

# Assessment of the effects of gabapentin on activity levels and owner-perceived mobility impairment and quality of life in osteoarthritic geriatric cats

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## OBJECTIVE

To evaluate effects of gabapentin on activity levels and owner-perceived mobility impairment and quality of life (QOL) in osteoarthritic geriatric cats.

## DESIGN

Blinded, placebo-controlled, randomized crossover-design study.

## ANIMALS

20 osteoarthritic cats ( $\geq 10$  years old).

## PROCEDURES

Cats received gabapentin (10 mg/kg [4.5 mg/lb]) or placebo treatment, PO, every 12 hours for 2 weeks, followed by the alternate treatment (with no washout period). Activity was assessed with a collar-mounted accelerometer. A client-specific outcome measure (CSOM) questionnaire was used weekly to collect owner assessments of 3 selected activities in which their cats had impaired mobility; QOL ratings (worse, the same, or improved) following crossover to each treatment and for the overall study period were collected at the end of the investigation. Activity counts, CSOM and QOL data, and deterioration in impaired activities (ie, decrease of  $\geq 2$  points in CSOM scores) associated with treatment crossover were assessed statistically. Adverse events were recorded.

## RESULTS

Gabapentin administration was associated with significantly lower mean daily activity counts (48,333 vs 39,038 counts/d) and significantly greater odds (approx 3-fold change) of CSOM ratings indicating improvement in impaired activities, compared with results for the placebo treatment. A greater proportion of cats had deterioration in impaired activities after the crossover from gabapentin to placebo than when the opposite occurred, but the proportion of cats with worsened QOL did not differ between sequences. Adverse events were noted for 10 cats (9 that completed the study) during gabapentin treatment (sedation, ataxia, weakness, and muscle tremors) and 1 cat during placebo treatment (lethargy).

## CONCLUSIONS AND CLINICAL RELEVANCE

Gabapentin treatment was associated with improvement in owner-identified impaired activities of osteoarthritic cats. Activity levels were lower than those during placebo treatment, and sedation was the most common adverse effect. (*J Am Vet Med Assoc* 2018;253:579–585)

**O**steoarthritis is an important clinical problem in cats, particularly among older patients, as it can be associated with signs of pain and impaired mobility.<sup>1–7</sup> Osteoarthritis appears to involve a complex pain state with nociceptive, inflammatory, and neuropathic components.<sup>8,9</sup> In cats, it has been found to be associated with central sensitization as identified by a facilitation of nociceptive temporal summation<sup>7</sup> and punctate tactile hypersensitivity,<sup>10</sup> neither of which was responsive to the cyclooxygenase inhibi-

tor meloxicam.<sup>10,11</sup> A positron-emission tomographic imaging study<sup>12</sup> revealed significant metabolic changes in the secondary somatosensory cortex, thalamus, and periaqueductal gray matter in cats with osteoarthritis, compared with findings for healthy control cats, suggesting that the condition is accompanied by sustained nociceptive inputs and increased activity of descending inhibitory pathways. Interestingly, multimodal therapy with tramadol and meloxicam, which is expected to simultaneously modulate ascending nociceptive input and descending inhibition, was associated with a significant decrease in central hypersensitivity in cats with osteoarthritis as assessed by mechanical temporal summation of pain.<sup>11</sup>

Gabapentin, a structural analog of GABA that was originally developed as an antiepileptic drug,

## ABBREVIATIONS

CSOM Client-specific outcome measure  
GABA  $\gamma$ -Aminobutyric acid  
QOL Quality of life

was found to be effective in the treatment of neuropathic pain in people.<sup>13,14</sup> Although gabapentin resembles GABA, it does not act at GABA receptors.<sup>14</sup> Instead, it selectively inhibits voltage-gated calcium channels containing the  $\alpha 2\delta$ -1 subunit.<sup>14</sup> Gabapentin decreases nociceptive input through suppression of dorsal horn nociceptive neurons<sup>15</sup> and stimulates descending inhibition by increasing glutamatergic neurotransmission in the locus coeruleus.<sup>16</sup> In cats, the disposition of gabapentin is characterized by a small volume of distribution and low clearance rate.<sup>17</sup> It does not reduce inhalant anesthetic requirements or increase thermal nociceptive thresholds in healthy cats.<sup>18,19</sup> In veterinary medicine, analgesic benefits of the drug were reported for 2 cats with multiple injuries<sup>20</sup> and 1 horse with signs of neuropathic pain.<sup>21</sup> Gabapentin is frequently recommended for the management of chronic pain associated with various conditions in cats, including osteoarthritis,<sup>5,22-26</sup> but to the author's knowledge, no controlled studies have been published.

