

Effects of a single preappointment dose of gabapentin on signs of stress in cats during transportation and veterinary examination

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OBJECTIVE

To determine the effects of oral gabapentin administration prior to veterinary examination on signs of stress in cats.

DESIGN

Randomized, blinded, crossover clinical trial.

ANIMALS

20 healthy pet cats with a history of fractious behavior or signs of stress during veterinary examination.

PROCEDURES

Cats were scheduled for 2 veterinary visits 1 week apart and randomly assigned to receive a capsule containing 100 mg of gabapentin (13.0 to 29.4 mg/kg [5.9 to 13.4 mg/lb]) or placebo (lactose powder) prior to the first visit and the opposite treatment prior to the second visit. Owners were instructed to administer the assigned capsule orally 90 minutes prior to placing the cat into a carrier and transporting it to the veterinary hospital. Standardized physical examinations and blood pressure readings were performed. Owners assigned a cat stress score during transportation and examination, and the veterinarian assigned a compliance score at the visit. Scores were compared between treatments, controlling for various factors.

RESULTS

Owner-assessed cat stress scores during transportation and veterinary examination and veterinarian-assessed compliance scores were significantly lower when cats received gabapentin than when they received the placebo. Sedation was a common effect of gabapentin administration, and ataxia, hypersalivation, and vomiting were also reported. All effects resolved within 8 hours after gabapentin administration.

CONCLUSIONS AND CLINICAL RELEVANCE

Owners' perception of stress in their cats is a primary reason for failing to seek veterinary care. Results of this study suggested that gabapentin is a safe and effective treatment for cats to help reduce stress and aggression and increase compliance for transportation and veterinary examination. (*J Am Vet Med Assoc* 2017;251:1175–1181)

Cats are the most popular type of pet in the United States,¹ yet the number of feline visits to veterinary clinics decreased 14% from 2001 to 2011. Owners' perception of their cats' stress level during transportation and veterinary examination is a recognized barrier to cats receiving preventive veterinary care.² Lack of preventative care is detrimental to the health and welfare of cats owing to missed opportunities for prevention or early recognition and treatment of disease.

ABBREVIATIONS

AS	Aggression score
CI	Confidence interval
CS	Compliance score
CSS	Cat stress score
MAP	Mean arterial blood pressure
SAP	Systolic arterial blood pressure
SS	Sedation score

Several strategies have been explored for their ability to reduce stress in cats and increase their compliance during veterinary examinations, including behavioral conditioning,³ low-stress handling,^{4,5} and fast-acting anxiolytic medications.⁶ Veterinarians may recommend one of many short-acting medications such as trazodone or dexmedetomidine hydrochloride to sedate and help ameliorate the signs of stress in their patients; this strategy has been effective for some pets.^{7,8}

One medication that has been suggested for reducing stress in cats during veterinary visits is gabapentin,^{9,10} although the mechanism underlying its anxiolytic properties remains unclear. Data suggest that gabapentin has an inhibitory effect on voltage-gated calcium channels in neural tissues,¹¹ but the clinical effects of this action have not been determined. The drug is used clinically in cats and other species for various therapeutic purposes, including

the treatment of chronic pain^{12,13} and epilepsy.¹⁴ The anxiolytic effects of gabapentin in reducing signs of anxiety have been reported for humans¹⁵ and rats¹⁶ but, to the authors' knowledge, not for cats. However, pharmacokinetic properties of the drug have been evaluated in cats, in which mean \pm SD oral bioavailability is reportedly $88.7 \pm 11.1\%$, time to maximum plasma concentration is 100 ± 22 minutes, and half-life is 177 ± 25 minutes.¹⁷

Gabapentin is inexpensive, nonscheduled in most US states, and easily available for oral administration in capsule or liquid form. Although some commercial liquid formulations of gabapentin contain xylitol, xylitol has no known toxic effects in cats.^{18,19} The drug has a mild taste, and many cats will consume it voluntarily when mixed with wet food or placed in a small, flavored treat.¹⁰ Although the authors' experience suggests that gabapentin is commonly used in clinical practice, the effectiveness and safety of this drug for providing fast-acting anxiolysis in cats for transportation and veterinary visits have not been reported. The purpose of the study reported here was to determine whether oral administration of a single 100-mg dose of gabapentin by cat owners prior to a veterinary visit would be effective at reducing signs of stress and aggression and increasing compliance in cats during travel and veterinary examination, compared with placebo administration, as assessed by owners, the examining veterinarian, and video observers, all of whom were blinded to treatment received.

