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Calcium Disorders

Usually measuring total calcium

Methods for determining ionized Ca are available

Degree of protein binding affected by pH

Ionized Ca decreases by 0.15 mg/dl for every 0.1 unit increase in pH

DISTRIBUTION OF CALCIUM

Total calcium is divided into:

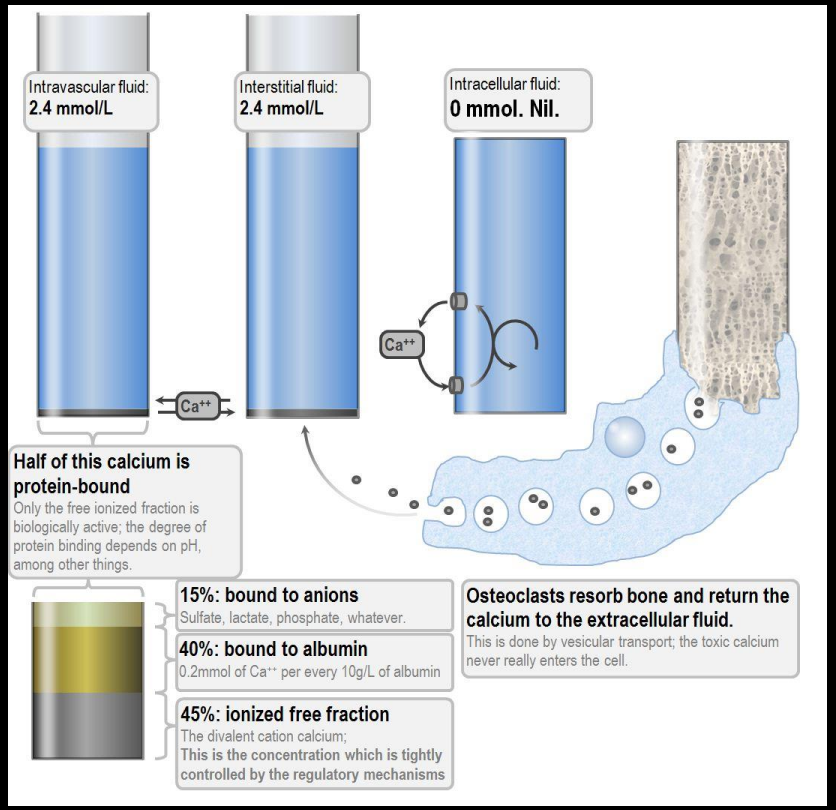
Protein bound (50%)

90% bound to albumin

Ultrafiltrable (50%)

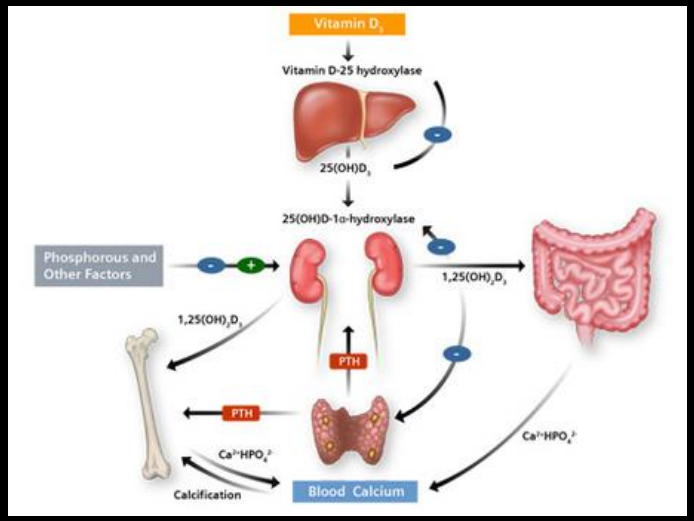
Complexed Ca (15%)

Ionized Ca (45%)



CALCIUM REGULATION

Vitamin D



Liver converts D_3 to 25-D_3

Kidney converts 25-D_3 to 1,25-D_3

Enhances GI absorption of Ca and PO_4

Mobilizes Ca and PO_4 release from bone

Enhances renal re-absorption of Ca and PO_4

Suppresses PTH release

CALCIUM REGULATION

Parathyroid hormone (PTH)

- 84 amino acid polypeptide
- Biologic effects mediated through amino terminus
- PTH acts through adenyl cyclase increasing cAMP
  - Results in phosphaturia and hypocalciuria

CALCIUM REGULATION

PTH Related Peptide (PTH-rp)

- Responsible for humoral hypercalcemia of malignancy (HHM)
  - Lymphoma, anal sac carcinoma, others
  - Binds to the PTH receptor
  - Actions similar to PTH
  - Results in hypercalcemia; PTH levels low to undetectable

Classification of Types of Cancer-Associated Hypercalcemia.*

Table 1. Classification of Types of Cancer-Associated Hypercalcemia.*

Feature	Humoral Hypercalcemia			Local Osteolytic Hypocalemia	
Mediator	PTHrP	1,25 dihydroxyvitamin D	Parathyroid hormone	TNF, interleukin-6, interleukin-1, macrophage inhibitory protein, and others	PTHrP, TNF, interleukin-6, interleukin-1, and others
Tumor type	Lung, breast, renal, and many others	Hematologic cancer, T-cell lymphoma	Parathyroid cancer, neuroendocrine, ovarian, and others	Myeloma or lymphoma in bone	Breast, lung, kidney
Bone metastases, tumor in bone	None or few	None or few	None or few	Extensive	Extensive
Parathyroid hormone	Low	Low	High	Low	Low
PTHrP	High or normal	Low	High	Low	Variable
1,25-dihydroxyvitamin D	Variable	High	High	Variable	Low
Phosphorus	Low	High	Low	Variable	Variable
Osteoclast activity	High	High	High	High	High

* PTHrP denotes parathyroid hormone–related protein, and TNF tumor necrosis factor.

TA Guise, JJ Wysolmerski. N Engl J Med 2022;386:1443-1451.

