Safety and efficacy of intralesional triamcinolone administration for treatment of mast cell tumors in dogs: 23 cases (2005–2011)

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OBJECTIVE
To evaluate the safety and efficacy of intralesional triamcinolone administration, as a sole or adjuvant treatment, in dogs with mast cell tumors.

DESIGN
Retrospective case series

ANIMALS
23 dogs with mast cell tumors.

PROCEDURES
Medical records of dogs treated for a confirmed diagnosis of a mast cell tumor between 2005 and 2011 were reviewed. Patients with a confirmed diagnosis and measurable disease (tumor longest dimension ≥ 0.5 cm) that had received ≥ 1 intralesional treatment with triamcinolone, regardless of prior, concurrent, or adjuvant treatments, were eligible for inclusion. Data collected included patient characteristics, results of cytologic and histologic testing and tumor staging, triamcinolone dosage, treatment response, and adverse events.

RESULTS
23 dogs with 24 tumors were included. Tumors were treated by means of intralesional triamcinolone administration alone (n = 5), intralesional triamcinolone administration with concurrent oral administration of glucocorticoids (6), and intralesional triamcinolone administration with concurrent cytotoxic chemotherapy, with or without oral administration of corticosteroids and radiation therapy (13). Of 5 dogs treated with intralesional triamcinolone administration alone, 1 achieved a complete response, 3 achieved a partial response, and 1 maintained stable disease. The response rate for all 24 tumors (23 dogs) was 67% (16/24), including 4 with a complete response and 12 with a partial response. The median time to progression was 63 days (range, 6 to 447 days). Three dogs experienced adverse events (local hemorrhage [n = 1]; suspected gastrointestinal ulceration [2]).

CONCLUSIONS AND CLINICAL RELEVANCE
Intralesional triamcinolone administration may be well tolerated and effective for treatment of nonresectable mast cell tumors in dogs. (*J Am Vet Med Assoc* 2018;252:84–91)

Mast cell tumors are a frequently encountered malignancy in dogs.[1–3] Mast cell tumors most commonly develop in the dermis and subcutis and range in biological behavior from benign to highly malignant. Numerous studies have sought to correlate the variable clinical characteristics of these tumors with survival time, reporting conflicting results. Studies[4–12] that have relied on histologic grade, mitotic index, argyrophilic nuclear organizing regions, proliferating cell nuclear antigen, and c-kit mutation status have provided somewhat consistent means of assessment of tumor behavior and patient outcomes; nevertheless, inconsistencies persist.

For patients with cutaneous mast cell tumors without evidence of distant metastasis, complete excision of the primary tumor is considered the treatment of choice, with many studies[13] demonstrating a greater rate of local recurrence or metastatic disease after incomplete excision. Therefore, current recommendations include achieving 2- to 3-cm lateral surgical margins (although 2-cm margins may be adequate for low grade tumors) and 1 tissue plane deeper than the tumor.[14,15] This recommendation is founded on the tenet that any malignant mast cells located beyond the bulk of the grossly visible tumor will be removed, thus offering a longer disease-free interval and improved likelihood of survival. Nonetheless, a recurrence rate of 11% was noted in 1 report[6] of incomplete surgical excision in 46 dogs. The reason for this outcome is unknown; however, it has been theorized that immune surveillance triggering clearance of residual tumor cells may play a role.[5,17] For tumors deemed nonresectable because of size, location, patient comorbidities, or some combination of these factors, several options are available. These include definitive or palliative radiation therapy, neo-

adjuvant or adjuvant chemotherapy, treatment with tyrosine kinase inhibitors, or a combinations of these treatments.

