

“Colecalciferol: Além da nutrição vitamínica”

Prof. Dr. Thiago H. A. Vendramini



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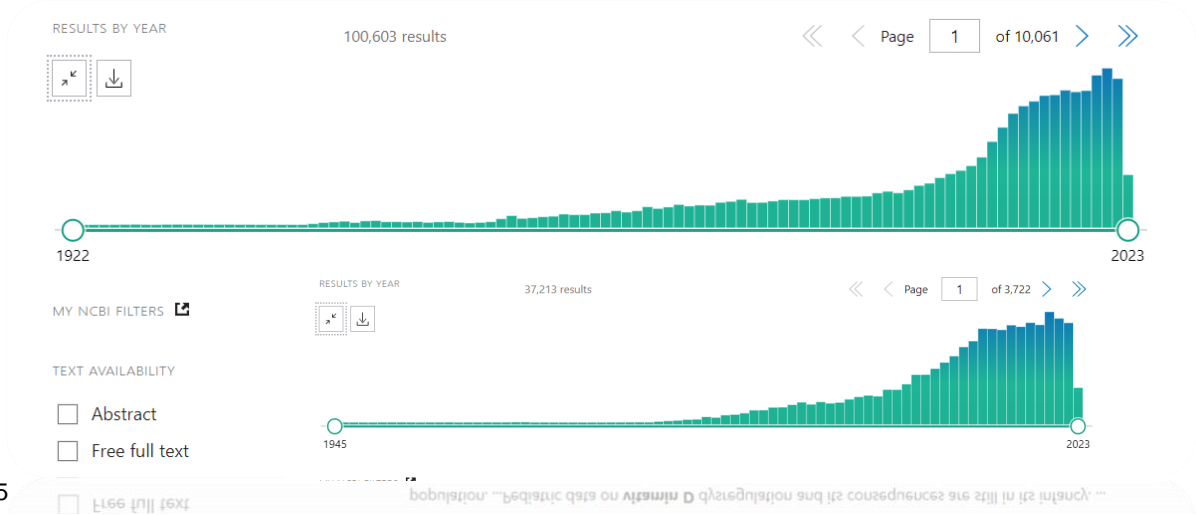
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Vou tentar fazer o meu melhor...

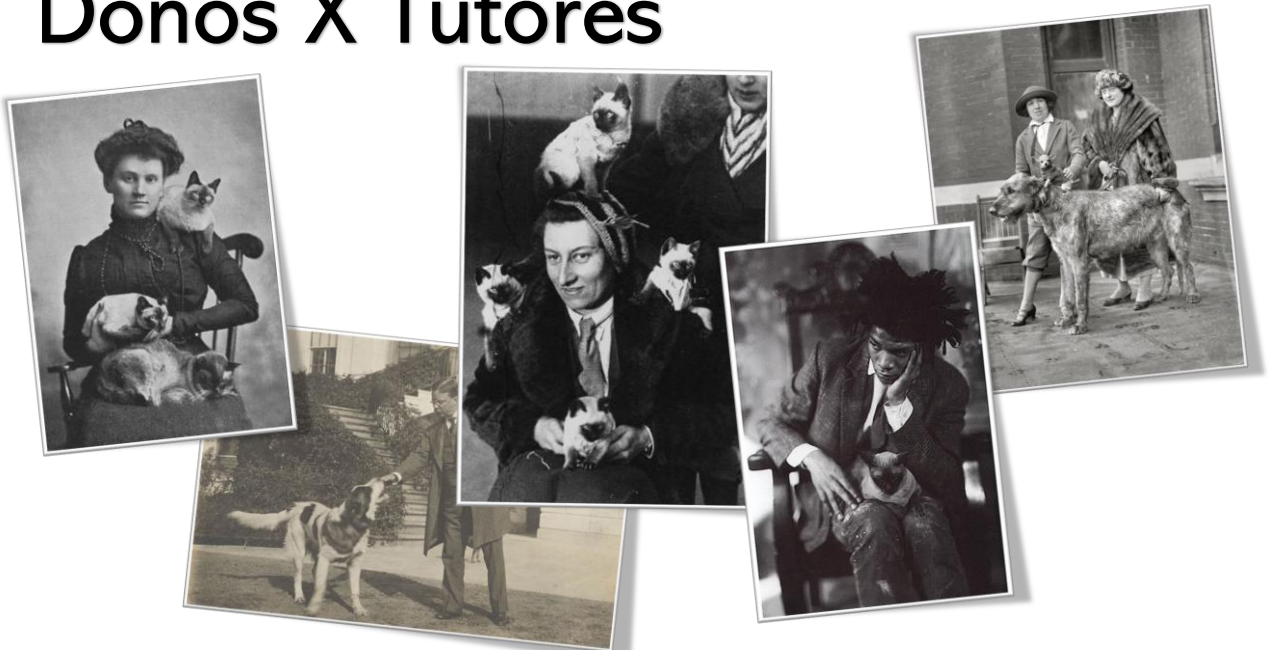


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A queridinha do momento...



Donos X Tutoros



Donos X Tutoros

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CLÍNICA E NUTRIÇÃO

Vitamina D é essencial para os animais e deve se fornecida, diariamente, pela dieta



12 de setembro de 2022

Conhecida pelo seu importante papel na manutenção do cálcio no organismo, Vitamina D está cada vez mais em evidência na Medicina Humana e na Veterinária. Mas, diferentemente dos seres humanos, os pets não conseguem sintetizar a vitamina D por meio da exposição à luz solar, o que faz com que todo o metabolismo desta vitamina dependa de sua ingestão.

É preciso suplementar?

A profissional explica que o nutriente é considerado essencial, ou seja, o pet deve obter por meio da dieta diária, mas que, na maioria dos casos, as dietas comerciais já são enriquecidas com a vitamina em sua formulação. "A atenção para suplementação aos animais saudáveis precisa estar principalmente nos pets que comem comida caseira ou têm a dieta vegetariana ou vegana, já que os pets não conseguem sintetizar a vitamina D2 em D3".

Suplementos de vitaminas para cachorro: veja quando usar com seu pet

O pet precisa de suplementação alimentar equilibrada

Especialistas explicam os benefícios da reposição de vitaminas e nutrientes em cães e gatos e orientam sobre o risco do uso em quantidade excessiva.

Queridinha do momento, vitamina D também é essencial para cães e gatos

Por Irce Falcão
12/03/21 às 07H15 atualizado em 12/03/21 às 07H15

5 suplementos alimentares importantes para cães e gatos

Entenda como os nutracêuticos podem contribuir para a qualidade de vida e o bem-estar do seu pet



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Se vocês tiverem qualquer dúvida, vocês sabem à quem perguntar né?



2021



2020



Calcium, Phosphorus, and Vitamin D in Dogs and Cats Beyond the Bones

Jonathan Stockman, DVM¹, Cecilia Villaverde, BVSc, PhD², Ronald Jan Corbee, DVM, PhD^{1,2*}

KEYWORDS

- Metabolism • Renal • Urinary tract • Gastrointestinal • Cancer

KEY POINTS

- Calcium, phosphorus, and vitamin D have a key role in skeletal development and health as well as other important metabolic functions.
- Insufficient or unbalanced dietary provision of these nutrients can have multiple negative health impacts.
- Excess vitamin D intake may cause hypercalcemia and negative health effects in dogs and cats, and the health-related effects of high calcium and phosphorus intake are being studied.
- The dietary provision of calcium, phosphorus, and vitamin D and their interactions must be considered in patients with renal-urinary diseases.
- The role of vitamin D in chronic conditions, such as enteropathies and neoplasia, is receiving considerable attention, but research is still inconclusive, and no clinical recommendations can be made at this time.

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ADVANCES IN SMALL ANIMAL CARE

Vitamin D in Health and Disease in Dogs and Cats

Ronald Jan Corbee, DVM, PhD, Dipl ECVN
Department of Clinical Sciences, Faculty of Veterinary Medicine, Utrecht University, Yalelaan 106, Utrecht 3584 CM, the Netherlands

KEYWORDS

- Calcitriol • Cholecalciferol • Calcitriol • Canine • Feline

KEY POINTS

- 25-hydroxyvitamin D is not a sensitive indicator of vitamin D status in dogs and cats.
- Food intake and food ingredient analysis are often absent in studies on vitamin D in dogs and cats.
- 1,25-dihydroxyvitamin D is the most potent vitamin D metabolite with the greatest binding affinity to the vitamin D receptor.
- Determination of other vitamin D metabolites rather than 25-hydroxyvitamin D in vitamin D studies will provide better insight in cause-effect relationships.



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REVIEW ARTICLE

WILEY

The Role of Vitamin D in Small Animal Bone Metabolism

Rafael Vescechi Amorim Zafalon 1, Bruna Ruberti 2, Mariana Fragoas Rentas 1, Andressa Rodrigues Amara 3, Thiago Henrique Amabile Vendramini 1, Fernanda Chicharo Chacar 4, Marcia Mery Kogika 5 and Marco Antonio Brunetto 1,*

- 1 Pat Natology Research Center, Nutrition and Production Department, School of Veterinary Medicine and Animal Science, University of São Paulo, Jaridim Elito, Pracaunanga 136/05-900, Brazil; rafael.zafalon@usp.br (R.V.A.); mariana.rentas@usp.br (M.F.R.); thiago.vendramini@usp.br (T.H.A.V.)
2 Small Animal Internal Medicine Service, Veterinary Teaching Hospital, School of Veterinary Medicine and Animal Science, University of São Paulo, Cidade Universitária, São Paulo 05508-270, Brazil; brunaruberti@usp.br (B.R.); mkogika@usp.br (M.M.K.)
3 Veterinary Natology Service, Veterinary Teaching Hospital, School of Veterinary Medicine and Animal Science, University of São Paulo, Cidade Universitária, São Paulo 05508-270, Brazil; andressa.rodrigues.amara@usp.br
4 Department of Internal Medicine, Federal Institute of Education, Science and Technology of South of Minas Gerais, IFSU/LEMINAS, Muzambinho 37890-000, Brazil; fernanda.chacar@fzsu.ifsu.edu.br
5 Correspondence: mabrunetto@usp.br; Tel.: +55-19-3565-4226

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Abstract: Dogs and cats have differences in vitamin D metabolism compared to other mammalian species, as they are unable to perform vitamin D cutaneous synthesis through sun exposure. Therefore, they are dependent on the dietary intake of this nutrient. The classic functions of vitamin D are to stimulate intestinal calcium and phosphate absorption, renal calcium and phosphate reabsorption and regulate bone mineral metabolism. Thus, it is an important nutrient for calcium and phosphorus homeostasis. This review highlights the evidence of the direct and indirect actions of vitamin D on bone mineral metabolism, the consequences of nutritional imbalances of this nutrient in small animals, as well as differences in vitamin D metabolism between different size dogs.

Keywords: 1,25(OH)2D3; 25(OH)D; calcium; cat; dog; nutrition; osteomimetic homeostasis; phosphate

1. Introduction

Vitamin D is an essential nutrient for dogs and cats since they are unable to synthesize vitamin D3 through skin sun exposure; thus, it is essential that they receive this nutrient in their diet [1,2]. Vitamin D has two nonactive forms in nature: cholecalciferol or vitamin D2, and ergocalciferol or vitamin D2. After ingestion, vitamin D undergoes a multistep enzymatic conversion until conversion to an active vitamin known as 1,25-dihydroxyvitamin D (1,25(OH)2D3) [3]. After activation, vitamin D binds to the vitamin D receptor (VDR), a representative receptor for the steroid receptors family, which mediates its biological functions [4] that go beyond the traditional role of calcium and phosphate homeostasis [5].

Regarding bone metabolism vitamin D functions, calcitriol target organs are intestine, kidneys, bone tissue and the parathyroid gland [6,7]. In the intestine, calcitriol acts on transcellular and passive paracellular calcium transport besides phosphate absorption [8,9]. In the kidneys, calcitriol stimulates renal calcium and phosphate reabsorption. Finally, calcitriol acts in the parathyroid gland regulating parathyroid hormone (PTH) secretion. All these functions can indirectly regulate bone growth and mineralization. In addition, it is known that both osteoblasts and chondrocytes express the enzyme

School of Veterinary Medicine and Animal Science, University of São Paulo, São Paulo, Brazil

Correspondence: Marco A. Brunetto, School of Veterinary Medicine and Animal Science, University of São Paulo, São Paulo, Brazil. Email: mabrunetto@usp.br

Abstract

Due to the presence of receptors in the cells of numerous body tissues, vitamin D is associated with several physiological functions that go beyond calcium and phosphorus homeostasis and control of bone metabolism in the body. In humans, several studies have associated lower vitamin D concentrations with numerous diseases, such as cancer, heart disease, autoimmune diseases and infectious diseases, and also with an increase in the total mortality rate of the population. Recently, this nutrient started to gain importance in veterinary medicine, and several articles have shown a correlation between low vitamin D status and diseases unrelated to bone metabolism. The present review aims to highlight the recent publications that investigated this relationship, bringing the evidence that exists so far in dogs and cats.