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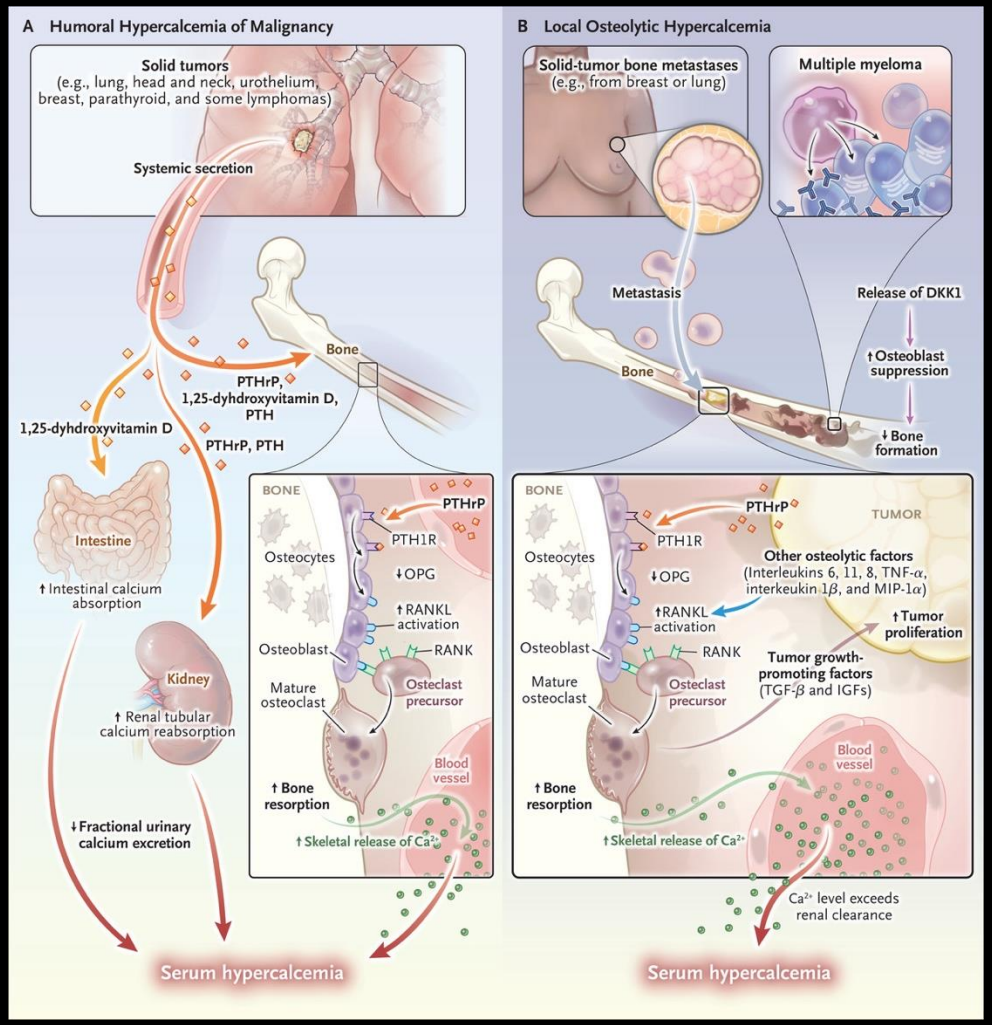
Pathophysiology of Humoral Hypercalcemia of Malignancy.



TA Guise, JJ Wysolmerski. N Engl J Med 2022;386:1443-1451.

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DIAGNOSTIC APPROACH TO HYPOCALCEMIA

Clinical Signs

- Weakness; lethargy
- Focal trembling; twitching
- Generalized muscle fasiculations
- Ataxia; stiff gait
- Seizures
- Polyuria, polydipsia
- Cataracts

DIFFERENTIAL DIAGNOSIS OF HYPOCALCEMIA

Laboratory error

Hypoalbuminemia

Chronic or acute renal failure

Primary hypoparathyroidsim

Puerperal tetany

Hypomagnesemia

Malabsorption; enemas

Pseudo-hypoparathyroidism

TREATMENT OF HYPOCALCEMIA INITIAL MANAGEMENT

Ca gluconate 10% solution

- 0.5 - 1.5 ml/kg IV slowly
- Monitor EKG
- Do not use CaCl

- After initial control
  - Ca gluconate SQ every 6-8 hours
  - Dilute 50% with saline

TREATMENT OF HYPOCALCEMIA

Daily monitoring of Ca

Calcitriol

25 - 40 ng/kg PO q 24 hours

DIFFERENTIAL DIAGNOSIS OF HYPERCALCEMIA

Laboratory error

Malignancy

- Lymphoma
- Anal sac carcinoma
- Multiple myeloma
- Bone tumors
- Others (mammary, prostate, SCC)

DIFFERENTIAL DIAGNOSIS OF HYPERCALCEMIA

- Primary hyperparathyroidism
- Chronic renal failure
- Hypoadrenocorticism
- Young animals
- Hypervitaminosis D
- Granulomatous disease
  - Blastomycosis
  - Granulomatous skin disease

FELINE HYPERCALCEMIA

- Neoplasia
  - SCC, LSA
- Renal Failure
- Primary Hyperparathyroidism
- Diet
  - Acidifying diets
    - Role of fiber
    - Role of prednisone
- Granulomatous disease
  - Cryptococcus

DIAGNOSTIC APPROACH TO HYPERCALCEMIA

- Repeat Ca
- Correction for albumin
- Rule-out exposure to Vit D
- Good physical examination
  - Lymph node
  - Anal sac

DIAGNOSTIC APPROACH TO HYPERCALCEMIA

- CBC/SMA
  - Rule-outs
  - Ca x PO_4 product
  - With PTH or PTH-rp
    - Hypercalcemia with low or low normal PO_4
- Urinalysis
  - Increased incidence of UTI
  - Specific gravity < 1.020