At present, there is no gold standard for evaluation of chronic pain and response to analgesics in cats. Objective evaluation modalities such as ground reaction forces,<sup>10</sup> mechanical paw withdrawal thresholds,<sup>10</sup> positron emission tomography,<sup>12</sup> and goniometry<sup>27</sup> have been used in some studies. Changes in mobility assessed subjectively with CSOM questionnaires or objectively with accelerometers have been used commonly to assess analgesic efficacy in cats with osteoarthritis.<sup>10,11,28</sup> The placebo effect can be a problem when CSOMs are used, and it should be properly controlled for,<sup>28,29</sup> whereas accelerometer-based activity assessment correlates well with distance traveled<sup>30</sup> and has more consistently detected treatment effects in cats with osteoarthritis.<sup>10,11,28</sup> However, drugs that alter CNS activity (ie, depression or excitation) could also affect activity levels independent of analgesic effects.<sup>31</sup>

The objective of the study reported here was to evaluate the effects of gabapentin in geriatric cats with osteoarthritis and owner-identified mobility impairment in a randomized, placebo-controlled, crossover study by use of CSOMs, owner-perceived QOL, and accelerometer-based activity assessments. We hypothesized that gabapentin treatment would be associated with significant improvement in owner-identified mobility impairment in these patients.

## Materials and Methods

### Animals and inclusion criteria

Geriatric ( $\geq 10$ -year-old) cats of either sex with owner-identified mobility impairment were recruited for participation in the study. Owners enrolled their cats and participated in the study voluntarily. Written informed consent was obtained from owners prior to enrollment. The University of California-Davis Institutional Animal Care and Use Committee reviewed and approved the study protocol.

All cats underwent general physical, orthopedic, and neurologic examinations; a CBC; and serum biochemical analysis. Orthogonal radiographs of joints were obtained if manipulation elicited an aversive response during physical examination or if signs of muscle atrophy were present. Cats were included in the study if the following criteria were met: the owners reported decreased or impaired patient mobility, radiographic evidence of osteoarthritis was identified in  $\geq 1$  synovial appendicular joint, the cat was kept exclusively indoors, and the owners had a stable routine of daily living during the study period (ie, no impending changes such as moving to another house, vacations, or introduction of new pets or people into the household).

### Exclusion criteria

Cats were excluded from enrollment if they had any detectable systemic disease or clinically important abnormalities on hematologic examination or if they were receiving any anti-inflammatory drug, other analgesic medications, or glucosamine-chondroitin sulfate and similar products (eg, chondroprotectants) at the time of enrollment in the study. In addition, cats were removed from the study and excluded from the statistical analyses if inclusion requirements were violated at any time after enrollment, if frequent or serious adverse effects developed, or if cats missed  $> 2$  doses of gabapentin or the placebo treatment. Owners were allowed to remove cats from the study at any time at their own discretion.

### Procedures

Cats were randomly assigned to receive 1 capsule of gabapentin or a placebo treatment, PO, every 12 hours for 2 weeks, followed by the alternate treatment in a crossover-design study. All cats were weighed at the start of the study, and the contents of 300-mg gabapentin capsules<sup>a</sup> were repackaged into gelatin capsules at a calculated dose of 10 mg/kg (4.54 mg/lb) for each cat. Identical-looking capsules were prepared with a similar weight of sucrose to be used as the placebo treatment. Body weights were not reassessed, and there was no washout period between treatments. The dosage of gabapentin was selected on the basis of the clinically recommended range for use in cats (2.5 to 20 mg/kg [1.1 to 9.1 mg/lb], PO, q 12 h)<sup>5,26,32</sup> and a report<sup>20</sup> of its use in 2 cats with polytrauma. More frequent administrations of lower<sup>17</sup> and higher<sup>26</sup> doses have been suggested, but such a regimen would likely adversely affect dosing compliance.<sup>26</sup> Owners had the option of inserting the capsule into a flavored pill delivery pouch<sup>b</sup> to facilitate oral administration.

