prevent the vomiting reflex. All antiemetic drugs simultaneously prevent nausea (Pirri et al., 2013). Antiemetics commonly used in the veterinary field are phenothiazines, dopamine receptor antagonists, serotonin 5-hydroxy tryptophan-3 (5-HT3) and neurokinin 1 (NK-1) class drugs (Trepanier, 2010; Martin-Flores et al., 2016). In cats, antiemetics targeting NK-1 or 5-HT3 receptors are licensed and effective (Batchelor, 2012).However, there is little data on the antiemetic efficacy of these drugs in cats, most of which is based on experimental models of anesthesia-induced vomiting (Santos et al., 2011).

Maropitant and ondansetron are among the commonly preferred and extensively investigated drugs as antiemetic and antinausea agents (Burke et al., 2022). Maropitant is a selective NK-1 antagonist that shows antiemetic activity by inhibiting substance P binding to central and peripheral NK receptors (Hickmann et al., 2008). Ondansetron is a 5-HT3 receptor antagonist antiemetic that is widely found in the central nervous and gastrointestinal system (Milne and Heel, 1991).Comparing these two agents is crucial because they target different receptors and pathways, which might result in varying efficacy and side effect profiles in clinical settings (Kenward et al., 2017;Burke et al., 2022). Such comparisons help determine the most effective and safest treatment options for managing vomiting and nausea in veterinary practice, providing insights into their efficacy, side effect profiles, and potential cost implications.

The aim of this study was to evaluate andcompare the efficacyof maropitant and ondansetron in cats with acute vomitingfollowing a single parenteral administration,bymonitoringtheir clinical response over 24hours.

MATERIALS AND METHODS

Study design

This study was designed as a randomized, prospective clinical trial to evaluate and compare the efficacy of maropitant and ondansetron in cats with acute vomiting. Prior to participation, all cat owners provided informed consent regarding the administration of antiemetic drugs. The study protocol was approved by the Animal Experiments Local Ethics Committee of Aydın Adnan Menderes University (No: 64583101/2022/125), ensuring compliance with ethical standards.

Animals

A total of 40 client-owned cats of various breeds and ages, from both genders that presented to the clinics with acute vomiting were enrolled in the study (Table 1). Animals were randomly divided into two groups: Maropitant (n=20) and Ondansetron (n=20) group, according to the administration of a single subcutaneous dose of either Maropitant (Cerenia®, Zoetis, Istanbul)at a dose of 1 mg/kg/day (Hickman et al., 2008) or ondansetron (Zofer® 2 ml/8 mg ampoule, ADEKA, Samsun)at a dose of 0.4 mg/kg/day (Quimby et al., 2014).Both groups were monitored by an observer for the first 24hafteradministration.

Inclusion criteria included cats with acute onset of vomiting (occurring more than twice within 12 hours), absence of chronic systemic illness, and clinical signs consistent with nausea such as hypersalivation orretching, with the deliberate inclusion of cats of various breeds, ages, and clinical presentations. The exclusion criteria included severe dehydration, epileptic seizures, a Glasgow coma score lower than 9, pregnancy or lactation, a history of antiemetic use, and suspected poisoning. Following diagnostic procedures (such as rapid test kits, complete blood count, biochemical analyses, etc.) to determine the etiological conditions of the cases, the remaining cats were randomly assigned to receive either maropitant or ondansetron without etiological treatment. After these diagnostic evaluations, cats meeting the exclusion criteria were excluded from the study. Each group received a single dose of their respective antiemetic, and their clinical response was monitored over a 24-hour period. The assessment of nausea and vomiting was conducted using clinical scoring at multiple time points (0 min, 30 min, 4 h, and 24 h), including a visual analog scale, a numer-

Table 1. Demographic distribution of the cats

		Group	
		Maropitant (n=20)	
		$\bar{X}$ ± SE	**Min-Max**
Age (month)		44,55 ± 40,28	2-120
Body weight (kg)		3,50 ± 1,33	1,50-6,90
Gender	Male	50	-
	Female	50	-
Pure breeds (%)		65	-
Mixed breed (%)		35	
		Ondansetron (n=20)	
		$\bar{X}$ ± SE	**Min-Max**
Age (month)		54,60 ± 50,04	6-204
Body weight (kg)		4,21 ± 1,33	2,20-6,60
Gender	Male	55	-
	Female	45	-
Pure breeds (%)		25	-
Mixed breed (%)		75	-

ical rating scale, appetite and activity scores, and a pain score (Figure 1).

Clinical Scoring systems

Various scoring systems have been described by different researchers for the assessment of vom-