Intralesional treatments, including intralesional brachytherapy and intralesional administration of deionized water, have been previously investigated for patients with cutaneous mast cell tumors, with variable results.[18–20] Anecdotal references to intralesional glucocorticoid treatment have been reported[21–23]; however, no data evaluating efficacy or tolerability of this treatment modality currently exists in the veterinary literature. The premise underlying intralesional chemotherapy is the delivery of high drug concentrations at the primary tumor site, thereby improving treatment response rate. The ultimate goal is to achieve an effective drug concentration with avoidance of systemic adverse effects. Triamcinolone is an intermediate-acting glucocorticoid that is 4 to 10 times as potent as hydrocortisone.[24] When administered parenterally, activity can be detected for several weeks.[24] Reported therapeutic indications for this drug in veterinary patients include the treatment of inflammatory reactions such as acute allergic pruritus and otitis.[25,26] Intralesional triamcinolone administration has been described anecdotally for treatment of mast cell tumors in dogs and for treatment of rectal strictures and lipomas.[21–23,27,28] However, to our knowledge, there are no studies evaluating the efficacy or tolerability of this treatment administered alone or in combination with other treatments in dogs with mast cell tumors. Therefore, the goal of the study reported here was to retrospectively evaluate the tolerability and efficacy of intralesional triamcinolone administration alone or in combination with other treatments in dogs with mast cell tumors. We hypothesized that intralesional triamcinolone administration would be a safe and effective treatment for measureable mast cell tumors, and that triamcinolone could be administered safely in conjunction with other treatments.

Materials and Methods

Case selection criteria

Electronic medical records of client-owned dogs treated for a confirmed diagnosis of a mast cell tumor of any grade, stage, or tumor location at the Cummings Veterinary Medical Center at Tufts University between January 1, 2005, and December 31, 2011, were reviewed. Only dogs with measurable mast cell disease (tumor longest dimension ≥ 0.5 cm) that received at least 1 intralesional treatment with triamcinolone[a] and that had tumor measurements recorded before and after intralesional triamcinolone treatment were eligible for study inclusion. Patients were included regardless of prior or concurrent treatments or illnesses. Dogs without cytologic or histologic confirmation of the diagnosis of a mast cell tumor were excluded.

Medical records review

Patient variables—Data collected included signalment (age, breed, sex, and neuter status), weight, CBC results, results of cytologic and histologic testing, tumor location, and presence of metastatic disease (if applicable). When available, data regarding clinical signs at the time of diagnosis, staging results, results of serum biochemical analyses, previous treatments (including surgery, chemotherapy, orally administered corticosteroids, and radiation therapy), and neoadjuvant or concurrent treatments with chemotherapy, orally administered corticosteroids, and radiation therapy were also recorded. Data regarding surgery or margin analysis were not routinely noted in patients' medical records and thus were not collected. Staging designation was determined on the basis of the World Health Organization tumor grading system for dogs with mast cell tumors.[11] Data regarding supportive treatments were also not typically noted in the medical record and thus were not recorded.

Treatment variables—Data regarding intralesional treatment with triamcinolone included amount (mg/cm) injected per treatment, frequency of administration, response (tumor size [longest dimension in cm] at each visit), and adverse events as noted in the medical record. The timing of patient reevaluation varied according to the discretion of the treating clinician. Because of the variety of protocols, dosage regimens, and drugs employed, details of individual chemotherapy agents administered were not recorded for analysis, although it was noted when chemotherapy agents were administered concurrently or prior to intralesional triamcinolone treatment.

Patients were considered to have undergone concurrent treatments if they received any orally administered corticosteroids, chemotherapy, or radiation therapy at any time during intralesional triamcinolone treatment, even if triamcinolone treatment was initiated prior to other treatments. Patients were also considered to have undergone concurrent treatments if intralesional triamcinolone treatment was incorporated into an existing chemotherapy, corticosteroid (PO), or radiation therapy protocol. If patients only received concurrent orally administered corticosteroids, they were grouped into the concurrent orally administered corticosteroid group. If patients had received any chemotherapy with or without orally administered corticosteroids, or with or without radiation therapy, they were grouped into the concurrent chemotherapy group.

Patients were considered to have received previous treatment if they had been treated with chemotherapy, orally administered corticosteroids, radiation therapy, or some combination of these treatments within 1 year prior to but ≥ 7 days prior to initiation of triamcinolone treatment and if they had evidence of progressive disease during this treatment period. If patients had evidence of progressive disease when receiving a treatment, but this occurred < 7 days prior to initiation of intralesional triamcinolone treatment, it was considered concurrent treatment.