Activity level (assessed with a collar-mounted activity monitoring device<sup>c</sup> as previously described<sup>28,30</sup>), changes in owner-selected impaired activities (assessed with the CSOM questionnaire<sup>28</sup>), and owner-assessed patient QOL were the outcome measures of the study. The 17.5-g activity monitoring device,

which was secured with a hook-and-loop fastener to a nonbreakaway neck collar, monitored activity by means of an omnidirectional piezoelectric accelerometer. Accelerometer-based activity counts were previously shown to correlate well with distance moved and mobility in freely moving cats.<sup>30</sup> Epoch duration (the period of time during which a data value is created) was set at 60 seconds (ie, 1 data value or activity count/min), and the time stamp was synchronized with local time. The CSOM questionnaire was composed of 3 place- and time-specific activities for which the owner considered the pet to have signs of impairment prior to the start of the study. As such, the CSOMs were unique for each cat and owner. At each assessment time, owners were asked to rate the changes in these impaired activities relative to the week prior to study entry (ie, days -7 through -1) according to the following scale: 1 = deteriorated or worse, 2 = same, 3 = slightly improved, 4 = moderately improved, and 5 = very improved. Because 3 activities were included, the possible sum of scores for each week ranged from 3 (ie, deteriorated or worse in all 3 activities) to 15 (ie, very improved in all 3 activities).

On day 0 of the study, the cats were fit with a collar that included an attached activity monitoring device, the owners received study instructions, and the first CSOM questionnaire was answered. Week 1 was allowed for acclimation, and baseline assessments of activity level and the CSOMs were obtained via a telephone call with the owners on day 7. Treatments began on day 7, and subsequent assessments via telephone occurred on day 14 (week 2), day 21 (week 3), day 28 (week 4), and day 35 (week 5). Owners were reminded how to answer the questionnaire prior to each assessment. At these contact times, owners were also asked to provide information regarding compliance (ie, whether treatments were given according to schedule, the cat had remained indoors and worn the accelerometer at all times, and the owner had no changes in schedule that prevented the required assessments) and adverse events and were allowed to provide additional comments. One trained individual performed all telephone calls to collect the data. At the end of week 5, each owner was asked 2 additional questions that were used to assess changes in the cat's QOL. The first question asked whether the owner thought the cat's QOL during the study was worse, the same, or improved, compared with that before the study, and the other question asked whether the owner thought the cat's QOL was worse, the same, or improved in the last 2 weeks of treatment, compared with that during the previous 2 weeks. For each question, owners were also asked to estimate the percentage change in QOL.

The authors downloaded accelerometer data at the end of the study. Owner-reported adverse events were recorded throughout the study, and affected cats were examined by a veterinarian at the owner's

discretion. Physical examination, a CBC, and serum biochemical evaluation were performed for each cat upon completion of the study.

