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Adverse Effects of Chemotherapy in Dogs

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ABSTRACT

Owners of dogs with cancer are often offered chemotherapeutic treatment. However, clients who seek veterinary care for pets with cancer are often concerned about the potential negative impact of chemotherapeutic treatments on their animals' quality of life. The purpose of this retrospective case series was to investigate the delayed acute effects of chemotherapy drugs in dogs receiving cancer treatment and their owners' opinions regarding chemotherapy acceptance by their pet. In this study, 292 dogs that were treated with chemotherapy as a definitive and/or adjuvant treatment for cancer. Medical records were reviewed to determine the chemotherapy agent used and if they had any delayed adverse effects or not. Side effects were classified according to VCOG-CTCAE grading of adverse effect severity veterinary co-operative oncology group. Lomustine, carboplatin, vincristine, doxorubicin, cyclophosphamide, mitoxantrone, and vinblastine were administered in 16%, 20%, 15%, 18%, 16%, 8%, and 7% of the cases respectively. The most common adverse effects were neutropenia (22%), vomiting (21%), diarrhea (20%) and inappetence (20%). Cyclophosphamide and vincristine were the agents that had caused more adverse gastrointestinal effects, while lomustine was the drug that had caused more hematologic effects. In some dogs receiving lomustine and carboplatin, neutropenia (some of them severe) had occurred as early as in the sixth day. According to the current grading system of adverse effects induced by chemotherapy, general tolerance to chemotherapy is referred to as grade 1, which was observed in 83% of the cases. Owner opinion was positive in most cases, and 77% of the owners had evaluated that the treatment was well tolerated by their dogs. In contrast, 8% of the treatments were poorly tolerated and they had negatively impacted the affected dogs' quality of life. Based on the data examined, we would recommend that gastrointestinal adverse effects must be prevented with antiemetic medication, especially in dogs receiving cyclophosphamide, vincristine, carboplatin and doxorubicin. Hematologic profile must be performed as early as in the 6-7th day after lomustine and carboplatin, as severe neutropenia can occur. Adverse chemotherapy effects may occur in about 20-25% of canine patients.

Key words: Canine, Oncology, Chemotherapy, Side effect, Tolerability

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INTRODUCTION

Owners of dogs with cancer are often offered chemotherapeutic treatment. However, clients who seek veterinary care for pets with cancer are often concerned about the potential negative impact of chemotherapeutic treatments on their animals' quality of life. This concern may arise from the owner's knowledge or experience with chemotherapy in human medicine, and often owners hesitate in proceeding with chemotherapy (Vail, 2009; Vols et al., 2016).

Anticancer drugs primarily target dividing cells to interfere with the processes involved in the mediating progression of the cell cycle (Gustafson and Page, 2013). The toxicity profiles associated with anticancer agents include immediate and evident toxicities (e.g., those that develop within 24–48 hrs after treatment), acute delayed effects (e.g., those that develop within 2–14 days after treatment), and/or cumulative/chronic toxicity (effects extending over weeks,

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months, or years). Immediate toxicity may result from infusion hypersensitivity due to histamine release associated with allergic reactions or vehicle-induced mast cell de-granulation (Gustafson and Page, 2013). Routine management of these effects with antihistamines and steroids may significantly reduce or eliminate these side effects. Acute nausea and vomiting may also occur with specific agents or if an infusion is performed too rapidly. Delayed acute effects from chemotherapy often include bone marrow suppression and nausea, vomiting, and diarrhea. In the majority of instances, these effects are self-limiting and the incidence of hospitalization for such problems is rare (Vail, 2009; Gustafson and Page, 2013; Vols, 2016). Examples of potential cumulative and/or chronic toxicity include hepatic dysfunction after multiple doses of Chloroethyl Cyclohexyl Nitrosourea (CCNU, also known as lomustine), cardiac abnormalities after exceeding a safe cumulative dose of doxorubicin, and renal disease after cisplatin use (Gustafson and Page, 2013).A consensus currently exists in veterinary oncology regarding the quantification and rating of adverse treatment effects in dogs and cats in response to chemotherapy agents. This grading system is referred to as Veterinary Cooperative Oncology Group - Common Terminology Criteria for Adverse Events (VCOG-CTCAE) (Veterinary Co-operative Oncology Group, 2016). The purpose of this retrospective case series was to investigate the delayed acute effects of chemotherapy drugs in dogs receiving cancer treatment and their owners' opinions regarding chemotherapy acceptance by their pet.

MATERIALS AND METHODS

This retrospective study involved 292 dogs treated with chemotherapy between August 2011 and August 2016, in Rio de Janeiro, Brazil. All of the dogs had been previously diagnosed with malignant neoplasia and chemotherapy was prescribed as a definitive and/or adjuvant treatment.

Medical records were reviewed to determine if the chemotherapy agents used had any observed delayed acute toxicity effects (between 12 h and 21 d after the administration of chemotherapy) or not. The chemotherapy agents administered included vincristine, vimblastine, compounded lomustine, cyclophosphamide, doxorubicin, mitoxantrone, and carboplatin, according to neoplasm histologic type, treatment protocol, and each animal´s concomitant diseases.