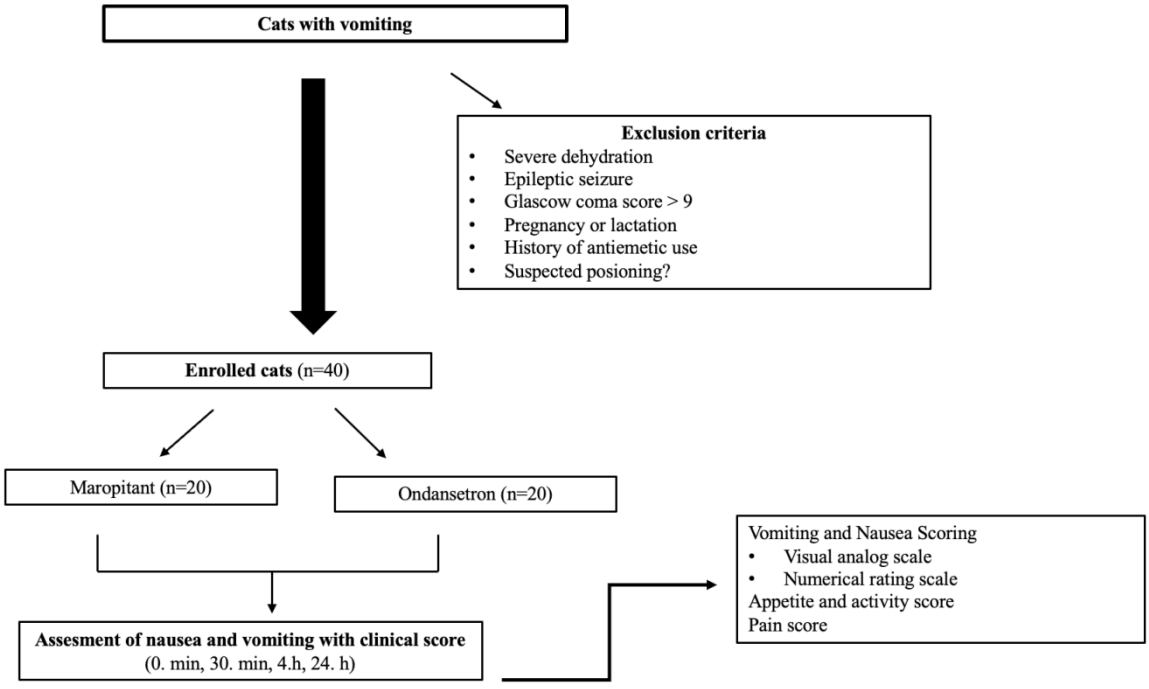

Figure 1. A diagram outlining the evaluation process for eligibility, enrollment, allocation and clinical evaluation of cats with acute vomiting.

iting and nausea. These include the visual analog scale (McCaffery and Pasero, 1999), numerical rating scale(Santos et al., 2011; Papastefanou et al., 2015), appetite and activity score (Quimby et al., 2015), and pain score (Fudge et al., 2021). In this study, each of these scoring systems, as detailed in the literature, was individually analyzed to ensure comprehensive evaluation.

The clinical scoring was based on physical examination and follow-up question-answer sessions with the patient owner. Clinical follow-ups were repeated 4 times before (0 min) and after (30 min), (4 h) and (24 h) antiemetic administration. During the physical examination, heart rate (beats/min), respiratory rate (breaths/min), body temperature (°C) were all recorded. These scores, mostly based on subjective assessment, were performed by a single investigator (K.T).

Visual Analog Scale and Numerical Rating Scale

Unlike in humans, in cats there is no known and validated scoring system for the assessment of vomiting and nausea. The visual analog scale (McCaffery and Pasero, 1999) and numerical rating scale (Santos et al., 2011; Papastefanou et al., 2015) are mostly used in this field.

A visual analog scale, evaluated by a single blinded observer, was utilized to measure the clinical symptoms of nausea, with 0 indicating no nausea and 10 representing the most severe possible nausea. Clinical indicators of nausea included drooling, excessive licking, and changes in body posture, among others (McCaffery and Pasero, 1999; Hickman et al., 2008).

Nausea was assessed using a numerical rating scale at multiple time points (0 min, 30 min, 4 h, and 24 h). The behaviors monitored included vocalization, lip licking, and retching. Each behavior was scored on a scale from 0 to 3, where 0 represented the absence of the behavior and 3 indicated the most severe manifestation. The scores for each behavior were recorded and summed to obtain a total score for each time point. The cumulative scores provided a comprehensive assessment of nausea severity over the 24-hour observation period (Santos et al., 2011; Papastefanou et al., 2015).

In addition to these two scales, the number of times vomiting, or nausea occurred within 24 h after antiemetic administration, when vomiting occurred more frequently (after a meal, at rest, after drug administration, etc.), whether vomiting and nausea occurred together or separately, and the number and frequency of vomiting/nausea were recorded.

Appetite and Activity Score

Clinical scoring of appetite and activity was performed as reported by Quimby et al. (2015), with decreased appetite or activity -1, unchanged appetite or activity 0, and increased appetite or activity 1, scored according to severity.

Pain Score

For pain assessment, we synthesized three previously validated pain scales into a combined system. These included the 0-10 numerical pain rating scale (McCaffery and Pasero, 1999), the Glasgow Feline Composite Measure Pain Scale (Shipley et al., 2019), and the Feline Grimace Scale (Evangelista et al., 2019). The combined system evaluated pain based on behavioral indicators, facial expressions, and physiological parameters such as body posture, ear position, and vocalization. Each cat's pain score was assessed by a single blinded observer at predefined time points (0 min, 30 min, 4 h, and 24 h) to ensure consistency and reduce subjective bias.

Statistical Analysis

Descriptive statistics were performed for the scores and clinical findings, with the data presented as mean and median values. The homogeneity of the data distributions was assessed using the Shapiro-Wilk test, which indicated that the data did not follow a normal distribution. Even after logarithmic transformation, the data remained non-normally distributed, necessitating the use of non-parametric tests. Accordingly, the Mann-Whitney U test was utilized to evaluate inter-group differences for each scoring criterion at specific time points, while the Friedman's Two-Way Analysis of Variance test was employed to assess time-dependent changes within each group. Statistical significance was determined at $p < 0.05$, and all analyses were conducted using SPSS version 26.0 (IBM, USA).