KEYWORDS

1,25(OH)2D3; 25(OH)D; calcitriol; calcitriol; cholecalciferol; hypovitaminosis D

1 | INTRODUCTION

The effects of vitamin D as an important regulator of bone metabolism and calcium homeostasis have been well known for almost 100 years (McCollum, Simmons, Becker, & Shipley, 1922). For a long time, this was believed to be the only role of this vitamin in the metabolism of humans and animals. However, after the discovery of vitamin D receptors (VDR) in various human immune cells (Provedini, Tsoukas, Delfino, & Manolagas, 1983), research into the pleiotropic effects of vitamin D intensified, and it was discovered that cells of almost all body tissues express VDR. This receptor is believed to be directly or indirectly involved in the regulation of about 2,000 genes, which correspond to almost 10% of the human genome (Ramagopalan et al., 2010).

In human medicine, although the cause and effect relationship is not proven, the relationship between vitamin D status and diseases unrelated to bone metabolism has been extensively studied in recent years, and lower vitamin D concentrations has been associated with increased cancer incidence (Djurastinovic et al., 2018; Yin & Amin, 2019; Anon. Nat., 2019-001-21).

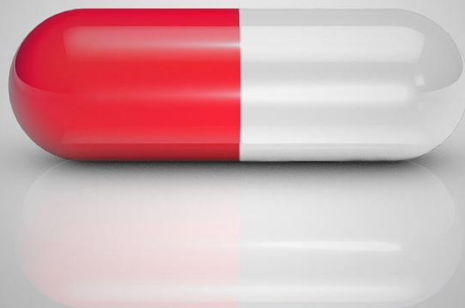
et al., 2013); cardiovascular diseases, such as myocardial infarction (Giovannucci, Liu, Holm, & Rimm, 2008), stroke and heart failure (Chowdhury et al., 2012; Muzocquliri et al., 2017), as well as autoimmune diseases (e.g., diabetes mellitus type I) (Pudowski et al., 2013), multiple sclerosis (Martiniello et al., 2014), rheumatoid arthritis (Kerr et al., 2011) and infectious diseases (White, 2008).

The relationship of vitamin D (D status and diseases) has also been investigated in dogs and cats, and some studies found association between low vitamin D status and some types of cancer (Selting, Sharp, Ringold, Thamm, & Backus, 2010; Wackling et al., 2011; Weisner et al., 2017), congestive heart failure (Witas et al., 2014; Ouga et al., 2015), gastrointestinal diseases (Allenspach, Rizzo, Jergens, & Chang, 2017; Gow et al., 2011; Lator et al., 2014; Tienarsh, Gow, Kilpatrick, Cartwright, et al., 2015; Tienarsh, Gow, Kilpatrick, Sinclair, et al., 2015), acute pancreatitis (Kim et al., 2017), acute polyradiculoneuritis (Lawa, Kalthani, Harcourt-Brown, Granger, & Rose, 2018), chronic kidney disease (Cortadellas, Fernandez del Palacio, Talavera, & Bayón, 2010; Galler et al., 2012; Parker, Hässig, & Reusch, 2003; Gerber, Hauser, & Reusch, 2004; Parker, Hässig, et al., 2017) and

11 Metabolites 2020, 10, 496. doi:10.3390/metabol10120496

www.mdpi.com/journal/metabolites

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Introdução

Vamos apenas lembrar...

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Introdução

Cães e gatos apresentam diferenças no metabolismo da vitamina D em relação a outras espécies de mamíferos

Incapazes de realizar a síntese cutânea de vitamina D por meio da exposição solar

Acredita-se - consumo de presas que armazenam a vitamina D3 no fígado e no tecido adiposo

Portanto - dependentes da ingestão dietética desse nutriente

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Introdução

As funções clássicas da vitamina D

- Estimular a absorção intestinal de cálcio e fosfato
- Reabsorção renal de cálcio e fosfato
- Regular o metabolismo mineral ósseo

Assim, é um nutriente importante para a homeostase do cálcio e do fósforo

Mas não somente...

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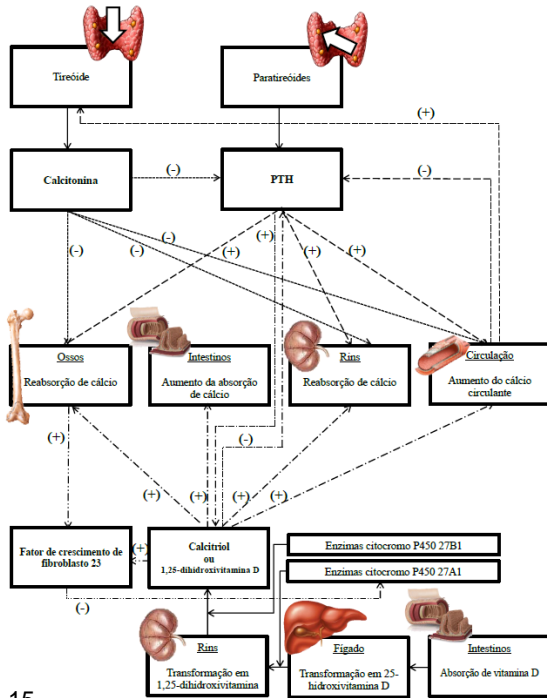


Figura 01. Metabolismo básico do cálcio em cães e gatos e sua regulação hormonal da homeostase. *Feedback* positivo (+) é indicado pelo tracejado. *Feedback* negativo (-) é indicado pelas linhas contínuas. Relação de transporte e atuação é indicado pelo pontilhado

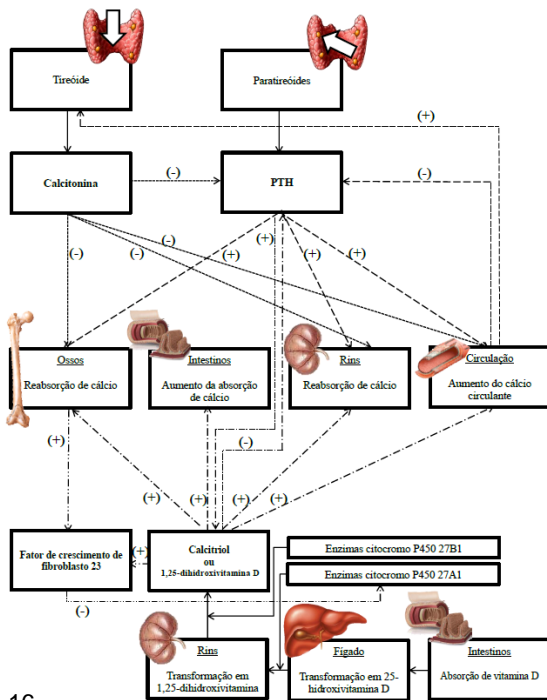
A vitamina D tem duas formas inativas na natureza:

- Colecalciferol ou vitamina D3
- Ergocalciferol ou vitamina D2

Após a ingestão

A vitamina D sofre uma conversão enzimática em várias etapas até a conversão em uma vitamina ativa conhecida como 1,25-di-hidroxicitriol (1,25(OH)₂D) - calcitriol

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Após a ativação, a vitamina D se liga ao receptor de vitamina D

Um receptor representativo da família dos receptores de esteróides, que medeia suas funções biológicas

Vão além do papel tradicional da homeostase de cálcio e fósforo

Em relação às funções da vitamina D no metabolismo ósseo, os órgãos-alvo do calcitriol são:

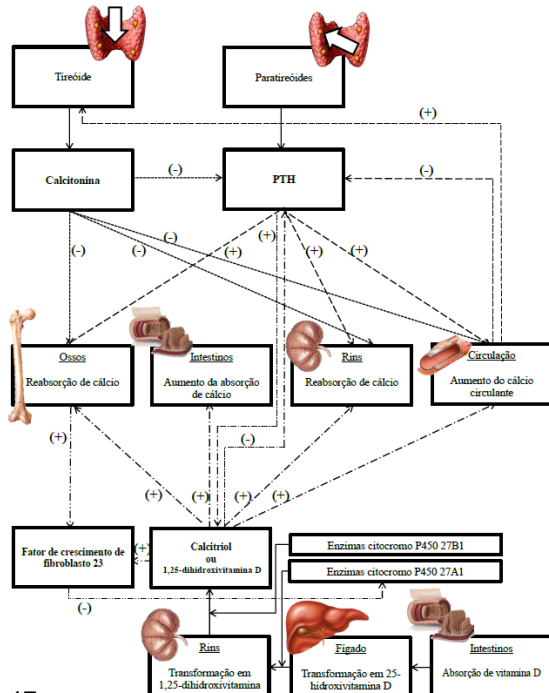
- Intestino
- Rins
- Tecido ósseo
- Glândula paratireoide

No intestino, o calcitriol atua no transporte transcelular e paracelular passivo de cálcio, além da absorção de fosfato

Nos rins, o calcitriol estimula a reabsorção renal de cálcio e fosfato

Na glândula paratireoide regulando a secreção do paratormônio (PTH)

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Todas essas funções podem indiretamente regular o crescimento ósseo e a mineralização

Além disso, sabe-se que tanto os osteoblastos quanto os condrócitos expressam a enzima 1- α -hidroxilase e VDR

Foi demonstrado que a vitamina D pode atuar diretamente no crescimento e mineralização óssea, bem como na remodelação óssea

Alimentos comerciais completos e balanceados, houve uma diminuição no diagnóstico de casos de deficiência de vitamina D... comum no passado

No entanto...

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Tratado de **Ortopedia de Cães e Gatos** Volume I

Bruno Watanabe Minto
Luís Gustavo Goussen Gonçalves Dias

Editora MedVet

56 **Osteoartropatias Nutricionais**

Marcos Antonio Brunetto
Thiago Henrique Anísio Vendramini

INTRODUÇÃO

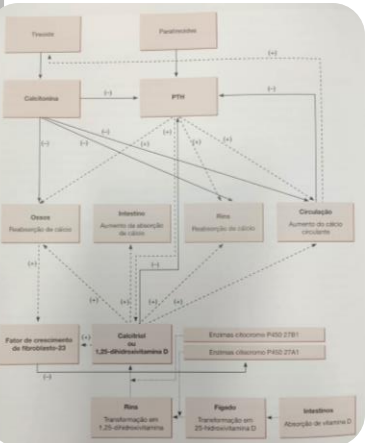
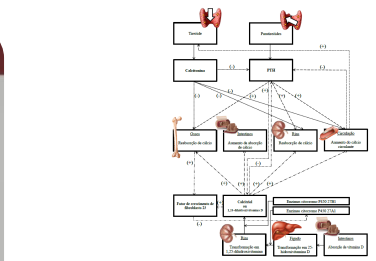
As lesões osteoartropatias induzidas em um indivíduo podem resultar em quadros de limitação funcional grave e gravidade variável, de acordo com o segmento corporal afetado e o tipo de lesão apresentada. A associação está intimamente ligada a erros genéticos e tem sua origem tanto no surgimento, aproximadamente na sexta semana de desenvolvimento, podendo reverter e progredir e melhorar a qualidade de vida dos pacientes com doença de um indivíduo.

Osteoartropatia nutricional é definida como qual quer alteração degenerativa óssea e articular que tem como causa de base a má nutrição do paciente.

Pouco se conhece de nutrição óssea se comparado aos demais tecidos. Em tempos não tão remotos, o desenvolvimento do alimento comercial para cães e gatos era imprevisível, sobras de consumo humano e os resíduos de animais abatidos faziam parte do cardápio de alimentação dos animais de companhia e a consequente falta de substâncias e deficiências de proteínas, por exemplo, rapidamente, foi percebido que os animais apresentavam alterações estruturais em seus ossos e acompanhadas de sinais de má nutrição do período.

Após a Segunda Guerra Mundial diversos estudos em alimentação, desenvolvimento alimentar, controle para animais de companhia e desde então, o desenvolvimento de tal alimento, completo e balanceado, representa a principal forma de consumo alimentar. Acompanhando essa mudança as nutrições veterinárias necessariamente por deficiências foram realizadas, porém o aumento da ligação de alimentos comestíveis e os animais, aliados ao aumento de proteínas, desenvolvimento dos animais, por exemplo, desenvolvimento dos ossos e artropatias, a osteoartropatia nutricional (Osteoartropatia Nutricional) é considerada.