Materials and Methods

Animals

Owners of healthy cats with a history of signs of stress or fractious behavior during transportation or veterinary examination were recruited by email (to student groups) and word of mouth within the University of California-Davis School of Veterinary Medicine community, with a goal of enrolling 20 cats. Recruitment took place over a period of 2 weeks. The study was explained to interested owners, and consent was obtained for their cats to participate. The study protocol was approved by the Institutional Animal Care and Use Committee of the University of California-Davis.

Procedures

Cats were scheduled for 2 veterinary visits, 1 week apart. A simple randomization table was used to assign the cats to receive prior to the first visit a capsule containing 100 mg of gabapentin or placebo and then the opposite capsule prior to the second visit. To ensure blinding of observers to treatment, the contents of each original gabapentin capsule^a were transferred by a veterinary pharmacist (LREF) into a clear No. 3 gelatin capsule, and placebo capsules were prepared by filling a similar clear gelatin capsule with 100 mg of lactose powder.^b The result was identical capsules containing a white powder. These capsules were labeled as "Drug A" and "Drug

B" by a pharmacist at the teaching hospital who was uninvolved in the study. All investigators and study participants were blinded to the treatment given until after data collection was complete. The assigned capsules were personally delivered to participating cat owners.

Owners were instructed to orally administer the assigned capsule 90 minutes prior to placing the cat into a carrier and bringing it to the veterinary hospital. This timing was chosen on the basis of species-specific pharmacokinetic data indicating that peak plasma concentrations of gabapentin are achieved at a mean \pm SD of 100 ± 22 minutes following oral administration.¹⁷ Owners were instructed to withhold food from their cat for at least 2 hours prior to capsule administration and then deliver the capsule directly PO or hide it inside a small, soft, flavored cat treat.

On arrival at the hospital, each owner was asked to wait with the cat in a cat-only waiting area (4 X 4 m) for 5 minutes before being taken to a standard examination room (3 X 3 m). The hospital was closed to other appointments during these times. The carrier was placed on the examination table for 1 minute to allow the cat to acclimate to the examination room. The owner was seated in clear view of their cat, but asked not to assist with restraint or interact with their cat during the examination. The carrier door was opened, and the cat was given 2 minutes to exit the carrier on its own, with only verbal encouragement. If a cat did not exit the carrier on its own, it was gently removed from the carrier by the veterinarian (KAVH).

A standardized physical examination was performed by the veterinarian. The same assistant manipulated all cats for the examination using minimal and gentle handling. Heart rate was recorded, and arterial blood pressure was measured at the base of the tail with a noninvasive oscillometric blood-pressure reader.^c The evaluation was aborted if the cat attempted to bite or scratch or seemed overly stressed to the veterinarian. All examinations were recorded with a digital video recorder.^d Video recordings were reviewed by 2 independent expert observers (MJB and EAS, both board-certified veterinary behaviorists). The owners, veterinarian, and video observers were all blinded to treatment given.

Assessments

Owners were asked to score signs of stress in their cat during transportation and veterinary examination by use of a published CSS system (1 = fully relaxed, 2 = weakly relaxed, 3 = weakly tense, 4 = very tense, 5 = fearful or stiff, 6 = very fearful, and 7 = terrorized).²⁰ The veterinarian and assistant assigned a single CS to the cat's behavior during the examination using a system developed by the authors for the study (0 = no resistance to handling, 1 = minimally resistant to handling, 2 = struggling and difficult to handle, and 3 = extreme struggling with or without urination or defecation). Video observers used the video recording of the examination to assign a CSS,

CS, and SS (0 = no sedation, 1 = standing but wobbly, 2 = sternal recumbency, 3 = can lift head, and 4 = asleep or no response to hand clap)²¹ and an AS (developed for the study by the authors; 0 = no aggressive behaviors; 1 = hiss, growl, or spit; and 2 = attempt to bite or swat).