RESULTS

A total of 40 cats with acute vomiting were included in the study. The breed distribution, age range (months), gender and body weight of the animals were shown in Table 1. In this study, the demographic and physical characteristics of cats treated with maropitant (n=20) and ondansetron (n=20) were analyzed. The mean age of the maropitant group was 44.55 ± 40.28 months, with a range of 2 to 120 months, while the ondansetron group had a mean age of 54.60 ± 50.04 months, ranging from

6 to 204 months. Regarding body weight, cats in the maropitant group weighed an average of 3.50 ± 1.33 kg (range: 1.50–6.90 kg), whereas those in the ondansetron group had a mean body weight of 4.21 ± 1.33 kg (range: 2.20–6.60 kg). The gender distribution in the maropitant group was balanced, with 50% males and 50% females. In contrast, the ondansetron group included 55% males and 45% females. Breed distribution showed that 65% of the cats in the maropitant group were purebred, while 35% were mixed breed. In the ondansetron group, the majority (75%) were mixed breed, and only 25% were purebred.

The etiology of vomiting varied in the cats and the etiology/suspected diagnosis of vomiting were as shown in Figure 2.Among the observed conditions, panleukopenia was the most frequent diagnosis, with a total of 3 cases, primarily in the maropitant group. Intestinal parasitic infections followed, with approximately 2.5 cases, predominantly in the ondansetron group. Other frequently observed conditions included enteroliths and feline leukemia virus (FeLV), each reported in around 2 cases. These conditions were evenly distributed across both treatment groups. Acute gastritis and acute hepatic failure were notable causes, appearing in approximately 1.5 cases, with a slight tendency toward the ondansetron group. Less common diagnoses, such as acute renal injury, acute renal failure, idiopathic vomiting, and hepatic lipidosis, were observed in fewer than 1 case on average, scattered across both groups. Similarly, conditions like intestinal foreign bodies and trichobezoar were infrequent but present in both treatment groups, albeit minimally. Conditions such as feline infectious peritonitis (FIP), chronic renal failure, and hepatic encephalopathy were recorded with lower frequency and were sparsely distributed between the groups.

Time-dependent mean changes in clinical examination findings according to the groups are shown in Table 2. There was no time related difference between the groups for T (˚C) and P (beats/min) except for R (breath/min). Significant difference for R (breaths/min) was observed between groups at 0 min ($p= 0.04$), 30 min ($p= 0.017$), 4 h ($p= 0.02$) and 24 h ($p=0.02$).Within the maropitant group, there was statistically significant time-dependent changes in physical examination finding for R (breaths/min) rate at 0 min, 30 min, and 4 h compared to 24h ($p<0.05$) (Table 2).

In cats treated with ondansetron and maropitant, no significant statistical difference was observed be-

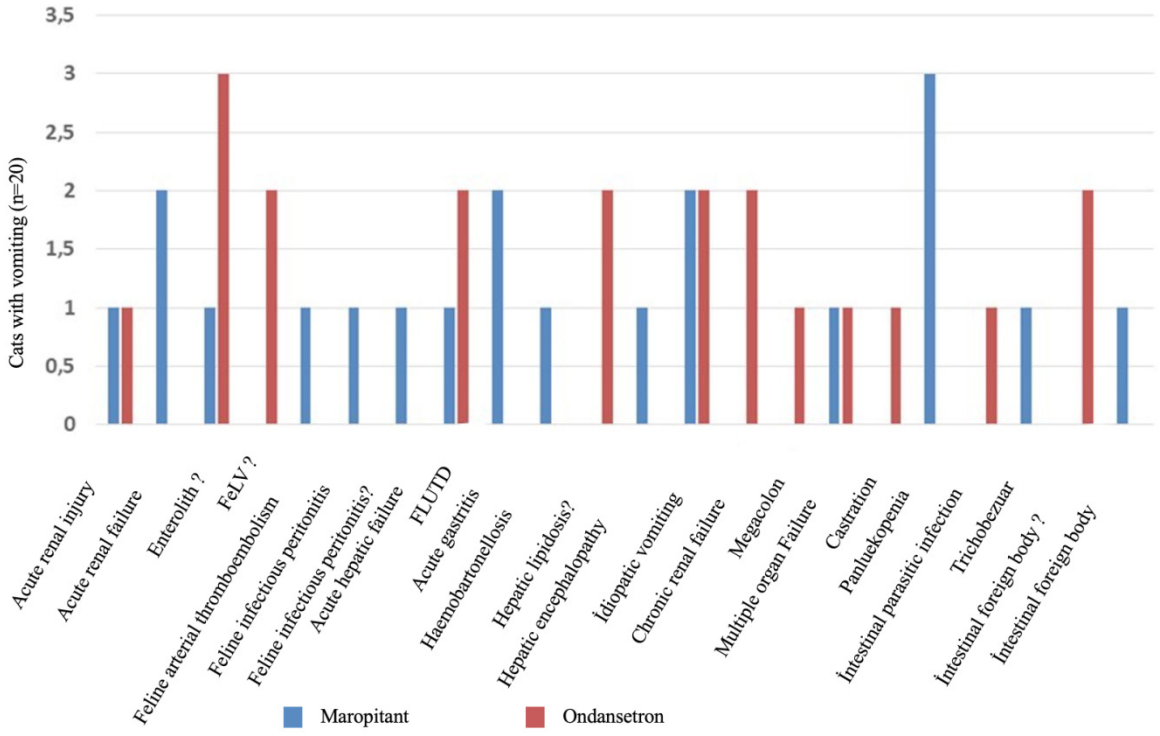

Figure 2. Presumptive cause of acute vomiting in maropitant and ondansetron treated cats.