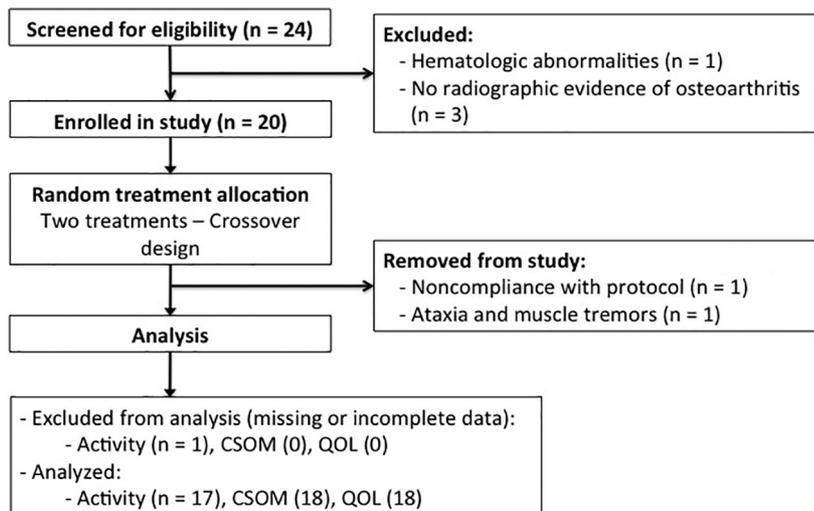
## Statistical analysis

Statistical analysis was performed with commercially available software.<sup>d</sup> Activity data were normally distributed according to the D'Agostino and Pearson omnibus normality test. Total activity counts over the 2-week treatment periods were divided by the number of days to obtain mean daily total activity for each treatment period and were subsequently analyzed with 2-tailed paired *t* tests. The sums of CSOM scores (the mean of 2 weekly sums) were compared between treatments with a Wilcoxon matched-pairs signed rank test. The weekly CSOM scores for each of the 3 activities were also dichotomized as not improved (ie, score  $\leq 6$ ) or improved (ie, score  $> 6$ ) and analyzed with a McNemar test. To assess deterioration in the owner-selected impaired activities associated with crossing over from one treatment to the other, the difference in CSOM scores (the mean of 2 weekly sums) between the two 2-week treatment periods was calculated for each cat. Owner-observed deterioration in the selected activities during the second treatment period was defined as a decrease of  $\geq 2$  points in the CSOM score as in a previous study,<sup>29</sup> and both the presence and magnitude of deterioration were recorded. Deterioration was investigated because the results of a previous study<sup>29</sup> indicated that owners may be more likely to detect deterioration in clinical condition of cats with joint disease after withdrawing an analgesic medication than improvement in signs during analgesic treatment. A 1-tailed Fisher exact test was used to compare frequencies of deterioration in impaired activities (on the basis of CSOM scores) and of owner ratings indicating a worsened QOL between cats that crossed over from gabapentin to placebo treatment and those that crossed over from placebo to gabapentin treatment. The magnitude of QOL deterioration (percentage change) was compared between the 2 treatment sequences with a 1-tailed paired *t* test. Data with normal and non-normal distributions were summarized as mean  $\pm$  SD or as median and range, respectively. Values of *P*  $\leq 0.05$  were considered significant.

## Results

### Animals

Twenty-four cats were evaluated for inclusion in the study, and 20 (11 spayed females and 9 neutered males) fulfilled the enrollment inclusion criteria (**Figure 1**). None of the enrolled cats had received analgesic or anti-inflammatory medications for  $\geq 4$  weeks before the study, and none had received chondroprotectants within the previous year. Breeds included domestic shorthair (*n* = 14), domestic longhair (5), and Persian (1). Median age and body weight were 14 years (range, 11 to 18 years) and 5.3 kg (11.7 lb; range,



**Figure 1**—Flow diagram for a blinded, placebo-controlled, crossover-design study to evaluate the effects of gabapentin on activity levels and owner-perceived mobility impairment and QOL in osteoarthritic geriatric ( $\geq 10$ -year-old) cats. Cats were randomly assigned to receive gabapentin (repackaged into capsules at a dose of 10 mg/kg [4.5 mg/lb] for each cat) or a placebo treatment (sucrose provided in the same type of capsules), PO, every 12 hours for 2 weeks, followed by the alternate treatment with no washout period between experiments. A collar-mounted accelerometer, CSOM questionnaire scores, and owners' evaluation of changes in their cats' QOL were used to assess outcomes for each treatment.

2.7 to 8.1 kg [5.9 to 17.8 lb]), respectively. Median ages and body weights of females and males were 14 years (range, 11 to 18 years) and 14 years (range, 12 to 17 years) and 4.9 kg (10.8 lb; range, 2.7 to 6.6 kg [5.9 to 14.5 lb]) and 5.7 kg (12.5 lb; range, 4.2 to 8.1 kg [9.2 to 17.8 lb]), respectively.

Eighteen cats completed the study. The 2 cats that did not complete the study were withdrawn during week 2 (the first week of the first treatment period); one was removed because of noncompliance with the study protocol (the owner could not successfully administer the assigned capsules), and the other had adverse effects (severe ataxia and muscle tremors) after the first dose of gabapentin. Erroneous setup of the activity monitor resulted in an incomplete activity data set for 1 other cat, which was excluded from the activity level analyses.

### Activity counts and owner-assessed outcomes

Mean  $\pm$  SD daily activity counts were significantly ( $P < 0.001$ ) greater during placebo administration than during gabapentin administration ( $48,333 \pm 12,674$  counts/min and  $39,038 \pm 9,536$  counts/min, respectively). The CSOM scores for the first and second weeks of each treatment were summarized (**Figure 2**). The median sum of CSOM scores for the 3 owner-selected impaired activities was 6 (range, 5 to 9) during placebo administration (corresponding to no change) and 8 (range, 4 to 14) during gabapentin administration (corresponding to a slight improvement). The difference was not significant ( $P = 0.55$ ). Analysis of the CSOM ratings (weekly scores for each

of the 3 activities) synthesized as improved or not improved revealed that the proportion of improved ratings was significantly ( $P = 0.003$ ) greater during gabapentin treatment than during placebo administration (OR, 3.1; 95% confidence interval, 1.4 to 7.5).