The reported effects included: hematologic effects (e.g., neutropenia, thrombocytopenia, increases in liver enzymes, and azotemia), gastrointestinal effects (e.g., vomiting, diarrhea, and inappetence), and sepsis. A summary of the reported adverse events is provided in Table 1. Late, cumulative, and/or chronic toxicity (e.g., hepatic dysfunction, cardiac abnormalities, and chronic renal disease) were not studied.

Table 1. Common terminology criteria for adverse events following chemotherapy or biological antineoplastic therapy in dogs, of veterinary cooperative oncology group

Adverse Event	Grade				
	1	2	3	4	5
Neutropenia (μL^{-1})	1500 to <LLN	1000–1499	500–999	<500	Death
Thrombocytopenia (μL^{-1})	100 000 to <LLN	50 000–99 000	25 000–49 000	<25 000	Death
Creatinine	>1–1.5× bl	>1.5–3× bl	>3× bl	>3× bl	-
ALT	>ULN to 1.5× ULN	>1.5–4.0× ULN, transient (<2 weeks)	>4.0–10× ULN	>10× ULN	-
Anorexia	Coaxing or dietary change required to Maintain appetite	Oral intake altered (≤3 days) without significant weight loss; oral nutritional supplements/appetite stimulants may be indicated	Of >3 days duration; associated with significant weight loss (≥10%) or malnutrition; IV fluids, tube feeding or force feeding indicated	Life-threatening consequences; TPN indicated; >5 days duration	Death
Vomiting	<3 episode in 24 h, medical intervention not indicated	3–10 episodes in 24 h; <5 episodes/day for ≤48 h; parenteral fluids (IV or SC) indicated ≤48 h; medications indicated	Multiple episodes >48 h and IV fluids or PPN^{+}/TPN^{+} indicated >48 h	Life-threatening (e.g.haemodynamic collapse)	Death
Diarrhea	Increase of up to 2 stools per day over bl; no increase in frequency, however, consistency decreased	Increase of 3–6 stools per day over bl; medications indicated; parenteral (IV or SC) fluids indicated ≤48 h; not interfering with ADL	Increase of >6 stools per day over baseline; incontinence >48 h; IV fluids >48 h; hospitalization; interfering with ADL	Life-threatening (e.g.haemodynamic collapse)	Death

LLN = lower limit of normal; ULN = upper limit of normal; bl = baseline; ADL = activities of daily living (eating, sleeping, defecating and urinating); PPN = partial parenteral nutrition; TPN = total parenteral nutrition

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The following factors were statistically examined to determine their relationship to the chemotherapy agents used and their impact on the owners' opinions about treatment: age (< 7 y, 8–11 y, or > 12 y), breed (divided into divided into mixed breed, retrievers, daschunds, companion, guard, terriers, pastor, greyhound, spitz and pitbull dogs), neoplasm histologic type (Lymphoma, carcinoma, mast cell tumor, melanoma, sarcoma, cerebral tumors and transmissible venereal tumor), and presence of concomitant disease (hemoparasitosis, endocrine, cardiovascular, renal and gastrointestinal).

Side effects were classified according to VCOG-CTCAE grading of adverse effect severity (Veterinary co-operative oncology group, 2016) as follows: grade 1; asymptomatic, or mild symptoms, clinical signs or diagnostic observations only, intervention not indicated, grade 2; moderate, minimal, outpatient, or noninvasive intervention indicated, moderate limitation of daily living activities, grade 3; severe or medically significant but not immediately life-threatening, hospitalization or prolongation of hospitalization indicated, disabling, significantly limited daily living activities, grade 4; life-threatening consequences, urgent interventions indicated, and grade 5; death related to adverse events.

All of the dogs in this study were treated according to the same protocol. Animals receiving chemotherapy received ondasetron, 0.5 mg/kg (Plumb, 2015) orally twice daily, and omeprazol, 1 mg/kg orally once daily, in the first five days following chemotherapy administration, independent of the chemotherapy drug administered. If vomiting occurred with oral medication, then maropitant, 2mg/kg (Plumb, 2015), was administered subcutaneously for three consecutive days, as oral medication was maintained. In addition, the animals were fed a special diet in case of vomiting/anorexia (Hill´s prescription a/d or royal canin gastrointestinal). When necessary, feeding was forced, and in some cases, an e-tube was recommended. If diarrhea (> grade 2) occurred, probiotics were administered for seven days. Hematologic examination was performed 6–14 days after chemotherapy. If neutropenia (> grade 3) occurred, filgrastim, 5 ug/kg, was administered subcutaneously for three consecutive days together with prophylactic antibiotics.

The dog owners' opinions were collected 7–21 days after each chemotherapy. The owners were surveyed about their perception of their animal's tolerance to chemotherapy, changes in activities of daily living (eating, sleeping, defecating, and urinating), and quality of life during oncologic treatment. No classification or graduation was presented and owners were free to state their opinion. The owners were asked to categorize their overall perceptions regarding the tolerance of their pets to chemotherapy as: good, regular, bad, or poor.