Atualmente, nos últimos anos, a preferência por alimentos comerciais, orgânicos ou naturais, a redução de aditivos e possíveis contaminantes das dietas comerciais e o desejo de controlar para um pet são fatores



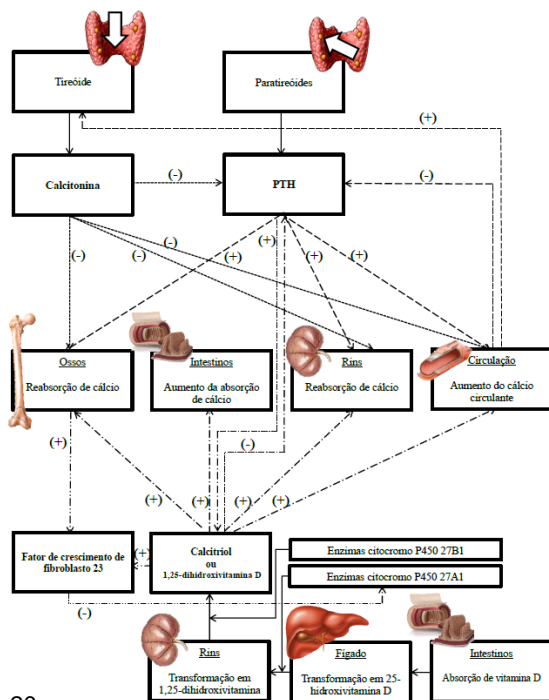
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Absorção

Incorporar, assimilar...

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Após a ingestão, tanto o colecalciferol quanto o ergocalciferol são absorvidos em um processo que depende de enzimas digestivas, ácidos biliares e quilomícrons

Após a absorção, o colecalciferol e/ou ergocalciferol são transportados através dos vasos linfáticos intestinais e do sistema portal

Ligados a uma glicoproteína até o fígado onde sofrem um processo de hidroxilação no Carbono 25

Pode ocorrer por meio de enzimas da família do citocromo P450 e também conhecidas como 25-hidroxilases, formando 25-hidroxivitamina D (25(OH)D) ou calcidiol

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Além da nutrição vitamínica

Se o animal apresentar altas concentrações circulantes de calcidiol, o colecalciferol absorvido pode ser armazenado no tecido adiposo e, em menor extensão, no tecido muscular, ao invés de ser transportado para hidroxilação no fígado

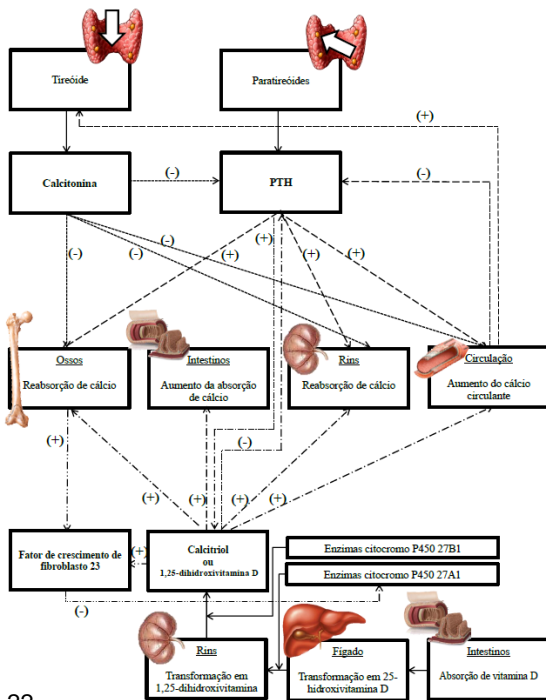


Os cães convertem ergocalciferol em calcidiol, bem como em colecalciferol

No entanto, os gatos usam colecalciferol - tipo de alimentação durante o processo evolutivo

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Após a síntese hepática, o calcidiol é transportado para os túbulos renais proximais

Onde sofre um processo de hidroxilação no carbono 1 (1- α -hidroxilase) através de uma enzima mitocondrial da família CYP450

Dando origem a 1,25 dihidroxivitamina D [1,25(OH)₂D] ou calcitriol

O metabólito ativo da vitamina D que realiza todas as suas ações hormonais conhecidas

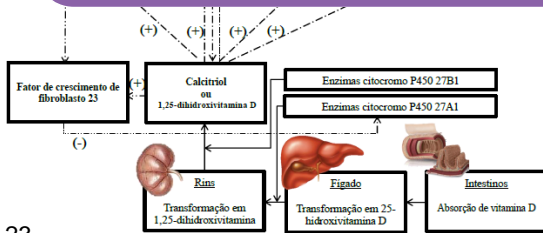
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Além da nutrição vitamínica

Vale ressaltar que a síntese renal é a grande responsável pelo calcitriol circulante

No entanto, foi demonstrado em humanos que vários outros tecidos expressam 1- α -hidroxilase (catalisa a hidroxilação de 25(OH)D), incluindo mama, glândula paratireoide, cólon, próstata, células beta-pancreáticas, placenta, cérebro, células imunes, células endoteliais e queratinócitos



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From vitamin D to hormone D: fundamentals of the vitamin D endocrine system essential for good health¹⁻⁴

Anthony W Norman

ABSTRACT

New knowledge of the biological and clinical importance of the steroid hormone 1 α ,25-dihydroxyvitamin D₃ [1,25(OH)₂D₃] and its receptor, the vitamin D receptor (VDR), has resulted in significant contributions to good bone health. However, worldwide reports have highlighted a variety of vitamin D insufficiency and deficiency diseases. Despite many publications and scientific meetings reporting advances in vitamin D science, a disturbing realization is growing that the newer scientific and clinical knowledge is not being translated into better human health. Over the past several decades, the biological sphere of influence of vitamin D₃, as defined by the tissue distribution of the VDR, has broadened at least 9-fold from the target organs required for calcium homeostasis (intestine, bone, kidney, and parathyroid). Now, research has shown that the pluripotent steroid hormone 1,25(OH)₂D₃ initiates the physiologic responses of 236 cell types that possess the VDR. In addition to the kidney's endocrine production of circulating 1,25(OH)₂D₃, researchers have found a paracrine production of the steroid hormone in 210 extrarenal organs. This article identifies the fundamentals of the vitamin D endocrine system, including its potential for contribution to good health in 3 physiologic arenas in which investigators have clearly documented new biological actions of 1,25(OH)₂D₃ through the VDR. As a consequence, the nutritional guidelines for vitamin D₃ intake (defined by serum hydroxyvitamin D₃ concentrations) should be reevaluated, taking into account the contributions to good health that all 36 VDR target organs can provide. *Am J Clin Nutr* 2008;88(suppl):915-38.

INTRODUCTION

Vitamin D₃ is essential for life in higher animals. Research has shown, for example, that vitamin D₃ is one of the primary biological regulators of calcium homeostasis. Vitamin D₃'s important biological effects occur only as a consequence of its metabolism into a family of daughter metabolites, including the key kidney-produced metabolite 1,25-dihydroxyvitamin D₃ [1,25(OH)₂D₃]. Researchers consider 1,25(OH)₂D₃ to be a steroid hormone and believe that it functions the same way as other steroid hormones—by interacting with its cognate vitamin D receptor (VDR) (1).

The role of vitamin D₃ as a vitamin or essential dietary component, in concert with the biological and clinical importance of the steroid hormone 1,25(OH)₂D₃ and the VDR, has achieved increasing prominence over the past 3 to 4 decades in the public health arena because of its contribution to good health in the general public. However, despite the plethora of publications and scientific meetings focusing on advances in vitamin D science, there is the disturbing realization that all too "swift" with the translation of the newer

scientific and clinical knowledge into the achievement of better health. Scientists and nutrition experts at the 13th Vitamin D Workshop held in 2006 agreed in a consensus statement that "about half of the elderly in North America and two-thirds of the rest of the world are not getting enough vitamin D to maintain healthy bone density, lower their risks for fracture and improve tooth attachment. Such vitamin D insufficiency also decreases muscle strength and increases the risk for falls and is even associated with increased risk for colorectal and other major cancers" (2).

SOURCES OF VITAMIN D

Vitamin D is not technically a vitamin, i.e., it is not an essential dietary factor; rather, it is a prohormone produced photochemically in the skin from 7-dehydrocholesterol. The molecular structure of vitamin D is closely allied to that of classic steroid hormones (e.g., estradiol, cortisol, and aldosterone) in that they have the same most cyclopentanoperhydrophenanthrene ring structure. Technically, vitamin D is a secosteroid because one of the rings of its cyclopentanoperhydrophenanthrene structure has a broken carbon-carbon bond; in vitamin D₃, this occurs in the 9,10 carbon-carbon bond of ring B (Figure 1). Given that fact as a starting point, the reader must have access to some of the details of the sunlight-mediated photochemical conversion of 7-dehydrocholesterol into vitamin D₃; this information is provided in Figure 1.

The skin produces vitamin D₃ photochemically from the previtamin D₃ 7-dehydrocholesterol, which is present in the epidermis or skin of higher animals, by the action of sunlight in most geographical locations or of artificial UV light. The conjugated double-bond system in ring B (see Figure 1) allows the absorption of light quanta at

¹From the Department of Biotechnology and Division of Biomedical Sciences, University of California, Riverside, CA.

²Presented at the National Institutes of Health conference "Vitamin D: Past, Present, and Future," held in Bethesda, MD, September 5-6, 2007.

³Supported by NIH grant DK 09121-04.

⁴Reprinted in part. Address correspondence to AW Norman, Department of Biotechnology, University of California, Riverside, CA 92521. E-mail: anthony.norman@ucr.edu.

Além da nutrição vitamínica

Embora o calcitriol seja o metabólito ativo, o status da vitamina D é avaliado medindo as concentrações circulantes de calcidiol

Pois tem uma meia-vida biológica longa, variando de 10 dias a três semanas, enquanto a meia-vida biológica do calcitriol varia de três a seis horas

Além disso, o calcidiol circula em concentrações cerca de 1000 vezes maiores que o calcitriol

Vale ressaltar também que o calcitriol tem natureza mais hidrofóbica, o que dificulta sua mensuração além de ser menos estável



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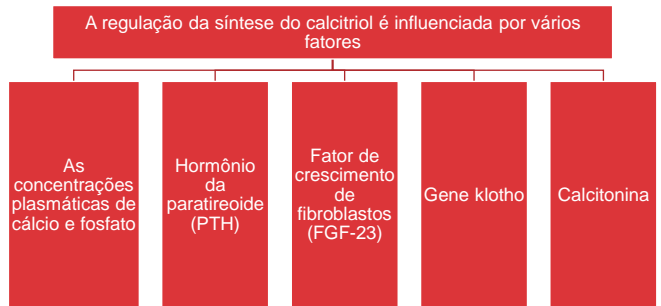
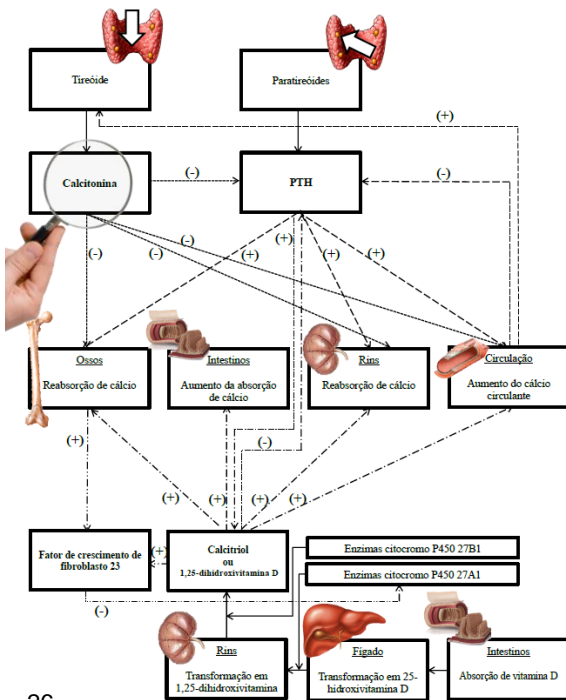
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Regulação

Controle ou descontrole

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Em condições hipocalcêmicas, há aumento da liberação de PTH, que pode estimular diretamente a atividade da 1- α -hidroxilase

Em condições normocalcêmicas, a calcitonina atua na manutenção das concentrações séricas de calcitriol, induzindo a transcrição da 1- α -hidroxilase nas células renais

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Regulação

A enzima 24-hidroxilase é responsável pelo catabolismo da vitamina D

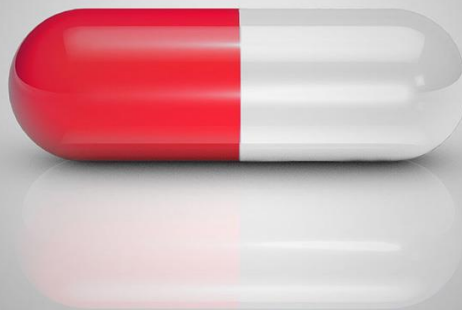
Esta enzima mitocondrial é encontrada principalmente nos túbulos renais proximais, mas também é expressa no intestino, queratinócitos, fibroblastos, linfócitos e macrófagos

Alto fósforo sérico - aumento da síntese e liberação do FGF-23, importante peptídeo produzido pelos osteoblastos e principalmente pelos osteócitos, com ação hipofosfatêmica, de modo que estimula a excreção renal de fósforo, aumenta a atividade da 24-hidroxilase, diminuindo a atividade da 1- α -hidroxilase

A regulação da síntese de calcitriol também é afetada por uma proteína transmembranar chamada Klotho, que é um co-receptor obrigatório e necessário para que o FGF-23 se ligue ao seu receptor

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Recomendações

É preciso saber o mínimo...