Table 2. Time-dependent physical examination findings in cats treated with maropitant and ondansetron

		Maropitant (n=20)		Ondansetron (n=20)	
Parameters	**Time**	$\bar{X}$ ± SE	**Min-Max**	$\bar{X}$ ± SE	**Min-Max**
T^{0}C	0. min	38,08 ± 0,16	36,50- 39,50	38,27 ± 0,21	36,9- 40,50
	30. min	38,24 ± 0,12	37,50- 39,20	38,23 ± 0,17	36,8- 40,10
	4. h	38,17 ± 0,11	37,50-38,90	38,21 ± 0,14	37,00- 39,70
	24. h	38,21 ± 0,11	37,3- 39,10	38,06 ± 0,01	37,20- 38,90
P (pulse/min)	0. min	120,45 ± 2,61	100- 140	120,50 ± 5,14	96- 200
	30. min	120,85 ± 3,72	100- 164	122,20 ± 4,89	96- 200
	4. h	119,55 ± 2,63	100- 145	121,60 ± 4,82	96- 200
	24. h	115,4 ± 2,90	100- 152	116,7 ± 3,97	96- 175
R (breath/min)	0. min	34,45 ± 1,16^a	28- 45	30,95 ± 2,26^b	19- 60
	30. min	34,4 ± 1,51^a	28- 54	30,20 ± 1,83^b	21- 50
	4. h	33,25 ± 1,36^a	23-46	29,45 ± 2,07^b	20- 51
	24. h	30,45 ± 1,46^a	20- 47	28,75 ± 1,85^b	18- 50

^{a,b}: letters in each row indicate significant differences of the means at each time point, p< 0.05.

tween the groups for the appetite and activity score, pain score, visual analog scale and numerical rating scale, that were generally evaluated for vomiting and nausea (p>0.05).

Evaluating intra-group time-dependent changes in pain score, it was observed that there was no significant change during the first 4 h following maropitant administration. However, a significant decrease was noted after 4 h (p = 0.037). Additionally, significant differences in pain scores were found at 0 min (p = 0.00) and 30 min (p = 0.00) compared to 24 h. In the ondansetron group, significant differences were observed at 0 min (p = 0.00), 30 min (p = 0.02), and 4 h (p = 0.01) compared to 24 h post-administration (Table 3). Upon detailed analysis of pain score, it was determined that both drugs similarly reduced pain levels.

The mean numerical rating scale between the groups did not show significant differences at each time point (p > 0.05). However, evaluating intra-group time-dependent changes in the numerical rating scale in the maropitant group revealed a significant reduction at 4 h (p = 0.17) and 24 h (p = 0.02) compared to the initial measurement, as well as from 30 min to 24 h (p = 0.012). In the ondansetron group, a significant decrease was observed only at the end

Table 3. Mean and standard error of the clinical scores in cats treated with maropitant and ondansetron

Clinical Scores	**Group (n=20)**	**Time**			
		0. min	**30. min**	**4. h**	**24.h**
		$\bar{X}$ ± SE	$\bar{X}$ ± SE	$\bar{X}$ ± SE	$\bar{X}$ ± SE
Nausea Score	Maropitant	2,4 ± 0,50^a	2,15 ± 0,48^c	1,05 ± 0,29^b	0,75 ± 0,21^{b,d}
	Ondansetron	1,6 ± 0,41^a	1,45 ± 0,43	1,45 ± 0,34	0,75 ± 0,32^b
Pain Score	Maropitant	11,15 ± 1,31^a	10,90 ± 1,31^d	9,30 ± 1,17^{b,d}	7,70 ± 1,17^{b,c}
	Ondansetron	9,75 ± 1,05^b	9,00 ± 1,12^b	8,30 ± 0,98^b	6,20 ± 1,03^a
Visual Analog Scale	Maropitant	6,60 ± 0,47^{b,d}	6,35 ± 0,51^{b,d}	5,40 ± 0,50^c	4,85 ± 0,47^a
	Ondansetron	6,05 ± 0,43^b	5,90 ± 0,46^b	5,20 ± 0,50	4,80 ± 0,56^a

SE: Standard error, ^{a,b,c,d}: letters in each row indicate significant differences in means at each time point, p< 0.05.

of the observation period (p = 0.023) compared to the pre-application measurement (Table 3).

The visual analog scale, a critical clinical observation tool for evaluating pain as well as assessing vomiting and nausea in cats, revealed a rapid and statistically significant decrease in scores at 4 h post-maropitant administration compared to pre-administration (0 min) (p = 0.02). Time-dependent changes of maropitant group were significant at 0 minutes (p = 0.00) and 30 minutes (p = 0.00) compared to 24 h. In the ondansetron-treated cats, significant differences were observed at 0 minutes (p = 0.02) and 30 minutes (p = 0.04) compared to 24 h post-administration (Table 3).

The initial median value for the appetite and activity score in the maropitant group was 0 (unchanged) at 0 h and 1 (increased) at 24 h. In the ondansetron group, it was -1 (decreased) at 0 h and 1 (increased) at 24 h. Both groups exhibited variable baseline median values. However, significant differences were observed at 4 h (p = 0.01) and 24 h (p = 0.00) compared to pre-maropitant administration, and at 0 min-4 h (p = 0.00), 0 min-24 h (p = 0.00), 30 min-4 h (p = 0.00), and 30 min-24 h (p = 0.00) in the ondansetron group (Table 4).