A database exploratory analysis was performed and comparisons between variables were made with the Pearson Chi-square, Kruskal-Wallis, and Mann-Whitney tests as appropriate. Descriptive statistics served as a basis for interpretation of the results. The level of statistical significance was 5%. Tests and studies were performed with the software, Statistical Package for the Social Sciences (SPSS; version 20.0, SPSS Inc., Chicago, IL, USA).

Ethical approval

The authors did a retrospective cohort study of oncologic patients treated with chemotherapy. They did not seek informed consent or ethical committee approval for their study, as the paper does not report on primary research and all data analysed were collected as part of routine oncologic treatment.

RESULTS

A total of 292 oncologic records of various canine breeds were reviewed. The breeds included: mixed (n=51), retrievers (n=92), dachshund (n=18), companion (n=57), guard (n=24), terriers (n=29), pastor (n=6), greyhounds (n=1), spitz (n=5) and pitbull (n=9).Most of the animals were8-12 years old (126; 43%), while 105 (36%) were older than 12 years and 60 (21%)were1-7 years old. One animal had unknown age.

The neoplasm histological types were highly variable and were categorized as: carcinoma [mammary (39/292), squamous cell (2/292), transitional cell (5/292), pharyngeal (2/292), sinonasal (1/292), perianal (2/292), sebaceous (4/292), pulmonary (1/292) and hepatocellular (3/292)], sarcoma [soft tissue (12/292), osteosarcoma (3/292), hemangiosarcoma (14/292), intestinal leiomyosarcoma (1/292) and sinonasal (1/292)], lymphoma (131/292), mast cell tumor (43/292), melanoma (20/292), sertolioma (1/292), thymoma (3/292), malignant trichoepithelioma (1/292), cerebral tumors (1/292) and TVT (2/292). Concomitant diseases were present in 33 (11%) animals, and these included renal (n=4), cardiovascular (n=14), endocrine (n=13), gastrointestinal (n=4) and hemoparasites (n=2).

Various chemotherapy agents were administered. The chemotherapy agent was compounded lomustine (CCNU) in 46 (16%) cases, carboplatin in 58 (20%) cases, vincristine in 43 (15%) cases, doxorubicin in 54 (18%) cases, cyclophosphamide in 47 (16%) cases (40 conventional therapy and 7 metronomic therapy), mitoxantrone in 22 (8%) cases and vimblastine in 22 (7%) cases. These doses are consistent with those previously published, although the author's preference determined the dose. Doses were 70 mg/m^2 for lomustine, 230-250 mg/m^2 for carboplatin, 0.75 mg/m^{2}for vincristine, 2 mg/m^{2}for vimblastine, 30 mg/m^2 for doxorubicin and 5.5 mg/m^2 for mitoxantrone.

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Cyclophosphamide was administered at a dose of 250 mg/m^2 in conventional therapy and 15 mg/m^2 in metronomic therapy.

Blood exams, including hematologic examination and biochemistry [Blood Urea Nitrogen (BUN), creatinine, Alanine aminotransferase (ALT) and Alkaline Phosphatase (ALP)] were performed 7-21 days after chemotherapy, according to chemotherapy agent nadir and author's previous experience. For example, the animals that received lomustine (CCNU) underwent their exams on day 6 and day 21. For the animals that received carboplatin, blood exams were performed between days 10–14.For the animals that received vincristine, vimblastine, mitoxantrone, or doxorubicin, their exams were performed between days 7–10.

Vomiting (despite prophylactic oral administration of antiemetics) was observed in62 (21%) cases, with severity grade 1 in 56 (19%), grade 2 in 4 (1%) and grade 3 in 2 (1%). Associations between the chemotherapeutic agents and vomiting did not exhibit statistically significant differences (P=0.078). However, most of these cases occurred with cyclophosphamide (n=15) and vincristine (n=15), followed by doxorubicin (n=12), carboplatin (n=10), mitoxantrone (n=4), lomustine (n=3), metronomic cyclophosphamide (n=2) and vimblastine (n=1) (Figure 1).

Diarrhea was observed in 58 (20%) cases, with severity grade 1 in 50 (17%) and grade 2 in 8 (3%). A comparison between the presence of diarrhea of various grades and chemotherapeutic agents revealed a statistically significant difference (p<0.001). Most of these cases occurred with cyclophosphamide (n=16) and vincristine (n=14), followed by doxorubicin (n=12), carboplatin (n=8), lomustine (n=3), mitoxantrone (n=2), metronomic cyclophosphamide (n=2) and vimblastine (n=1) (Figure 2).

Various grades of inappetence/anorexia occurred in 58 (20%) cases. Four cases were grade 1 (1%), 50 were grade 2 (17%), three cases were grade 3 (1%) and one case was grade 4 (1%).A statistically significant difference was observed when the presence of inappetence/anorexia was compared to chemotherapeutic agents (P =0.035). The agents that caused most cases of inappetence were conventional cyclophosphamide (13/40), carboplatin (12/58), doxorubicin (12/54) and vincristine (10/43) (Figure 3).