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As recomendações mínimas e máximas de colecalciferol para cães e gatos de acordo com o

- National Research Council (NRC)
- European Pet Food Industry Federation (FEDIAF)
- Association of American Feed Control Officials (AAFCO)

Item	Mínimo		Máximo	
	Cães	Gatos	Cães	Gatos
NRC (2006) (UI/Mkcal)	110 ^a /136 ^b	56 ^a /70 ^b	800	7520
FEDIAF (2021) (UI/Mkcal)	138 ^c /159 ^d	62,5 ^e /83,3 ^f	800	7500
AAFCO (2018) (UI/Mkcal)	125	70	750	7520

a Ingestão adequada; b Quantidade recomendada; c 110 kcal (kg de peso corporal)^{0,75} na alimentação; d 95 kcal (kg de peso corporal)^{0,75} na alimentação; e 100 kcal (kg de peso corporal)^{0,67} na alimentação; f 75 kcal (kg de peso corporal)^{0,67} na alimentação.

Item	Mínimo		Máximo	
	Cães	Gatos	Cães	Gatos
NRC (2006) (UI/Mkcal)	110 ^a /136 ^b	- ^a /56 ^b	800	7520
FEDIAF (2021) (UI/Mkcal)	125 ^c /138 ^d	70	800	7500
AAFCO (2018) (UI/Mkcal)	125	70	750	7520

a Ingestão adequada; b Quantidade recomendada; c 110 kcal (kg de peso corporal)^{0,75} na alimentação; d 95 kcal (kg de peso corporal)^{0,75} na alimentação; e 100 kcal (kg de peso corporal)^{0,67} na alimentação; f 75 kcal (kg de peso corporal)^{0,67} na alimentação.

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Recomendações



2020

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ADVANCES IN SMALL ANIMAL CARE

Vitamin D in Health and Disease in Dogs and Cats

Ronald Jan Corbes, DVM, PhD, Dipl. ECVIM
Department of Clinical Sciences, Faculty of Veterinary Medicine, Utrecht University, Yalelaan 101, Utrecht 3584 CM, The Netherlands

KEYWORDS
• Calcitriol • Cholecalciferol • Calcitriol • Canine • Feline

KEY POINTS
• 25-hydroxyvitamin D is not a sensitive indicator of vitamin D status in dogs and cats.
• Food intake and food ingredient analysis are often absent in studies on vitamin D in dogs and cats.
• 1,25-dihydroxyvitamin D is the most potent vitamin D metabolite with the greatest binding affinity to the vitamin D receptor.
• Determination of other vitamin D metabolites rather than 25-hydroxyvitamin D in vitamin D studies will provide better insight in cause-effect relationships.

TABLE 1
Nutritional Requirements of Vitamin D for Dogs and Cats

	Puppies Minimum	Adult Dogs Minimum	Dogs Maximum
AAFCO	500/125/29.9	500/125/29.9	3000/750/179
FEDIAF	552/138/33	639/159/38	2270 ^a /800/191
NRC	552/136/32.5	552/136/32.5	3200/800/191
	Kittens Minimum	Adult Cats Minimum	Cats Maximum
AAFCO	280/70/16.7	280/70/16.7	30,080/7520/1798
FEDIAF	280/70/16.7	333/83.3/19.9	2270 ^a /7500/1793
NRC	224/56/13.4	280/70/16.7	30,000/7500/1793

Data are expressed as amounts of vitamin D3 in IU per kg dry matter/1000 kcal metabolizable energy (ME)/MJ ME, respectively.

Abbreviations: AAFCO, Association of American Feed Control Officials; FEDIAF, Fédération Européenne de l'Industrie des Aliments pour Animaux Familiers; NRC, National Research Council.

^a FEDIAF has defined a legal maximum for vitamin D, on dry matter basis only.

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Recomendações

Início em 1918 por Mellanby et al...

1939 por Arnold e Elvehjem

No entanto, foi apenas em 1944 que a primeira recomendação de vitamina D para cães foi proposta...

Poucos estudos investigaram as necessidades de vitamina D para cães e gatos

Todos esses estudos foram realizados em filhotes

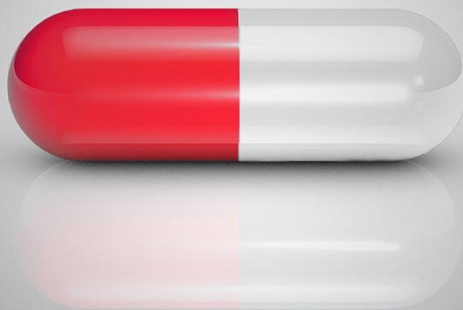
Pois a demanda por calcificação esquelética é maior nessa fase da vida e os animais em crescimento são mais sensíveis a dietas deficientes em vitamina D

Recomendações são baseadas em estudos de animais em crescimento



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Deficiência

Problemas de longo prazo...

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Deficiência

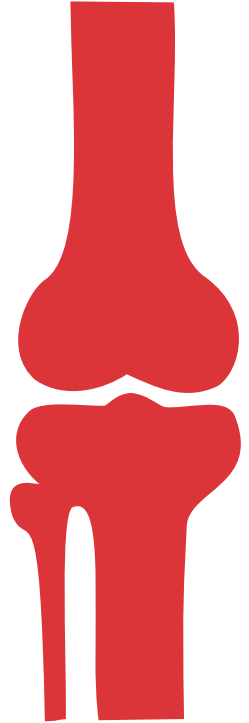
A deficiência de vitamina D pode ser causada pelo metabolismo anormal da vitamina D relacionado a **anormalidades congênitas** devido a mutações genéticas, bem como pela **ingestão de dietas desbalanceadas**

Alimentos comerciais completos e balanceados - diminuição no diagnóstico de casos de deficiência de vitamina D

No entanto - alimentos caseiros para animais de estimação, risco crescente de hipovitaminose D

Pode resultar em hipocalcemia e hipofosfatemia e, conseqüentemente, pode resultar em doença óssea caracterizada por mineralização óssea prejudicada associada a raquitismo ou osteomalacia

Além disso, a deficiência dietética de vitamina D pode resultar em hiperparatireoidismo secundário nutricional direto e indireto



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Deficiência

O raquitismo nutricional foi relatado em cães jovens e gatos, embora esta doença seja considerada rara

No entanto, o raquitismo pode ser causado por um erro inato no metabolismo da vitamina D em cães e gatos

O raquitismo dependente de vitamina D tipo I (VDDR-I) - é um distúrbio autossômico recessivo causado pela deficiência da enzima renal

O raquitismo tipo II dependente de vitamina D (VDDR-II) - resistência do órgão-alvo ao calcitriol e geralmente é um defeito secundário no gene que codifica o receptor



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Deficiência

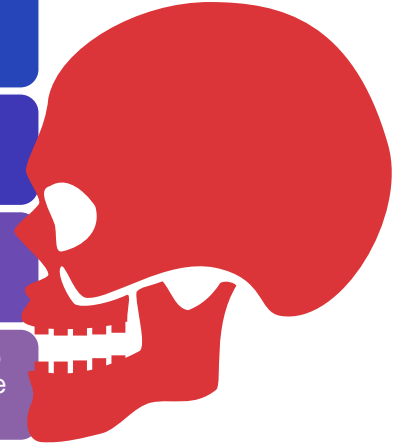
A incapacidade de detectar dor óssea e a insensibilidade das radiografias - condição pode ser subdiagnosticada

Em humanos, a incidência desta doença permanece amplamente subestimada em todo o mundo também

Proeminentes nos ossos longos nos locais de rápido crescimento

Fraturas são extremamente comuns, além de fraqueza muscular em pacientes idosos

O tratamento deve ser revertido por suplementação de vitamina D, o cálcio também é útil particularmente naqueles com ingestão pobre de cálcio



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Hiperparatireoidismo Secundário Nutricional

A deficiência de vitamina D na dieta pode resultar direta e indiretamente

O mRNA do receptor de calcitriol é altamente expresso na glândula paratireoide, de modo que a vitamina D também influencia diretamente a secreção de PTH

A baixa ingestão de vitamina D resulta em diminuição das concentrações circulantes de calcitriol, o que provoca aumento da síntese de PTH, uma vez que uma das funções do calcitriol é diminuir a síntese de PTH



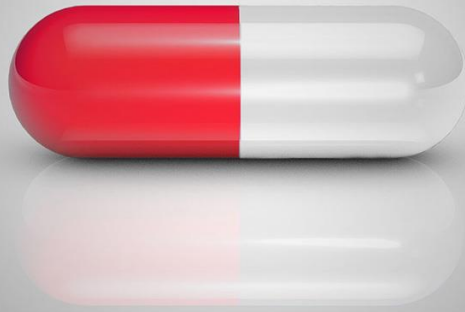
O tratamento inclui uma dieta completa e balanceada, mas às vezes é necessária a adição de suplementos de cálcio

Resposu para diminuir o risco de fraturas ósseas

O prognóstico bom e geralmente a correção dietética normaliza os níveis corporais de cálcio, fósforo e PTH

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Excessos

Comumente associadas às suplementações

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Excessos

O excesso de vitamina D também é prejudicial e causa hipervitaminose D

Erros de cálculo na formulação de alimentos comerciais, consumo acidental de raticidas, consumo de certas plantas que podem conter glicosídeos de calcitriol (como jessamina) e uso de pomadas tópicas para tratamento da psoríase, que são baseados em análogos da vitamina D

A “queridinha” do momento tem sido usada sem restrições e conhecimentos

Intoxicação aguda – hipercalcemia - causa sinais clínicos como polidipsia, poliúria, anorexia, vômitos, constipação, convulsões

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Excessos

Intoxicação crônica, osteocondrose e remodelação óssea retardada (cães de raças gigantes em crescimento)

Elevações apreciáveis nas concentrações de cálcio e fósforo levando à mineralização metastática dos tecidos moles

Elevações persistentes de cálcio e fósforo que levam à mineralização metastática geralmente afetam os rins e podem levar a lesão, disfunção ou insuficiência renal

No entanto, qualquer tecido mole, incluindo coração, pulmões e trato GI, pode ser afetado, e os sinais clínicos podem variar até certo ponto, dependendo do sistema de órgãos afetado

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Excessos, desde as recentes mudanças regulatórias

FDA U.S. FOOD & DRUG ADMINISTRATION

Home / Animal & Veterinary / Resources for You / Animal Health Literacy / Vitamin D Toxicity in Dogs

Vitamin D Toxicity in Dogs

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Animal Health Literacy

Vitamin D is an essential nutrient that helps dogs regulate the balance and retention of calcium and phosphorus. However, extremely high levels of vitamin D can cause serious health problems. Vitamin D is a fat-soluble vitamin, so unlike water-soluble vitamins, when a dog – or other animal – gets too much, the excess is not rapidly excreted in his or her urine. Instead, it's stored in fat tissue and the liver. Excessive vitamin D can lead to kidney failure and even death.

Content current as of: 02/09/2023

Em dezembro de 2018, o FDA notificou o público sobre relatórios de toxicidade da vitamina D

Janeiro de 2019, o FDA tomou conhecimento de um relatório de toxicidade da vitamina D

Em fevereiro de 2023, outro recall

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Ações não clássicas

É por aqui que estamos caminhando com maior velocidade...