Statistical analysis

Statistical analysis was performed to test the null hypothesis that there would be no difference between the gabapentin and placebo treatments regarding owner-assessed CSSs during transportation and examination; veterinarian-assessed CS, heart rate, and SAP and MAP during examination; and video observer-assessed CSS, CS, SS, and AS. The paired *t* test was used to determine whether the difference in mean values between gabapentin and placebo treatments was significant. All tests were 2 tailed, and values of *P* < 0.05 were considered significant.

Mixed-effects linear regression, with random effects for cat and treatment order, was performed to evaluate the effect of the gabapentin versus placebo on each of the following variables: transportation CSS, combined (owner and video observer) examination CSS, combined (veterinarian and video observer) CS, SS, and AS as well as physiologic variables (heart rate, SAP, and MAP). Multivariate mixed-effect linear regression was used to analyze the effect of potential confounders (gabapentin dose [on an mg/kg basis], visit number, cat age, and cat body weight) on the aforementioned outcome variables. Results are reported as mean (95% CI) difference. The 95% CI represents the interval within which the true coefficient would be 95% of the time if the experiment were repeated multiple times. Null hypothesis was only considered rejected if the 95% CI did not include 0.

Intraobserver agreement in cat scores was assessed through 2 statistical approaches. The Cohen κ statistic was calculated by use of a weighted matrix assuming a linear pattern between 0 and 7, with 0 indicating 0% agreement and 7 indicating 100% agreement. Intraclass correlations were calculated by use of a quadratic weighing pattern to assess agreement between scores assigned by the 2 video observers as well as between scores assigned by the owner and veterinarian. The κ values and intraclass correlation coefficients were considered to indicate excellent agreement when > 0.75, good agreement when between 0.60 and 0.74, fair agreement when between 0.40 and 0.59, and poor agreement when < 0.40.

Results

Animals

Twenty-five cats were evaluated for participation in this study. Five cats were excluded because they were receiving medications (*n* = 4) or had active disease (1), leaving 20 cats (10 neutered males and 10 spayed females) for enrollment. Ages ranged from 1 to 16 years (mean \pm SD, 4.95 \pm 3.74 years; median, 4 years). All cats were mixed breeds (17 domestic

shorthair, 2 domestic longhair, and 1 domestic medium hair). Body weights ranged from 3.4 to 7.7 kg (7.5 to 16.9 lb; mean \pm SD, 5.15 \pm 1.22 kg [11.33 \pm 2.68 lb]; median, 4.8 kg [10.6 lb]). Gabapentin doses ranged from 13.0 to 29.4 mg/kg (5.9 to 13.4 mg/lb; mean \pm SD, 20.5 \pm 4.7 mg/kg [9.3 \pm 2.1 mg/lb]; median, 20.0 mg/kg [9.1 mg/lb]).

Eleven cats were randomly assigned to receive gabapentin for their first visit, and the remaining 9 cats received placebo on their first visit. Owners chose to administer the capsule directly PO for 10 cats, and the other 10 cats voluntarily ate the capsule in a soft, flavored treat. Travel time to the hospital ranged from 5 to 45 minutes, for a mean \pm SD travel time of 12.0 \pm 10.3 minutes (median, 10 minutes).

Physical examination

The veterinarian was able to complete the physical examination on at least 1 visit for 19 of the 20 cats. One cat could not be removed from the carrier after either treatment because of aggression. For 4 cats after placebo administration, the examination could not be completed; however, after gabapentin administration, the examination could be completed. For all other cats, examination and blood pressure measurements were possible at both visits.

Heart rates during veterinary examination ranged from 124 to 220 beats/min (mean \pm SD, 168 \pm 36 beats/min; median, 172 beats/min). Values for MAP ranged from 63 to 161 mm Hg (mean, 101 \pm 35 mm Hg; median, 92.5 mm Hg) and for SAP ranged from 109 to 228 mm Hg (mean, 141 \pm 29 mm Hg; median, 134.5 mm Hg).

Treatment effects

The paired *t* test revealed that owner-assessed CSSs for cat behavior during transportation and veterinary examination were significantly (*P* < 0.001) lower when cats received gabapentin than when they received the placebo (**Figure 1**). Veterinarian-assessed CSs were also significantly lower when cats received gabapentin than when they received the placebo (**Figure 2**).

Video observer data revealed significantly (*P* = 0.02) lower CSs and ASs and significantly (*P* < 0.001) higher SSs in cats after gabapentin versus placebo treatment. No significant differences were identified between treatments in values for SAP, MAP, heart rate, or video observer-assessed examination CSS.

