Prospective evaluation of the utility of the vasovagal tonus index (VVTI) as an indirect assessment of remission status in canine multi-centric lymphoma undergoing multi-drug chemotherapy

Evi Pecceu, Yolanda Martinez-Pereira, Ian Handel, Brittainy Stebbing, Geoff Culshaw, Hannah Hodgkiss-Geere, Jessica Lawrence

Edinburgh University, R(D)SVS Small Animal Hospital, Edinburgh, UK

INTRODUCTION

Heart rate variability has frequently been used in human medicine as an indicator of prognosis for cardiovascular and non-cardiovascular diseases. Vasovagal tonus index (VVTI) is a simple non-invasive time-domain method to assess heart rate variability, and has been used in dogs as a prognostic indicator in cardiac disease. VVTI may also serve as an indirect marker of severity in other systemic diseases, such as canine lymphoma. The primary hypothesis of this study was that VVTI in dogs with lymphoma would increase when dogs were in partial or complete remission compared to VVTI obtained when out of remission at diagnosis or relapse. The primary objectives were to determine serial VVTI scores for dogs undergoing chemotherapy to evaluate if consistent changes in VVTI scores were associated with lymphoma remission status and if VVTI scores when out of remission were predictive of complete remission.

METHODS

Dogs with lymphoma were prospectively enrolled if they had a confirmed diagnosis of intermediate or high-grade multicentric lymphoma and underwent standard multidrug chemotherapy. Electrocardiogram (ECG) data were recorded with dogs in right lateral recumbency. A minimum of 20 R-R intervals were recorded and all ECGs were obtained in a quiet room prior to any further diagnostics or treatments. ECGs were repeated at various intervals through chemotherapy; remission status was documented at each visit. VVTI scores were compared using a random effects linear model with an autocorrelation term. Predictability of remission by means of a VVTI score was evaluated with a binary logistic regression model.

RESULTS

Twenty-seven dogs were enrolled in the study. Overall, 242 VVTI scores were collected; 63 from dogs in partial remission status, 142 from dogs in complete remission status and 37 from dogs out of remission. VVTI scores from dogs in partial remission were significantly different from dogs in complete remission, however VVTI scores from dogs out of remission were not significantly different from dogs in partial or complete remission. VVTI scores obtained from dogs out of remission were not predictive of remission status.

CONCLUSION

Preliminary investigation indicates that VVTI score may be associated with remission status in dogs with lymphoma, however further standardization of VVTI protocols may better elucidate its prognostic utility.

A questionnaire-based survey of chemotherapy drug-handling practices in UK first opinion veterinary small animal surgeries

Elsa Edery

Pride Veterinary Centre, Derby, UK

BACKGROUND

Hazards associated with the handling of cytotoxic agents have been recognized in human oncology for more than 3 decades. A large body of evidence documents environmental contamination in the workplace, healthcare workers exposure and biological effects following exposure to anti-neoplastic drugs. Efforts to reduce risks associated with exposure have resulted in a myriad of guidelines. In the UK, the Health and Safety at Work Act states that employers have a legal duty to protect their employees and the public and are expected to take measures to reduce exposure.

With an increasing demand from owners to treat their pet's cancer, it is likely that the administration of chemotherapeutic agents cannot be reserved exclusively to referral institutions anymore and first opinion practitioners are expected to handle cytotoxic agents more frequently.

STUDY DESIGN

A questionnaire-based survey of chemotherapy drug handling habits by first opinion UK veterinary surgeons and nurses was undertaken.

RESULTS

Completed replies were received from 65 veterinary surgeons and 5 veterinary nurses. 70.4% of the respondents were administering cytotoxic agents. 86% of them manipulated them infrequently (less than 20 times per year). Standards of care were defined according to available consensus and guidelines for safe handling of antineoplastic drugs. Compliance with standards of care was reported by 10%, 14%, 26.5%, 30% and 36% with regards to the use of mask, closed system transfer devices, chemotherapy-approved

Oral presentations

gowns and gloves and eye protection, respectively. Only 22% of participants were preparing cytotoxic drugs in a designated room while 68% used a dedicated room for administration to the patient. A cytotoxic spill kit was available in nearly half of the practices where the respondents worked. There was no association found between age, gender, time since graduation, university of graduation and type of practice and the use of recommended equipment for preparation of cytotoxic agents.

Although 80% of participants reported seeking training and advice from various sources, less than half

of them reported appropriate training in the safe handling of hazardous substances of other members of staff indirectly involved.