Response to treatment—Changes in mast cell tumor size were determined on the basis of measure-

ment of longest dimension with standard response evaluation criteria in solid tumors (RECIST) criteria.[29] Response to treatment was categorized as complete response (no clinical or gross evidence of disease), partial response (decrease in tumor burden of > 30% but < 100%), stable disease (decrease in tumor burden of < 30% or increase in tumor burden of < 20%), or progressive disease (increase in tumor burden of > 20%). Response was determined for patients regardless of the interval between intralesional triamcinolone treatment and reassessment of tumor size. Patients were grouped into 2 categories: responders and nonresponders. Responders were those patients with a complete or partial response and a response duration ≥ 14 days. This time interval was chosen on the basis of an expected duration of therapeutic action following intralesional triamcinolone administration of several (eg, 1 to 3) weeks and repeated injection at a median interval of 2 weeks in other treatment settings (eg, rectal strictures).[27] Nonresponders were patients with stable disease or progressive disease or with a response duration < 14 days. Data on evaluation of clinical improvement, time to progression, and the decision to incorporate intralesional triamcinolone treatment into the patient treatment plan were collected, when available, from review of medical records.

Adverse events—All clinical, hematologic, and serum biochemical evidence of adverse events were graded according to the Veterinary Comparative Oncology Group Common Terminology criteria for Adverse Events[30] on the basis of data obtained from medical records review.

Statistical analysis

Response to intralesional triamcinolone treatment was the primary outcome of interest, and time to progression was a secondary outcome. Clinicopathologic variables for responders (ie, patients that achieved a complete or partial response) and nonresponders (ie, patiens with stable or progressive disease) were compared. Dichotomous variables, including previous treatment, concurrent treatment, and sex, and ordinal variables, including grade (assigned on the basis of the Patnaik grading scheme[4] [grade I and II vs grade III]) and tumor location, were evaluated with χ^2 tests or the Fisher exact test when expected counts were < 5. Mast cell tumors on the muzzle of dogs (including the oral mucosa, oral mucocutaneous junction, and perioral region) have been associated with a high rate of metastasis (57 to 59%) and significantly shorter survival times.[31,32] Furthermore, a significantly shorter survival time was also reported for dogs with preputial or scrotal mast cell tumors.[33] Therefore, in the present study, we elected to evaluate patients with oral mucosal, oral mucocutaneous, and preputial mast cell tumors separately, compared with patients with tumors at other locations. Differences in age and median dose between responders and nonresponders were evaluated with the Mann-Whitney *U* test. Patients for which the diagnosis was made on the basis of cytologic analysis of biopsy samples, including those with metastatic lymph nodes treated with intralesional triamcinolone administration, were excluded from statistical analysis of tumor grade. Only those patients in which a primary lesion was treated with intralesional triamcinolone administration were included in the analysis of location (eg, anatomic site). Time to progression was defined as time to progressive disease of the primary tumor (or lymph node being injected, if applicable), development of a metastatic lymph node (or new metastatic lymph node if applicable), death, initiation of treatment with a new drug because of inadequate response, or loss to follow-up. If cause of death was unknown, it was assumed to be the result of progressive disease. Time to progression was assessed with the Kaplan-Meier method. Patients were censored from time to progression analysis if they had definitive surgery after intralesional triamcinolone treatment. All analyses were performed with a commercial software program[b]; values of $P \leq 0.05$ were considered significant.

Results

Twenty-three patients met the study inclusion criteria. One patient had 2 tumor sites that were treated with intralesional triamcinolone administration (24 total tumors treated). The median age at diagnosis was 8 years (range, 4 to 13 years). There were 12 spayed females and 11 castrated males. Dogs represented included Labrador Retrievers (n = 5), Golden Retrievers (4), Shepherd crosses (2), Pugs (2), 2 mixed-breed dogs, and 1 each of the following breeds: Miniature Pinscher, Boxer, Collie, Doberman Pinscher, Boston Terrier, Cocker Spaniel, Greyhound, and Redbone Coonhound. Staging tests and results were variable and not always complete, or results were not recorded in the medical record. Eleven dogs were deemed stage II. Nine dogs had confirmed lymph node metastasis, and 2 had suspected lymph node metastasis. One dog with confirmed stage II disease was suspected to have distant disease (spleen) on the basis of results of transabdominal ultrasonography.