Results of mixed-effects linear regression analysis revealed that, controlling for cat and treatment order, gabapentin treatment (vs placebo treatment) was associated with lower transportation CSSs, combined (owner and video observer) examination CSSs, combined (veterinarian and video observer) CSs, ASs, and heart rates and higher SSs (**Table 1**). Values of SAP and MAP did not differ significantly between treatments.

Multivariate linear regression analysis to adjust for potential confounders revealed that as gabapentin dose increased, transportation CSSs, combined exam-

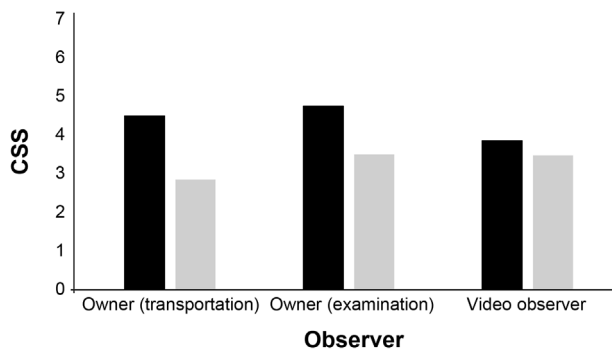


Figure 1—Mean values for CSSs (1 = fully relaxed, 2 = weakly relaxed, 3 = weakly tense, 4 = very tense, 5 = fearful or stiff, 6 = very fearful, and 7 = terrorized) for cats ($n = 20$) as assessed by owners for behaviors observed during transportation and veterinary examination and by 2 observers of examination video recordings (results averaged). Cats were scheduled for 2 veterinary visits 1 week apart and randomly assigned to receive prior to the first visit a capsule containing 100 mg of gabapentin (13.0 to 29.4 mg/kg [5.9 to 13.4 mg/lb]; gray bars) or placebo (black bars) and then the opposite treatment prior to the second visit. Owners were instructed to administer the assigned capsule orally 90 minutes prior to placing the cat into a carrier and transporting it to the veterinary hospital. All observers were blinded to treatment received. Owner-assessed CSSs for cats after receiving gabapentin were significantly ($P < 0.001$) lower than after receiving the placebo, but video observer-assigned scores did not differ significantly ($P = 0.06$) between treatments.

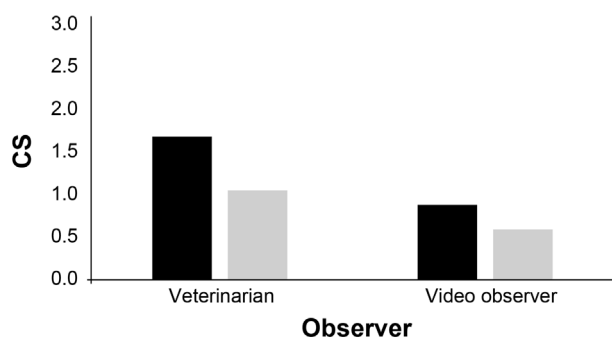


Figure 2—Mean values for CSs (0 = no resistance to handling, 1 = minimally resistant to handling, 2 = struggling and difficult to handle, and 3 = extreme struggling with or without urination or defecation) for the cats in Figure 1 as assessed by the veterinarian during physical examination and by 2 expert observers of examination video recordings (results averaged). Both sets of scores differed significantly ($P \leq 0.02$) between treatments.

ination CSSs, combined CSs, ASs, and heart rates decreased and SSs increased (**Table 2**). Transportation CSSs and combined examination CSSs significantly decreased from the first to second visit; although SSs increased, the difference between visits was not significant. Combined examination CSSs decreased with increasing body weight. As cat age increased, CSs decreased; however, inclusion of only 1 geriatric (16-year-old) cat in a group with a median age of 4 years rendered the value of this finding unclear. In each of these analyses, adjustment for these confounding variables had no significant effect on the measured outcome variables.

Observer agreement

Intraobserver agreement in scores assigned by the 2 expert observers of examination video recordings varied. Cohen κ calculations revealed that agreement between observers in AS assessments was excellent, but it was poor for the other score types (CSS, CS, and SS; **Table 3**). Interclass correlation coefficients suggested excellent agreement in AS assessments and fair agreement in CSS and CS assessments, but poor agreement in SS assessments (**Table 4**). Agreement was fair between video observer- and owner-assessed CSSs, but poor between video observer- and veterinarian-assessed CSs.

