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EFFICACY AND SIDE EFFECTS OF VINCristINE SULPHATE TREATMENT ON CANINE TRANSMISSIBLE VENEREAL TUMOUR - 438

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Introduction
Vincristine sulphate belongs to a group of medications known as vinca alkaloids and is obtained from the plant Vinca rosea Linn. Vinca alkaloids act as antimicrotubule agents that block mitosis by arresting cells in the metaphase. This agent represents the treatment of choice for canine transmissible venereal tumour (TVTc). The treatment is effective for 90% of TVTc cases, by intravenous (IV) administration, at the dose of 0.5-0.7 mg/m² of body surface, once a week (Withrow & Macewen 2001). Vincristine is safe for most patients, but potential side effects can occur, as gastrointestinal alterations, myelosuppression and extravasation injury. The purpose of this work was to document the efficacy and side effects of vincristine sulphate treatment on TVTc.

Materials and Methods
Fifteen cross-bred canines, that both male and female, were selected after the diagnostic of naturally occurring TVTc, confirmed by cytology (Thangathurai et al. 2008). Two weeks prior the treatment and during all the treatment the animals received the same balanced canine diet, for warranty of the experimental standard. The vincristine administrations, at the dose of 0.5 mg/m² of body surface (IV), were done considering all the manufacturers’ warnings recommendations. The treatment was performed until the tumour totally regression, confirmed by weekly clinical and cytological examination. Blood sample were collected weekly for complete blood count. The owners were oriented to observe the animal’s behavior, food and water intake, digestion alteration, including vomiting, constipation and diarrhea. This clinical research is in the accordance with the principles of guidance for the care and use of animals at Universidade Estadual de Santa Cruz (CEUA/UESC).

Results
Vincristine was an effective chemotherapeutic agent for genital TVTc, showing tumours totally regression in 13 dogs, among them the therapy was also efficient for one case of diffuse cutaneous TVTc. One dog died after the third dose of vincristine, and in one case the tumour was vincristine resistant, and the doxorubicin treatment was required. Clinical evaluation of the dogs revealed progressive decreases of tumour masses and stoppage of exudation. By cytological examination decreases on cellularity, with small-sized cells and few or no mitotic figures were also observed, and at the end of treatment no TVT cells were detected on the 13 dogs. No changes were recorded on body temperature or weight, during the treatment. The owners reported decrease on food intake (five dogs), diarrhea (two dogs), constipation (one dog), claudication (one dog). Dermatological alteration were observed on seven animals, with diffuse alopecia (five dogs), descamation (one dog), and hypersensibility reaction (one dog). These symptoms showed progressively improvement after treatment discontinuation. Nine dogs developed mild to moderate normocytic normochromic anaemia post-commencement of therapy. The total leukocyte count dropped below 37.3% (± 24.3) of the initial counts and five dogs have leucocopenia (reference range 6,000 to 15,000/μL), with relative neutropenia and lymphocytosis. The platelet count dropped below 55% (± 28.9) of the initial counts, and twelve dogs developed thrombocytopenia (reference range, 170,000-400,000/μL). No changes were recorded on total proteins during the treatment. When the The total leukocyte count and platelet counts were less than 3,000/μL and/or 80,000/μL, respectively, the intervals treatment were prolonged for fourteen days, for safety assurance. Nine dogs received weekly treatment while six received at fourteen days period. No changes were seen on the number of treatment (mean 5.4 ± 1.6), despite the different interval adopt.

Discussion and Conclusions
Vincristine sulphate, at the dose of 0.5 mg/m² of body surface (IV), on 7-14 days intervals, reveal high efficiency (86.6%) for TVTc treatment. One tumour (6.6%) was refractory to vincristine, while at the treatment beginning we observed a mass reduction. So we recommend the change for another agent if there is no response after six vincristine’s administrations. The extravasation injury was totally avoid by performing the treatment according to all manufacturers’ warnings recommendations. Before the therapy sections it is necessary to execute the clinical evaluation, the cytological exam and the complete blood count for monitoring the side effects related to vincristine. The main side effect observed on this study was the thrombocytopenia that affected 80% of the dogs, 60% of dogs developed anaemia and 33.3% leucocenia. These hematological alteration were also reported by others authors (Nak et al. 2005;
It is important to note that animals have a reduction on the platelet count values on 55% (± 28.9) of the initial counts, and on 37.3% (± 24.3) of the total leukocyte count. These results could be used for estimating the risk of hematological alterations after vincristine treatment, considering the initial references. One animal (6.6%) that has TVTc for more than two years, died after the third dose of vincristine, as a consequence of its severe thrombocytopenia developed (less than 3,000/μL). Some reports associated the use of vincristine with thrombocytosis (Adams 2003), and recommended its use for thrombocytopenia treatment. In this study, one animal developed thrombocytosis, but considering the thrombocytopenia observed in majority of the animals, caution should be taken. The animals also had digestive alteration, as decrease in food intake (33.3%), diarrhea (13%), constipation (6.6%). The constipation is associated with neuropathy (Das & Das 2000), as the sign of claudication observed in one dog (6.6%). Dermatological alteration also occurred, and alopecia is the most frequent lesion reported (33%), and the hypersensitivity reaction the most severe lesion. All the digestive and dermatological alteration were resolved after therapy discontinuation. According to the side effects the risk-benefit should be considered, and a prolonged interval treatment could be an alternative to minimize these effects. In conclusion, vincristine was found to be effective chemotherapeutic agent, but that are many side effects associated, which have to be monitored by clinical and hematological evaluation, for assurance treatment safety.

**References**


**Keywords**: Oncology, therapy, oncovin, veterinary