

The Role of Vitamin D₃ in Regulation of Calcium Homeostasis in Dairy Cattle Metabolism

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Introduction

Vitamin D plays a major role in the regulation of calcium homeostasis, affecting skeletal development, Calcium (Ca) and Phosphorus (P) metabolism, cellular differentiation and proliferation, and activation of the immune system. Research in other species with high metabolic demand for Ca has led to a re-evaluation of the importance of vitamin D for dairy cattle. In addition, the housing of dairy cattle in total confinement facilities, the feeding of prepartum negative DCAD diets, and the recognition of the impacts of subclinical hypocalcemia on dairy cattle health and performance have all placed more emphasis on the potential benefits of dietary vitamin D supplementation during the transition period of the dairy cow. The aim of this report is to discuss the role of vitamin D₃ on dietary Ca absorption, bone resorption, and regulation of calcium metabolism.

Vitamin D Metabolism

Sources of vitamin D include vitamin D₂ from plants, vitamin D₃ synthesized endogenously in skin exposed to sunlight, and from supplemental sources of vitamin D₃ in the diet (Nelson et al., 2016). Once vitamin D is synthesized or absorbed, it needs to be converted into the active form of 1,25(OH)₂D₃ through a metabolic pathway to exert its effects on calcium metabolism.

Vitamin D₃ and Ultraviolet Radiation

Provitamin D (7-dehydrocholesterol) is synthesized from the cholesterol-forming system and can be converted to vitamin D₃ from photoconversion in epithelial cells exposed to sunlight. This can be a primary source of vitamin D for dairy cattle housed outdoors and has the advantage of not being degraded by ruminal fermentation (Nelson and Merriman, 2014). The synthesized vitamin D₃ enters the blood and binds to vitamin D-binding protein. The half-life of vitamin D₃ in blood ranges from 36 to 78 hours, but is extended to approximately two months if stored in adipose tissue (Mostafa and Hegazy, 2015).

Dietary Vitamin D

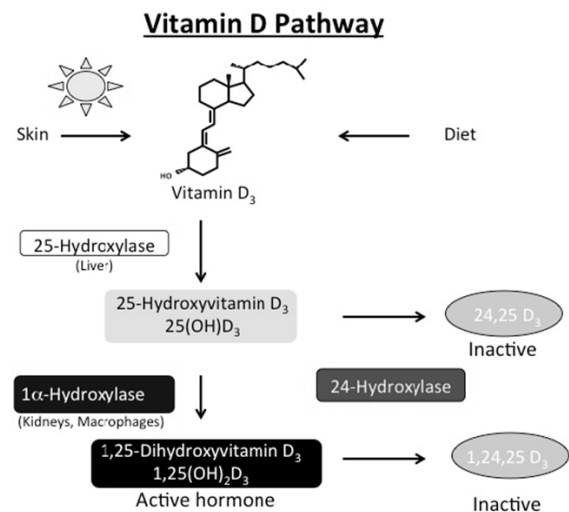
In most dairy production systems, the vitamin D₃ synthesized in the epithelial cells alone is not able to meet animals' requirements for vitamin D, so dietary sources of vitamin D become important to support a healthy and productive animal. Vitamin D₂ is obtained naturally by the ingestion of fungal ergosterol growing on the feed and vitamin D₃ is provided through nutritional supplements (Weir et al., 2016). As most of the ingredients used in dairy cattle feed are low in vitamin D₂, it is normal practice to add supplemental sources of vitamin D₃ to the diet (Nelson et al., 2016).

Vitamin D Metabolic Pathway

Vitamin D₂ and vitamin D₃ are inactive forms of vitamin D which need to be activated via a metabolic pathway. In the first step of this pathway (Figure 1), vitamin D₂ and D₃ are hydroxylated to 25-hydroxyvitamin D₃ (25-OH-D₃) in the liver. With that, 25-OH-D₃ is the most abundant vitamin D form in the blood of dairy cattle. Normal serum concentrations of 25-OH-D₃ for cattle are typically defined as 20 to 50 ng/ml (Horst et al., 1994). Conversion of vitamin D₃ to 25-OH-D₃ in the liver can be a limiting step, particularly when liver metabolism is impaired, such as during ketosis, and potentially throughout the transition period. Under such conditions, providing dietary 25-OH-D₃ may improve calcium homeostasis by reducing the total dependence on the liver to activate the Vitamin D.