DIAGNOSTIC APPROACH TO HYPERCALCEMIA

Thoracic radiographs

If animal is symptomatic

- Abdominal radiographs
- Bone marrow
- Abdominal US

If animal is asymptomatic

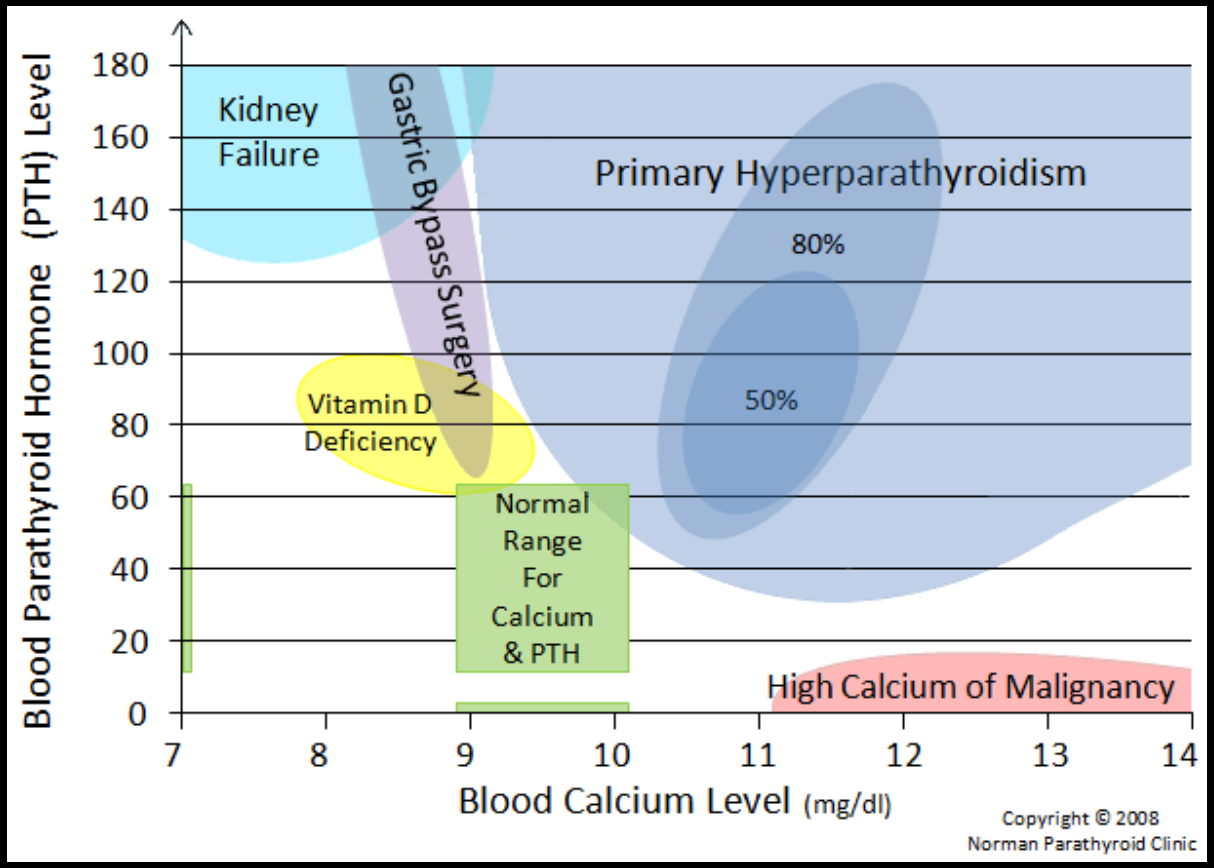
- PTH, ionized Ca, PTH-rp

DIAGNOSTIC APPROACH TO HYPERCALCEMIA

PTH and Ionized Ca

- PTH and iCa are elevated
  - Primary hyperparathyroidism
- PTH elevated, iCa low
  - Renal secondary hyperparathyroidism
- PTH low, iCa high
  - HHM

DIAGNOSTIC APPROACH TO HYPERCALCEMIA



Treatment Options for Cancer-Associated Hypercalcemia.

Table 2. Treatment Options for Cancer-Associated Hypercalcemia.

Treatment	Mechanism	Dose	Expected Effect	Adverse Events	Comments
Intravenous fluids	Corrects volume deficit and induces calciuresis	Sodium chloride solution (0.9%) in initial bolus of 1–2 liters, followed by continuous intravenous infusion at 200–500 ml/hr intravenously	Lowers calcium by 1–1.5 mg/dl over first 24 hr	Volume overload	Adjust to urinary output of 100–150 ml/hr. Carefully assess for volume overload.
Furosemide	Acts through natriuresis-induced calciuresis	20–40 mg	Lowers calcium by 0.5–1.0 mg/dl after resolution of volume depletion	Potential volume depletion and worsening of hypercalcemia if volume not replete when initiated	Administer only after volume status restored. Particular benefit in patients at risk for volume overload.
Salmon calcitonin	Inhibits osteoclast activity	Subcutaneous or intramuscular infusion of 4–8 IU per kg of body weight, subcutaneous or intramuscular, every 8–12 hr for 48–72 hr	Rapidly lowers calcium by 1–2 mg/dl		Consider in patients with calcium level >15 mg/dl or altered consciousness. Tachyphylaxis may occur after 48–72 hr.
Pamidronate	Inhibits osteoclast activity, causes osteoclast apoptosis	Intravenous infusion of 60–90 mg over 2 hr in 50–200 ml of saline or 5% dextrose in water	Normalizes calcium in 60–70% of patients over 48–72 hr; median treatment duration of 11–14 days	Acute-phase response relatively common, with hypocalcemia especially likely if vitamin D deficiency present; renal insufficiency possible if administered in presence of decreased GFR or volume depletion or if administered too quickly; osteonecrosis of jaw and atypical femoral fractures possible but rare	Can be repeated every 2–3 wk. May cause kidney damage, especially if GFR <30–35 ml/min.
Zoledronate	Inhibits osteoclast activity, causes osteoclast apoptosis	Intravenous infusion of 4 mg over 15 min in 50 ml of saline or 5% dextrose in water	Normalizes calcium in 80–90% of patients over 48–72 hr, with median treatment duration of 30–40 days	Same as pamidronate; dose adjustment required if GFR <60 ml/min (see package insert)	Rehydrate before administration. Do not administer loop diuretics until patient is adequately rehydrated and use with caution in combination with zoledronate to avoid hypocalcemia (refer to package insert). Treatment can be repeated in 7 days if sufficient lowering of calcium level not achieved and every 3–4 weeks thereafter. May cause kidney damage, especially in patients with GFR <30–35 ml per minute.
Denosumab	Inhibits osteoclast formation, differentiation, and activity	Subcutaneous administration of 120 mg	Normalizes calcium in at least 70% of patients; median duration of response, 104 days	Acute-phase response less common than with bisphosphonates; osteonecrosis of jaw and atypical fractures rare. Rebound osteoclastogenesis may occur when denosumab discontinued without initiation of other therapy (e.g., bisphosphonate).	Not as well studied as bisphosphonates in cancer-associated hypercalcemia. Patients with GFR <30 have a higher risk of hypocalcemia, and a lower dose should be considered (see package insert). Can be given weekly for 4 wk, then monthly for maintenance.
Glucorticoid	Inhibits 1-alpha hydroxylase and lowers 1,25-dihydroxyvitamin D levels	Oral administration of 60 mg of prednisone per day for 10 days†	Has variable effects. Normalization of calcium levels possible if 1,25-dihydroxyvitamin D levels are significantly reduced. Response typically transient unless tumors are treated.	Hyperglycemia, altered mental status, hypertension, increased risk of infection and thromboembolism	Most commonly used in patients with lymphoma. Consider adding to bisphosphonate or denosumab in patients with humoral hypercalcemia and elevated circulating levels of 1,25-dihydroxyvitamin D.
Cinacalcet	Binds calcium-sensing receptor and inhibits secretion of parathyroid hormone in patients with parathyroid carcinoma and may increase renal calcium absorption through renal calcium-sensing receptor in nonparathyroid hypercalcemia	Oral administration of 30 mg per day initially. Can increase to 90 mg four times daily as needed to control hypercalcemia	Reduced calcium by at least 1 mg/dl in approximately 60% of patients with inoperable parathyroid carcinoma. Case reports of normalization of calcium in some nonparathyroid cancers in combination with other treatments.	Nausea, vomiting, headache, fractures	Approved for treatment of hypercalcemia related to parathyroid cancer. Case reports indicate reduction of calcium levels in patients with refractory hypercalcemia related to non–small-cell lung, neuroendocrine, breast, or renal cancer.
Dialysis	Removes excess calcium directly	Administration of low-calcium or calcium-free dialysate through peritoneal dialysis or hemodialysis	Transient reduction of calcium during dialysis		Can be useful initially in patients with severe chronic kidney disease or acute, life-threatening hypercalcemia

* GFR denotes glomerular filtration rate.
† Other glucocorticoids may be used alternatively.