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Além da nutrição vitamínica

É importante lembrar que a vitamina D também está relacionada a inúmeras funções não associadas ao metabolismo ósseo

1983 - descoberta a presença de receptores de vitamina D em células imunológicas humanas
Pesquisa sobre os efeitos não relacionados da vitamina D no metabolismo ósseo se intensificou e descobriu-se que células em quase todos os tecidos do corpo expressam receptores

Cães e Gatos foi demonstrada uma associação entre baixas concentrações circulantes de vitamina D e doenças não associadas ao metabolismo ósseo, tais como:



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Além da nutrição vitamínica

Concentrações séricas/plasmáticas de 25(OH)D observadas em cães e gatos com diferentes doenças, bem como aquelas observadas em animais saudáveis (grupos controle) em todos os estudos que avaliaram o status de vitamina D em cães e gatos, e o resultados observados em cada estudo



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REVIEW ARTICLE

WILEY

Vitamin D metabolism in dogs and cats and its relation to diseases not associated with bone metabolism

Rafael V. A. Zafalon | Larissa W. Risolia | Vivian Pedrinelli | Thiago H. A. Vendramini | Roberta B. A. Rodrigues | Andressa R. Amaral | Marcia M. Kogika | Marcio A. Brunetto

School of Veterinary Medicine and Animal Science, University of São Paulo, São Paulo, Brazil

Correspondence: Marcio A. Brunetto, School of Veterinary Medicine and Animal Science, University of São Paulo, São Paulo, Brazil. Email: mabrunetto@usp.br

Abstract

Due to the presence of receptors in the cells of numerous body tissues, vitamin D is associated with several physiological functions that go beyond calcium and phosphorus homeostasis and control of bone metabolism in the body. In humans, several studies have associated lower vitamin D concentrations with numerous diseases, such as cancer, heart disease, autoimmune diseases and infectious diseases, and also with an increase in the total mortality rate of the population. Recently, this nutrient started to gain importance in veterinary medicine, and several articles have shown a correlation between low vitamin D status and diseases unrelated to bone metabolism. The present review aims to highlight the recent publications that investigated this relationship, bringing the evidence that exists so far in dogs and cats.

KEYWORDS

1,25(OH)₂D, 25(OH)D, calcidiol, calcitriol, cholecalciferol, hypovitaminosis D

1 | INTRODUCTION

The effects of vitamin D as an important regulator of bone metabolism and calcium homeostasis have been well known for almost 100 years (McCollum, Simmons, Becker, & Shipley, 1923). For a long time, this was believed to be the only role of this vitamin in the metabolism of humans and animals. However, after the discovery of vitamin D receptors (VDR) in various human immune cells (Provvedini, Toussas, Defize, & Manolagas, 1993), research into the pleiotropic effects of vitamin D intensified, and it was discovered that cells of almost all body tissues express VDR. This receptor is believed to be directly or indirectly involved in the regulation of about 2,000 genes, which correspond to almost 20% of the human genome (Ramagopalan et al., 2010).

In human medicine, although the cause and effect relationship is not proven, the relationship between vitamin D status and diseases unrelated to bone metabolism has been extensively studied in recent years, and lower vitamin D concentrations has been associated with increased cancer incidence (Juracinski et al., 2018; Yin

et al., 2013); cardiovascular diseases, such as myocardial infarction (Giovannucci, Liu, Hollis, & Rimm, 2008), stroke and heart failure (Chowdhury et al., 2012; Muscoffari et al., 2017), as well as autoimmune diseases (e.g., diabetes mellitus type 1) (Pitsova et al., 2013), multiple sclerosis (Martelli et al., 2018), rheumatoid arthritis (Kerr et al., 2011) and infectious diseases (White, 2008).

The relationship of vitamin D and diseases has also been investigated in dogs and cats, and some studies found association between low vitamin D status and some types of cancer (Gelling, Sharp, Ringold, Thamm, & Backus, 2016; Wakshlag et al., 2011; Weidner et al., 2017), congestive heart failure (Kraus et al., 2014; Ouga et al., 2015), gastrointestinal diseases (Allenspach, Rizzo, Jergens, & Cheng, 2017; Gow et al., 2011; Laker et al., 2014; Titmarsh, Gow, Kilpatrick, Cartwright, et al., 2015; Titmarsh, Gow, Kilpatrick, Sinclair, et al., 2015), acute pancreatitis (Kim et al., 2017), acute polyradiculoneuritis (Laws, Kathari, Harcourt-Brown, Granger, & Rosa, 2018), chronic kidney disease (Cortés-Escalona, Fernandez del Pulgo, Tabares, & Baeza, 2010; Geller et al., 2015; Gerber, Hising, & Reusch, 2003; Gerber, Hauser, & Reusch, 2004; Parker, Harjes, et al., 2017) and



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Além da nutrição vitamínica

TABLE 1 Serum/plasma concentrations of 25(OH)D in dogs and cats with various diseases and in healthy animals observed in different studies

Reference	Species	Disease	25(OH)D (ng/ml) disease group	25(OH)D (ng/ml) control group	Material	Methodology	Observed results
Wakshlag et al. (2011)	Dog	Cutaneous mast cell tumours	41.6 ± 12 ^a	48 ± 14 ^a	Serum	Radioimmunoassay	25(OH)D serum concentrations in dogs with mastocytoma were lower than those of healthy dogs
Setling et al. (2016)	Dog	Splenic hemangiosarcoma Splenic malignancies Benign neoplasia	49.2 (19.4–91.8) ^b 49.4 (19.4–151) ^b 59.5 (28.3–107) ^b	68.9 (9.5–249) ^b 68.9 (9.5–249) ^b 68.9 (9.5–249) ^b	Serum	Chemiluminescence immunoassay	An increased relative risk for cancer was observed as serum 25(OH)D levels decreased. The relative risk of cancer for 25(OH)D below 40 ng/ml of all-cancer group and of splenic hemangiosarcoma group were 3.9 and 4.1, respectively, compared with that of the control group
Willcox et al. (2016)	Dog	Osteosarcoma	34.95 ± 11.54 ^a	33.85 ± 10.27 ^a	Serum	Liquid chromatography-tandem mass spectrometry	No difference in serum concentrations of 25(OH)D in dogs affected by osteosarcoma, compared with a control group matched for age and body weight
Weidner et al. (2017)	Dog	Osteosarcoma Lymphoma Mast cell tumour	41.9 ± 20.6 ^a 41.1 ± 14.4 ^a 44.9 ± 12.3 ^a	51.3 ± 16.7 ^a 51.3 ± 16.7 ^a 51.3 ± 16.7 ^a	Plasma	Radioimmunoassay	The relationship between cancer and a change in vitamin D metabolism was suggested. In cancer patients, plasma 25(OH)D concentrations increased as ionized calcium increased, whereas in healthy dogs, plasma 25(OH)D concentrations decreased with the increase of ionized calcium concentrations
Gow et al. (2011)	Dog	Protein-losing enteropathy Inflammatory bowel disease Hospitalized patients with non-gastrointestinal illness	5.7 ^b 26.6 ^b 26.5 ^b	30.8 ^b 30.8 ^b 30.8 ^b	Serum	Radioimmunoassay	Serum 25(OH)D levels were lower in dogs with protein-losing enteropathy than in healthy dogs. Dogs hospitalized for causes unrelated to inflammatory bowel disease, and dogs with inflammatory bowel disease with albumin levels within reference range
Titmarsh, Gow, Kilpatrick, Sinclair, et al. (2015)	Dog	Chronic enteropathy (survivors) Chronic enteropathy (non-survivors)	24.90 (15.63–39.45) ^c 4.3 (1.6–17.0) ^c	—	Serum	Radioimmunoassay	Lower serum 25(OH)D concentrations at the time of diagnosis in dogs that died or were euthanized as a result of this disease than dogs who were alive or died due to causes unrelated to this disease
Allenspach et al. (2017)	Dog	Protein-losing enteropathy (negative outcome) Protein-losing enteropathy (positive outcome)	6.6 (0–26.4) ^b 14.8 (2.4–32.4) ^c	—	Serum	Radioimmunoassay	Serum 25(OH)D concentrations were lower in dogs that died up to 4 months after diagnosis (negative outcome group) than dogs that were alive or who died from other causes unrelated to protein-losing enteropathy



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Além da nutrição vitamínica



RESEARCH ARTICLE

Oral vitamin D supplementation at five times the recommended allowance marginally affects serum 25-hydroxyvitamin D concentrations in dogs

Lauren R. Young* and Robert C. Backus
Department of Veterinary Medicine and Surgery, College of Veterinary Medicine, University of Missouri, Columbia, MO 65211, USA
(Received 14 January 2016 – Final revised manuscript 28 April 2016 – Accepted 2 June 2016)

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Abstract
HTML

2016

doi:10.1017/jns.2016.23



É importante entender qual metabólito é mais eficaz para administrar

Estudos recentes demonstraram que a suplementação com vitamina D muitas vezes não é eficaz

Em humanos e cães, a suplementação com 25OHD (calcitrol) é muito mais eficaz em comparação com a colecalciferol

Avaliar uma dosagem oral de colecalciferol (D3) quanto à eficácia no aumento do status de vitamina D

A quantidade de vitamina D teve que ser 10 vezes maior em comparação com 25OHD para obter efeitos semelhantes

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Além da nutrição vitamínica Prognóstico

2015

PLOS ONE

Vitamin D Status Predicts 30 Day Mortality in Hospitalised Cats

Heena Tripathi*, Scott Klavans*, Jennifer Stronoff*, Andrew Blong*, Elizabeth P. Baker*, Elizabeth M. Suter*, Donald S. Borch*, Jonathan Berg*, John S. Berg*, Robert C. Backus*, Robert Ross*, Jani Hoshino*, Richard C. Anderson*

Abstract

Vitamin D insufficiency, defined as low serum concentrations of the major circulating form of vitamin D, 25-hydroxyvitamin D (25(OH)D), has been associated with the development of numerous infectious, inflammatory, and neoplastic diseases in humans. In addition, vitamin D insufficiency has been found to be predictive of mortality for many disorders. However, in comparison to human studies, to date, almost none of data is referenced to any feline, including feline neonates, lactating, and exposure to UV radiation. In contrast, administered with its end-product vitamin D₃ (cholecalciferol), and most studies are not commercialized, using a relatively standard amount of vitamin D₃. Consequently, alternative cats are an attractive model system in which to assess the relationship between serum 25(OH)D and health outcomes. The hypothesis of this study was that vitamin D status would predict short-term, all-cause mortality in hospitalized cats. Serum concentrations of 25(OH)D, together with a wide range of other clinical, hematological, and biochemical parameters, were measured in 60 consecutive hospitalized cats. Cats which died within 30 days of initial admission had significantly lower serum 25(OH)D concentrations than cats which survived. In a linear regression model including 10 clinical variables, serum 25(OH)D concentration in the lower tertile was significantly predictive of mortality. The odds ratio of mortality within 30 days was 2.7 (95% confidence interval 1.24 to 5.81) in cats with serum 25(OH)D concentration in the lower tertile. In conclusion, this study demonstrates that low serum 25(OH)D concentration relates to an independent predictor of short-term mortality in cats.

Introduction

*All authors contributed equally and significantly to the design, data collection, analysis, and interpretation of this study. All authors approved the final manuscript for submission and are accountable for all aspects of the accuracy and integrity of this work.

Gatos hospitalizados - a 25(OH)D foi representada como uma variável categórica - os gatos com concentrações circulantes de 25(OH)D no tercil inferior apresentaram maior risco de mortalidade em comparação com gatos na categoria de referência e no meio tercil

Cães hospitalizados em estado crítico, observou-se que as concentrações séricas de 25(OH)D no momento do diagnóstico eram um preditor da taxa de mortalidade para cães com enteropatia

Journal of Veterinary Internal Medicine

ACVIM

Open Access

J Vet Intern Med 2015;29:1473-1478

Association of Vitamin D Status and Clinical Outcome in Dogs with a Chronic Enteropathy

H. Timarsh, A.G. Gow, S. Kilpatrick, J. Sinclair, T. Hill, E. Milne, A. Philbey, J. Berry, I. Handel, and R.J. Mellorby

Background: Dogs with a chronic enteropathy (CE) have a lower vitamin D status, than do healthy dogs. Vitamin D status has been associated with a negative clinical outcome in humans with inflammatory bowel disease.