Of the 23 dogs, 1 had a primary tumor of the lip and philtrum that was treated with intralesional triamcinolone administration and concurrent chemotherapy; approximately 1 month later, the patient developed a second, presumably de novo, mast cell tumor of the left shoulder region that was also treated with intralesional triamcinolone administration. Five tumors of the oral mucosa or the oral mucocutaneous junction developed in 5 dogs: philtrum or lip (n = 3), right arytenoid cartilage (1), and soft palate (1). Three dogs had completely excised Patnaik grade III tumors that subsequently developed lymph node metastasis confirmed with cytological analysis. The primary tumors were axial, appendicular, and of the oral or mucocutaneous junction. All 3 patients developed

metastatic disease in adjacent draining lymph nodes (axillary, prescapular, and mandibular, respectively). In these patients, triamcinolone was injected into the affected peripheral lymph nodes only. The remaining 16 patients had cutaneous mast cell tumors at various locations; 8 were located on appendicular sites, 6 were axial, and 2 were preputial. The median size of tumors at the time of the first intralesional treatment (ie, longest dimension) was 3.2 cm (range, 0.8 to 11.7 cm). Except for 1 dog (arytenoid location), all intralesional injections were completed without the need for sedation or anesthesia.

A median of 2 intralesional triamcinolone treatments (range, 1 to 15) was administered to all 23 dogs (24 tumors) with a median dose of 2.0 mg/cm (range, 0.125 to 19 mg/cm). The frequency of administration varied from a single dose (n = 10) to weekly doses (4), or as needed at the discretion of the treating clinician (10). The median interval between treatments was 9 days (range 5 to 86 days). For the 10 dogs that received only a single intralesional injection of triamcinolone, the reasons varied and included neoadjuvant treatment prior to surgery, tumor control during delayed chemotherapy treatment, or emergency treatment for an obstructive airway lesion associated with the right arytenoid cartilage. For the 21 non–lymph node sites treated with triamcinolone, results of histologic examination of biopsy samples were available for 17; the remaining 4 were confirmed on the basis of results of cytologic analysis. One tumor was not graded because of mucosal location (right arytenoid). All others were graded with the Patnaik grading system, with results as follows: grade I = 1, grade II = 8, and grade III = 7.

Dosing regimens varied widely among clinicians. Most clinicians strived to inject approximately 1 mg of triamcinolone/cm of tumor (longest dimension). As a consequence, the amount of triamcinolone administered in milligrams was considered with respect to the size of the tumor. However, tumor size was not reliably noted in all medical records; therefore, the intralesional triamcinolone dose was estimated by dividing the milligram dose recorded by the longest dimension of the tumor.[34] Intralesional triamcinolone use in this study was extralabel, because treatment administered in this manner led to higher dosages, on a mg/kg basis, than recommended on the product label. Injections were administered weekly or to effect and were dispersed throughout the lesion to ensure adequate distribution of the drug. Each injection typically consisted of a single needle stick with an attempt to disperse the triamcinolone for maximum contact with tumor tissue. In larger tumors, in which fanning of a needle at a single injection site did not adequately contact all parts of the tumor, multiple injections were administered (eg, divided into 4 injections).

Twelve dogs (13 tumors) received no treatment for their mast cell tumors prior to intralesional triamcinolone treatment. Of these 12 patients, 5 were treated with intralesional triamcinolone administration alone, 2 were treated with concurrent orally administered corticosteroids, and 5 were treated with concurrent chemotherapy with or without corticosteroids (PO) and with or without radiation therapy. For these 12 patients (13 tumors), 3 had a complete response, 7 had a partial response, and 2 had stable disease.

