Feline idiopathic hypercalcaemia

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Calcium is an important electrolyte in the body which has many vital intra- and extracellular functions including skeletal support. Over 99% of the body’s calcium is stored in bone, less than 1% is in the extracellular fluid. In healthy cats, calcium exists in 3 different fractions: ionized (~52%), protein-bound (~40%) and complexed (~8%). Normally, the calcium concentration in the blood is maintained within a narrow range to ensure adequate supply for the various body functions. Regulation of the calcium concentration in the blood is complex and is under the control of PTH, vitamin D and calcitonin. Only ionized calcium (iCa) is biologically active and strictly spoken, the term hypercalcemia should only be used if this fraction is elevated. Often times, clinicians rely on the measurement of total calcium which comprises all 3 fractions and is easier to analyze. It has been shown, however, that there is a high level of diagnostic discordance and total calcium should not be used to predict iCa. Additionally, the use of adjustment formulas in case of total protein or albumin alterations is not recommended. For accurate assessment of the calcium, status measurement of iCa should be pursued. If iCa is used as a screening test, hypercalcemia is detected more commonly compared to the use of total calcium. Hypercalcemia is usually defined as an increase of total calcium > 2.75 mmol/l and iCa > 1.4 mmol/l; although reference ranges differ slightly between methods and laboratories. On one hand, hypercalcemia can be regarded as a marker of disease, on the other hand, it can cause disease. All tissues may be damaged by high iCa, clinically, the effects on the CNS, kidney, GI-tract and heart are the most important. Severity of clinical signs generally depend on the magnitude of hypercalcemia and on its rate of development. Differential diagnosis of hypercalcemia may be divided into nonpathological and pathological causes. Nonpathological causes include non-fasted blood sample, growth, hemoconcentration and laboratory error. The most important pathological causes comprise neoplasia, renal failure, hypoadrenocorticism, primary hyperparathyroidism, hypervitaminosis D (plants, rodenticide, antipsoriasis cream), granulomatous disease and idiopathic hypercalcemia (IHC). The most common causes for persistent hypercalcemia in cats are neoplasia and IHC; in some countries (e.g. USA) the latter is the most common cause. The term IHC describes a syndrome in cats which have ionized hypercalcemia for which no underlying cause can be identified, even after extensive medical evaluation. The phenomenon has started to be recognized since the early 1990 as an incidental finding on serum biochemistry profiles. At that time, acidifying diets designed to prevent struvite crystals were introduced and many people assume that feeding acidifying, magnesium restricted diets is a major predisposing factor for IHC: It is possible that IHC only develops if there is a particular genetic background. Another potential cause is excessive amounts of vitamin D in the diet; although blood levels of 25-hydroxyvitamin D and calcitriol in cats with IHC are usually normal. Cats of all ages may be affected, median/mean age at onset of hypercalcemia has been reported to be 5.4 and 9.8 years. There is no sex predisposition, long-hair cats seem to be overrepresented. Cats may be asymptomatic, especially in the early stages of the disease. For this reason, IHC often times is an incidental finding during pre-surgical or pre-dental blood work. In symptomatic cats, clinical signs include (mild) weight loss, anorexia, vomiting, diarrhoe, constipation, lethargy and signs of lower urinary tract disease (pollakiuria, stranguria, hematuria). Calcium oxalate stones may be present due to increased calciuresis. Hypercalcemia in IHC is usually mild to moderate, e.g. in most cases total calcium is not higher than 3.75 mmol/l and iCa is between 1.4 and 1.9 mmol/l. Serum phosphorus is usually normal, unless concurrent chronic renal disease is present. PTH concentration is low to low-normal, PTHrP is undetectable. Ionized magnesium, 25-hydroxvitamin D and calcitriol are usually normal. IHC is diagnosed by exclusion, e.g. work-up should include a thorough physical examination, laboratory evaluation (whenever possible PTH, PTHrP, 25-hydroxyvitamin D, calcitriol should be measured) and diagnostic imaging. There is no specific treatment because pathogenesis is unknown. It is controversial, if cats
with minor elevation of iCa should be treated as they are usually asymptomatic. In any case, treatment should be initiated when iCa continues to increase and/or clinical signs become obvious. Dietary modifications may be used as first-line treatment, although their choice is mostly empirical. Wet diets are preferred over dry diets, as they are usually more calcium-restricted. High-fiber diets, renal diets and diets developed to prevent calcium oxalate urolithiasis all have been used in cats with IHC with variable success. If a feeding trial fails to normalize iCa after approximately 6 – 8 weeks treatment with bisphosphonates should be considered. This class of drugs reduces the number and activity of osteoclasts thereby decreasing bone turnover. Recently, treatment success has been reported in a small number of cats using alendronate orally (10 mg/cat, once weekly). If treatment with bisphosphonates is unsuccessful, glucocorticoids may be considered. Initial dose of prednisolone is 5 mg/cat SID, if unsuccessful the dose may be increased to 10 mg/cat SID after approximately 4 weeks. However, chronic steroid treatment may be associated with substantial side effects and the risks should be weighed carefully against the benefits.

References