Neutropenia is a major side effect of chemotherapy and it was only observed in63 (22%) cases. The severity of neutropenia included grade 1 in 5/63 cases, grade 2 in 37/63 cases, grade 3 in 20/63 cases and grade 5 in 1/63 cases. There was no statistically significant difference when the presence of neutropenia and chemotherapeutic agents were compared (P =0.088). However, lomustine was the chemotherapy agent responsible for most of the cases of neutropenia (18/46), and grades 1–3 had an incidence of 1case, 8cases and9cases, respectively. Carboplatin also caused neutropenia in 45/58 dogs (including nine cases of grade 2, three cases of grade 3 and one case of grade 5), as did vincristine in 8/43dogs (including seven cases of grade 2 and one case of grade 3). Mitoxantrone caused neutropenia in six dogs (one case of grade 1, one case of grade 2 and four cases of grade 3). Doxorubicin administration leads to neutropenia in seven cases and vimblastine in two cases (Figure 4). Sepsis secondary to chemotherapy occurred in four dogs of this study (three had received carboplatin and 1mitoxantrone), and three of them died despite treatment.

Thrombocytopenia was observed in 24 (8%) cases, with grades 1–4 affecting18cases, 3cases, 3 cases and 1 case, respectively. There was no statistically significant difference when the presence of thrombocytopenia and chemotherapeutic agents were compared (p =0.37). In most cases, It was caused by lomustine (n=8), carboplatin (n=5) and cyclophosphamide (n=4), followed by mitoxantrone (n=3), doxorubicin (n=2) and vincristine (n=2) (Figure 5).

Azotemia occurred in three dogs, including one case of grade 2, one case of grade 3 and one case of grade 5. All dogs had been previously diagnosed with renal disease, and two cases had received carboplatin and one case metronomic cyclophosphamide. Elevated levels of ALT and/or ALP were observed in 16 dogs (including nine cases of grade 2 and seven cases of grade 3), and 13/16 occurred after lomustine administration.

According to the current VCOG-CTCAE system for grading the adverse effects of chemotherapy, general tolerance to chemotherapy was at grade 1 in 242(83%) cases, and grade 2-5 in 22 (8%) cases, 17 (6%) and11 (4%), respectively. VCOG was classified as grade 1 in 78-90% of cases in most chemotherapies (Figure 6)**.**There was no statistically significant difference when the VCOG-CTCAE grading and chemotherapeutic agents were compared (P =0.83).

For the cases examined, owner perception was positive in most of the cases; with 224 (77%) owners reporting that the treatments received were well tolerated by their dogs. Treatment was considered as regular in 44 (15%) cases and bad in 11 cases (4%) cases. For the 13 (4%) dogs that had poorly tolerated their treatments, a negative impact on quality of life was observed. Chemotherapy was considered well tolerated in most agents (67-96%) (Figure 7). There was no statistically significant difference when the owner perception and chemotherapeutic agents were compared (P =0.22)

A statistical association between neutropenia, vomiting, inappetence, azotemia, and owner's opinion was identified for the chemotherapy agents. For example, the Kruskall-Wallis test confirmed the presence of a statistically significant difference between the chemotherapy agents and the incidences of neutropenia, vomiting, diarrhea, azotemia and hepatopathy (P<0.05). To further identify these differences, the Mann-Whitney statistical test was applied. In this analysis, statistical association between azotemia and chemotherapy agents was not maintained.

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In paired comparisons, a statistical difference (P<0.05) was observed for hepatopathy with the administration of lomustine versus administration of the other chemotherapeutic agents. Lomustine contributed significantly to the occurrence of hepatopathy in dogs. Similar results were observed with the occurrence of neutropenia with this agent (P=0.02).

There was a significant statistical difference in the occurrence of diarrhea when comparing cyclophosphamide with carboplatin (P= 0.006), lomustine (P= 0.000), mitoxantrone (P= 0.01), and vimblastine (P= 0.003). The treatment with vincristine was also associated with the occurrence of diarrhea, with a statistically significant difference compared to the chemotherapeutics carboplatin (P= 0.04), lomustine (P= 0.002), and vimblastine (P= 0.008).

The occurrence of vomiting was statistically significant in dogs treated with cyclophosphamide when compared to the chemotherapeutics carboplatin (P = 0.03), lomustine (P= 0.000) and vimblastine (P= 0.005). The use of vincristine was also statistically associated with vomiting, compared to the use of lomustine (P= 0.001) and vimblastine (P= 0.01). The use of doxorubicin and lomustine also showed a significant statistical difference (P= 0.03), in this case, we observed a tendency of lomustine to be related to grade 1 vomiting, whereas doxorubicin with grade 1, 2 and 3 vomiting.