Adverse effects

Adverse effects were noted only in cats after gabapentin administration ($n = 6$). Vomiting was reported for 2 cats approximately 60 minutes after administration, and 1 other cat reportedly had hypersalivation and lip-licking behavior. One of the vomiting cats had received the gabapentin directly PO, and the other had voluntarily consumed the capsule with a soft, flavored treat, as had the cat with hypersalivation. For 3 additional cats, adverse effects were noted during veterinary examination and included minor muscle fasciculation ($n = 2$) and anisocoria (1). The owners of affected cats reported complete resolution of adverse effects within 6 hours after gabapentin administration.

Follow-up data on behavior observed by owners after returning home from the veterinary visit were available for 15 of the 20 cats. The most common

Table 1—Results of mixed-effects linear regression analysis of the effect of treatment received by pet cats ($n = 20$) before a veterinary appointment (100 mg of gabapentin vs 100 mg of placebo) on various outcome variables.

Outcome variable	Mean difference	95% CI	P value for variable	P value for model fit
Owner-assigned transportation CSS	-1.65	-2.21 to -1.09	< 0.001	< 0.001
Owner- and video observer-assigned examination CSS	-0.69	-0.99 to -0.39	< 0.001	< 0.001
Veterinarian and video observer-assigned CS	-0.41	-0.61 to -0.20	< 0.001	< 0.001
Video observer-assigned AS	-0.18	-0.26 to -0.09	< 0.001	< 0.001
Video observer-assigned SS	0.42	0.22 to 0.62	< 0.001	< 0.001
SAP during examination (mm Hg)	6.0	-8.9 to 20.9	0.43	0.43
MAP during examination (mm Hg)	2.2	-14.6 to 19.2	0.79	0.79
Heart rate during examination (beats/min)	-15.2	-29.5 to -0.8	0.04	0.04

Cats were scheduled for 2 veterinary visits 1 week apart and randomly assigned to receive prior to the first visit a capsule containing gabapentin (13.0 to 29.4 mg/kg [5.9 to 13.4 mg/lb]) or placebo and then the opposite treatment prior to the second visit. Owners were instructed to administer the assigned capsule orally 90 minutes prior to placing the cat into a carrier and transporting it to the veterinary hospital. All observers were blinded to treatment received; video observer scores represent the average of 2 expert observers' assessments during viewing of examination video recordings. Each regression model included random effects for cat and treatment order. Model fit was assessed with the Wald test.

Table 2—Results of multivariate mixed-effects linear regression analysis of the effect of potential confounders on the outcome variables in Table 1.

Outcome variable and confounder	Mean difference	95% CI	P value for confounder	P value for model fit
Owner-assigned transportation CSS				
Gabapentin dose (mg/kg)	−1.71	−2.20 to −1.22	< 0.001	< 0.001
Visit No.	−0.62	−1.11 to −0.13	0.01	—
Owner- and video observer–assigned examination CSS				
Gabapentin dose (mg/kg)	−0.71	−1.00 to −0.42	< 0.001	< 0.001
Visit No.	−0.33	−0.62 to −0.05	0.02	—
Cat body weight (kg)	−0.48	−0.79 to −0.17	0.002	—
Veterinarian and video observer–assigned CS				
Gabapentin dose (mg/kg)	−0.41	−0.61 to −0.20	< 0.001	< 0.001
Cat age (y)	−0.08	−0.14 to −0.02	0.007	—
Video observer–assigned AS				
Gabapentin dose (mg/kg)	−0.18	−0.26 to −0.09	< 0.001	< 0.001
Video observer–assigned SS				
Gabapentin dose (mg/kg)	0.43	0.24 to 0.63	< 0.001	< 0.001
Visit No.	0.23	0.04 to 0.43	0.18	—
Heart rate				
Gabapentin dose (mg/kg)	−15.2	−29.5 to −0.8	0.04	0.05

— = Not applicable.

See Table 1 for remainder of key.

Table 3—Results of Cohen κ testing for agreement between 2 observers who used examination video recordings to assign various scores to the cats in Table 1.