Eleven of the 23 (48%) dogs received treatment consisting of various protocols of vinblastine[c] (n = 10), lomustine[d] (9), vincristine[e] (1), cyclophosphamide[f] (3), toceranib[g] (1), paclitaxel[h] (1), prednisone (9), or radiation therapy (2) prior to starting intralesional triamcinolone treatment. The median time between previous chemotherapy and triamcinolone treatment was 20 days (range, 7 to 94 days). Two dogs had been previously treated with prednisone (concurrently with chemotherapy) that was discontinued 324 and 15 days prior to intralesional treatment. The remaining patients continued to be treated with corticosteroids while receiving triamcinolone. The median number of chemotherapy treatments prior to commencing intralesional triamcinolone treatment was 6 (range, 1 to 12). Eight dogs that were previously treated with chemotherapy received only 1 intralesional dose of triamcinolone. The decision to incorporate intralesional triamcinolone treatment was not always documented in the medical record; for 10 of 23 patients in which this information could be ascertained from the record, reasons included treatment of refractory disease (n = 7) or tumor control during delayed chemotherapy treatment (3).

Patients were grouped into 3 treatment groups: dogs receiving intralesional triamcinolone treatment alone, dogs receiving intralesional triamcinolone treatment and an orally administered corticosteroid, and dogs receiving intralesional triamcinolone treatment and other adjuvant treatment (eg, chemotherapy or a tyrosine kinase inhibitor, with or without radiation therapy and with or without concurrent orally administered corticosteroids).

Of the 5 patients that were treated with triamcinolone alone, there was 1 complete response, 3 partial responses, and 1 dog that maintained stable disease. The median time to progression was 28 days (range, 10 to 54 days). None of the 5 patients had received previous treatments. Of the 6 tumors (5 dogs) that were treated with intralesional triamcinolone administration and an orally administered corticosteroid (median dosage, 0.85 mg/kg [0.39 mg/lb]; range, 0.37 mg/kg [0.17 mg/lb], q 48 h, to 3.8 mg/kg/d [1.73 mg/lb/d]), there were 4 partial responses and 2 instances of stable disease. The median time to progression was 114 days (range, 17 to 169 days).

There were 13 patients that were treated with intralesional triamcinolone administration and concurrent chemotherapy (with or without radiation therapy and with or without orally administered corticosteroids). Of these patients, there were 3 with complete responses, 5 with partial responses, 3 with

stable disease, and 2 with progressive disease. The median time to progression for these 11 dogs was 148 days (range, 6 to 447 days). Of these 13 patients, 5 received intralesional triamcinolone treatment on the same day as chemotherapy. Four dogs initially received treatment with intralesional triamcinolone administration only and were subsequently treated with additional doses of triamcinolone with chemotherapy 7, 12, 28, and 112 days after the initial triamcinolone dose. Four patients had been on chemotherapy protocols, and intralesional triamcinolone treatment was incorporated into the protocol 3 days, 7 days (2 patients), and 14 days after the start of the chemotherapy protocol.

Overall, for the 24 tumors (23 dogs) treated with intralesional triamcinolone administration regardless of additional adjuvant treatment, 4 (16.7%) had a complete response, 12 (50%) had a partial response, 6 (25%) maintained stable disease, and 2 (8%) had evidence of progressive disease. There were 16 responding tumors (tumors with complete or partial responses and with duration of response > 14 days) and 8 nonresponding tumors (tumors with stable disease, progressive disease, or response duration < 14 days). Two dogs had responses lasting < 14 days. One of these dogs was euthanized 6 days after treatment; in this patient, the tumor was stable in size at the time of euthanasia. The second patient was lost to follow-up 10 days after the first triamcinolone treatment; in this patient, the tumor was stable in size at the time the patient was lost to follow-up. There was no significant difference between responders and nonresponders with regard to age ($P = 0.569$), sex ($P = 0.772$), tumor location ($P = 0.123$), previous treatment ($P = 0.082$), concurrent treatment ($P = 0.854$), or tumor grade ($P = 0.077$). There was no significant ($P = 0.559$) difference in response between patients treated with intralesional triamcinolone alone and those receiving intralesional triamcinolone and orally administered prednisone. The median intralesional triamcinolone dose for patients achieving a complete response was 11.0 mg/cm, and was significantly ($P < 0.001$) greater than the median dose for all other groups (1.9 mg/cm).