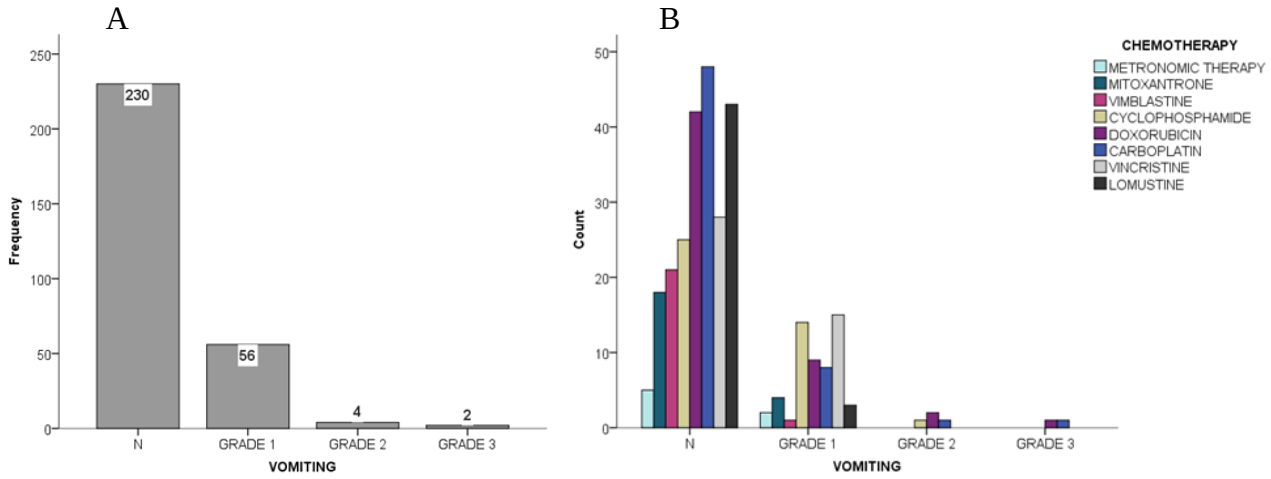

Figure 1. Adverse events of chemotherapy in dogs - vomiting. A: Presence of vomiting and its veterinary cooperative oncology group toxicity criteria grade in studied dogs. B: Presence of vomiting according to chemotherapy in studied dogs

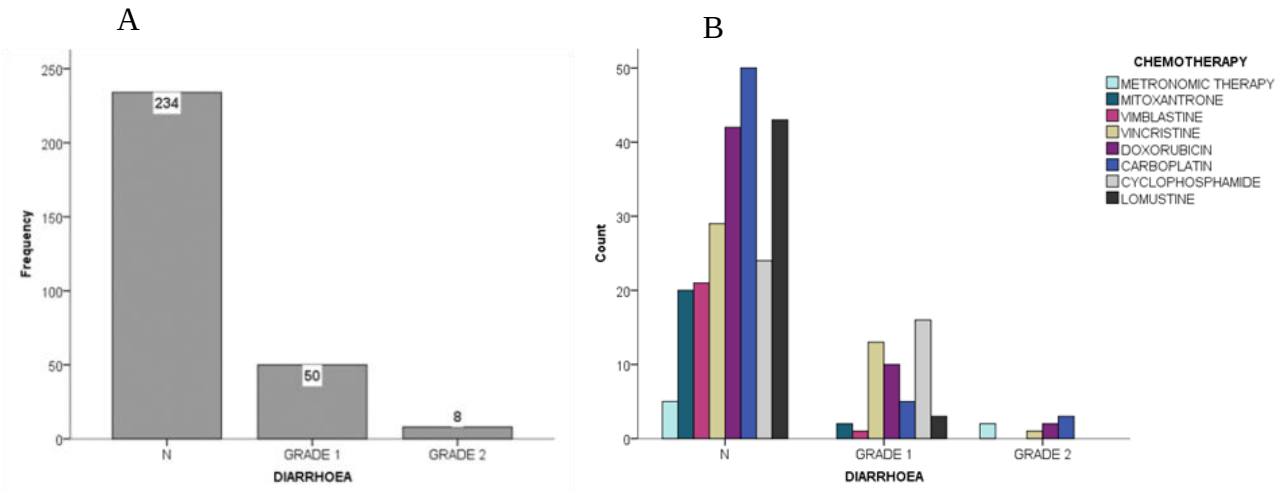

Figure 2. Adverse effects of chemotherapy in dogs - diarrhea. A: Presence of diarrhea and its veterinary cooperative oncology group toxicity criteria grade in studied dogs. B: Presence of diarrhea according to chemotherapy in studied dogs