DISCUSSION

Maropitant and ondansetron are widely used antiemetics in cats and dogs. Maropitant, an NK1 receptor antagonist, is approved for preventing and treating vomiting and is also used in managing postoperative visceral pain (Sullivan et al., 2011). Ondansetron, a 5-HT3 receptor antagonist, is approved for controlling postoperative nausea and vomiting and for preventing chemotherapy-associated nausea and vomiting (Santos et al., 2011). Both agents provide central and peripheral prevention of vomiting and nausea.

In a previous two-stage study conducted by De la Puente-Redondo et al. (2007), the antiemetic effect of maropitant was assessed in dogs with various etiologies and vomiting occurring twice in the last eight h, with metoclopramide used as a positive control. It was noted that vomiting recurred within the first h after maropitant administration in very few dogs, and its efficacy during the first 24 h was higher than that of metoclopramide. Additionally, maropitant administered as a single 1 mg/kg dose via the subcutaneous route was reported to be generally reliable for controlling vomiting up to five days post-administration (De la Puente-Redondo et

Table 4. Descriptive data of activity-and appetite score in cats treated with maropitant and ondansetron

Activity-and appetite score (n=20)	Times											
	0. min			30. min			4. h			24. h		
	Median	Range	Variance	Median	Range	Variance	Median	Range	Variance	Median	Range	Variance
Maropitant	0,00[a]	2,00	0,45	0,00	2,00	0,52	1,00[b]	2,00	0,15	1,00[b]	2,00	0,13
Ondansetron	-1,00[b,d]	1,00	0,91	-1,00[b,d]	1,00	0,11	1,00[a]	2,00	0,21	1,00[c]	2,00	0,18

[a,b,c,d]: letters in each row indicate significant differences in means at each time point, p< 0.05..

al., 2007). Observations indicated that both agents demonstrated high antiemetic efficacy in controlling acute vomiting due to different etiologies within the first 24 h following single-dose subcutaneous administration.

In the present randomized prospective clinical study, maropitant at a dose of 1 mg/kg/day (Hickman et al., 2008) and ondansetron at a dose of 0.4 mg/kg/day (Quimby et al., 2014) were administered subcutaneously once to cats with acute vomiting of different etiologies, randomly divided into two groups. Both drugs demonstrated positive effects on the management of vomiting over a 24-hour period. It was observed that the antiemetic efficacy of maropitant and ondansetron did not differ significantly over time, regardless of the underlying etiologic agent. This finding suggests that both maropitant and ondansetron are effective options for the short-term management of acute vomiting in cats.

Unlike in humans, there is no known and validated scoring system for the assessment of vomiting and nausea in cats. Especially in the veterinary field, the evaluation of postoperative vomiting and nausea in cats is mostly based on pain scoring criteria (Santos et al, 2011; Corrêa et al, 2019;Evangelista et al, 2019; Do Nascimento et al, 2019). In this context, our study was based on different scoring systems, including numerical rating scale, visual analogue scale, activity and appetite score and pain score to evaluate vomiting and nausea. In addition, the combination of all of them could provide a valid scoring system for the observation of vomiting and nausea in cats.

In our study, time-dependent changes in the mean numerical rating scale showed a significant decrease from 2.4 ± 0.50 before maropitant administration to 1.05 ± 0.29 ($p = 0.17$) at 4 h and 0.75 ± 0.21 ($p = 0.02$) at 24 h. A significant difference was also noted between the values at 30 min (2.15 ± 0.48) and 24 h (0.75 ± 0.21, $p = 0.012$). Previous studies, such as Quimby et al. (2015), showed that maropitant reduced vomiting frequency in cats with chronic renal failure when administered orally at 4 mg/cat for two weeks. Martin-Flores et al. (2016) found that maropitant reduced vomiting incidence for approximately 20 h without affecting nausea in cats administered dexmedetomidine and morphine. Behavioral symptoms such as vocalization, lip licking, and retching were evaluated, and vomiting was monitored. Vomiting recurred in 7 out of 20 cats treated with maropitant, with varying frequencies. Maropitant reached peak plasma concentration within 0.5-2 h, providing a long-lasting effect of less than 20 h. This, along with its high subcutaneous bioavailability, explains the observed decrease in nausea and vomiting (Hickman et al., 2008). Efficacy of maropitant is linked to its role as an NK1 receptor antagonist, blocking substance P, which is involved in pain transmission, vasodilation, inflammation, and vomiting. Its involvement in the vomiting reflex led to the development of NK1 antagonists for treating vomiting in human and veterinary medicine. Maropitant is licensed for use in dogs and cats for preventing and treating vomiting and motion sickness and significantly reduces opioid-induced vomiting and nausea when administered before anesthetic premedication (Hay Kraus, 2017).

Pain scores, as previously assessed by Fudge et al. (2021), showed a significant decrease at 4 h (9.30 ± 1.17) compared to pre-administration (11.15 ± 1.31) ($p = 0.01$). Time-dependent changes were also significant at 24 h (7.70 ± 1.17) compared to baseline (11.15 ± 1.31, $p = 0.00$) and 30 min (10.90 ± 1.31, $p = 0.00$) in the maropitant group. Various studies have investigated the anti-analgesic effect of maropitant on acute opioid-induced hyperalgesia, using hot-plate and tail-flick tests to model nociceptive pain caused by tissue injury in rats and ovariohysterectomy in cats and dogs (Aguado et al., 2015; Marquez et al., 2015; Swallow et al., 2017; Corrêa et al., 2019; Karna et al., 2019). Additionally, no analgesic effect was observed when evaluated by mechanical nociceptive responses in rats, with standardized mean differences and 95% confidence intervals for mechanical responses being 0.27 (-0.40, 0.94) and a p-value of 0.43 (Kinobe and Miyake, 2020). Martin-Flores et al. (2016) reported higher visual analogue scale score ($p < 0.001$) in the maropitant compared to the control group when evaluating behavioral changes during injection. In cats undergoing ovariohysterectomy under sevoflurane anesthesia, the minimum alveolar concentration of sevoflurane decreased by 15% due to maropitant, indicating its potential role as an adjunct analgesic, particularly for visceral pain (Niyom et al., 2013).