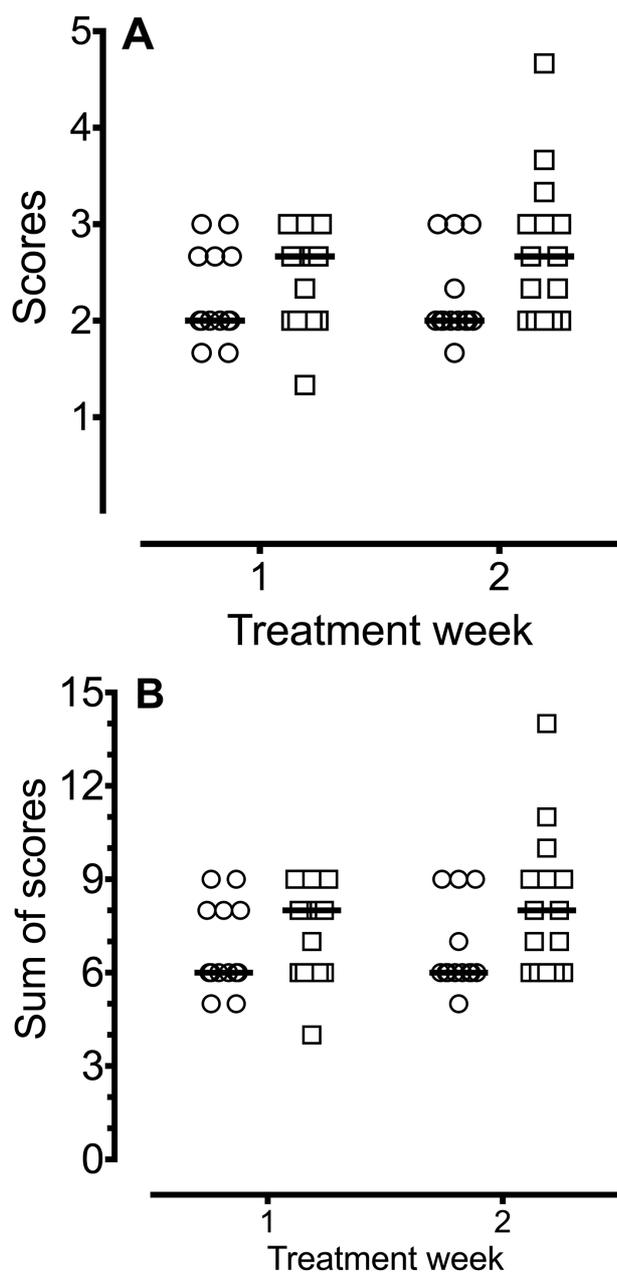
Thirteen of 18 owners who assessed the global QOL for their cats throughout the study (compared with that observed in the week prior to study participation) indicated that they had observed improvement; the mean  $\pm$  SD estimated change was  $45 \pm 24\%$ . Four owners reported that their pet's QOL remained the same during the study, and 1 reported that it was worse (an estimated change of 80%) during the study. In the analysis of crossover effects, 8 of 9 owners whose cats had a crossover from gabapentin to placebo treatment indicated that their cats' QOL had worsened during the second treatment period (mean  $\pm$  SD estimated difference,  $40 \pm 20\%$ ), and 5 of 9 owners whose cats had

crossed over from placebo to gabapentin treatment reported that QOL had worsened with the change (mean  $\pm$  SD estimated difference of  $29 \pm 27\%$ ). The proportions of owners who reported worsened QOL were not significantly different between these groups. Of the 5 owners who indicated a worsened QOL after their cats had crossed over to gabapentin treatment, 3 also reported adverse effects. None of the 8 owners who indicated that QOL had worsened when cats crossed over to placebo treatment reported adverse effects.

When the criterion of a 2-point decrease in the mean of 2 weekly sums of CSOM scores associated with treatment crossover was applied as a determinant for owner-observed deterioration in clinical signs, 4 of 9 cats had deterioration following the crossover from gabapentin to placebo treatment, whereas 0 of 9 cats had deterioration following the crossover from placebo to gabapentin treatment. These frequencies were significantly ( $P = 0.041$ ) different.