CONCLUSION

The study suggests that, despite training and concerns with health and safety issues associated with manipulation of hazardous drugs, compliance with recommended protocols was generally poor amongst veterinary healthcare workers in first opinion UK practices.

Prognostic significance of immunophenotype in canine acute myeloid leukaemia

Jennifer Lowe, Maciej Guzera, Joy Archer, Tim Williams

Cambridge University, Department of Veterinary Medicine, Cambridge, UK

Acute myeloid leukaemia (AML) is known to carry a poor prognosis in dogs, but little is known of any prognostic factors related to this disease. Immunophenotype is of prognostic value in chronic lymphocytic leukaemia, and anaemia is associated with a poorer prognosis in acute leukaemias. This study investigated the use of immunophenotype, classified using flow cytometry, and other clinical parameters as prognostic indicators in canine AML.

Dogs diagnosed with AML on flow cytometry at one institution between 1st January 2005 and 1st January 2013 were reviewed and a follow up history was obtained. Dogs were excluded if the diagnosis was uncertain; there was no follow up history; were CD34 negative (indicating chronic leukaemia), or were negative for all three myeloid markers (CD14, myeloperoxidase [MPO] or neutrophil specific antibody [anti-neut]). The relationship between survival time and the following variables were analysed using log rank analysis: breed, immunophenotype (divided into the following groups: [CD14+, MPO+, anti-neut+], [CD14+, MPO+],

[CD14+], [MPO+ and/or anti-neut+]), treatment type (palliative only, prednisolone or various chemotherapy protocols), haematological parameters at diagnosis and clinical signs. Survival time was calculated from the date of flow cytometric diagnosis to the date of natural death or euthanasia. Data are presented as median [range] and statistical significance was defined as $P < 0.05$.

Twenty four dogs met the inclusion criteria with an age of 7 [1-14] years; Labrador Retrievers, Golden Retrievers and German Shepherds were the most commonly represented breeds. Survival time was 3 [0-29] days. No association was identified between the immunophenotype of the disease and the survival time. However dogs with anaemia ($HCT < 36\%$) at the time of diagnosis had significantly shorter survival times compared with dogs with a $HCT \geq 36\%$ (3[0-28] days, $n=21$ vs. 21[6-29] days, $n=3$, $P=0.025$). Dogs presenting with gastrointestinal signs had significantly shorter survival times than those with no signs (3[0-6] days, $n=10$ vs. 4[1-29] days, $n=11$; $P=0.03$). Four cases presented with shifting lameness. Dogs surviving ≥ 3 days were compared by treatment type; those treated with prednisolone had longer survival times compared to those treated with various chemotherapy protocols (21[3-28] days, $n=3$ vs. 7[3-29] days, $n=6$; $P=0.041$).

Immunophenotype does not appear to be associated with prognosis in canine AML. However anaemia at the time of diagnosis and gastrointestinal signs are associated with a poorer prognosis in dogs with AML, although prognosis is invariably poor.

Evaluation of a lomustine based chemotherapy protocol (LOP) to treat canine T-cell lymphoma in 7 dogs

Charles Pittaway, Sarah Mason, Aleksandra Marcinowska, Antonio Giulano, Jane Dobson

Department of Veterinary Medicine, Cambridge University, Cambridge, UK

High grade T-cell lymphoma in dogs is associated with a poorer prognosis compared to the B-cell phenotype when treated with COP and CHOP based protocols. One study previously reported that lomustine based protocols were more

effective at treating multicentric and mediastinal canine T-cell lymphoma with a similar response rate and a longer progression free interval when compared with a CHOP protocol.

This retrospective study evaluated cases diagnosed with T-cell lymphoma at a single referral institution and that were subsequently treated with a LOP (lomustine, vincristine and prednisolone) protocol. Mean lomustine dose was 57 mg/m² (range 40–65 mg/m²) every 4 weeks, and mean vincristine dose was 0.66 mg/m² (range 0.5–0.7 mg/m²) weekly for 4 weeks then every 2 weeks. Response rate was recorded and progression free interval (PFI) was calculated from the date of first chemotherapy administration until recurrence of disease. Time taken before change in protocol due to adverse effects was calculated where appropriate and treatment delays and hospitalisation events due to adverse effects were recorded. Seven cases of high grade T-cell lymphoma were included (3 multicentric, 2 mediastinal,