TA Guise, JJ Wysolmerski. N Engl J Med 2022;386:1443-1451.

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TREATMENT OF HYPERCALCEMIA

Identify and treat the underlying disorder

Correct dehydration

- Saline diuresis
- Fluctuations in ionized Ca
- Lasix 2 - 4 mg/kg BID to TID

TREATMENT OF HYPERCALCEMIA

Glucocorticoids
- Cytotoxic
- Decrease GI Ca absorption
- Pros and cons
- 1 - 2 mg/kg/day

Salmon calcitonin
- 4 U/kg IV then 4 - 8 U/kg SC BID

TREATMENT OF HYPERCALCEMIA

When dietary modification and prednisolone are not successful, use of bisphosphonates should be considered. A number of cats have been successfully treated with 10 mg of alendronate (Fosamax) orally once weekly for up to one year. It's extremely important to give the drug on an empty stomach to increase GI absorption of the drug. Erosive esophagitis is a known side effect of oral bisphosphonates in humans, but has not been reported in cats. However, we recommend that the owner give 5–6 ml of water to their cat with a dosing syringe immediately after administration of alendronate; they then can apply a small amount of butter on the cat's lips to increase licking and salivation, which might further promote the transit of the pill to the stomach.

TREATMENT OF HYPERCALCEMIA

Pamidronate is the most commonly used parenteral drug.

The recommended dosage in dogs is 1.0–2.0 mg/kg administered intravenously mixed in 0.9 % saline over 2 hours. Adequate hydration is essential when treating with bisphosphonates since these drugs may cause nephrotoxicity, especially at higher doses.

The drug can be repeated in 3–4 weeks if needed.

Prior dental extraction sites in patients concurrently treated with bisphosphonate medications were often associated with MRONJ lesions. Therefore, any needed dental surgery should be performed prior to the use of bisphosphonates where possible.

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A retrospective case series on bisphosphonate related osteonecrosis of the jaw in 20 cats

Suzanna L. Hatunen[1]*, Jamie G. Anderson[2], Cynthia M. Bell[3], Hugo C. Campos[4], Matthew D. Finkelman[4] and Bonnie H. Shope[1]

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Introduction: This retrospective study highlights the salient aspects of a series of feline patients affected with bisphosphonate related osteonecrosis of the jaw. Though more commonly published in human literature, this presentation is rare in cats. The authors hope that this study will assist in making this a more globally known entity with subsequent improved prognosis.

Methods: Data was retrospectively obtained from the medical records between 2015 and 2021 of 20 cats with Medication Related Osteonecrosis of the Jaw. Data included patient information, clinical history, presenting complaint, systemic diseases, details referable to hypercalcemia and treatment thereof, bisphosphonate specifics (dose and duration), clinical presentation of the lesion, diagnostic testing including radiographic and histopathologic descriptions, treatment, and outcome.

Results: Pertinent results include that all 20 cats who developed Medication Related Osteonecrosis of the Jaw had been treated for idiopathic hypercalcemia with the bisphosphonate medication alendronate. Eighty-five percent of the cases had prior dental extractions at the site of MRONJ lesion. Ninety-five percent of the affected cats required a surgical procedure to control the disease. Thirty-five percent of cases required at least one revision surgery after the initial procedure was performed. Diagnosis of MRONJ was made by a correlation of diagnostic findings and patient history. No single diagnostic, or combination was pathognomonic for lesion diagnosis. As well, there were no statistically significant associations between patient variables assessed and the overall patient outcome.

Discussion: The case series reveals that cats with feline idiopathic hypercalcemia treated with alendronate may be at a risk for development of MRONJ, a serious oral condition with significant morbidity. Prior dental extraction sites in patients concurrently treated with bisphosphonate medications were often associated with MRONJ lesions. Therefore, any needed dental surgery should be performed prior to the use of bisphosphonates where possible. The authors have also included a relevant comparative literature review.

KEYWORDS

bisphosphonate, alendronate, MRONJ, BRONJ, osteonecrosis, jaw, feline, hypercalcemia

PRIMARY HYPERPARATHYROIDISM

Etiology:

Adenomas >>> carcinomas
Hyperplasia (< 8%)

Pathogenesis:

Inappropriate secretion of parathyroid hormone (PTH) by autonomously functioning neoplastic or hyperplastic parathyroid "chief" cells.

Signalment:

>/= 7 yo (1), 11.2yrs (2)
Keeshonds over represented

Few reported cases in the cat.
Siamese overrepresented

CLINICAL SIGNS OF HYPERPARATHYROIDISM

PU/PD

Listlessness, Muscle weakness

Development of renal insufficiency is rare

Gastrointestinal Signs

LUTS attributed to urolithiasis or UTI (stranguria, pollakiuria, hematuria)

PE generally unremarkable

Seizures: one case report

In general, signs are mild to moderate.

