

Too Much of a Good Thing, Feline Hypercalcemia

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Calcium is essential for many normal physiological processes within the body. Changes in calcium homeostasis leading to hypercalcemia can result in clinical signs such as polyuria and polydipsia, lethargy and weakness due to depressed excitability of muscle and nervous tissue, and gastrointestinal (GI) signs due to effects on GI smooth muscle. Hypercalcemia in cats is mostly idiopathic, with chronic kidney disease and neoplasia also being common causes. Hypercalcemia can be a diagnostic challenge and a good understanding of the regulation of calcium homeostasis can aid in interpreting results of diagnostic tests. Furthermore, the management approach may depend on the underlying cause of hypercalcemia, and also its severity and chronicity.

Calcium plays a key role in many normal physiological processes. It is important in neuromuscular transmission, enzyme activity, blood coagulation and muscle contraction (including skeletal, smooth and cardiac muscle), and is required for intracellular signaling and normal cellular function. Calcium mediates vascular smooth muscle contraction and maintains blood vessel tone and hence blood pressure. It enters vascular smooth muscle cells via voltage-dependent calcium channels (L-type calcium channels) or can be released from intracellular stores; the resultant increase in the intracellular concentration of calcium stimulates vascular smooth muscle contraction. Calcium is also the most abundant component of the skeleton, being required both for bone formation/resorption and for maintaining the structural integrity of bones and teeth.

The normal physiological response to hypercalcemia includes decreased production of parathyroid hormone (PTH) from the parathyroid gland, increased production of calcitonin from C cells in the thyroid gland, and decreased calcitriol production in the kidneys due to direct inhibition and also decreased PTH production. Identification of hypercalcemia and implementation of appropriate therapy is important as soft tissue calcification is a likely sequela if the calcium x phosphate product becomes increased. Mineralization of renal tissue may result in nephron injury or changes in renal blood flow, causing a decline in renal function and azotemia. Hypercalcemia may promote formation of calcium oxalate uroliths, which can lead to urinary tract obstruction.

Ionized calcium should be measured to confirm hypercalcemia if total calcium is increased. Hypercalcemia should also be demonstrated to be persistent. A cat with an ionized calcium concentration >1.40 mmol/l is generally considered to be hypercalcemic. Full biochemical analysis should be undertaken, ensuring the panel includes assessment of renal function and phosphate concentration. If available, acid-base analysis should also be performed. If PTH concentration is in the upper two-thirds of the reference interval or is increased, it suggests a parathyroid-dependent cause. Parathyroid hormone-related peptide (PTH-rp) can be measured if malignancy is suspected – but can be normal. Thus, a normal value does not fully exclude neoplasia. 1,25 dihydroxycholecalciferol (calcitriol) and 25-hydroxyvitamin D₃ (caldiol) can be measured as well. Calcitriol reflects metabolically active vitamin D and caldiol reflects cholecalciferol or ergocalciferol ingestion following hydroxylation. Caldiol is the major circulating form of vitamin D. Thoracic and abdominal imaging can be helpful in screening for neoplasia or granulomatous lesions.

The management approach will depend not only on the severity of the hypercalcemia but also the time frame of development (eg., acute vs chronic). Patients with mild hypercalcemia (ionized calcium <0.25 mmol/l above the reference interval) that are asymptomatic and have a normal calcium x phosphate product may require no immediate treatment, whereas patients experiencing a severe acute rise in calcium concentration may require more aggressive treatment. No single treatment is recommended for managing all cases of hypercalcemia and, therefore, the underlying cause should be addressed. Supportive therapy is aimed at

enhancing renal excretion of calcium and preventing calcium resorption from bone. Dietary change is perhaps one of the most important aspects of management in cats with idiopathic hypercalcemia. High fiber diets can be fed to bind intestinal calcium, thus reducing its absorption. Wet diets can also be helpful in promoting diuresis and generally have a lower calcium content than dry diets. Hypercalcemia has been noted in cats fed a renal diet and so this diet should be discontinued if hypercalcemia develops on a renal diet. Glucocorticoids act to reduce bone resorption, decrease intestinal absorption and increase renal excretion of calcium. It is important to avoid steroids if the underlying etiology remains unclear and further investigations to determine a definitive diagnosis are to be pursued. Bisphosphonates exert their effect by reducing the number and activity of osteoclasts. There are few reports on the use of these drugs in cats. Recently alendronate has been evaluated in a small study of cats with idiopathic hypercalcemia but bisphosphonate related osteonecrosis has been reported and these should be used in caution in cats.

References:

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