Scoring system	Observed agreement (%)	Expected agreement (%)	Weighted κ	P value
CSS	88.0	83.2	0.29	< 0.001
AS	97.5	77.1	0.89	< 0.001
CS	80.2	74.3	0.23	< 0.001
SS	86.8	84.4	0.16	0.02

The κ values were considered to indicate excellent agreement when > 0.75, good agreement when 0.60 to 0.74, fair agreement when 0.40 to 0.59, and poor agreement when < 0.40.

See Table 1 for remainder of key.

Table 4—Intraclass correlation coefficients for agreement between 2 video observers, the 2 video observers and cat owners, and the 2 video observers and the examining veterinarian in assignment of various types of scores to the cats in Table 1.

Variable	Intraclass correlation coefficient	95% CI
Video observer CSS	0.56	−0.09 to 0.84
Video observer AS	0.97	0.97 to 0.99
Video observer CS	0.47	−0.10 to 0.78
Video observer SS	0.24	−0.05 to 0.50
Examination CSS	0.46	0.24 to 0.66
(video observers vs owner)		
CS (video observers vs veterinarian)	0.36	0.12 to 0.58

The same definitions of agreement level as used for κ values were used for intraclass correlation coefficients.

See Tables 1 and 3 for remainder of key.

reported effect of gabapentin administration was sedation ($n = 12$), and in 3 cats, the degree of sedation was marked. These 3 cats had the lowest body weights and, consequently, had received the highest gabapentin dose (25.6 to 29.4 mg/kg [11.6 to 13.4 mg/lb]). Other reported effects included ataxia ($n = 6$; all ataxic cats also had signs of sedation), greater than typical affectionate behavior (4; 2 also had signs of se-

dation), and reduced signs of fear of dogs (1; no sedation reported). In all circumstances, owners reported complete resolution of these effects within 8 hours after gabapentin administration. Owner-reported perceived peak effect of gabapentin occurred 2 to 3 hours after administration.

Discussion

Overall, the present study yielded good evidence that oral administration of a 100-mg gabapentin capsule to cats 90 minutes before transporting them to the veterinary hospital led to a significant reduction in stress-related behaviors during transportation and examination. Gabapentin administration also decreased aggression and increased compliance of cats during veterinary examination.

Compliance improved for most cats in the present study, and for 4 (20%) cats, full examination was possible only with gabapentin treatment. However, for 1 (5%) cat, an examination could not be completed regardless of treatment received. Historically, this cat has needed to be anesthetized to allow safe performance of veterinary procedures, suggesting that the anxiolytic effects of the 100-mg dose of gabapentin (16.4 mg/kg [7.5 mg/lb] in this particular cat) may

not be potent enough to allow safe handling of cats with behavior indicative of extreme fear. A higher gabapentin dose, injectable sedative, or anesthesia may be warranted for similar cats.

Gabapentin at the 100-mg dose appeared to be well tolerated by most cats. However, the 2 smallest cats in the study (which received doses from 25.6 to 29.4 mg/kg) reportedly had marked signs of sedation after returning home. The finding that as body weight increased, CSS decreased indicated that the effects of gabapentin may have been somewhat dose dependent, with smaller cats having greater sedation. For clinical use, the authors recommend adjusting the dose for the size of the cat. For cats with a body weight close to the mean in this study (5.15 kg), a gabapentin dose of 100 mg (approx 20 mg/kg [9.1 mg/lb]) appeared to result in the best balance of clinical effect with adverse effects. However, pharmacokinetics data suggest a wide range of individual variation in peak plasma concentration with oral gabapentin administration in cats¹⁷; consequently, doses may need to be tailored to the individual patient.

Owner-perceived peak effect of gabapentin was reportedly achieved between 2 and 3 hours after administration. These data suggested that administration of the drug earlier than was done in the study (eg, 2 to 3 hours instead of 90 minutes prior to placing the cat in a carrier) may result in improved outcomes. Clients should be warned about the potential for ataxia and advised to keep gabapentin-treated cats from having access to stairs or other raised surfaces until the effects have resolved. Additionally, cats with outdoor access should be kept indoors until the effects pass.

