THE IMPACT OF FORTETROPIN® SUPPLEMENTATION ON DOGS RECOVERING FROM TIBIAL-PLATEAU LEVELING OSTEOTOMY (TPLO) SURGERY.

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Background - Fortetropin® is a non-thermal pasteurized, freeze-dried fertilized egg yolk product that has been shown to reduce serum myostatin levels and demonstrate a change in downstream signaling pathways, supportive of muscle hypertrophy with a resultant increase in lean body mass. Cranial cruciate ligament (CCL) rupture is a common injury in dogs and can result in disuse muscle atrophy of the affected limb, both at the time of presentation or during the post-operative period.

Objectives – To determine whether Fortetropin® supplementation in the post-operative period will help reverse or prevent disuse muscle atrophy in the affected limb, resulting in improved force distribution at standing and measurable differences in muscle thickness at the 8-week (end of the period of forced exercise restriction) and 12-week (end of the first 4-week period of increasing activity level) evaluations as compared to dogs receiving a placebo.

Primary End-Points - Thigh circumference, ultrasonographic measurement of thickness of coxofemoral extensors and flexors, stance analysis, and serum myostatin levels.

Secondary End-Points – Ultrasonagraphic measurements of epaxial muscle thickness, muscle condition score, and serum C-reactive protein levels.

Methods - 100 dogs with confirmed, naturally-occurring CCL rupture with no concurrent disease were randomly assigned to receive either Fortetropin or a placebo in a double-blinded study. Dogs received a minimum of 300 mg/kg daily of either powder (one scoop (6600 mg)/22 kg, dosed to the closest ½ scoop without under-dosing). All measurements and samples for evaluation of the primary and secondary end-points were obtained at time 0 (at the time of admission for TPLO surgery), week 8, and week 12.

Statistical analyses for measurements within a group were performed by t-test with a right- or left-tail (or two-tail) post-hoc analysis depending on whether the expected change was an increase, decrease, or not predicted. Statistical analyses between groups was by ANOVA. Significance was set at $p<0.10$. All statistical analyses were performed by Dr. M. Singh (Biometrics and Statistics, Toronto, Canada).

Results

86 dogs completed the study: 77 dogs had complete data sets for stance force analysis and muscle measurement (85 had measurements at week 8) and 69 dogs had complete data sets for serum myostatin levels (81 had measurements at week 8). The following analyses were not statistically analyzed: C-reactive protein, as only 17 of 241 samples had measurements above the reference range; and muscle condition score, as the subjective nature of the evaluation and breed/conformation differences precluded meaningful interpretation. Although statistically analyzed, there was significant interobserver variation of ultrasonographic measurement of muscle thickness as the force applied to the muscle at the time of measurement could not be standardized, invalidating the results.

Stance Analysis: As expected, dogs in both groups had a statistically significant improvement in the stance force applied to the affected limb at week 8 and week 12, as measured by % overall weight supported by the limb in comparison to week 0. Dogs in the Fortetropin-supplemented group had a statistically significant increase in % stance force of the affected limb from week 0 to week 8 as compared to the control group (p=0.097).

Thigh circumference**:** In the affected limb, dogs supplemented with Fortetropin had no significant change in thigh circumference as compared to baseline at either week 8 or week 12. Dogs in the control group had a significant reduction in thigh circumference from baseline to week 8 (p=0.03). In the unaffected limb, dogs supplemented with Fortetropin had no significant change in thigh circumference as compared to baseline at either week 8 or week 12. Dogs in the control group had a significant reduction in thigh circumference from baseline to week 8 (p=0.02).

Myostatin measurements**:** In dogs supplemented with Fortetropin, there was a mean increase in serum myostatin levels of 45 pg/ml/week, but the mean myostatin levels at week 8 were not statistically significantly different from baseline. Additionally, there was a mean decrease in serum myostatin levels of 43 pg/ml/week from baseline to week 12, but mean myostatin levels at week 12 were not statistically significantly different from baseline. In the control dogs, there was a significant increase in mean serum myostatin levels from baseline at both week 8 (358.9 pg/ml/week; p=0.02) and week 12 (186 pg/ml/week; p=0.07). In comparison of the changes in mean serum myostatin levels between Fortetropin-supplemented and control dogs, control dogs had a statistically significant increase from baseline to week 8 (p=0.08).

Conclusions – During the period of forced exercise restriction from week 0 to week 8, when comparing Fortetropin® supplementation to placebo (cheese powder):

- Fortetropin® prevented a rise in serum myostatin levels.
- Fortetropin® minimized the loss of muscle mass as measured by thigh circumference in the affected and unaffected limbs.
- Fortertropin® supplemented dogs had a more significant improvement in percent of weight supported by the affected limb as determined by force plate stance analysis (more rapid return to normal stance force distribution).

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