

Fortetropin® inhibits disuse muscle atrophy in dogs after tibial plateau leveling osteotomy

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Summary

Cranial cruciate ligament (CCL) rupture is the most common stifle injury in medium and large breed dogs, ultimately resulting in pain, lameness, and secondary muscle atrophy of the affected limb. There have not been any studies addressing the effect of disuse muscle atrophy on stifle joint stability or on interventions to mitigate disuse muscle atrophy in dogs with CCL rupture. The purpose of this study was to assess if a myostatin reducer would have an effect on preventing or reversing disuse muscle atrophy in patients undergoing a tibial plateau leveling osteotomy. Our hypothesis was that Fortetropin® supplementation in the post-operative period would help reverse disuse muscle atrophy in the affected limb, resulting in improved force distribution at standing and measurable difference in muscle thickness at the rechecks compared to dogs receiving the placebo. Patients were randomly assigned into the Fortetropin® or placebo group and clients were instructed to add the assigned supplement to the dog's normal diet once daily for twelve weeks. Enrolled patients had ultrasound measurements of muscle thickness, tape measure measurements of thigh circumference, serum myostatin level assays, and static stance analysis evaluated at weeks 0, 8, and 12.

Registration details

Status of the study	Accessible
Date of registration	2019-06-14
Date of publication	2024-05-30
DOI	10.17590/asr.0000141
Planned start of the study	2018-05-31
Planned end of the study	2018-07-25
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1. General Information

Keywords

disuse muscle atrophy, myostatin, tibial plateau leveling osteotomy, Fortetropin

Funding sources

MYOs RENS Technology Inc.

International code of classification

IDC-15

2. Study design

Introduction

The loss of lean body mass due to disuse muscle atrophy can result from immobilization or inactivity associated with recovery from surgery or reduction in the use of a limb secondary to pain. During periods of immobilization, disuse atrophy occurs because increased myostatin mRNA expression results in both an increase in muscle protein breakdown and a reduction in muscle protein synthesis. The inhibition or reduction of serum myostatin has been described in dogs.

Fortetropin®, a non-thermal pasteurized, freeze-dried, fertilized, egg yolk product, is considered a natural myostatin-reducing agent. When administered to healthy adults, Fortetropin® reduced serum myostatin levels and increased lean mass and muscle thickness in comparison to a placebo.

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The purpose of this study was to assess if a myostatin reducer would have an effect on preventing or reversing disuse muscle atrophy in patients undergoing a tibial plateau leveling osteotomy. Currently the manuscript is being prepared for publication.

Type of research

Confirmatory

Hypothesis of your study

Our hypothesis was that Fortetropin® supplementation in the post-operative period would help reverse disuse muscle atrophy in the affected limb, resulting in improved force distribution at standing and measurable difference in muscle thickness at the rechecks compared to dogs receiving the placebo.

Study design

A prospective randomized, double-blinded, placebo-controlled clinical trial.

Enrolling 100 client owned dogs undergoing a tibial plateau leveling osteotomy.

Placebo group received a cheese powder, while the treatment group received Fortetropin®, a non-thermal pasteurized, freeze-dried, fertilized, egg yolk product.

Method of blinding

Both clients and investigators were blinded to the treatment and placebo agent.

Method of randomization

Treatment or placebo was randomly assigned to each dog with use of a published random numbers table

3. Methods

3. 1. Thigh Circumference

Description of the method

Thigh circumference was measured by one of two investigators with a single retractable tape measure device at the mid-point of the femur for both the affected (leg on which the TPLO was performed) and unaffected (contralateral) leg.

Thigh circumference was measured in cm.

Narcotic/analgesic treatment

Not provided

Drugs/substances

Not provided

Antibodies

Not provided

Cell lines, viruses, DNA or RNA constructs and bacteria

Not provided

3. 2. Ultrasound Measurements

Description of the method

B-mode ultrasonography was used to determine the muscle thickness of the thigh, cranial to the mid-femur and lateral to the mid femur of both the affected and contralateral hindlimbs, and of the epaxial muscles at the level of the 13th rib.

Muscle thickness was evaluated in mm.

Narcotic/analgesic treatment

Not provided

Drugs/substances

Not provided

Antibodies

Not provided

Cell lines, viruses, DNA or RNA constructs and bacteria

Not provided

3. 3. Stance Analysis

Description of the method

The percent body weight placed on each limb at a static stance was recorded with a PetSafe Stance Analyzer for all dogs prior to sedation. Measurements were recorded as percent body weight on the ipsilateral front limb, contralateral front limb, affected hindlimb, and contralateral hindlimb.

Narcotic/analgesic treatment

Not provided

Drugs/substances

Not provided

Antibodies

Not provided

Cell lines, viruses, DNA or RNA constructs and bacteria

Not provided

3. 4. Serum Myostatin

Description of the method

For myostatin measurements 3-6ml of blood was collected from a peripheral vein and the serum was routinely separated after clot formation. Serum was stored at -80° C until the time of the assay. Batched samples were thawed and serum myostatin concentrations were measured in duplicate using a GDF-8 Myostatin Quantikine ELISA kit according to the manufacturer's instructions.

Narcotic/analgesic treatment

Not provided

Drugs/substances

Not provided

Antibodies

Not provided

Cell lines, viruses, DNA or RNA constructs and bacteria

Not provided

4. Statistics

4. 1. Group t-test

Assigned method(s)

Thigh Circumference
Ultrasound Measurements
Stance Analysis
Serum Myostatin

Main endpoints

Measurements at week 8 and week 12

Secondary endpoints

Not provided

Sample size calculation

The sample size was not calculated, but was selected based on the number of dogs presenting to the hospital for a tibial plateau leveling osteotomy in one year.

Primary statistical analysis

ANOVA

Exclusion criteria

Data from animals that did not reach the 8 week and 12 week time marks were excluded.

5. Animals

5. 1. Dogs (*Canis familiaris*)

Animal strain/breed

Client owned dogs of various breeds

Genetically modified

No

Sex

Female
Male

Further characteristics of the animals (e.g. age, body weight, size)

Age ranged from 18-126 months

Body weight ranged from 18-75kg

Housing conditions

Single group housing

Case size: 3'x6' runs

Bedding: blankets and comforters

Enrichment: walks every 4 hours outside

Cage changing: kennels cleaned and bedding changed every 4 hours as needed

Feeding: offered commercial diet twice daily

Water: tap water provided at all times

Refinement

Not provided