Food was withheld from cats in the present study for 2 hours prior to treatment administration for consistency, but food withholding is likely not necessary for clinical use. To the authors' knowledge, the adverse effect of vomiting in cats after gabapentin administration has not been reported previously. It remains unclear from the study data whether the food withholding or administration method contributed to the vomiting. In clinical practice, it is common to mix the contents of a gabapentin capsule or liquid form of the medication with a small amount of wet food.

Veterinarians examining gabapentin-treated cats should take into consideration the potential for drug effects on their clinical examination findings. Mild sedation should be expected. Mixed-effects linear regression analysis revealed that heart rate was influenced by gabapentin treatment, with a mean decrease of 15.2 beats/min. Considering that the heart rate data from this study ranged from 124 to 220 beats/min, this decrease was unlikely to have been clinically important. Gabapentin has been shown to have analgesic properties in humans²²⁻²⁴ and rodents,^{25,26} but evidence of analgesic effects in placebo-controlled clinical trials has been lacking in cats²⁷ and dogs.²⁸ Nevertheless, veterinarians should be mindful that gabapentin treatment may mask signs of pain on clinical examination.

Transportation and examination CSSs decreased with increasing visit number, whereas SSs increased. This finding may have been attributable to the use of minimal and gentle handling and lack of invasive procedures during these visits. If the cats had a positive or neutral experience during their first visit, they may have had less stress during subsequent visits, underscoring the importance of providing low-stress veterinary experiences. Simple actions such as carrier training and low-stress handling of cats as well as treat provision during the examination may augment this effect.

One limitation of the present study was the poor agreement identified between the expert video observers (with the exception of AS assessment). Video observer- and owner-assessed examination CSSs and veterinarian-assessed CSs also had variable agreement. Data collected by the owners and the veterinarian indicated clearer differences between gabapentin and placebo than demonstrated with video observer data. These findings could have been attributable to greater familiarity of owners (vs the veterinarian and video observers) with their cat's typical behaviors and, therefore, a greater sensitivity to subtle changes in behavior. The examining veterinarian, with hands-on contact, is best placed to evaluate compliance, which may be difficult to assess through video analysis. However, in-room observers may also be more sensitive to bias than observers of examination video recordings. To minimize bias, linear regression analysis was performed involving the mean of scores reported by multiple observers. Additional studies are warranted to evaluate the effectiveness of video observation for evaluating behavior during veterinary examination.

In the study reported here, only minimal and gentle handling methods were used during veterinary examination. No invasive procedures were performed. Future studies could explore the effects of gabapentin administration on handling tolerance, such as during physical restraint of cats for procedures such as blood collection or cystocentesis. No significant differences were identified between treatments in SAP and MAP values, and only a mild difference in heart rate was found in the present study. Future studies could investigate differences in stress biomarker values, such as circulating cortisol or norepinephrine concentrations, in response to handling after treatment with gabapentin, another medication, or placebo.

Findings of the present study supported the use of gabapentin administered orally at 20 mg/kg for short-term anxiolysis in cats. Administration 2 to 3 hours prior to onset of a stressful event such as placing a cat in a carrier may provide best results, and efforts to minimize stress during veterinary visits may improve the cat's experience and compliance on subsequent visits.

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Footnotes

- a. Gabapentin capsules (100 mg), Teva Pharmaceuticals, North Wales, Pa.
- b. Fisher Scientific, Waltham, Mass.
- c. Cardell 9402, Paragon Medical, Coral Springs, Fla.
- d. HandyCam DCR-SR300, Sony Corp of America, New York, NY.