Three patients received intralesional triamcinolone treatment as neoadjuvant treatment prior to surgery; these 3 patients were censored from the Kaplan-Meier analysis. The median time to progression was 63 days (range, 6 to 447 days). The median time to progression for responders (patients that achieved a complete or partial response, with a response duration ≥ 14 days) was 161 days (range, 21 to 447 days). This was significantly ($P < 0.001$) longer than that for nonresponders (patients with stable disease, progressive disease, or a response of < 14 days [median, 14 days; range, 6 to 55 days]). There was no significant ($P = 0.341$) difference in the time to progression between patients with grade I or grade II tumors versus patients with grade III tumors. Likewise, there was no significant ($P = 0.061$) difference between patients that received concurrent therapy versus those treated with intralesional triamcinolone administration alone. Similarly, there was no significant ($P = 0.082$) difference between patients that received previous treatment and those that did not, or between patients with tumors located at sites reportedly associated with a worse prognosis (eg, oral mucosa, oral mucocutaneous junction, and preputial sites), compared with other locations ($P = 0.336$).

Adverse events after intralesional triamcinolone treatment were noted in 3 patients. One dog developed grade I vomiting and grade II anemia 1 week after intralesional injection of triamcinolone at 2 different primary tumor sites. One site had been treated with a dose of 6 mg/cm, previously administered 3 times, 12 and 7 days apart. The second site was previously treated for the first time with a dose of 12 mg/cm; this patient was receiving omeprazole and famotidine at the time of injection. Because of the acute onset of clinical signs, gastric ulceration was suspected, and triamcinolone treatments were discontinued while treatment with gastroprotectants was continued. The clinical signs improved and no further intralesional triamcinolone treatments were administered. That patient was not receiving concurrent oral corticosteroid treatment. The second affected patient had a grade II increase in BUN concentration (52 mg/dL; reference range, 8 to 30 mg/dL) after receiving 6 intralesional doses of triamcinolone (0.7 to 2 mg/cm; most recent dose, 1.4 mg/cm) with concurrent orally administered corticosteroids (prednisone, 0.37 mg/kg, PO, q 48 h), omeprazole, and famotidine over a 2-month period. Gastrointestinal ulceration was suspected; treatment with triamcinolone was discontinued, and treatment with gastroprotectants was continued. Treatment with prednisone also continued at the same dosage; a persistent grade II increase in BUN concentration was noted 5 weeks later, but concentration was within the reference range at an 8-month follow-up visit. The third patient had grade II hemorrhage at the primary tumor site after the third intralesional triamcinolone injection, which resulted in a decrease in the Hct from 45% to 23% (reference range, 39% to 55%). This dog had no adverse effects after the first 2 doses and was receiving concurrent orally administered prednisone treatment (1.1 mg/kg [0.5 mg/lb], PO, q 48 h). Because of this complication, further treatments with triamcinolone were discontinued and no additional treatment was pursued. None of the remaining patients experienced adverse events including clinical signs consistent with local inflammation or irritation, nor were there any reported signs indicating injection site pain or discomfort. None of the patients receiving neoadjuvant intralesional triamcinolone treatment experienced postoperative surgical site complications (eg, dehiscence or infection). Details of individual patient treatment protocols are available (**Supplementary Table S1**; available at: www.avmajournals.avma.org/doi/suppl/10.2460/javma.252.1.84).

Discussion

Results of the present single-center retrospective study conducted over a 6-year period (2005–2011) suggested that intralesional triamcinolone administration alone or combined with systemic treatments, including orally administered corticosteroids, chemotherapy, and radiation therapy, may be a safe and efficacious treatment for mast cell tumors in dogs. However, larger studies involving various tumor locations, grades, and stages and matched controls are necessary to understand the biologic behavior and define ideal treatment approaches. The results of the present study were comparable with those of previous studies[23,35,36] evaluating the outcome for patients with mast cell tumors treated with orally administered glucocorticoids, with reported response rates ranging from 20% to 75%. Notably, the response rate in the present study (including complete and partial responses) of 67% (16/24) may have been an underestimation of efficacy as a consequence of selection bias. In the present study, 11 of the 23 dogs had failed to respond to previous treatments including orally administered corticosteroids, conventional (ie, typical) chemotherapy regimens, radiation therapy, or some combination of these modalities. As such, we suggest that dogs with a mast cell tumor refractory to prior treatment may also have been unresponsive to intralesional triamcinolone treatment because of a more aggressive tumor phenotype with inherent resistance to medical treatment. Most treatment-naïve dogs in the present study (10/12 [83%]) responded with either a complete or partial response to intralesional triamcinolone administration, and all dogs that achieved a complete response were treatment-naïve. Nevertheless there was no significant difference in the likelihood of response to intralesional triamcinolone administration for dogs with treatment-refractory disease, compared with treatment-naive disease, although this may have been a consequence of the small number of cases in the present study.