DIAGNOSIS

Clinical Signs

CBC

Chemistry Panel

- Calcium [hypercalcemia, elevated iCa]
- Phosphorus [hypophosphatemia]
- Chloride [mild hyperchloremia]
- ALP [possibly mild elevation]

Urinalysis

- Low USG
- UTI

DIAGNOSIS- LOCALIZATION PROCEDURES

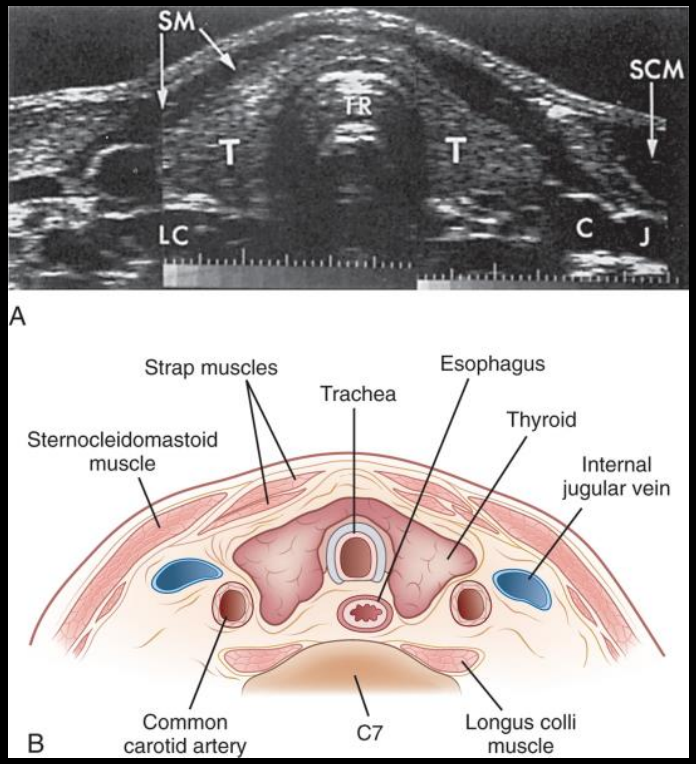
Approximately 10 % of parathyroid tissue is ectopic in location, and furthermore, approximately two thirds of "missed" adenomas are within the thyroid bed.

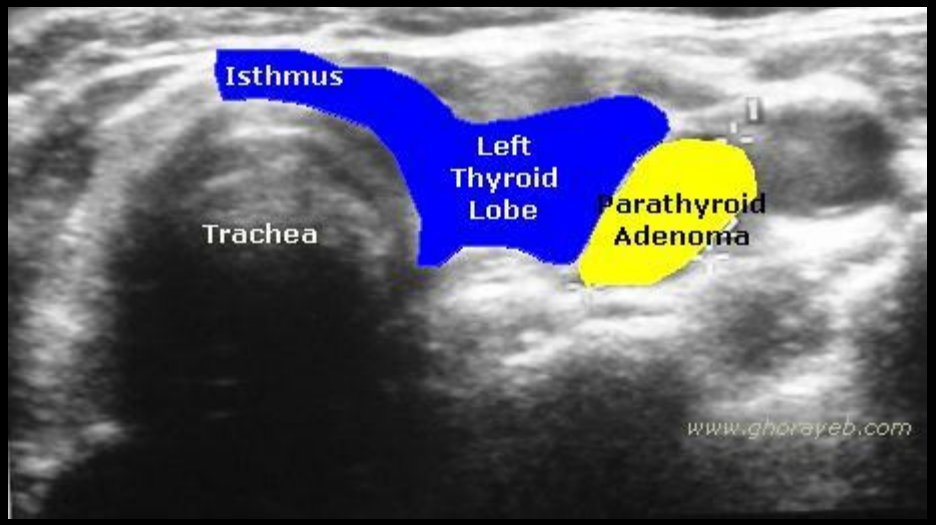
Historically CT, MRI, and US- these modalities are very insensitive for ectopic and mediastinal glands

Angiography and venography with venous sampling for parathormone are cumbersome and invasive