Objectives: To examine the relationship between serum 25-hydroxyvitamin D (25(OH)D) concentrations at diagnosis and clinical outcome in dogs with a CE.

Animals: Forty-one dogs diagnosed with CE admitted to the Royal Dick School of Veterinary Studies, Hospital for Small Animals between 2007 and 2013.

Methods: Retrospective review. Serum 25(OH)D concentrations were compared between dogs which were alive at follow up or had died because of non-CE-related reasons (survivors) and dogs which died or were euthanized due to their CE (non-survivors). A binary logistic regression analysis was performed to determine significant predictors of death in dogs with CE.

Results: Serum concentrations of 25(OH)D at the time a CE was diagnosed were significantly lower in non-survivors ($n = 15$) (median non-survivors 4.36 ng/mL, interquartile range 1.6–17.0 ng/mL), median survivors ($n = 26$) (24.9 ng/mL, interquartile range 15.63–39.43 ng/mL, $P < .001$). Serum 25(OH)D concentration was a significant predictor of death in dogs with CE (odds ratio 1.08 [95% CI 1.02–1.15]).

Conclusion: Serum 25(OH)D concentrations at diagnosis are predictive of outcome in dogs with CE. The role of vitamin D in the initiation and outcome of chronic enteropathies in dogs is deserving of further study.

Key words: 25(OH)D; Prognostic; Inflammatory bowel disease.

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2015

Além da nutrição vitamínica Doenças gastrointestinais

2011

Observaram que os níveis séricos de 25(OH)D eram mais baixos em cães com doença inflamatória intestinal (DII) e hipoalbuminemia do que em cães saudáveis

Observada associação negativa entre as concentrações séricas de 25(OH)D e marcadores de inflamação gastrointestinal e sistêmica



Journal of Veterinary Internal Medicine

Association of Vitamin D Status and Clinical Outcome in Dogs with a Chronic Enteropathy

H. Titmarsh, A.G. Gow, S. Kilpatrick, J. Sinclair, T. Hill, E. Milne, A. Philbey, J. Berry, I. Handel, and R.J. Mellanby

Background: Dogs with a chronic enteropathy (CE) have a lower vitamin D status, than do healthy dogs. Vitamin D status has been associated with a negative clinical outcome in humans with inflammatory bowel disease.
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Methods: Retrospective review. Serum 25(OH)D concentrations were compared between dogs which were alive at follow up or had died because of non-CE-related reasons (survivors) and dogs which died or were euthanized due to their CE (non-survivors). A binary logistic regression analysis was performed to determine significant predictors of death in dogs with CE.
Results: Serum concentrations of 25(OH)D at the time a CE was diagnosed were significantly lower in non-survivors ($n = 15$) (median non-survivors: 4.26 ng/mL, interquartile range: 1.6-17.0 ng/mL), median survivors ($n = 26$) (24.9 ng/mL, interquartile range: 15.63-39.45 ng/mL, $P < .001$). Serum 25(OH)D concentration was a significant predictor of death in dogs with CE (odds ratio: 1.08 [95% CI: 1.02-1.18]).
Conclusion: Serum 25(OH)D concentrations at diagnosis are predictive of outcome in dogs with CE. The role of vitamin D in the initiation and outcome of chronic enteropathies in dogs is deserving of further study.
Key words: 25(OH)D; Prognostic; Inflammatory bowel disease.

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2015

Além da nutrição vitamínica Doenças gastrointestinais

2015 2017

Dois estudos avaliaram a relação entre o estado de vitamina D no momento do diagnóstico das enteropatias e a expectativa de vida desses animais, e ambos observaram que a 25(OH)D pode ser considerada um preditor de evolução clínica

Gatos com DII ou linfoma do intestino delgado apresentaram concentrações séricas de 25(OH)D mais baixas do que animais saudáveis e animais hospitalizados por outras causas



Vitamin D Status Predicts 30 Day Mortality in Hospitalised Cats

Kevin Freeman, David Chapman, Jennifer Stocker, Elizabeth Boyd, Elizabeth F. Bards, Stephanie M. Lohr, Donna O'Brien, Jacqueline Berry, Melissa S. Bampton, Danielle Gunn-Rosell, Mike Ross, Sam Ross, Richard A. Bellenger

1 Royal Dick School of Veterinary Studies and The Ross School, The University of Edinburgh, Roslin, Midlothian, United Kingdom, 2 Diagnostic Services Laboratory, The University of Edinburgh, Roslin, Midlothian, United Kingdom, 3 Diagnostic Services Laboratory (Veterin D), Clinical Biochemistry, Manchester Royal Infirmary, Oxford Road, Manchester, United Kingdom

† These authors contributed equally to this work.

* k.freeman@ed.ac.uk



Hypovitaminosis D is associated with negative outcome in dogs with protein losing enteropathy: a retrospective study of 43 cases

K. Alenqach, J. Ross, A. E. Jorgens and Y. M. Chang

Abstract Hypovitaminosis D has previously been shown to be prevalent amongst dogs with protein losing enteropathy (PLE).
Background: The hypothesis of this study was that low 25 hydroxyvitamin D (25(OH)D) serum concentrations could be a risk factor for negative outcome in dogs with PLE.
Methods: Eighty-four dogs were included in the study: 23 in the healthy group, 41 in the hospitalized ill group, and 26 in the euthanized group.
Results: Although there was overlap in serum 25(OH)D concentrations among the 3 groups, serum 25(OH)D concentrations were significantly lower in the cats with IBD or IEL, compared to healthy cats ($P < .0001$) and hospitalized ill cats ($P = .014$). In the IBD/IEL group, there was a significant moderate positive correlation between serum 25(OH)D and 25(OH)D concentrations ($r = 0.56$, $P = .001$).
Conclusion and Clinical Importance: The median serum concentration of 25(OH)D was significantly lower in cats with IBD/IEL than in healthy cats and in hospitalized ill cats. Additional studies are required to elucidate the mechanism of hypovitaminosis D in cats with gastrointestinal diseases, to define the best management strategy to treat this complication, and to investigate its potential prognostic implications.
Key words: Small cell lymphoma, Inflammatory bowel disease, Vitamin D, Calcium.

48

48

2014

Além da nutrição vitamínica Doenças gastrointestinais

Nenhum desses estudos mencionados monitorou o status de vitamina D dos animais antes do desenvolvimento da doença –
ALIMENTAÇÃO?

A etiologia da DII ainda não foi totalmente elucidada, mas acredita-se que a desregulação da resposta imune às bactérias intestinais comensais possa estar envolvida na sua patogênese

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Além da nutrição vitamínica Doenças gastrointestinais

Vários estudos demonstraram a implicação da vitamina D na regulação do sistema imunológico em humanos

Além de sua expressão em diversos tecidos, principalmente nas células intestinais humanas, o receptor de vitamina D também está presente nas células T, neutrófilos e células apresentadoras de antígenos (macrófagos e células dendríticas)

Ou seja, a sinalização da vitamina D pode influenciar tanto o sistema imunológico inato quanto o adaptativo

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Além da nutrição vitamínica Doenças gastrointestinais



Até o momento, não se sabe se menores concentrações de vitamina D são a causa ou apenas consequência de doenças intestinais

Acredita-se que uma diminuição na ingestão ou absorção de vitamina D, causada pela doença, possa estar associada

Mas, pacientes internados por outras causas não relacionadas a enteropatias, que também poderiam causar redução do apetite, apresentavam concentrações séricas de 25(OH)D maiores



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Além da nutrição vitamínica Doenças gastrointestinais

Além disso, a inflamação da mucosa gastrointestinal pode prejudicar a absorção da vitamina D, contribuindo para a diminuição do seu estado sérico

No entanto, há evidências de que baixas concentrações de 25(OH)D podem influenciar o desenvolvimento do processo inflamatório intestinal - IL-8 - essa citocina desempenha um papel importante na iniciação e manutenção da DII

O papel da suplementação de vitamina D no desenvolvimento e tratamento da DII em cães e gatos necessita de mais estudos para ser elucidado

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Journal of Steroid Biochemistry & Molecular Biology 190 (2015) 179–181

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Review

Critical roles of intestinal epithelial vitamin D receptor signaling in controlling gut mucosal inflammation

Yan Chun Li^{a,*}, Yunzi Chen^{a,b}, Jie Du^b

^aDepartment of Medicine, Institute of Biological Sciences, The University of Texas, Houston, Texas, U.S.A. 77030, USA
^bLaboratory of Molecular Disease Research and Drug Development, China Medical University, Shenyang, Liaoning 110001, China

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 Intestinal epithelial cells
 Inflammation bowel diseases

ABSTRACT

Although vitamin D receptor (VDR) is highly expressed in the intestine, the role of VDR signaling in the gut is not fully understood. Our recent studies unveil a regulatory circuit that controls gut epithelial VDR as a key molecule in the control of mucosal inflammation and colitis development. On the one hand, intestinal epithelial VDR signaling protects the integrity of the mucosal barrier by inhibiting inflammation-induced epithelial cell apoptosis. This barrier-protecting, anti-cellular activity is independent of the non-epithelial immune VDR activity. A healthy and intact mucosal barrier prevents bacterial invasion and thus reduces mucosal inflammation. On the other hand, inflammation in turn down-regulates epithelial VDR expression by inducing VDR-targeting microRNA-34c, thus compromising mucosal barrier functions. Consistently, colonic epithelial VDR levels are markedly reduced in patients with inflammatory bowel diseases or in experimental colitis models, whereas vitamin D analog therapy that ameliorates colitis up-regulates epithelial VDR. Thus, gut epithelial VDR signaling appears to play an essential role in controlling mucosal inflammation and thus could be a novel therapeutic target in the management of inflammatory bowel diseases.

This article is part of a special issue entitled "The Vitamin D Workshop".

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1. Introduction

The gut, particularly the large intestine, contains an enormous amount of commensal bacteria and other immune-activating substances in the lumen that can cause mucosal inflammation once invading the lamina propria, where the immune-activating components of the bacteria activate the immune cells. The gut mucosal epithelial barrier separates the body from the luminal microorganisms and inflammatory and toxic substances. This mucosal barrier consists of a monolayer of epithelial cells with intercellular junctions formed between adjacent cells that seal the paracellular space and regulate permeability of the barrier [1]. Dysfunction of the barrier leads to increased translocation of luminal substances to the lamina propria, triggering inflammatory

* Corresponding author at: Department of Medicine, The University of Texas, 6603 B.5763 Street, MC301900, Houston, TX 77030, USA. Tel.: +1 281 242 2477; fax: +1 281 242 2281.
 E-mail address: yanchunli@bcm.tmc.edu (Y.C. Li).

http://dx.doi.org/10.1016/j.jstbmb.2015.01.011
 0964-6529/© 2015 Elsevier Ltd. All rights reserved.