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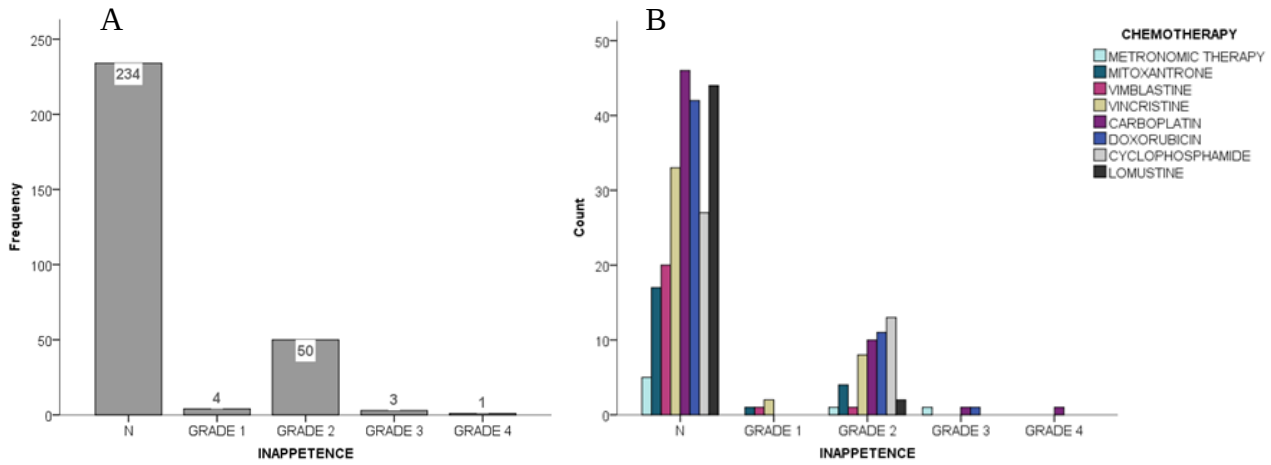

Figure 3. Adverse effects of chemotherapy in dogs - inappetence. A: Presence of inappetence and its veterinary cooperative oncology group toxicity criteria grade in studied dogs. B: Presence of inappetence according to chemotherapy in studied dogs

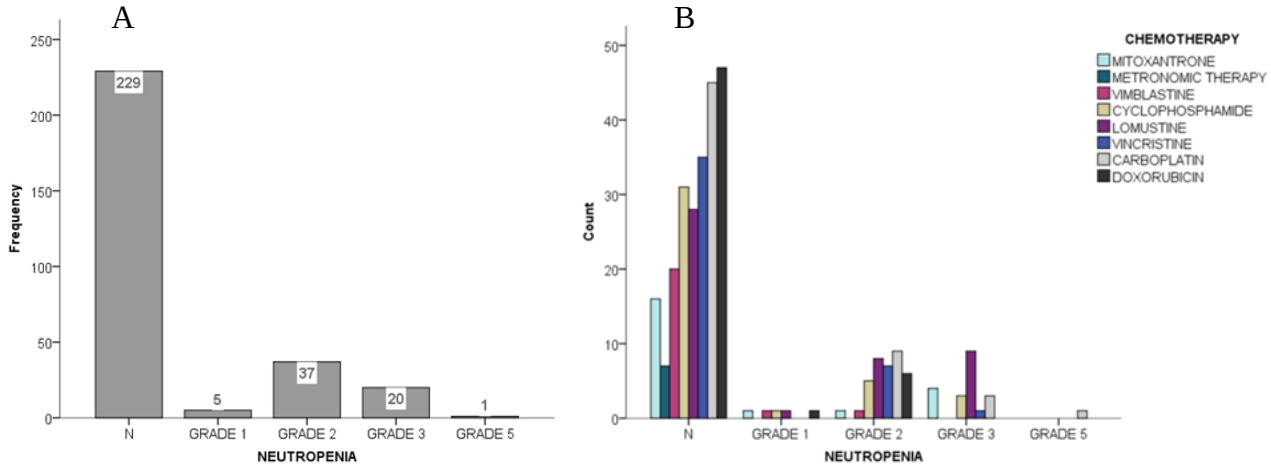

Figure 4. Adverse effects of chemotherapy in dogs - neutropenia. A: Presence of neutropenia and its veterinary cooperative oncology group toxicity criteria grade in studied dogs. B: Presence of neutropenia according to chemotherapy in studied dogs

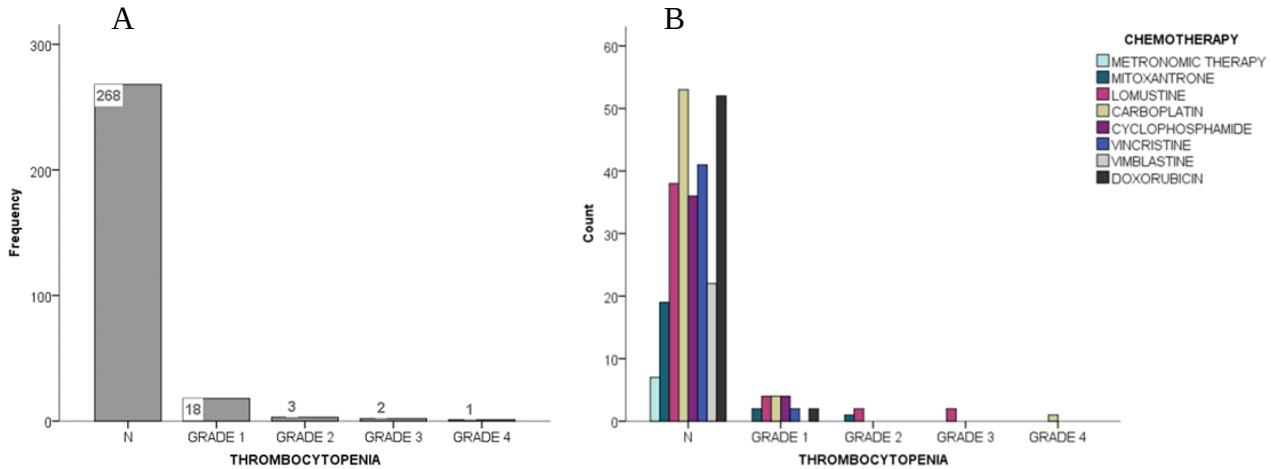

Figure 5. Adverse effects of chemotherapy in dogs - thrombocytopenia. A: Presence of thrombocytopenia and its veterinary cooperative oncology group toxicity criteria grade in studied dogs. B: Presence of thrombocytopenia according to chemotherapy in studied dogs.

