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ELECTROCHEMOTHERAPY: EXPERIENCE AT THE UNIVERSITY OF PISA

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Abstract

Electrochemotherapy (ECT) is a local treatment for cutaneous and subcutaneous tumours, that uses electric pulses (electroporation), combined with the administration (local or systemic) of non- or poorly-permeable cytotoxic drugs. Electroporation causes a transient permeabilization of cellular membranes in the treated tissue and allows the passage and accumulation of cytotoxic drugs within the neoplastic cells. Once inside the targeted cells the drugs provoke cytotoxicity *(Mir et al., Eur J Cancer, Suppl*., *2006; Mir et al., Adv Drug Deliv Rev*., *1999; Tozon et al., J Vis Exp., 2016)*. Currently only bleomycin and cisplatin have been proven effective combined with ECT (*Čemažar et al., J Vet Intern Med., 2008; Serša et al., Eur J Surg Oncol., 2008)*. In addition, ECT induces the so called vascular-lock and vascular disrupting mechanism, a rapid and profound abrogation of local blood flow of exposed tissue that leads to ischemic cell death. Finally, ECT studies showed a potential role of the immune system in anti-tumour effectiveness *(Jarm et al., Expert Rev Anticancer Ther*., *2010; Calvet et al., Oncoimmunology*, *2014)*. Guidelines for ECT in veterinary medicine were published by Tozon and others in 2016. *(Tozon et al., J Vis Exp., 2016)*

The experience at the University of Pisa is mostly based on retrospective studies.

The latest study was arranged to evaluate the feasibility of ECT in the treatment of non-tonsillar squamous cell carcinoma (ntSCC). Twelve dogs with ntSCC were treated with ECT combined with systemic bleomycin. The response rate was 92% and the overall recurrence rate was 27.3%. All dogs with tumours smaller than 2 cm obtained complete response. Overall treatment toxicity was very low *(Simčič et al., ready for submission to VCO, 2019)*.

The first study was about the use of ECT with systemic bleomycin in canine mast cell tumour (MCT) with or without surgical excision. A group of 51 dogs was divided in 4 groups based on treatment modality (1-ECT only, 2-intra-surgery, 3-neoadjuvant ECT, 4-ECT recur). Complete remission ranging from 64-93% and partial remission from 7-36% were observed. The group where ECT was used intra-surgically obtained the best and longest disease-free interval. In conclusion, ECT could be applied in small size MCTs as an alternative to surgery. However, for larger tumours ECT should be applied intra- or post-surgery without causing high toxicity *(Lowe et al., Vet Comp Oncol., 2017).*

Recently, we published a study on the safety and efficacy of ECT with systemic bleomycin in the treatment on canine soft tissue sarcomas (STSs). Fifty-two dogs included in the study were divided in three groups (1-ECT alone, 2-intra-operative, 3-adjuvant ECT). Recurrence rate ranged 23-25% and disease-free interval ranged 81-243 days. Local treatment toxicity was mild in 66.7% of the patients and higher toxicity was associated with higher pulse voltage. In conclusion, ECT could be considered safe and efficient in treatment of canine STSs *(Torrigiani et al., Vet Comp Oncol*., *2019)*.
In all three studies the results achieved after ECT treatment are good and, in the future, more prospective studies should be performed to confirm the success of ECT as a treatment modality for solid tumours in veterinary medicine.

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