### Adverse events

Owner comments and owner-reported adverse events for all cats (including those removed from the study) during gabapentin administration were summarized (**Supplemental Table S1**, available at [avmajournals.avma.org/doi/suppl/10.2460/javma.253.5.579](http://avmajournals.avma.org/doi/suppl/10.2460/javma.253.5.579)). Adverse events during gabapentin treatment were reported for 9 of 18 cats that completed the study. These included sedation ( $n = 7$ ), hind limb weakness or ataxia (3), periodic muscle tremors (1), and diarrhea (1). One cat was reported to be lethargic during placebo treatment.



**Figure 2**—Scatterplots depicting median (A) and sum (B) of CSOM scores for 3 owner-selected impaired activities of 18 geriatric cats ( $\geq 10$  years old) with osteoarthritis. After a 1-week acclimation and baseline data collection period, cats received gabapentin (10 mg/kg [4.5 mg/lb], PO, q 12 h; squares) or a placebo (sucrose) treatment (circles) for 2 weeks each in a randomized, blinded, crossover-design study with no washout period between experiments. At the end of each week, owners were contacted by telephone and asked to rate changes in the previously identified impaired activities (compared with their observations during the week before entering the study) according to the following scale: 1 = deteriorated or worse, 2 = same, 3 = slightly improved, 4 = moderately improved, and 5 = very improved. Horizontal lines in panel B correspond to the median sum of scores for each group.

## Discussion

Osteoarthritis is a complex, painful condition in cats that involves changes in central nociceptive neuronal pathways characteristic of central sensitiza-

tion.<sup>7,10,12</sup> In osteoarthritic geriatric cats of the present study, gabapentin administration was significantly ( $P = 0.003$ ) associated with improvement (vs no improvement) in owner-identified impaired activities, and crossover from gabapentin to placebo treatment was significantly ( $P = 0.041$ ) associated with deterioration in the selected activities on the basis of CSOM scores. Gabapentin decreases nociceptive input via suppression of dorsal horn nociceptive neurons<sup>15</sup> and activates descending inhibition via increasing glutamatergic neurotransmission in the locus coeruleus.<sup>16</sup> These mechanisms are expected to counter the increased central nociceptive input documented for osteoarthritic cats<sup>12</sup> and might underlie the analgesic effects observed in the present study.

Research in mice has shown that chronic joint inflammation can transition to a neuropathic state that becomes insensitive to cyclooxygenase inhibitors but responds to gabapentin and tumor necrosis factor- $\alpha$  inhibitors.<sup>33</sup> Some of the signs of pain associated with osteoarthritis in cats can also be insensitive to cyclooxygenase inhibition,<sup>10,11</sup> although they may respond to combined treatment with a cyclooxygenase inhibitor and tramadol.<sup>11</sup> Recent findings suggest that tramadol alone may improve impaired activities in geriatric cats with osteoarthritis.<sup>31</sup> Both tramadol and gabapentin have multiple mechanisms of action that are potentially useful for treatment of neuropathic pain states.<sup>13</sup> The evidence for central sensitization<sup>7,10-12</sup> and positive responses to drugs such as tramadol and gabapentin suggest that such a neuropathic state may exist in cats with osteoarthritis and may need to be addressed for adequate pain management.

Owner-related placebo effect is an important concern that should be addressed in studies evaluating pain and analgesic efficacy in animals with conditions involving chronic pain. In 1 placebo-controlled parallel-design study<sup>29</sup> of cats with degenerative joint disease, a lack of differences between owner-identified improvements following meloxicam versus placebo treatment was attributed to a placebo effect. The owners of cats that received meloxicam in that study<sup>29</sup> did detect recurrence of clinical signs during a masked withdrawal period after meloxicam treatment ceased, and the authors suggested that focusing on worsening of clinical signs after discontinuation of a treatment might be a useful means of circumventing such placebo effects in evaluating analgesic efficacy. In the present study, the odds of owner-identified signs of improvement (vs no improvement) in cats during gabapentin treatment were 3 times those for the same cats during placebo treatment. These findings supported the hypothesis that gabapentin is superior to placebo treatment and may be a useful treatment for some signs of pain in cats with osteoarthritis.