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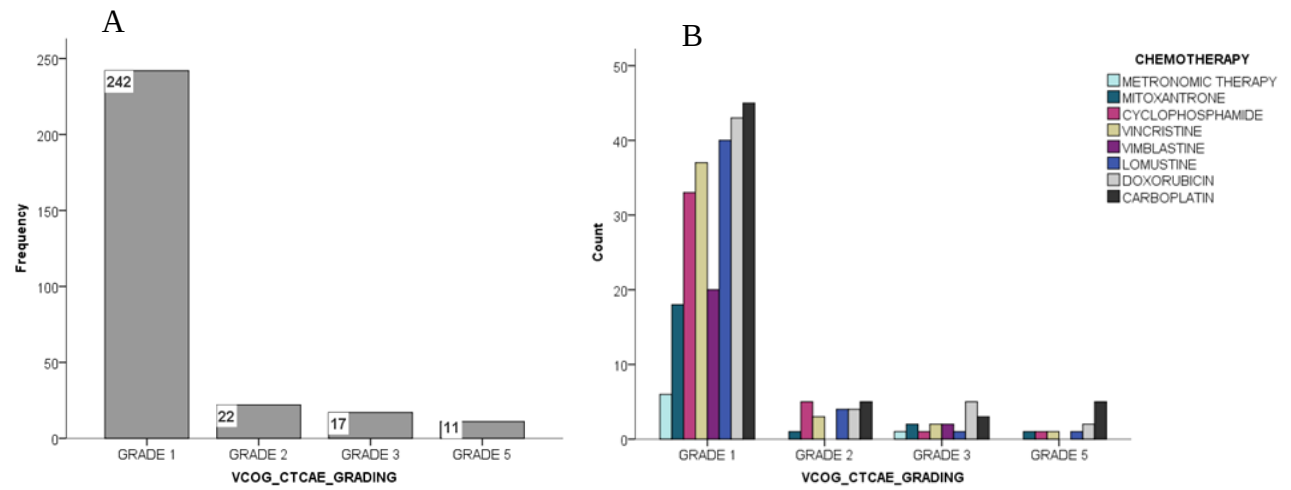

Figure 6. Grading system of adverse events to chemotherapy according to veterinary oncology group in studied dogs. A: General chemotherapy veterinary cooperative oncology group toxicity criteria grade in studied dogs. B: Veterinary cooperative oncology group toxicity criteria grade according to chemotherapy in studied dogs

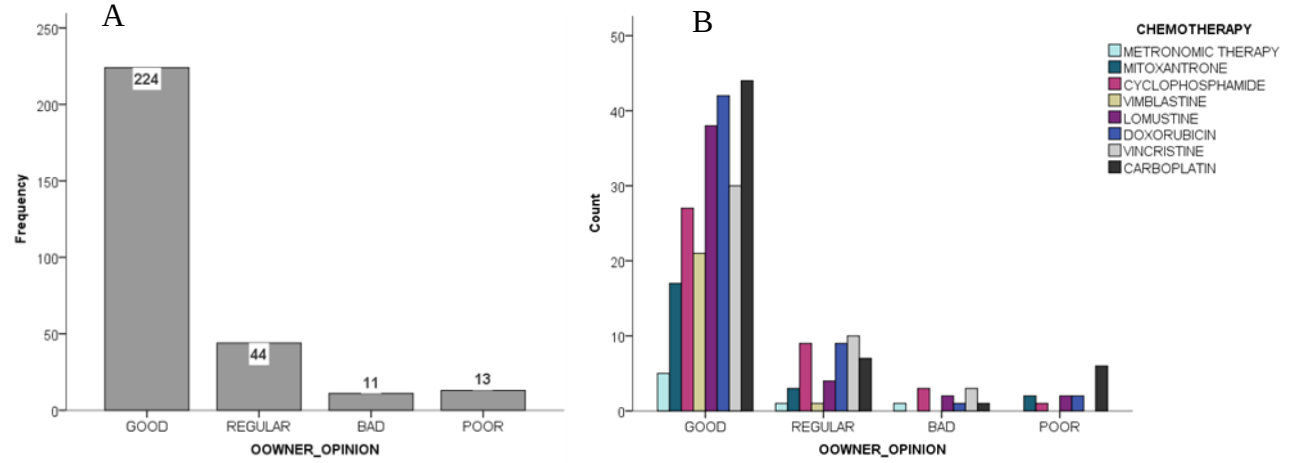

Figure 7. Owner's perception of chemotherapy in studied dogs. A: General owner perception. B: Owner perception according to chemotherapy

