ABSTRACTS

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COMPARISON OF THE EFFECT OF THE AROMATASE INHIBITOR, ANASTRASOLE, TO THE ANTIESTROGEN, TAMOXIFEN CITRATE, ON CANINE PROSTATE AND SEMEN

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Introduction - Estrogens are thought to play a considerable causative or permissive role in benign prostatic hyperplasia (BPH) [1], therefore, antiestrogens and aromatase inhibitors may be useful in the medical treatment of BPH. Aromatase inhibitors would be superior to antiestrogens due to their lack of agonistic effects. Anastrazole is a potent, highly selective, fourth generation aromatase inhibitor [7].

Objectives - The objective of this study was to compare the efficiency and safety of the aromatase inhibitor, anastrazole, to the antiestrogenic receptor blocker, tamoxifen, on normal and hyperplasic prostate. Additionally the effect of this compound on semen characteristics was described.

Materials and methods - Thirty-eight dogs 6.8 ± 1.1 of age, weighing 29.8 ± 3.5 were included in this study. The animals, which were otherwise normal, were ultrasound and radiologically classified according to their prostate into normal (NRL; n= 12) or abnormal with BPH (ABN; n= 14) [1]. The NRL and ABN dogs were randomly assigned to one of the following treatment groups during 60 days. Placebo tablets PO (NRL- PLC; n = 6) and (ABN-PLC; n = 6), anastrazole (Asiolex, Zenca) 0.25 (< 5 kg BW), 0.5 (5 ≥ 10 kg body weight, BW), 0.75 (10 ≥ 25 kg BW), 1 (25 ≥ 5 kg BW) mg/day, PO (NRL-ANZ, n = 6) and (ABN-ANZ, n = 8) and tamoxifen citrate (Tamoxifeno, Filaxis): 2.5 (animals < 15 kg BW), 5 (15 ≥ 25 kg BW) or 10 (25 ≥ 5 kg BW) mg/ day PO (NRL-TMX; n = 6) and (ABN-TMX; n = 8). The dogs were evaluated before the beginning of the treatments and then monthly during four months. Evaluation included physical examination, ultrasound exam of prostatic parenchyma and volume, scrotal diameter, testicular consistency, libido, semen analysis, hemogram and routine biochemical serum determinations.

Quantitative parameters were analyzed by least square analysis of variance using the General Linear Model Procedure (PROC GLM; SAS®). The model included the main effect of treatment and time point and their interaction. Orthogonal contrasts were also used to test biologically interesting differences. Categorical data were analyzed by PROC CATMOD (SAS®) using the same model.

Results - There was a significant interaction between treatment and time points for percentage prostatic volume change in both ABN and NRL animals (P < 0.01). Percentage prostatic volume change significantly varied in both drug-treated groups but not in the PLC (P < 0.01). At the end of the treatment percentage change decreased to -28.5±4.3, -21.6± 6.3 and -0.7±1.0 in the ABN-TMX, ABN-ANZ and ABN-PLC, respectively. From then on, it began to increase (-18.9±3.5, -16.7±0.0 and 2.7±1.2 for the same groups) without reaching pretreatment values at the end of the study. In the ABN animals there were no differences for this parameter between ANZ and TMX (P > 0.1) while in the NRL animals TMX presented a steeper decrease (P < 0.05). In some drug- treated dogs prostatic parenchyma became more homogenous and cysts disappeared throughout treatments (> 0.05).

In TMX, but not in ANZ nor PLC groups, libido, erection, testicular consistency and scrotal diameter decreased during treatment (P > 0.05). In ANZ and PLC groups sperm volume, count, motility and morphological abnormalities remained unaltered and non different between themselves throughout the study (P > 0.05). These characteristics impaired to
aspermia and/or astenoligonecrozoospermia up to the third month in the TMX group (P < 0.05). No animal presented hematological, biochemical nor clinical side effects related to the treatments. In dogs, data about aromatase inhibitors are scarce and controversial [3,6,8]. In line with a previous report [8] in the present study, the aromatase inhibitor used decreased prostatic volume in both normal and hyperplasic dogs. In these latter animals the decreasing percentage change was similar to that of tamoxifen, which is known for its rapidity of effect [2]. In anastrazole treated dogs, libido, testicular, semen and hematological characteristic remained unaltered which is in coincidence with previous findings in this and other species [4,5,9]. These results warrant further studies of aromatase inhibitors in the treatment of BPH in dogs.

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References