The possible effect of maropitant in pain management is likely directed towards the inhibition of NK1 receptors and substance P, which are found in many regions of pain pathways, including sensory afferents, dorsal root ganglia, dorsal spinal cord, and

brain centers involved in pain perception (Boscan et al., 2011). Furthermore, more than 80% of visceral afferents contain the substance P neuropeptide, compared to only 21% of somatic afferents, suggesting that NK1 receptor antagonists play a greater role in visceral antinociception than in somatic pain (Niyom et al., 2013).

The initial median value in the time-dependent appetite and activity score was 0 (unchanged) and increased to 1 at 24 h in the maropitant group. Significant differences were observed at 4 h ($p = 0.01$) and 24 h ($p = 0.00$) compared to pre-maropitant administration. While maropitant used as premedication in dogs has been shown to improve postoperative return to feeding and food intake (Marquez et al., 2015; Ramsey et al., 2014), it was found that cats undergoing gastrointestinal and urogenital surgery under buprenorphine anesthesia did not recover their postoperative appetite more quickly when premedicated with maropitant (Park and Hoelzler, 2021). During the postoperative recovery period in dogs, a greater percentage of the maropitant, compared to the morphine, ate when offered food, and a greater postoperative return to and interest in food was observed (Marquez et al., 2015).Several factors can influence appetite in cats and dogs, such as environmental factors, postoperative anxiety, food type and presentation, the effects, amount and frequency of medication given for pain, or the persistence of nausea or pain (Marquez et al., 2015). The reason for the increased interest in food during the recovery period cannot be fully explained, but it is thought to be related to the cessation of vomiting.

In the present study, a significant decrease in the numerical rating scale (0.75 ± 0.32) was observed in maropitant-treated cats at 24 h post-treatment compared to pre-treatment (1.6 ± 0.41, $p = 0.023$). Ondansetron, administered as a preoperative antiemetic with dexmedetomidine and buprenorphine, was reported to reduce postoperative vomiting and nausea, though one-third of the cats still experienced vomiting (Santos et al., 2011). Similarly, Martin-Flores et al. (2016) found maropitant to be more effective as an antiemetic than metoclopramide, ondansetron, dexamethasone, and promethazine, albeit without a different comparison group. In a study of six healthy cats with normal complete blood count, serum biochemistry, and urinalysis, ondansetron's bioavailability was 32% (oral) and 75% (subcutaneous) after cross-administration of 2 mg orally, subcutaneously, and intravenously (Quimby et al., 2014). The half-life was determined to be 1.84 ± 0.58 h (intravenous), 1.18 ± 0.27 h (oral), and 3.17 ± 0.53 h (subcutaneous). The calculated elimination half-life of subcutaneous ondansetron was significantly longer ($p < 0.05$) than oral or intravenous administration, similar to maropitant (Hickman et al., 2008). Bioavailability was higher with subcutaneous administration of ondansetron in healthy cats (Quimby et al., 2014). Ondansetron, also administered subcutaneously in our study, is a 5-HT3 receptor antagonist designed to treat anesthesia-associated nausea induced by chemotherapy in humans (Fox-Geiman et al., 2001). Recognized as the 'gold standard' in chemotherapy, 5-HT3 receptor antagonists have both peripheral and central antiemetic effects due to their presence in the abdominal vagal afferent nerves and the chemoreceptor trigger zone. Ondansetron has demonstrated superior efficacy and safety profiles compared to other antiemetic agents, including antidopaminergics, antihistamines, and anticholinergics (Ye et al., 2001). It also shows some affinity for other receptor subtypes, including 5-HT1B, 5-HT1C, 5-HT4, opioid, and α1-adrenergic receptors (Goodin and Cunningham, 2002). Therefore, the reduction in vomiting and nausea in the ondansetron group is thought to be related to the broad pharmacological effects of ondansetron.

Although studies comparing the antiemetic efficacy of maropitant and ondansetron exist for dogs, similar studies for cats are lacking. It has been reported that ondansetron is more effective than maropitant in controlling nausea and vomiting induced in dogs treated with cisplatin(Kenward et al., 2017). Conversely, a similar study found maropitant to be more effective than ondansetron in reducing the incidence of vomiting and nausea (Burke et al., 2022). Another study demonstrated that maropitant and ondansetron were equally effective in controlling associated clinical signs in dogs with parvoviral enteritis (Sullivan et al., 2018). In our study, similar results were obtained, aligning with Sullivan et al. (2018), showing a statistically significant difference ($p< 0.05$) in clinical scores for vomiting and nausea for both the maropitant and ondansetron. In our observation, both maropitant and ondansetron exhibited similar efficacy in managing vomiting of various etiologies in cats, reducing the incidence of vomiting and nausea within the first 24 h. Although the time-dependent changes in clinical scores were not statistically significant between the groups ($p <$

0.05), the decreases in clinical scores observed in the maropitant group were more pronounced when considering time-dependent intra-group evaluation. However, the differing baseline values of clinical scoring in both groups suggest that the variability in etiologies may have influenced these differences.