DISCUSSION

This retrospective study studied adverse effects of 292 dogs treated with chemotherapy. In a general manner, chemotherapy was very well tolerated in most dogs of this study. According to the current grading system of chemotherapy adverse effects of VCOG-CTCAE (Veterinary Co-operative Oncology Group, 2013), general tolerance to chemotherapy was at grade 1 in 83% dogs, which means most dogs had only mild, asymptomatic or mild symptoms, and medical intervention was not needed. In the previous studies with dogs and cats, authors believed that less than 1 in 4 animals will have an unpleasant adverse event following chemotherapy, and only approximately 3% to 5% have a serious adverse event leading to hospitalization (Bowles et al., 2010; Vols et al., 2016). In the present study, only 4%of the dogs had experienced serious and life threatening adverse events.

Cyclophosphamide in conventional therapy and vincristine were the agents that caused more gastrointestinal adverse events (vomiting, diarrhea and inappetence), while lomustine was the drug that caused more hematologic events (neutropenia, thrombocytopenia and hepatopathy). Carboplatin and doxorubicin lead to intermediate gastrointestinal and hematologic adverse events. Vimblastine was the agent that caused less adverse events. Cyclophosphamide is a nitrogen mustard, commonly included in multi-agent protocols for lymphoma in both dogs and cats (Gustafson and Page, 2013; Matsuyama et al., 2017). Even with antiemetic preventive administration, inappetence and nausea were observed in some dogs (24% and 33% respectively). For those dogs, maropitant was administered subcutaneously, together with oral ondasetron and omeprazol, and provided a good antiemetic effect, as previously reported by Mason et al. (2014). The

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high percentage of vomiting and diarrhea after vincristine administration was also observed in a study by Mason et al. (2014). Lomustine is a drug with known myelotoxicity (Burton et al., 2015), and in a previous study, 25% of dogs given compound lomustine (similarly to this study) had neutropenia (Burton et al., 2015).

Neutropenia, a major concern of chemotherapy, was observed in only 22% cases, most of them following lomustine administration. Carboplatin, doxorubicin, mitoxantrone and cyclophosphamide caused intermediate neutropenia in some dogs. According to Vail (2009), neutropenia is likely to be seen 7 to 10 days after the administration of most chemotherapy drugs. Exceptions to this rule includes vinblastine and paclitaxel, which can cause neutropenia as early as 4 to 5 days after administration, and carboplatin, which can occasionally cause neutropenia as late as 2 to 3 weeks after administration in dogs and cats. However, in this study, some dogs receiving lomustine and carboplatin had neutropenia (some of them severe) in the sixth day. Most companion animals have a low risk of infection if their neutrophil count remains greater than 1000/L. The severity of neutropenia and associated sepsis can be extremely variable, ranging from clinically silent to overwhelming and fatal (Vail, 2009).Sepsis occurred only in 4 animals but could have occurred in more cases if hematology was not performed in the 6-7 day of these chemotherapies.

Azotemia occurred in 3 dogs which had been previously diagnosed renal disease, and 2 had received carboplatin. This drug is considered nephrotoxic in dogs, and should have been avoided in these patients. However, it was considered for chemotherapy because it was the best oncologic treatment for these histologic types of tumor.

Elevation of ALT and/or ALP was observed 13/16 after lomustine administration. This result is similar to previous studies, which lomustine was considered to cause acute and chronic hepatotoxicity in dogs (Kristal et al., 2004).

Owner opinion was positive in most cases, and 77% of the owners evaluated that the treatment was well tolerated by their dogs. Bad and poor tolerance, and negative impact in quality of life, corresponded only to 8% of cases. This result agrees with other authors experience in dogs, where most canine patients tolerate chemotherapy very well (Bronden et al., 2003; Mellanby et al., 2003; Vail, 2009; Giuffrida and Kerrigan, 2014). In a study of the owners' perception about chemotherapy in dogs and cats, 62 of the 69 the owners thought that the anticancer chemotherapy was worthwhile for cats and dogs in general.

Chemotherapy was very tolerated well in most dogs, with positive owner opinion and minimal impact on the dog´s quality of life. This result may encourage veterinarians to perform chemotherapy in canine patients. The most common adverse effects were neutropenia (22%), vomiting (21%), diarrhea (20%) and in appetence (20%). Gastrointestinal adverse events must be prevented with antiemetic medication, especially in dogs receiving cyclophosphamide, vincristine, carboplatin and doxorubicin. Hematologic profile must be performed as early as in the 6-7th day after lomustine and carboplatin, as neutropenia can occur. Adverse chemotherapy effects may occur in about 20-25% of canine patients.

Competing of interests

The authors have no competing interests to declare.

Author`s contribution

The authors Simone Cunha and Katia Corgozinho were responsible for the clinical, oncological, and chemotherapeutic treatment of the cats, as well as the article writing. The authors Kassia Silva, Franciele Silva and Ana Ferreira performed the statistical analysis and review of the manuscript.

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