The lack of significant improvement in owner-reported QOL for cats in the present study during gabapentin (vs placebo) treatment was discordant with other results that indicated a significant association between gabapentin treatment and improvement in owner-reported impaired activities. A high proportion

of cats had adverse effects reported during gabapentin treatment (9/18 that completed the study), most commonly sedation, and this could have negatively affected QOL. Most owners who indicated that their cat's QOL worsened with the crossover to gabapentin treatment (5/9) also reported adverse effects (3/5), whereas no owners reported adverse effects when cats crossed over to placebo treatment, but most (8/9) still indicated that the change was associated with a worsened QOL. Considering that the proportion of cats with a  $\geq 2$ -point decrease in CSOM scores following the crossover to placebo treatment was significantly greater than that following the crossover to gabapentin (4/9 vs 0/9), the reported negative change in QOL during placebo treatment was likely attributable to clinical deterioration. Sedation, the most common adverse effect as in previous reports,<sup>17-19,25,32</sup> was likely the reason for the observed decrease in activity level, but seemed to decrease in intensity over the course of treatment. Overall, most (13/18) owners appeared satisfied, as they reported that their cats' global QOL had improved while participating in the study. Clinically, a strategy to minimize adverse events may include starting with a lower dose of gabapentin that could be titrated up until a balance between sedation and efficacy, and thus suitable QOL, is achieved. A lower dosage than that used in the present study (6.5 mg/kg [2.95 mg/lb], PO, q 12 h) was reportedly effective and well-tolerated in long-term treatment of 3 cats with musculoskeletal disease and trauma,<sup>34</sup> and doses up to 50 mg/kg (22.7 mg/lb) have been recommended.<sup>32</sup>

Investigation of gabapentin at only 1 dose and lack of a washout period between experiments could be considered shortcomings of the present study. The lack of a washout period could have led to a carryover effect of gabapentin during placebo treatment. However, gabapentin has a relatively short half-life in cats (2.5 to 3.3 hours),<sup>17</sup> such that the carryover effect on the 2-week-long placebo treatment would likely have been very small; therefore, a washout period was deemed unnecessary. Although it would have been potentially more informative to evaluate a range of drug doses, the dose selected was within the low-to-middle range of clinically recommended doses (2.5 to 50 mg/kg)<sup>5,20,26,27,34,35</sup> and was significantly associated with improvement in some owner-reported outcome measures for cats. Dose adjustment for individual cats is likely to be required in clinical settings.

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The authors declare there were no conflicts of interest.

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## Footnotes

a. Gabapentin capsules USP, Actavis Pharma Manufacturing Pvt Ltd, Tamilnadu, India.

- b. Feline Greenies Pill Pockets (salmon flavor), The Nutro Co, Franklin, Tenn.
- c. Actical Mini Mitter, Phillips Respironics, Bend, Ore.
- d. GraphPad Prism, version 5.0c for MAC OS, GraphPad Software Inc, San Diego, Calif.

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## From this month's AJVR

### Prognostic value of CD44 variant isoform expression in dogs with multicentric high-grade B-cell lymphoma

Tomoki Motegi et al

#### OBJECTIVE

To determine the prognostic value of CD44 variant isoform expression in dogs with multicentric high-grade B-cell lymphoma (BCL).

#### ANIMALS

45 dogs with multicentric BCL and 10 healthy control Beagles.

#### PROCEDURES

The medical record database of a veterinary teaching hospital was searched to identify dogs with BCL that were treated between November 2005 and April 2015. Information regarding overall response to chemotherapy, progression-free survival (PFS) time, and overall survival time was extracted from each record. Archived lymph node aspirate specimens from dogs with BCL and lymph node aspirate specimens from the 10 control dogs underwent real-time PCR analysis to determine mRNA expression of CD44 variant isoforms of exons 3, 6, and 7 and the CD44 whole isoform. For each isoform, mRNA expression was compared between dogs with BCL and control dogs. The mean relative expression of each isoform was used to classify dogs with BCL into either a high- or low-expression group, and overall response rate, PFS time, and overall survival time (ie, indices of prognosis) were compared between the 2 groups.

#### RESULTS

For all isoforms evaluated, mean relative mRNA expression for dogs with BCL was numerically lower than that for control dogs. Dogs with BCL and high CD44 isoform expression had a lower overall response rate, median PFS time, and median overall survival time, compared with dogs with BCL and low CD44 isoform expression.

#### CONCLUSIONS AND CLINICAL RELEVANCE

Results indicated that, for dogs with BCL, high expression of exons 3, 6, and 7 was associated with a poor prognosis. (*Am J Vet Res* 2018;79:961-969)



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