2015

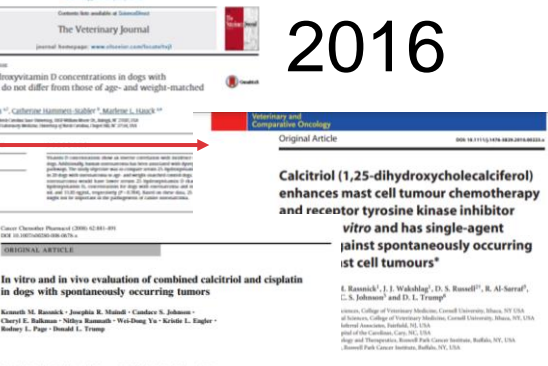
Além da nutrição vitamínica Oncologia

Avaliaram a relação entre as concentrações séricas de 25(OH)D e mastocitoma em Labrador Retrievers

33 animais acometidos por esta doença foram avaliados e comparados com um grupo controle composto por 54 animais saudáveis, sendo observadas menores concentrações séricas de 25(OH)D em cães com mastocitoma

As concentrações séricas de 25(OH)D de um grupo de cães saudáveis foram comparadas com as concentrações séricas de 25(OH)D de um grupo de cães com neoplasias

O grupo controle apresentou maiores concentrações séricas de 25(OH)D quando comparado a todos os outros grupos



2011 e 2016

Além da nutrição vitamínica Oncologia

Em contraste - não encontraram diferenças nas concentrações séricas de 25(OH)D em 20 cães afetados por osteossarcoma

Demonstraram que 1,25(OH)2D, usado isoladamente para tratamento de mastocitoma, induziu remissão em 4 dos 10 cães que participaram do experimento

Ransnick et al. (2008) também observaram efeito sinérgico in vivo do 1,25(OH)2D com o quimioterápico cisplatina

2008



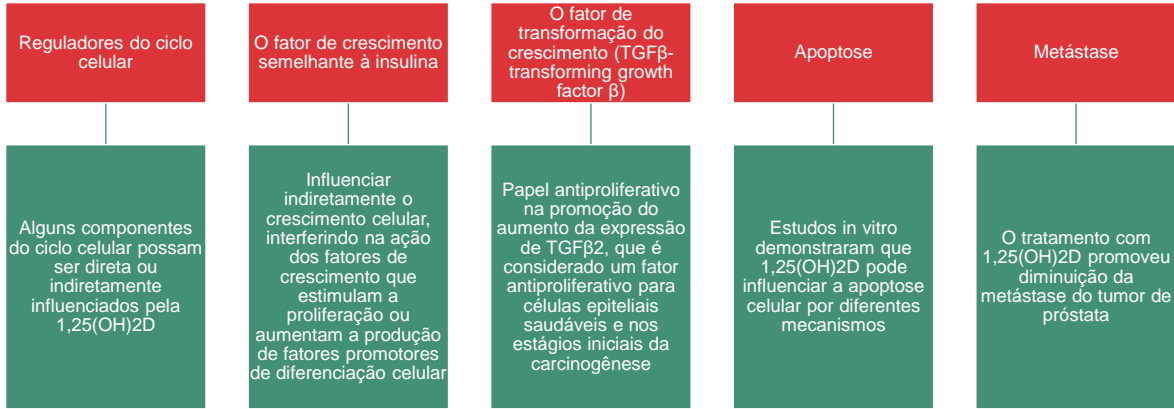
Além da nutrição vitamínica Oncologia

Calcitriol and Calcipotriol Modulate Transport Activity of ABC Transporters and Exhibit Selective Cytotoxicity in MRP1-overexpressing Cells

Xiao W, Tan, Angeline Sarrajoo, Brannan, Chai-Andrew, and Suraj H. Iam.
Drug Metabolism and Disposition December 2010, 40(12):1886-1890; DOI: 10.1124/dmd.103.038122

2018

Mecanismos pelos quais o calcitriol desempenha efeitos anticancerígenos:



A angiogênese é necessária para o desenvolvimento de metástases
Esse processo depende de vários fatores pró-angiogênicos

57 Calcitriol parece diminuir a expressão de fatores pró-angiogênicos e aumentar a expressão de proteínas antiangiogênicas

57

Além da nutrição vitamínica Doença renal crônica

- Existem vários estudos que avaliaram o metabolismo da vitamina D em pacientes com doença renal crônica (DRC)
- Uma vez que seu metabólito ativo (1,25(OH)2D) é produzido nos túbulos renais por meio da enzima 1-α-hidroxilase
- Cães com DRC apresentam concentrações séricas e plasmáticas dos metabólitos 25(OH)D e 1,25(OH)2D menores que cães saudáveis
- Em pacientes com DRC, vários fatores podem influenciar o status de vitamina D no corpo

- Diminuição da atividade da enzima 1-α-hidroxilase
- Redução da conversão hepática de colecalciferol em 25(OH)D
- Diminuição da ingestão dietética de vitamina D
- Alto fósforo, promove FGF-23 e inibe a atividade da 1-α-hidroxilase
- Receptor de megalina – proteína de ligação da 25(OH)D no túbulo renal diminui - proteinúria

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Journal of Veterinary Internal Medicine

Standard Article
J Vet Intern Med 2013;31:791-798

Association of Vitamin D Metabolites with Parathyroid Hormone, Fibroblast Growth Factor-23, Calcium, and Phosphorus in Dogs with Various Stages of Chronic Kidney Disease

V.J. Parker, L.M. Harjes, K. Dembek, G.S. Young, D.J. Chew, and R.E. Toribio

Background: Hypovitaminosis D is associated with progression of renal disease, development of renal secondary hyperparathyroidism (RHPT), chronic kidney disease-mineral bone disorder (CKD-MBD), and increased mortality in people with CKD. Despite what is known regarding vitamin D dysregulation in humans with CKD, little is known about vitamin D metabolism in dogs with CKD.

Objectives: The purpose of our study was to further elucidate vitamin D status in dogs with different stages of CKD and to relate it to factors that affect the development of CKD-MBD, including parathyroid hormone (PTH), fibroblast growth factor-23 (FGF-23), calcium, and phosphorus concentrations.

Methods: Thirty-seven dogs with naturally occurring CKD were compared to 10 healthy dogs. Serum 25-hydroxyvitamin D [25(OH)D], 1,25-dihydroxyvitamin D [1,25(OH)2D], and 24,25-dihydroxyvitamin D [24,25(OH)2D], and PTH and FGF-23 concentrations were measured. Their associations with serum calcium and phosphorus concentrations and IRIS stage was determined.

Results: Compared to healthy dogs, all vitamin D metabolite concentrations were significantly lower in dogs with Interstitial Renal Interest Society (IRIS) stages 3 and 4 CKD (*r* [correlation] = -0.49 to -0.60; *P* < .05) but not different in dogs with stages 1 and 2 CKD. All vitamin D metabolites were negatively correlated with PTH, FGF-23, and phosphorus concentrations (*r* = -0.39 to -0.64; *P* < .01).

Conclusion and Clinical Importance: CKD in dogs is associated with decreases in all vitamin D metabolites evaluated suggesting that multiple mechanisms, in addition to decreased renal mass, affect their metabolism. This information could have prognostic and therapeutic implications.

ORIGINAL INVESTIGATION

25-Hydroxyvitamin D Levels and the Risk of Mortality in the General Population

Michael J. Holmbeck, MD, MPH; Eric D. Michos, MD, MPH; Wanda Post, MD, MS; Brad Astor, PhD

Background: In patients undergoing dialysis, therapy with all-cis-calcitriol or paricalcitol or other vitamin D agonists is associated with reduced mortality. Observational studies suggest that low 25-hydroxyvitamin D levels (25(OH)D) are associated with diabetes mellitus, hypertension, and cancer. However, whether low serum 25(OH)D levels are associated with mortality in the general population is unknown.

Methods: We tested the association of low 25(OH)D levels with all-cause, cancer, and cardiovascular disease (CVD) mortality in 13 131 nationally representative adults 20 years of age from the Third National Health and Nutrition Examination Survey (NHANES III) linked mortality data. Participants' serum 25(OH)D levels were collected from 1990 through 1994, and individuals were primarily followed for mortality through 2000.

Results: In cross-sectional multivariate analyses, increasing age, female sex, nonwhite race/ethnicity, diabetes, hypertension, and hypercholesterolemia were all independently associated with higher odds of 25(OH)D

deficiency (lowest quartile of 25(OH)D level, <17.8 ng/mL, vs. controls in women only, multiply by 2.49); while greater physical activity, vitamin D supplementation, and nonwhite women were inversely associated. During a median 8.7 years of follow-up, there were 1065 deaths, including 777 from CVD. In multivariate models (adjusted for baseline demographics, season, and residential and social CVD risk factors), compared with the highest quartile, being in the lowest quartile (25(OH)D levels <17.8 ng/mL) was associated with a 20% increased rate of all-cause mortality (mortality rate ratio, 1.20; 95% CI, 1.08-1.40) and a population attributable risk of 1.1%. The adjusted models of CVD and cancer mortality revealed a higher risk, which was not statistically significant.

Conclusion: The lowest quartile of 25(OH)D level (<17.8 ng/mL) is independently associated with increased mortality in the general population.

Arch Intern Med. 2008;168(13):1629-1637.

2017

2008

Além da nutrição vitamínica Doença renal crônica



Outro fator importante – DRC - influenciar o status de vitamina D - FGF-23, um hormônio produzido pelo tecido ósseo que estimula a excreção renal de fosfato e promove a supressão da síntese de 1,25(OH)2D pela inibição da enzima 1 α -hidroxilase e estimulação 24-hidroxilase

Uma das consequências da DRC é o desenvolvimento de hiperparatireoidismo renal secundário

Novos estudos são necessários para avaliar os efeitos de dosagens de calcitriol na redução do PTH sérico em pacientes com DRC, bem como avaliar se poderiam promover os efeitos observados em humanos, como efeito antiproteinúrico e o aumento da expectativa de vida

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Além da nutrição vitamínica Doença renal crônica

Porém, vale ressaltar que deve-se ter cuidado com o uso do calcitriol, pois a superdosagem desse metabólito pode causar hipercalcemia, que pode resultar em necrose tubular renal aguda e calcinose, como a nefrocalcinose

Isso é extremamente prejudicial, principalmente para animais que já possuem DRC, portanto a recomendação deve garantir uma oferta adequada, mas não excessiva

60

60

2013



Além da nutrição vitamínica Dor e cuidados paliativos



Critical Reviews in Food Science and Nutrition



ISSN: 1040-4398 (Print) 1549-7852 (Online) journal homepage: <http://www.tandfonline.com/loi/brfn20>

Falta de vitamina D está claramente associada à dor devido a condições esqueléticas patológicas

Current knowledge of vitamin D in dogs

Nicole Weidner & Adronie Verbrugghe

To cite this article: Nicole Weidner & Adronie Verbrugghe (2016): Current knowledge of vitamin D in dogs, *Critical Reviews in Food Science and Nutrition*, DOI: 10.1080/10404398.2016.1171202
To link to this article: <http://dx.doi.org/10.1080/10404398.2016.1171202>

2017

Além disso, como a vitamina D também contribui para o funcionamento correto do músculo, estudos também mostraram que baixos níveis séricos de vitamina D estão ligados a dores

O baixo status corporal de vitamina D pode representar um importante fator de risco para o desenvolvimento e/ou manutenção de dores agudas e crônicas em várias dores musculo esqueléticas inespecíficas

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Por outro lado, descobriu-se que a suplementação de vitamina D melhora a dor em indivíduos ambulatoriais com dor musculo esquelética, fibromialgia, de joelho e em cuidados paliativos

PLOS ONE

2017

RESEARCH ARTICLE
Vitamin D supplementation to palliative cancer patients shows positive effects on pain and infections—Results from a matched case-control study

Maria Hilda-Franklin^{1*}, Jonas Högl², Jenny Bergqvist³, Linda Björkstén-Bergman^{4,5,6}

Abstract

Background
 We previously showed an association between low vitamin D levels and high opioid doses to alleviate pain in palliative cancer patients. The aim of this case-controlled study was to investigate if vitamin D supplementation could improve pain management, quality of life (QoL) and decrease infections in palliative cancer patients.

Methods
 Thirty-five palliative cancer patients with levels of 25-hydroxyvitamin D < 75 nmol/L were supplemented with vitamin D 4000 IU/day, and were compared to 39 untreated, matched 'control'-patients from a previous study at the same ward. Opioid doses, antibiotic consumption and QoL-scores measured with the Edmonton Symptom Assessment Scale (ESAS) were monitored. The primary endpoint was the change from baseline after 1 and 3 months compared between the groups using linear regression with adjustment for a potential confounding factor.

Results
 After 1 month the vitamin D-treated group had a significantly decreased benzylal dose compared to the untreated group with a difference of 46 µg/d; 95% CI 24–78, which increased further at 3 months to 91 µg/d; 95% CI 56–140 µg/d. The ESAS QoL-score improved in the Vitamin D group the first month; -1.4; 95% CI -2.8 (-0.35). The vitamin D-treated group had significantly lower consumption of antibiotics after 3 months compared to the untreated group, the difference was -20%; 95%CI -0.41%–-16.12%. Vitamin D was well tolerated by all patients and no adverse events were reported.

OPEN ACCESS
 Citation: Hilda-Franklin M, Högl J, Bergqvist J, Björkstén-Bergman L (2017) Vitamin D supplementation to palliative cancer patients shows positive effects on pain and infections—Results from a matched case-control study. *PLOS ONE* 12(8): e0182048. doi:10.1371/journal.pone.0182048

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Data Availability Statement: The raw data is available in the Supporting Information file. However, in accordance with the approved application to the National Ethical Review Board we have removed the age and date of the personal data of the included subjects from the dataset to make it impossible to identify single patients.