One of the limitations of this study is the heterogeneity in age, breed, and underlying etiologies among the cases, which could potentially influence the outcomes and limit the generalizability of the findings. Additionally, the absence of a control group prevents direct comparisons to untreated cases, which may have provided clearer in sights into the efficacy of the treatments. The wide range of etiologies, including conditions such as panleukopenia and intestinal parasitic infections, may have affected the pharmacological response differently in each group.

These limitations highlight the need for future studies with more homogeneous populations, narrower etiological scopes, and the inclusion of a control group to provide more robustand definitive conclusions.

CONCLUSION

The findings of this study demonstrate that both maropitant and ondansetron are effective in managing acute vomiting in cats of various etiologies within the first 24 h post-administration, with significant improvements observed in clinical nausea and pain scores. This suggests that both agents can be reliably used in veterinary practice for short-term control of vomiting and nausea, providing similar efficacy in the management of these symptoms. However, the study's limitations, including heterogeneity in age, breed, and underlying etiologies, as well as the absence of a control group, should be considered when interpreting these results. Future studies with more homogeneous populations and narrower etiological scopes are needed to confirm and expand upon these findings.

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REFERENCES

Aguado D, Abreu M, Benito J, García-Fernández J, de Segura IAG (2015) Amitriptyline, minocycline and maropitant reduce the sevoflurane minimum alveolar concentration and potentiate remifentanil but do not prevent acute opioid tolerance and hyperalgesia in the rat: a randomised laboratory study. Eur J Anaesthesiol 32(4):248-254.

Batchelor DJ, Devauchelle P, Elliott J, Elwood CM, Freiche V, Gualtieri M, German AJ (2013) Mechanisms, causes, investigation and management of vomiting disorders in cats: a literature review. J Feline Med Surg 15(4):237-265. DOI: 10.1177/1098612X12473466

BatchelorD (2012) Vomiting and Antiemetic Use in Cats: What's the Evidence? In: WSAVA/FECAVA/BSAVA World Congress,Birmingham, The United Kingdom.

Boscan P, Monnet E, Mama K, Twedt DC, Congdon J, Steffey EP (2011) Effect of maropitant, a neurokinin 1 receptor antagonist, on anesthetic requirements during noxious visceral stimulation of the ovary in dogs. Am J Anim Vet Sci 72(12):1576-1579. DOI:10.2460/ajvr.72.12.1576

Brondani JT, Luna SPL, Padovani CR (2011) Refinement and initial validation of a multidimensional composite scale for use in assessing acute postoperative pain in cats. Am J Anim Vet Sci 72(2):174-183. DOI:10.2460/ajvr.72.2.174

Burke JE, Hess RS, Silverstein DC (2022) Effectiveness of orally administered maropitant and ondansetron in preventing preoperative emesis and nausea in healthy dogs premedicated with a combination of hydromorphone, acepromazine, and glycopyrrolate. JAVMA 260(S1):40-45. DOI: 10.2460/javma.21.02.0082

Butler A, Hill JM, Ireland SJ, Jordan CC, Tyers MB (1988) Pharmacological properties of GR38032F, a novel antagonist at 5-HT3 receptors. Br J Pharmacol 94(2):397-412.

Corrêa JMX, Niella RV, Oliveira JNSD, Silva Junior AC, Marques CSDC, Pinto TM, Lavor MSLD (2021) Antinociceptive and analgesic effect of continuous intravenous infusion of maropitant, lidocaine and ketamine alone or in combination in cats undergoing ovariohysterectomy. Acta Vet Scand 63:1-8.

De la Puente-Redondo VA, Siedek EM, Benchaoui HA, Tilt N, Rowan TG, Clemence RG (2007) Anti-emetic efficacy of maropitant (Cerenia®) in the treatment of ongoing emesis caused by a wide range of underlying clinical aetiologies in canine patients in Europe. JSAP 48(2).

Diemunsch P, Grélot L (2000) Potential of substance P antagonists as antiemetics. Drugs 60:533-546.

Do Nascimento Arruda É, da Silva Marques M, Galera PD, de Sousa Filho RP, Monteiro CLB (2021) GastricObstructionbyTricobezoar in CatAssociatedwithLynxacarusradovskyi: a Case Report. BJCR 1(2):26-31. DOI: 10.52600/2763-583X.bjcr.2021.1.2.26-31

Evangelista MC, Watanabe R, Leung VS, Monteiro BP, O'Toole E, Pang DS, Steagall PV (2019) Facial expressions of pain in cats: the development and validation of a Feline Grimace Scale. Sci Rep 9(1):19128.

Fox-Geiman MP, Fisher SG, Kiley K, Fletcher-Gonzalez D, Porter N, Stiff P (2001) Double-blind comparative trial of oral ondansetron versus oral granisetron versus IV ondansetron in the prevention of nausea and vomiting associated with highly emetogenic preparative regimens prior to stem cell transplantation. Biol Blood Marrow Transplant 7(11):596-603. DOI:10.1053/bbmt. 2001. v7.pm11760147

Fudge JM, Page B, Lee I (2021) Evaluation of targeted bupivacaine, bupivacaine-lidocaine-epinephrine, dexamethasone, and meloxicam for reducing acute postoperative pain in cats undergoing routine ovariohysterectomy. Top Companion Anim Med 45:100564.

Goodin S, Cunningham R (2002) 5-HT3-receptor antagonists for the treatment of nausea and vomiting: a reappraisal of their side-effect profile. Oncologist 7(5):424-436.