Scintigraphy - Technetium-99m Sestamibi

CERVICAL ULTRASOUND

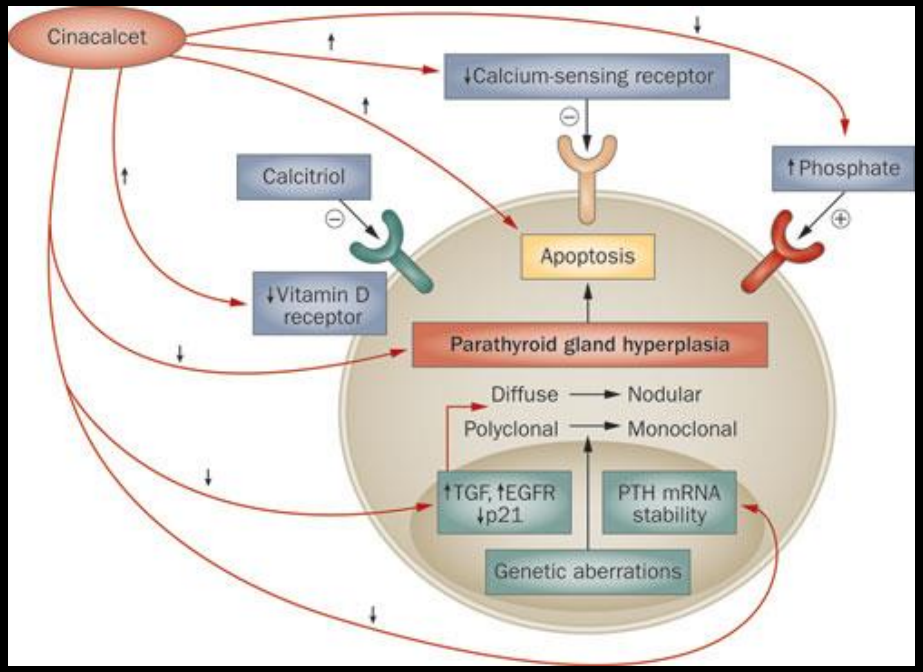


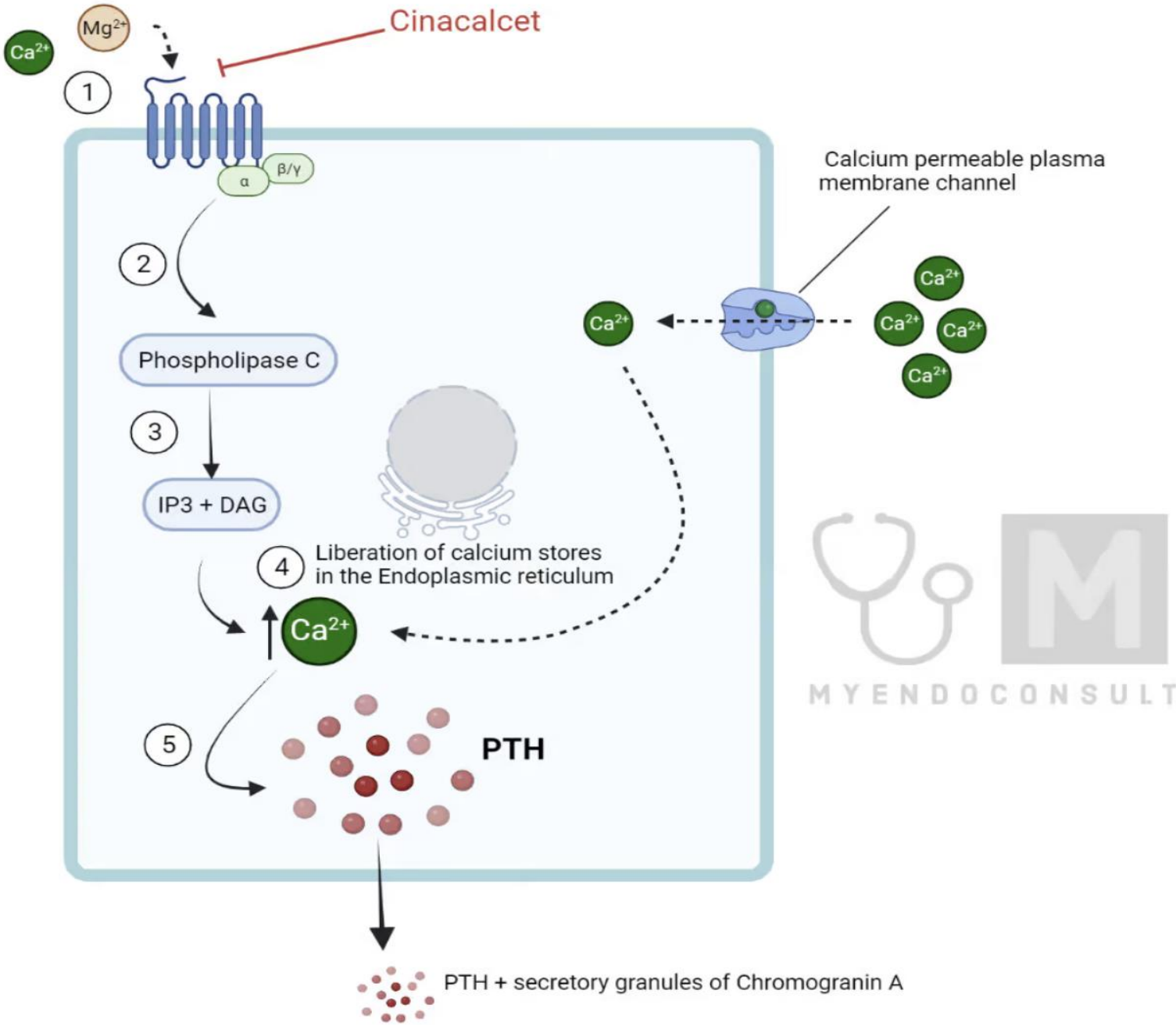


TREATMENT

Medical Options:

To treat or not treat: Discuss the reasons why we treat and reasons why we might tell an owner we don't have to treat.




Cinacalcet
Ca2+
Mg2+
1
α
β/γ
2
Phospholipase C
3
IP3 + DAG
4
Liberation of calcium stores
in the Endoplasmic reticulum
Ca2+
5
PTH
Calcium permeable plasma
membrane channel
Ca2+
Ca2+
Ca2+
Ca2+
Ca2+
PTH + secretory granules of Chromogranin A
MYENDOCONSULT

Research Abstract - Oral | Small Animal Internal Medicine

EN17 - Efficacy and Tolerability of Generic Cinacalcet in Dogs with Primary Hyperparathyroidism

Thursday, June 23, 2022 | 3:45 PM – 4:00 PM CT | Location: ACC 18CD | CE: .25

Research Abstract - Oral Presenter(s)

Heidi Ward, DVM, DACVIM(Oncology)
Clinician
Gulfcoast Veterinary Oncology and Internal Medicine
Sarasota, Florida, United States

Slides | Proceedings/Handout

Abstract: Background: Cinacalcet is approved to treat severe hypercalcemia in humans with primary hyperparathyroidism (PHPT) who are unable to undergo parathyroidectomy. In 2018, generic cinacalcet became available and potentially affordable for veterinary patients. Hypothesis: Cinacalcet will be well-tolerated and effective in the management of hypercalcemia associated with PHPT in dogs. Animals: 14 dogs diagnosed with symptomatic PHPT and ionized calcium values greater than 1.5 mmol/L as measured by the Zoetis iSTAT Alinity. Methods: Cinacalcet was initially dosed at 0.5 mg/kg once daily. Dosages were increased weekly until the iCa fell below 1.45 mmol/L, side-effects developed, or a dose of 10 mg/kg bid was reached. PTH was measured at baseline, and again when the target iCa was achieved. SPSS v24 was used to analyze the data with significance at $p < 0.05$. Results: Mean iCa concentration was 1.74 ± 0.19 mmol/L at baseline and 1.39 ± 0.28 mmol/L post-cinacalcet ($p= 0.033$). PTH levels were 13.68 ±7.35 pmol/L pretreatment and 9.96 ± 7.31 pmol/L post-cinacalcet ($p = 0.194$). With doses ranging from 1 mg/kg every 4 days to 9.4 mg/kg bid, 11 (78%) dogs achieved the target iCa < 1.45 mmol/L. The average number of days dogs remained within target iCa was 33.6 days (7-84). Side-effects were observed in 64% of dogs: lethargy and anorexia (9), vomiting (2), and nonhypocalcemic associated episodes of shaking (3). Conclusion: Cinacalcet was effective in significantly decreasing iCa in dogs with PHPT. However, there was considerable inter-individual variation in dose response, side-effects, and the duration of within-target iCa.

Starting dose is 0.5 mg/kg/day and can titrate upwards every 7-10 days.

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ORIGINAL ARTICLE

JOURNAL OF Veterinary Pharmacology and Therapeutics WILEY

Oral cinacalcet administration decreases serum ionized calcium and parathyroid hormone concentrations in healthy dogs

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Abstract

Cinacalcet is an oral calcimimetic that has potential to non-invasively treat primary hyperparathyroidism in dogs (*Canis lupis familiaris*). There is minimal data assessing its efficacy in dogs. This study aimed to determine whether a single dose of cinacalcet decreases serum ionized calcium (iCa), total calcium (tCa), and parathyroid hormone (PTH) concentrations. Twelve dogs received a median dose of 0.49 mg/kg (range 0.30–0.69 mg/kg) cinacalcet per os. Venous blood samples were collected at time 0 (before cinacalcet administration), 3, 8, and 24 h following cinacalcet administration. PTH, iCa, and tCa concentrations were measured at each time point and compared to 0 hour concentrations. A significant (50%) decrease in serum PTH occurred at 3 h with a median PTH of 4.6 pmol/L (range 2.7–10.8) at baseline and 1.65 pmol/L (range 0.5–14.7) at 3 h; $p = .005$. A significant, but not clinically relevant, decrease in serum iCa from a median baseline of 1.340 mmol/L (range 1.32–1.41) to a 3 h median of 1.325 mmol/L (range 1.26–1.39), $p = .043$, was also observed. tCa concentrations were not different. This study showed that a single dose of cinacalcet leads to transient decreases in iCa and PTH concentrations in healthy dogs.

