PARATHYROID HORMONE, IONIZED CALCIUM, AND 25-HYDROXYVITAMIN D CONCENTRATIONS IN THE DOMESTIC FERRET (*MUSTELA PUTORIUS FURO*)

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Abstract

The objective of this study was to measure parathyroid hormone (PTH), ionized calcium, and 25-hydroxyvitamin D concentrations in healthy intact adult ferrets. Serum was collected from 16 clinically healthy adult ferrets (8 males and 8 females). Concentrations of PTH and 25-hydroxyvitamin D were measured via commercially available radioimmunoassays validated for humans, dogs, and cats (PTH) plus horses (25-hydroxyvitamin D). Concentrations of ionized calcium (at pH 7.4) were measured using an ion-specific electrode. Median (minimum, maximum) concentrations were as follows: PTH 8.7 (2.2, 24.4) pmol/L, ionized calcium 1.15 (1.09, 1.25) mmol/L, and 25-hydroxyvitamin D 94 (61, 138) nmol/L). Female ferrets had significantly higher concentrations of PTH than male ferrets (female median: 17.1 pmol/L; male median: 6.9 pmol/L). Associations among PTH, ionized calcium, 25-hydroxyvitamin D, calcium, phosphorus, magnesium, and weight were evaluated. There was a weak negative correlation between PTH concentration and total calcium concentration in female ferrets. As none of these assays have been validated for use in ferrets, results may provide a baseline for clinicians evaluating ferrets for disorders of calcium homeostasis, parathyroid glands, and paraneoplastic syndromes. Copyright 2017 Elsevier Inc. All rights reserved.

Key words: ferret; mustelid; parathyroid hormone; ionized calcium; 25-hydroxyvitamin D

The parathyroid glands are endocrine organs that are closely associated with the thyroid. In ferrets, the parathyroid glands are discrete, pinkish discs usually found medially on the cranial pole of the thyroid gland at the level of the fourth or fifth tracheal rings.[1] The parathyroid glands secrete parathyroid hormone (PTH). In its biologically active form, PTH is an 84-amino acid peptide that is highly conserved in mammals,[2] and is secreted by the chief cells of the parathyroid in response to hypocalcemia or low concentrations of ionized calcium, the biologically active form of calcium.[3] PTH is the primary regulatory hormone for calcium and phosphate metabolism, while its secretion is inhibited by increased serum concentrations of ionized calcium and vitamin D. PTH targets the bone, intestines, and the kidneys to increase serum concentrations of ionized calcium by mobilizing calcium and phosphate from bones and increasing gastrointestinal absorption of calcium in the presence of vitamin D. In the kidneys, PTH promotes calcium reabsorption in the ascending loop of Henle, distal tubule, and collecting tubule, and promotes reabsorption of phosphate in the proximal tubule.

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Ionized calcium refers to the fraction of calcium that is unbound in plasma, highly controlled, hormonally regulated, and involved in pathologic conditions, such as disorders of the endocrine, renal, and skeletal systems, granulomatous diseases, and neoplasia.[4] The calcium analyte in a serum or plasma chemistry is the total calcium, which includes free or ionized calcium, calcium bound to anionic proteins, and calcium bound to nonprotein anions, or complexed calcium.[4] Total calcium measurements are influenced by the total protein concentration, particularly the albumin concentration, and therefore, hypoproteinemia or hypoalbuminemia can result in a hypocalcemia that does not reflect a calcium regulation dysfunction. To evaluate biologically active calcium without this influence, ionized calcium is measured. In humans and dogs, ionized calcium is a more sensitive indicator of primary hyperparathyroidism and a more reliable calcium measurement in critically ill patients.[5-8]

Vitamin D plays an important role in calcium homeostasis and it targets the same organs as PTH. The largest fraction of vitamin D in the blood is 25-hydroxyvitamin D.[9] It is synthesized in the liver from Vitamin D_3 (cholecalciferol). 25-hydroxyvitamin D is then hydroxylated by 1-α-hydroxylase in the kidney to the active 1,25-dihydroxyvitamin D (calcitriol). Synthesis of the renal 1-α-hydroxylase enzyme is stimulated by PTH. Vitamin D promotes calcium reabsorption by the renal tubules, calcium and phosphate absorption in the intestines, and osteolysis to liberate calcium and phosphate from bones.[9] Vitamin D also provides negative feedback on the secretion of PTH, and therefore deficiencies in vitamin D can cause a secondary hyperparathyroidism. Chronic renal failure can lead to decreased conversion of 25-hydroxyvitamin D to the metabolically active 1,25-dihydroxyvitamin D, which inhibits PTH secretion. Vitamin D deficiencies can also result from all-meat diets in ferrets.[10]

There is a lack of published information regarding reference values for PTH, ionized calcium, and 25-hydroxyvitamin D in domestic ferrets and other mustelids. While these assays have not been validated for use in ferrets, results will expand the reference material available to clinicians, especially for consideration of endocrine, renal, or neoplastic diseases in a ferret patient.

MATERIALS AND METHODS

Animals

This project was approved by the North Carolina State University (NCSU) Institutional Care and Animal Use Committee. Sixteen ferrets (8 males and 8 females) were obtained from a commercial breeding facility (Marshall Bioresources, North Rose, NY, USA) for a course in ferret medicine and surgery offered to veterinary students biennially at the NCSU College of Veterinary Medicine. The age of the ferrets ranged from 0.6 to 1.4 years (median 1 year) and they weighed 0.5 to 1.6 kg (median 1.1 kg; females 0.5 to 1.0, median 0.8 kg; males 1.2 to 1.6, median 1.4 kg). There were no abnormalities detected in the physical examinations of the ferrets. The ferrets were housed individually in standard stainless steel cages within a temperature-controlled room with no other occupants. The light cycle provided 12 hours of light daily. The ferrets were fed a commercial ferret diet (Premium Marshall Ferret Diet, Marshall Pet Products, Inc., Wolcott, NY, USA).

Venipuncture

Venipuncture was performed on the same day at approximately the same time for all ferrets in early December 2015. The ferrets were sedated with 0.25 mg/kg detomidine gel administered transmucosally (Dormosedan Gel; Orion Corporation, Turku, Finland). Full physical examinations were performed on all ferrets. Blood was collected from the jugular vein or the cranial vena cava with a 22-gauge, 1.6 cm needle and 6 mL syringe. A maximum of 5 mL/kg of blood was collected. After venipuncture, detomidine gel was reversed with 0.25 mg/kg atipamezole (Antisedan; Zoetis, New York, NY, USA) administered intramuscularly. For each ferret, a subsample of whole blood was transferred to heparinized microhematocrit tubes for determining packed cell volumes (PCV) and total solids. The remaining blood was transferred to a 7.0 mL no additive serum tube (BD Vacutainer; Becton, Dickinson, Franklin Lakes, NJ, USA). Samples were allowed to clot for at least 30 minutes and then centrifuged at 563*xg* for 10 minutes to separate the serum. Serum was transferred to cryovials, which were submitted to the Clinical Pathology Laboratory at NCSU College of Veterinary Medicine for serum chemistries or the Diagnostic Center for