Hay Kraus BL (2017) Spotlight on the perioperative use of maropitant citrate. Veterinary Medicine: Research and Reports 41-51. DOI:10.2147/VMRR.S126469

Hickman MA, Cox SR, Mahabir S, Miskell C, Lin J, Bunger A, McCall RB (2008) Safety, pharmacokinetics and use of the novel NK-1 receptor antagonist maropitant (CereniaTM) for the prevention of emesis and motion sickness in cats. J Vet PharmacolTher 31(3):220-229. DOI:10.1111/j.1365-2885.2008.00952.x

Karna SR, Kongara K, Singh PM, Chambers P, Lopez-Villalobos N (2019) Evaluation of analgesic interaction between morphine, dexmedetomidine and maropitant using hot-plate and tail-flick tests in rats. Vet AnaesthAnalg 46(4):476-482.

Kenward H, Elliott J, Lee T, Pelligand L (2017) Anti-nausea effects and pharmacokinetics of ondansetron, maropitant and metoclopramide in a low-dose cisplatin model of nausea and vomiting in the dog: a blinded crossover study.BMC Vet Res 13(1):1-12.

Kinobe RT, Miyake Y (2020) Evaluating the anti-inflammatory and analgesic properties of maropitant: A systematic review and meta-analysis. Vet J 259:105471.

McCaffrey M,Pasero C (1999) Pain: Clinical manual. 2nd ed, Mosby, St Louis: pp 796.

Marquez M, Boscan P, Weir H, Vogel P, Twedt DC (2015) Comparison of NK-1 receptor antagonist (maropitant) to morphine as a pre-anaesthetic agent for canine ovariohysterectomy. PLoS One 10(10):e0140734. DOI:10.1371/journal.pone.0140734

Martin-Flores M, Sakai DM, Mastrocco A, Learn MM, Campoy L, Kirch PJ, Gleed RD (2016) Evaluation of oral maropitant as an antiemetic in cats receiving morphine and dexmedetomidine. J Feline Med Surg 18(11):921-924. DOI:10.1177/1098612X156133

Milne RJ, Heel RC (1991) Ondansetron: therapeutic use as an antiemetic. Drugs 41:574-595.

Niyom S, Boscan P, Twedt DC, Monnet E, Eickhoff JC (2013) Effect of maropitant, a neurokinin-1 receptor antagonist, on the minimum alveolar concentration of sevoflurane during stimulation of the ovarian ligament in cats. Vet AnaesthAnalg 40(4):425-431. DOI:10.1111/vaa.12017

Papastefanou AK, Galatos AD, Pappa E, Lymperis AG, Kostoulas P (2015) The effect of butorphanol on the incidence of dexmedetomidine-induced emesis in cats. Vet AnaesthAnalg 42(6):608-613.

Park LS, Hoelzler MG (2021) Retrospective evaluation of maropitant and perioperative factors affecting postoperative appetite in cats. Can Vet J 62(9):969.

Pirri C, Bayliss E, Trotter J, Olver IN, Katris P, Drummond P, Bennett R (2013) Nausea still the poor relation in antiemetic therapy? The impact on cancer patients' quality of life and psychological adjustment of nausea, vomiting and appetite loss, individually and concurrently as part of a symptom cluster. Support Care Cancer 21:735-748.

Quimby JM, Brock WT, Moses K, Bolotin D, Patricelli K (2015) Chronic use of maropitant for the management of vomiting and inappetence in cats with chronic kidney disease: a blinded, placebo-controlled clinical trial.JFelineMedSurg 17(8):692-697. DOI:10.1177/1098612X14555441

Quimby JM, Lake RC, Hansen RJ, Lunghofer PJ, Gustafson DL (2014) Oral, subcutaneous, andintravenouspharmacokinetics of ondansetron in healthycats. J Vet PharmacolTher 37(4):348-353. DOI:10.1111/jvp.12094

Ramsey D, Fleck T, Berg T, Nederveld S, DeLong D, Tena JK, McCall R (2014) Cerenia Prevents Perioperative Nausea and Vomiting and Improves Recovery in Dogs Undergoing Routine Surgery.Intern J ApplResVetMed 12(3):228-237.

Santos LCP, Ludders JW, Erb HN, Martin-Flores M, Basher KL, Kirch P (2011) A randomized, blinded, controlled trial of the antiemetic effect of ondansetron on dexmedetomidine-induced emesis

in cats. Vet AnaesthAnalg 38(4):320-327. DOI:10.1111/j.1467-2995.2011.00619.x

Shipley R, Wright E, Selden D, Wu G, Aegerter J, Fooks AR, Banyard AC (2019) Bats and viruses: emergence of novel lyssaviruses and association of bats with viral zoonoses in the EU. Int J Infect Dis 4(1):31.

Stern RM, Koch KL, Andrews P (2011) Nausea: mechanisms and management. 1st ed, Oxford, NewYork.

Sullivan LA, Lenberg JP, Boscan P, Hackett TB, Twedt DC (2018) Assessing the efficacy of maropitant versus ondansetron in the treatment of dogs with parvoviral enteritis.J Am Anim Hosp Assoc 54(6):338-343. DOI:10.5326/JAAHA-MS-6650

Swallow A, Rioja E, Elmer T, Dugdale A (2017) The effect of maropitant on intraoperative isoflurane requirements and postoperative nausea and vomiting in dogs: a randomized clinical trial. Vet AnaesthAnalg 44(4):785-793.

Trepanier (2010) Acute vomiting in cats: rational treatment selection. J Feline Med Surg 12(3):225-230. DOI:10.1016/j.jfms.2010.01.

Ye JH, Ponnudurai R, Schaefer R (2001) Ondansetron: a selective 5-HT3 receptor antagonist and its applications in CNS-related disorders. CNS Drug Rev 7(2):199-213.