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ATTI DEL LXIX CONVEGNO SISVET

Perugia, 15-17 Giugno 2015

Università degli Studi di Perugia

Dipartimento di Medicina Veterinaria

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CLINICAL AND HEMATOLOGICAL ADVERSE EFFECTS AFTER ADMINISTRATION OF TWO DIFFERENT CHEMOTHERAPY PROTOCOLS IN DOGS AFFECTED BY LYMPHOMA

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Lymphoma is the most common canine hemopoietic neoplastic disorder. Chemotherapy can prolong the survival time of patients, even if Adverse Effects (AEs) may occur. The rate and severity of common AEs of two chemotherapy protocols were investigated.

Medical records (2007-2014) of 24 dogs with multicentric lymphoma were reviewed. Thirteen dogs were treated with COP protocol (cyclophosphamide, vincristine, and prednisone) at the Veterinary Teaching Hospital, while 11 were treated with Wisconsin-Madison (UW) protocol (cyclophosphamide, vincristine, prednisone and l-asparaginase) at a Private Veterinary Clinic. The appearance of fever, weight loss, vomiting, diarrhea, anorexia, anemia, neutropenia, and thrombocytopenia, during the first nine weeks of therapy were evaluated. The occurrence of dogs showing different severity of AEs weekly (AEsW) or during the entire period of treatment (AEsT), were collected. Each AE was classified into 6 grades using VCOG criteria and 101 and 99 observations (dogs treated with COP and UW, respectively) were carried out. Results underwent statistical analysis (Fisher's exact test for AEsW and Chi Square tests for AEsT).

In UW-treated dogs anemia of grade 2 at 4th week was statistically significant in comparison to COP-treated dogs ($p= 0.01$). Other AEs during the several weeks of treatment were not statistically significant. The comparison between the severity of AEs during the entire period showed the following results. Fever was an uncommon sign (23% COP-treated vs. 36% UW-treated) while weight loss was detected in the early weeks of treatment especially in COP patients (62% COP vs. 55% UW; $p=0.0019$). Gastrointestinal AEs were common but rarely affected the patient quality of life (vomiting 46% COP vs. 27% UW; diarrhea 23% COP vs. 36% UW; anorexia 46% COP vs. 55% UW) ($p> 0.05$). The common hematological AEs were anemia (85% COP vs. 82% UW; $p> 0.05$) and neutropenia (85% COP vs. 55% UW; $p=0.0018$) compared to thrombocytopenia (38% COP vs 45% UW; $p> 0.05$).

This retrospective survey pointed out some interesting findings. Fever was not associated to neutropenia, probably because UW-treated patients have never showed severe neutropenia and in COP-treated dogs antibiotics were preventively administered. Both protocols caused severe weight loss during the first weeks of treatment (grade 2 or higher); in COP-treated patients there was a significant weight loss. The gastrointestinal AEs were mild and cases of severe vomiting or diarrhea (grade 3 or higher) were not observed. Vincristine causes more gastrointestinal and hematological AEs; vincristine/cyclophosphamide combination could be the trigger of neutropenia that has been reported more frequently and severe in COP-treated cases. Regarding anemia and thrombocytopenia, the possible myelo-suppressive effect of drugs used could worsen the clinical condition of some patients (dogs with stage V lymphoma and bone marrow involvement); for these two AEs a correct etiology is difficult to trace. Chemotherapy drugs used in the present study for the canine lymphoma treatment are well tolerated, they prolong the survival time and assure a good quality of life with low frequency and severity of AEs.

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