Funding: Financial support was provided through the Regenera agreement on basic and clinical research (R1) between Karolinska Institutet and PLOS ONE | <https://doi.org/10.1371/journal.pone.0182048> August 21, 2017



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Além da nutrição vitamínica Dor e cuidados paliativos

39 pacientes com câncer paliativo com níveis de 25-hidroxivitamina D <75 nmol/L foram suplementados com vitamina D e foram comparados a 39 pacientes não tratados e correspondentes-pacientes de um estudo anterior na mesma enfermaria

Doses de opioides, consumo de antibióticos e escores de qualidade de vida foram monitorados

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Além da nutrição vitamínica Dor e cuidados paliativos

Após 1 mês, o grupo tratado com vitamina D teve uma dose de fentanil significativamente diminuída em comparação com o grupo não tratado

Isso aumentou ainda mais em 3 meses

O escore da qualidade de vida melhorou no grupo de vitamina D no primeiro mês

O grupo tratado com vitamina D apresentou um consumo significativamente menor de antibióticos após 3 meses em comparação com o grupo não tratado

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PLOS ONE

2017

RESEARCH ARTICLE
Vitamin D supplementation to palliative cancer patients shows positive effects on pain and infections—Results from a matched case-control study

Maria Hilda Frankhøj^{1*}, Jonas Höjler², Jenny Bergqvist³, Linda Ekblom-Bergqvist^{1,4,5}

Abstract

Background
 We previously showed an association between low vitamin D levels and high opioid doses to alleviate pain in palliative cancer patients. The aim of this case-controlled study was to investigate if vitamin D supplementation could improve pain management, quality of life (QoL) and decrease infections in palliative cancer patients.

Methods
 Thirty-nine palliative cancer patients with levels of 25-hydroxyvitamin D < 75 nmol/L were supplemented with vitamin D 4300 IU/day, and were compared to 39 untreated, matched 'control'-patients from a previous study at the same ward. Opioid doses, antibiotic consumption and QoL-scores measured with the Edmonton Symptom Assessment Scale (ESAS) were monitored. The primary endpoint was the change from baseline after 1 and 3 months compared between the groups using linear regression with adjustment for a potential confounding factor.

Results
 After 1 month the vitamin D treated group had a significantly decreased fentanyl dose compared to the untreated group with a difference of 46 µg/h; 95% CI 24–78, which increased further at 3 months to 91 µg/h; 95% CI 56–140 µg/h. The ESAS QoL-score improved in the Vitamin D group the first month; -1.4-3.9% D -0.4 (-0.3%). The vitamin D-treated group had significantly lower consumption of antibiotics after 3 months compared to the untreated group, the difference was -26%; 95%CI -0.41%–-6.12%. Vitamin D was well tolerated by all patients and no adverse events were reported.

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OPEN ACCESS
 Citation: Frankhøj M, Höjler J, Bergqvist J, Ekblom-Bergqvist L (2017) Vitamin D supplementation to palliative cancer patients shows positive effects on pain and infections—Results from a matched case-control study. PLoS ONE 12(6): e0178208. doi:10.1371/journal.pone.0178208

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Data Availability Statement: The raw data is available in the Supporting Information file. However, in accordance with the approved application to the Regional Ethical Review Board we have released the age and date of the personal data of the included patients from the dataset to make it impossible to identify single patients.

Funding: Financial support was provided through the Region Agreement on Nursing and Clinical Research (R-1) between Halmstad and Lund and research (R-1) between Halmstad and Lund and research (R-1) between Halmstad and Lund.

PLoS ONE | <https://doi.org/10.1371/journal.pone.0178208> August 21, 2017

PLOS ONE

2017

RESEARCH ARTICLE
Vitamin D supplementation to palliative cancer patients shows positive effects on pain and infections—Results from a matched case-control study

Maria Hilda Frankhøj^{1*}, Jonas Höjler², Jenny Bergqvist³, Linda Ekblom-Bergqvist^{1,4,5}

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OPEN ACCESS
 Citation: Frankhøj M, Höjler J, Bergqvist J, Ekblom-Bergqvist L (2017) Vitamin D supplementation to palliative cancer patients shows positive effects on pain and infections—Results from a matched case-control study. PLoS ONE 12(6): e0178208. doi:10.1371/journal.pone.0178208

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PLoS ONE | <https://doi.org/10.1371/journal.pone.0178208> August 21, 2017

Além da nutrição vitamínica Poderíamos conversar muito mais...

Doenças hepáticas 2014

Doenças cardiovasculares 2015

Controversy in the link between vitamin D supplementation and hypertension



2016

SCANDINAVIAN CARDIOVASCULAR JOURNAL, 2016, VOL. 30, NO. 1, 1-16

ORIGINAL ARTICLE

Effects of vitamin D supplementation as an adjuvant therapy in coronary artery disease patients*

Zhaoke Wu¹, Ting Wang², Shenshen Zhu¹ and Ling Li¹

¹Department of Gerontology, The Second Affiliated Hospital of Zhengzhou University at Zhengzhou, Zhengzhou, China; ²Department of Gerontology, Shanxi Provincial People's Hospital at Xi'a University at Zhengzhou, Zhengzhou, China



Potential Beneficial Effects of Vitamin D in Coronary Artery Disease

Christian Legarth¹, Daniela Grimm^{1,2,3}, Marcus Krüger^{2,3}, Manfred Infanger² and Markus Wehland^{1,4}

¹ Department of Biomedicine, Aarhus University, Høegh-Guldbergsgade 10, 8000 Aarhus C, Denmark
² Clinic for Plastic, Aesthetic and Hand Surgery, Otto von Guericke University, Leipziger Str. 44, 39120 Magdeburg, Germany
³ Correspondence: dgg@biomed.au.dk (D.G.), markus.wehland@med.au.dk (M.W.); Tel.: +45-871-47693 (D.G.); +49-391-4721267 (M.W.)

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The vitamin D₃ analog, maxacalcitol, reduces psoriasisform skin inflammation by inducing regulatory T cells and downregulating IL-23 and IL-17 production

Carren Yu Han¹, Teruo Shinohara¹, Yajun Tang^{1,2}, Masahiro Kaneko^{1,2,3}, Shizuka Sakurai¹, Sayaka Ohtsuka¹, Ota Mitsuo¹, Naohiko Aoyama¹, Makoto Sogayori¹, Takafumi Kishimoto¹, Shinya Imai¹, Shinya Watanabe¹

¹Department of Dermatology, Niigata University School of Medicine, Niigata, Japan; ²Department of Dermatology, Niigata University School of Medicine, Niigata, Japan; ³Department of Dermatology, Niigata University School of Medicine, Niigata, Japan



Skeletal and hepatic changes induced by chronic vitamin A supplementation in cats

Ri Corbera^{1,2}, M.A. Trifonidou¹, G.C.M. Crombos¹, B. Schotman¹, M.R. Molenaar¹, G. Voorhuis¹, A.B. Vanlangerak¹, J.C.M. Houwers¹, J.A.W. Hartwegh¹

¹Department of Food Quality and Food Safety, Wageningen University, Wageningen, The Netherlands; ²Department of Food Quality and Food Safety, Wageningen University, Wageningen, The Netherlands

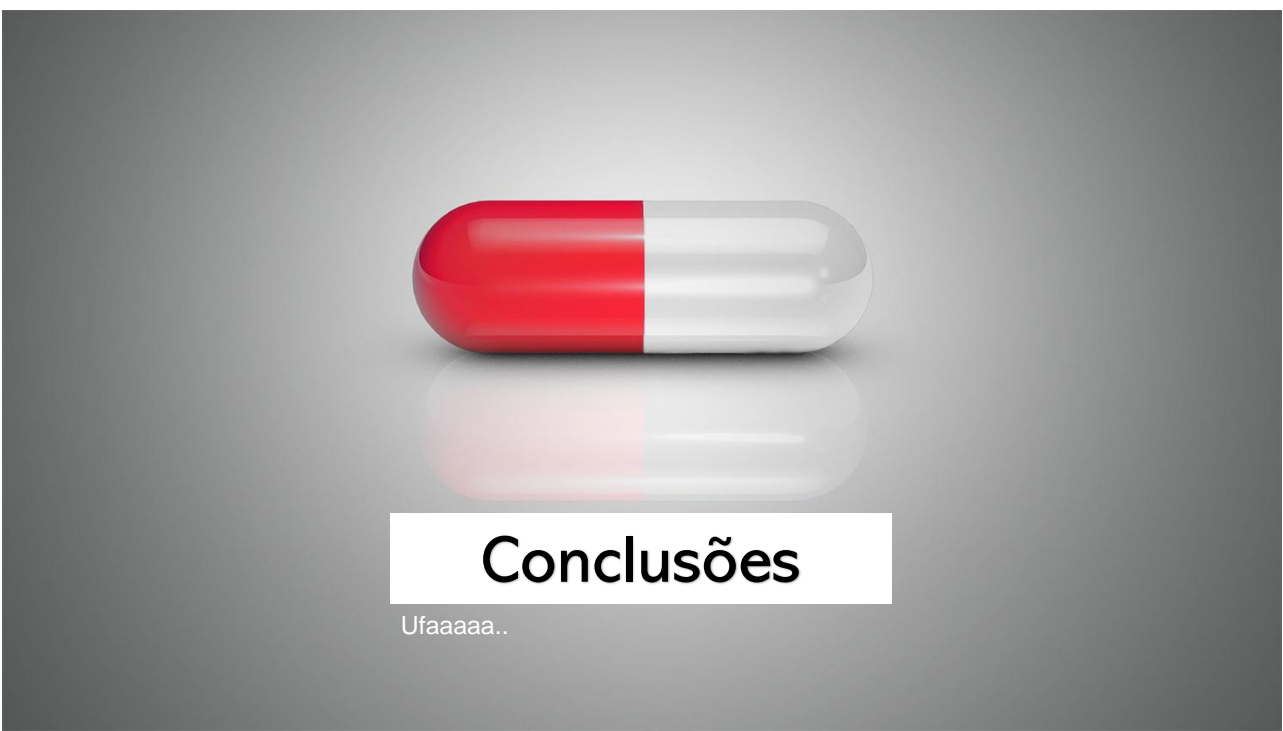
ABSTRACT
Objectives: Low vitamin D status has been shown to be associated with cardiovascular disease. We investigated the effect of 0.3 corrected, double-blind study in 90 stable outpatients with coronary artery disease. The study was conducted between January and June. 20-Hydroxyvitamin D deficiency was assessed by 25-hydroxyvitamin D levels. A significant baseline (19.9 ± 9.8 ng/ml) to 6 months (15.8 ± 1.1 ng/ml) difference in the fall of SYNTAX score for vitamin D₃ also had greater decreases in high in system activity (p < 0.05). Conclusions: Vitamin D₃ supplementation as an adjuvant in

Introduction
Vitamin D deficiency is associated with cardiovascular disease. The aim of this study was to investigate the effect of 0.3 corrected, double-blind study in 90 stable outpatients with coronary artery disease. The study was conducted between January and June. 20-Hydroxyvitamin D deficiency was assessed by 25-hydroxyvitamin D levels. A significant baseline (19.9 ± 9.8 ng/ml) to 6 months (15.8 ± 1.1 ng/ml) difference in the fall of SYNTAX score for vitamin D₃ also had greater decreases in high in system activity (p < 0.05). Conclusions: Vitamin D₃ supplementation as an adjuvant in

Doenças imunes 2018

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Conclusões

Cães e gatos têm um metabolismo diferente da vitamina D; portanto, eles são dependentes da ingestão dietética de vitamina D

Novas tendências na nutrição de cães e gatos, como uma dieta caseira, podem aumentar o risco de desenvolver deficiência de vitamina D

A intoxicação por vitamina D não é comum em cães e gatos, porém a "queridinha" do momento tem sido usada sem restrições e conhecimentos

Baixas concentrações de 25(OH)D estão associadas a várias doenças não relacionadas ao metabolismo ósseo, a maioria dos estudos foi realizada em humanos ou modelos e não especificamente em cães e gatos



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Conclusões

Mas algumas descobertas interessantes apontam possíveis semelhanças

Com base nos dados disponíveis na literatura até o momento, não é possível concluir se as menores concentrações de vitamina D estão influenciando no desenvolvimento dessas doenças ou são apenas consequência delas

Mais estudos são necessários para determinar as necessidades dietéticas de vitamina D para animais adultos, bem como determinar as concentrações circulantes ideais de 25(OH)D



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Conclusões

As interações de nutrientes também devem ser avaliadas e justificam a inclusão de PTH, cálcio e fósforo

A ingestão de alimentos, a quantidade de vitamina D, a forma da vitamina D (ou seja, D2 ou D3 ou metabólitos) têm efeito nos níveis de 25OHD e devem, portanto, ser medidos e relatados em estudos futuros

Para ai sim, em uma segunda etapa, realizar a avaliação dos potenciais benefícios da suplementação de vitamina D sobre o desfecho em doenças



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Muito OBRIGADO

✉ thiago.vendramini@usp.br

📷 @thiago.vendramini



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