Intralesional triamcinolone administration is an avenue of treatment for dogs with measurable cutaneous mast cell tumors that may otherwise not be candidates for more conventional treatments. Opportunities for this treatment may include owners declining conventional treatment, tumor location requiring immediate reduction in tumor size, or presence of comorbid conditions. Additionally, intralesional treatment may be beneficial for dogs requiring a delay in treatment because of adverse effects of chemotherapy. In this setting, intralesional treatment may preserve tumor control during a treatment break. Lastly, as previously reported,[36] neoadjuvant oral corticosteroid administration may be useful in facilitating surgical resection by down staging large inoperable tumors, thereby providing the best opportunity for long-term disease control.

Whereas the small number of dogs receiving prior treatment for mast cell tumors in this study may underestimate the efficacy of intralesional triamcinolone administration, the inclusion of dogs that received concurrent treatment may overestimate the efficacy of this treatment. In the present study, 12 of 23 patients received concurrent treatment with chemotherapy (with or without radiation therapy and with or without orally administered corticosteroids), making it difficult to determine the role of intralesional triamcinolone administration in the outcome for these patients. Nevertheless, our results suggested that triamcinolone can be administered safely with other treatments.

The most frequent confounding factor was insufficient record keeping whereby the decision to incorporate intralesional triamcinolone administration into patient treatment was not routinely documented. In view of the apparent short duration of response to intralesional triamcinolone administration alone, we suggest that this treatment may be most useful in the neoadjuvant setting prior to surgery or to maintain tumor response during a chemotherapy treatment delay.

Previous studies[31,32] have reported that patients with mast cell tumors of the muzzle, oral mucosa, and oral mucocutaneous junction have a high rate of metastasis. In addition, when preputial tumors were specifically analyzed as a subset of inguinal and perineal mast cell tumors, a significant decrease was seen in the disease-free interval.[33] In keeping with the indeterminate behavior of this tumor, dogs with tumors of these locations all responded to intralesional triamcinolone treatment in the present study; however, response to treatment and time to progression were not affected by tumor location.

Adverse effects were relatively uncommon for patients of the present study, with 2 of 23 patients developing signs of gastrointestinal distress that may have been associated with intralesional triamcinolone treatment. However, in view of the propensity for mast cell tumors to degranulate, resulting in a release of histamine, we could not determine whether the gastrointestinal signs were a result of triamcinolone treatment or because of underlying mast cell disease. In 1 patient, considerable local hemorrhage associated with triamcinolone injection occurred. This was attributed to mast cell degranulation with release of histamine, heparin, and other vasoactive amines. Degranulation is a risk with any locally administered treatment or mechanical manipulation of mast cell tumors and may produce erythema, wheal formation, and subcutaneous hemorrhage. Clients should be warned of these potential complications, and ideally, patients should receive appropriate prophylactic administration of histamine antagonists. Importantly, there were no apparent postoperative complications related to prior intra-

lesional triamcinolone injection in the patients of this report.

Limitations of the present study were attributable to its retrospective nature and reliance on the accuracy of medical records. Unfortunately, there were many instances in which the medical records failed to clarify the reason for choosing intralesional triamcinolone treatment, limiting the ability to assess success of treatment. Because adverse event data were collected from the medical records, the true frequency of adverse events could have been underestimated in this study. Likewise, the lack of standardization of dose precluded accurate determination of the optimal dose range for intralesional triamcinolone treatment in dogs with measureable cutaneous mast cell tumors. In the present study, doses varied widely and, on occasion, were difficult to ascertain from the medical records. Finally, only data that were reliably collected from each medical record were included in analyses; consequently, information regarding chemotherapy protocols and clinical staging was not fully assessed because of variability of treatment protocols used and limited patient testing.