KEYWORDS
calcium, cinacalcet, hyperparathyroidism, parathyroid, parathyroidectomy

1 | INTRODUCTION

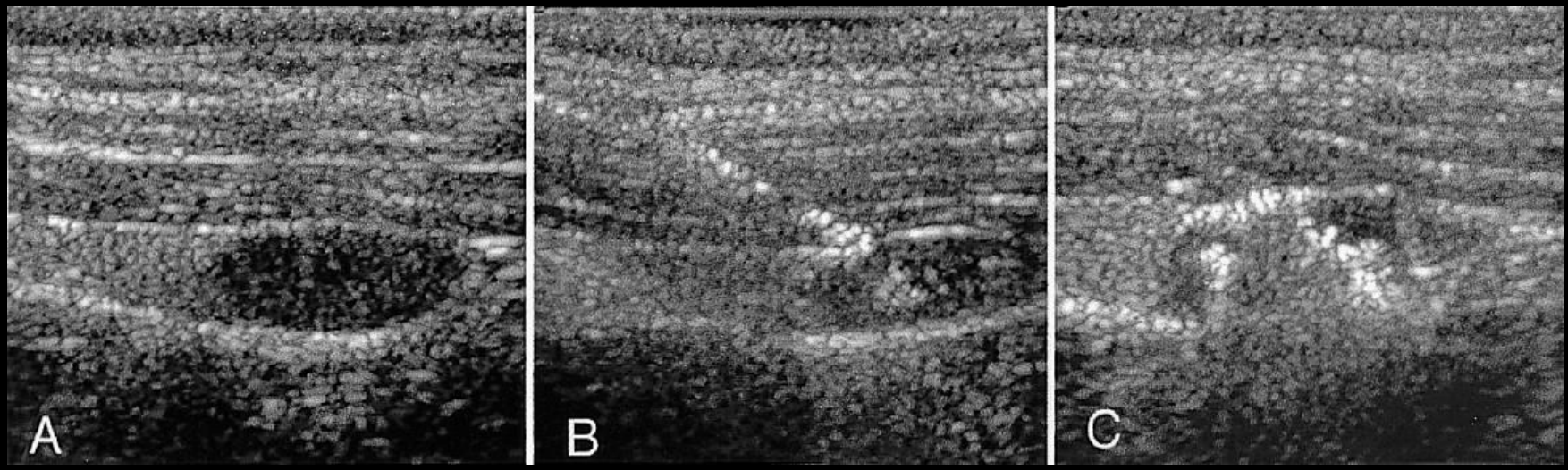
Primary hyperparathyroidism (PHP) is an uncommon endocrine disease that typically affects older dogs (*Canis lupus familiaris*) and leads to hypercalcemia, polyuria, polydipsia, gastrointestinal signs, weakness, urolithiasis, and potentially progressive renal damage (Greco, 2012). Standard treatments for PHP in dogs include surgical parathyroidectomy, percutaneous ultrasound-guided ethanol ablation, or radiofrequency heat ablation. All three options require general anesthesia and post-procedural hospitalization increasing the up-front costs associated with these procedures. Complications can occur including recurrent laryngeal nerve damage and post-procedural hypocalcemia (Bonczynski, 2007; Feldman, 2015; Greco, 2012). Hypercalcemia recurs in 8 to 10% of dogs following surgery (up to 50% in Keeshonds) and in 2%–28% of dogs following ethanol or radiofrequency heat ablation (Bucy et al., 2017; Feldman, 2015; Guttin et al., 2015; Ham et al., 2009; Thompson & Skelly, 2020). Given that 20%–50% of canine PHP patients have subclinical disease (Feldman, 2015; Feldman et al., 2005), the cost associated with the procedures, and the dogs are typically older with co-morbidities, some owners are averse to performing these invasive treatment options. A pharmacologic PHP treatment option could help to manage patients that are not good anesthetic candidates, or whose owners elect to not seek a definitive treatment option.

TREATMENT

Surgery -In experienced hands, surgical removal of an adenoma within the thyroid bed cures the hyperparathyroidism 90% to 95% of the time

Chemical or ethanol ablation

Heat Ablation



COMPLICATIONS OF TREATMENT

Hypocalcemia - Muscle fasiculations, tetany, and seizures, behavior and gait abnormalities

Trauma to recurrent laryngeal nerve

Hemorrhage

Recurrence

RETROSPECTIVE EVALUATION OF THREE TREATMENT METHODS FOR PRIMARY HYPERPARATHYROIDISM IN DOGS

The medical records of 110 dogs treated for primary hyperparathyroidism were reviewed. Dogs were treated via parathyroidectomy (n=47), percutaneous ultrasound-guided ethanol ablation (n=15), or percutaneous ultrasound-guided heat ablation (n=48). Forty-five of 48 (94%) parathyroidectomies resulted in control of hypercalcemia for a median of 561 days. Thirteen of 18 (72%) ethanol ablation procedures resulted in control of hypercalcemia for a median of 540 days. Forty-four of 49 (90%) heat-ablation treatments resulted in control of hypercalcemia for a median of 581 days.

SUMMARY

Think about primary hyperparathyroidism as a differential for hypercalcemia particularly in patients with…