References

1. AVMA. Cat-owning households. In: *US pet ownership & demographics sourcebook*. Schaumburg, Ill: AVMA, 2007;75-87.
2. Volk JO, Thomas JG, Collieran EJ, et al. Executive summary of phase 3 of the Bayer veterinary care usage study. *J Am Vet Med Assoc* 2014;244:799-802.
3. Gruen ME, Thomson A, Clary G, et al. Conditioning laboratory cats to handling and transport. *Lab Anim (NY)* 2013;42:385-389.
4. Rodan I. Understanding feline behavior and application for appropriate handling and management. *Top Companion Anim Med* 2010;25:178-188.
5. Anseeuw E, Apker C, Ayscye C, et al. Handling cats humanely in the veterinary hospital. *J Vet Behav* 2006;1:84-88.
6. Stevens BJ, Frantz EM, Orlando JM, et al. Efficacy of a single dose of trazodone hydrochloride given to cats prior to veterinary visits to reduce signs of transport- and examination-related anxiety. *J Am Vet Med Assoc* 2016;249:202-207.
7. Hopfensperger MJ, Messenger KM, Papich MG, et al. The use of oral transmucosal detomidine hydrochloride gel to facilitate handling in dogs. *J Vet Behav* 2013;8:114-123.
8. Gilbert-Gregory SE, Stull JW, Rice MR, et al. Effects of trazodone on behavioral signs of stress in hospitalized dogs. *J Am Vet Med Assoc* 2016;249:1281-1291.
9. Rodan I. Feline-friendly handling techniques, in *Proceedings*. 153rd Am Vet Med Assoc Annu Conv 2016.
10. Shafford H. Serenity now: practical sedation options for cats. Available at: vetanesthesiaspecialists.com/wp-content/uploads/2015/05/SedationOptions_DogsAndCats_Shafford_updated2017.pdf. Accessed Jun 26, 2017.
11. Cheng JK, Chiou LC. Mechanisms of the antinociceptive action of gabapentin. *J Pharmacol Sci* 2006;100:471-486.
12. Hellyer P, Rodan I, Brunt J, et al. AAHA/AAFP pain management guidelines for dogs and cats. *J Feline Med Surg* 2007;9:466-480.
13. Lorenz ND, Comerford EJ, Iff I. Long-term use of gabapentin for musculoskeletal disease and trauma in three cats. *J Feline Med Surg* 2013;15:507-512.
14. Thomas WB. Idiopathic epilepsy in dogs and cats. *Vet Clin North Am Small Anim Pract* 2010;40:161-179.
15. Ménigaux C, Adam F, Guignard B, et al. Preoperative gabapentin decreases anxiety and improves early functional recovery from knee surgery. *Anesth Analg* 2005;100:1394-1399.
16. de-Paris F, Busnello JV, Vianna MR, et al. The anticonvulsant compound gabapentin possesses anxiolytic but not amnesic effects in rats. *Behav Pharmacol* 2000;11:169-173.
17. Siao KT, Pypendop BH, Ilkiw JE. Pharmacokinetics of gabapentin in cats. *Am J Vet Res* 2010;71:817-821.
18. Court MH. Feline drug metabolism and disposition: pharmacokinetic evidence for species differences and molecular mechanisms. *Vet Clin North Am Small Anim Pract* 2013;43:1039-1054.
19. Peterson ME. Xylitol. *Top Companion Anim Med* 2013;28:18-20.
20. Kessler M, Turner D. Stress and adaptation of cats (*Felis silvestris catus*) housed singly, in pairs and in groups in boarding catteries. *Anim Welf* 1997;6:243-254.
21. Steagall PV, Taylor PM, Rodrigues LC, et al. Analgesia for cats after ovariohysterectomy with either buprenorphine or carprofen alone or in combination. *Vet Rec* 2009;164:359-363.
22. Al-Mujadi H, A-Refai AR, Katzarov MG, et al. Preemptive gabapentin reduces postoperative pain and opioid demand following thyroid surgery. *Can J Anaesth* 2006;53:268-273.
23. Cuignet O, Pirson J, Soudon O, et al. Effects of gabapentin on morphine consumption and pain in severely burned patients. *Burns* 2007;33:81-86.
24. Peng PW, Wijesundera DN, Li CC. Use of gabapentin for peri-operative pain-control: a meta-analysis. *Pain Res Manag* 2007;12:85-92.
25. Curros-Criado MM, Herrero JF. The antinociceptive effect of systemic gabapentin is related to the type of sensitization-induced hyperalgesia. *J Neuroinflammation* 2007;4:15.
26. Feng Y, Cui M, Willis WD. Gabapentin markedly reduces acetic acid-induced visceral nociception. *Anesthesiology* 2003;98:729-733.
27. Pypendop BH, Siao KT, Ilkiw JE. Thermal antinociceptive effect of orally administered gabapentin in healthy cats. *Am J Vet Res* 2010;71:1027-1032.
28. Wagner AE, Mich PM, Uhrig SR, et al. Clinical evaluation of perioperative administration of gabapentin as an adjunct for postoperative analgesia in dogs undergoing amputation of a forelimb. *J Am Vet Med Assoc* 2010;236:751-756.