On the basis of the results of the present study, we suggest that intralesional administration of triamcinolone may be considered as a single agent treatment for dogs with measureable cutaneous mast cell tumors. However, we suggest that use as a single agent would be best suited for cytoreduction of tumors that are not amenable to surgery (eg, oral tumors, large periocular tumors, tumors involving the distal portions of the limbs, and preputial tumors). Results suggested that intralesional triamcinolone administration may also be safely combined with systemic treatments, including orally administered glucocorticoids, chemotherapy, and radiation therapy, to aid in the management of nonresectable mast cell tumors in dogs. Intralesional triamcinolone treatment could also provide a benefit for patients receiving traditional chemotherapy that require a treatment break.

Acknowledgments

Presented in abstract form at the Annual Meeting of the Veterinary Cancer Society, St Louis, Mo, October 2014.

The authors thank Dr. Ryan King for assistance with the statistical analyses.

Footnotes

a. Vetalog Parenteral, Boehringer Ingelheim Vetmedica, St Joseph, Mo.
b. SPSS, version 21, SAS Institute Inc, Cary, NC.
c. Vinblastine powder for injection, Advacare Pharma, Wilmington, Del.
d. CeeNU (lomustine) capsules, Bristol-Myers Squibb Co, Princeton, NJ.
e. Vincristine powder for injection, Advacare Pharma, Wilmington, Del.
f. Cyclophosphamide injection, BDI Pharma, Columbia, SC.
g. Toceranib tablets, Zoetis, Kalamazoo, Mich.
h. Paccal Vet CA-1, Oasmia Pharmaceutical, Uppsala, Sweden.

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From this month's *AJVR*

Pharmacokinetics of a concentrated buprenorphine formulation in red-tailed hawks (*Buteo jamaicensis*)

Molly D. Gleeson et al

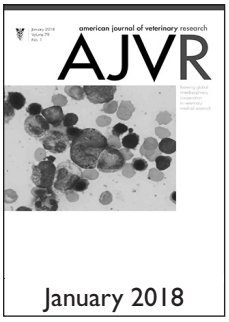
OBJECTIVE
To determine the pharmacokinetics and sedative effects of 2 doses of a concentrated buprenorphine formulation after SC administration to red-tailed hawks (*Buteo jamaicensis*).

ANIMALS
6 adult red-tailed hawks.

PROCEDURES
Concentrated buprenorphine (0.3 mg/kg, SC) was administered to all birds. Blood samples were collected at 10 time points over 24 hours after drug administration to determine plasma buprenorphine concentrations. After a 4-week washout period, the same birds received the same formulation at a higher dose (1.8 mg/kg, SC), and blood samples were collected at 13 time points over 96 hours. Hawks were monitored for adverse effects and assigned agitation-sedation scores at each sample collection time. Plasma buprenorphine concentrations were quantified by liquid chromatography–tandem mass spectrometry.

RESULTS
Mean time to maximum plasma buprenorphine concentration was 7.2 minutes and 26.1 minutes after administration of the 0.3-mg/kg and 1.8-mg/kg doses, respectively. Plasma buprenorphine concentrations were > 1 ng/mL for mean durations of 24 and 48 hours after low- and high-dose administration, respectively. Mean elimination half-life was 6.23 hours for the low dose and 7.84 hours for the high dose. Mean agitation-sedation scores were higher (indicating some degree of sedation) than the baseline values for 24 hours at both doses. No clinically important adverse effects were observed.

CONCLUSIONS AND CLINICAL RELEVANCE
Concentrated buprenorphine was rapidly absorbed, and plasma drug concentrations considered to have analgesic effects in other raptor species were maintained for extended periods. Most birds had mild to moderate sedation. Additional studies are needed to evaluate the pharmacodynamics of these doses of concentrated buprenorphine in red-tailed hawks. (*Am J Vet Res* 2018;79:13–20)



January 2018

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