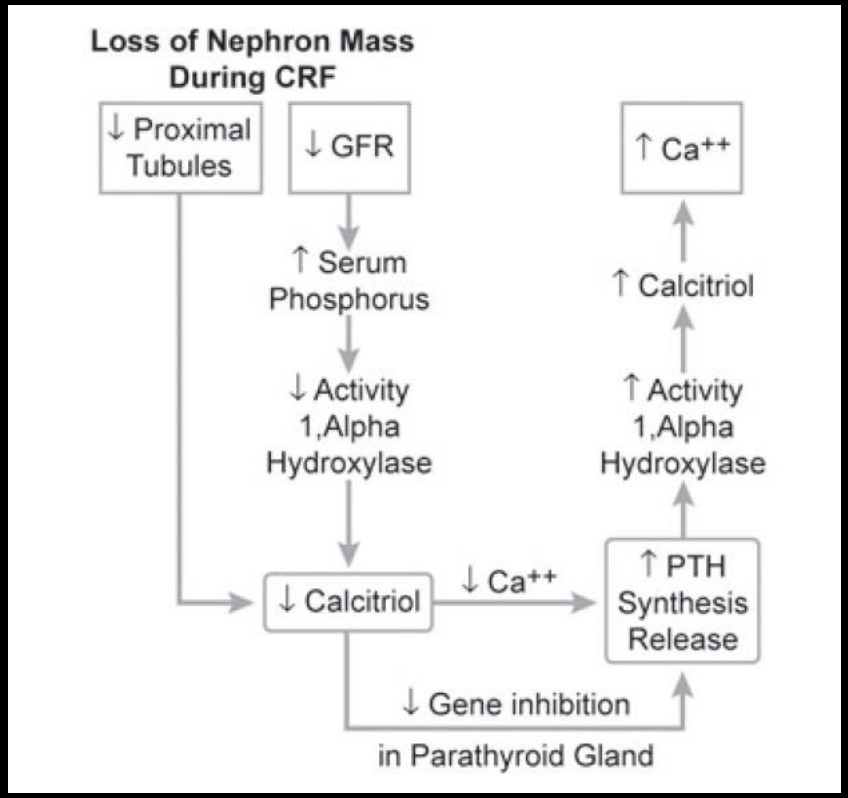
Mild to mod clinical signs

- High Ca, low Phos
- Older dogs, Keeshonds

Diagnosis is based on clinical signs, laboratory data, and imaging of the parathyroid nodule

Treatment options include surgical parathyroidectomy and heat ablation

The most common complication post-procedure is hypocalcemia



Journal of Veterinary Emergency and Critical Care

State of the Art Review

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Calcitriol, calcidiol, parathyroid hormone, and fibroblast growth factor-23 interactions in chronic kidney disease

Joao F. de Brito Galvao, MV, MS, DACVIM; Larry A. Nagode, DVM, MS, PhD; Patricia A. Schenck, DVM, PhD and Dennis J. Chew, DVM, DACVIM

Abstract

Objective – To review the inter-relationships between calcium, phosphorus, parathyroid hormone (PTH), parent and activated vitamin D metabolites (vitamin D, 25(OH)-vitamin D, $1,25(OH)_2$-vitamin D, $24,25(OH)_2$-vitamin D), and fibroblast growth factor-23 (FGF-23) during chronic kidney disease (CKD) in dogs and cats.
Data Sources – Human and veterinary literature.
Human Data Synthesis – Beneficial effects of calcitriol treatment during CKD have traditionally been attributed to regulation of PTH but new perspectives emphasize direct renoprotective actions independent of PTH and calcium. It is now apparent that calcitriol exerts an important effect on renal tubular reclamation of filtered 25(OH)-vitamin D, which may be important in maintaining adequate circulating 25(OH)-vitamin D. This in turn may be vital for important pleiotropic actions in peripheral tissues through autocrine/paracrine mechanisms that impact the health of those local tissues.
Veterinary Data Synthesis – Limited information is available reporting the benefit of calcitriol treatment in dogs and cats with CKD.
Conclusions – A survival benefit has been shown for dogs with CKD treated with calcitriol compared to placebo. The concentrations of circulating 25(OH)-vitamin D have recently been shown to be low in people and dogs with CKD and are related to survival in people with CKD. Combination therapy for people with CKD using both parental and activated vitamin D compounds is common in human nephrology and there is a developing emphasis using combination treatment with activated vitamin D and renin-angiotensin-aldosterone-system (RAAS) inhibitors.

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Keywords: angiotensin-II, calcium, canine, feline, hyperparathyroidism, KLOTHO, phosphorus, RAAS, TACE, vitamin D

Abbreviations

ARB	angiotensin II type 1 receptor blockers
Ang II	angiotensin II
BMP	bone morphogenic protein
CaR	calcium sensing receptor
CKD	chronic kidney disease
CTGF-β	connective tissue growth factor-beta
DHT	dihydrotachysterol
ECF	extracellular fluid
EGFR	epidermal growth factor receptor
EMT	epithelial-to-mesenchymal transition
ERK 1/2	extracellular regulated kinase 1 and 2
FGF-R	fibroblast growth receptor
FGF-23	fibroblast growth factor-23
GFR	glomerular filtration rate
HPTH	hyperparathyroidism
IRIS	International Renal Interest Society
iCa	ionized calcium
MEPE	matrix extracellular phosphoglycoprotein

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The authors declare no conflict of interests.

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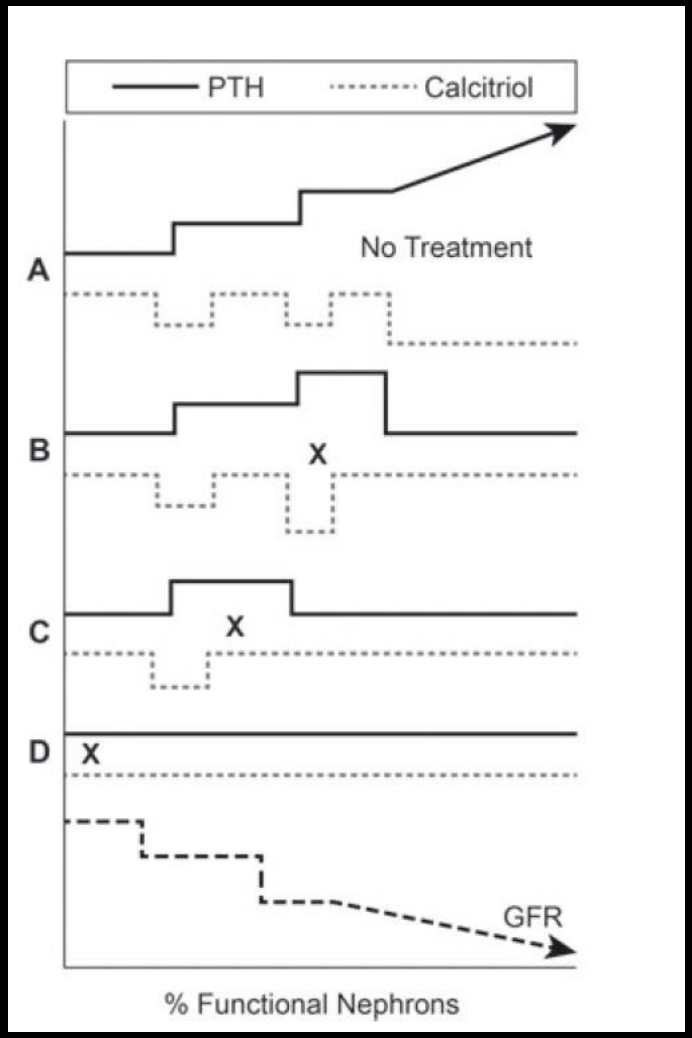

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Calcitriol, calcidiol, parathyroid hormone, and fibroblast growth factor-23 interactions in chronic kidney disease

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