Figure 1: General Vitamin D Metabolic Pathway

(Nelson and Merriman, 2014)



The final step of the pathway occurs in the kidney where 25-OH-D₃ is converted to the biologically active vitamin D₃ (1,25-dihydroxyvitamin D₃ (1,25-OH-2D₃)). The concentration of active vitamin D₃ in the blood is tightly regulated and typically ranges from 5 to 20 pg/mL in serum of cattle, but can be elevated to more than 300 pg/mL during severe hypocalcemia (Horst et al., 1994). In the circulation, the active vitamin D₃ binds to vitamin D binding protein and it is transported to target organs to regulate calcium and phosphate homeostasis.

Effects on Calcium Metabolism

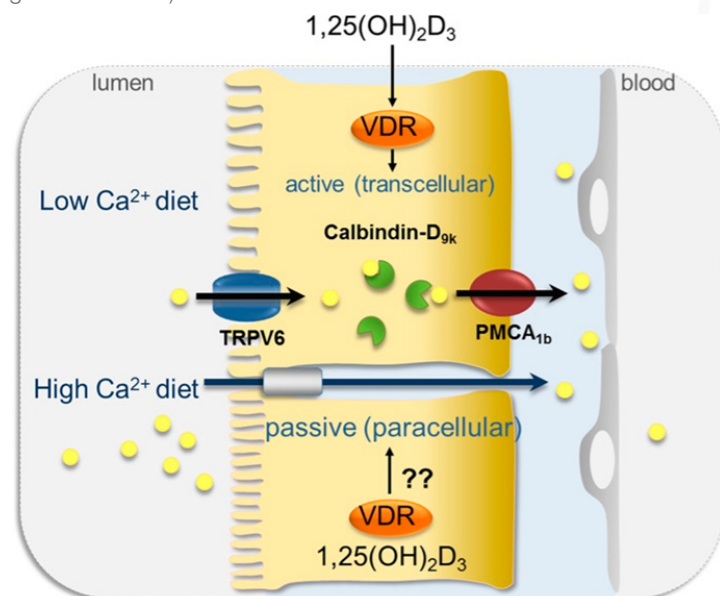
The active form of vitamin D₃ acts to upregulate the expression of genes related to calcium binding and transport, as well as bone remodeling (Nelson et al., 2016).

Intestinal Absorption of Ca

Calcium absorption in the intestine occurs via passive and active transport (Figure 2). Passive transport occurs when Ca concentration in the gut lumen is high. Active transport takes place when Ca concentration in the gut is low, and it is vitamin D-dependent. Active absorption is a three-step process that includes entry of Ca from the intestinal lumen through Ca channels, translocation of Ca from brush border to basolateral membrane, and the extrusion of Ca through the basolateral membrane into the blood. Each step in this process is under the regulation of the active form of vitamin D₃ and is initiated when 1,25-dihydroxyvitamin D₃ binds to the vitamin D receptor of intestinal cells and upregulates gene expression of proteins related to calcium binding and absorption.

Figure 2. Role of Vitamin D on Calcium Intestinal

Absorption (Christakos et al. 2014 - <https://pubmed.ncbi.nlm.nih.gov/24605213/>)



Bone Resorption

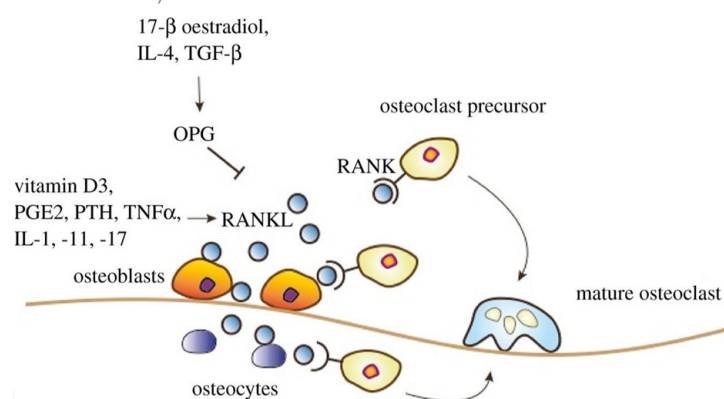
Vitamin D also regulates Ca metabolism through bone resorption (Figure 3). Active vitamin D₃ regulates the expression of RANK, a cell surface receptor that controls and regulates bone mass and calcium metabolism. Via RANK, 1,25-dihydroxyvitamin D₃ leads to bone resorption and initiates normal bone remodeling. This is an important mechanism to maintain the pool of available Ca to the animal.

Summary

Vitamin D increases Ca availability by promoting Ca intestinal absorption and bone resorption. These effects on Ca metabolism become extremely important during the periparturient period when Ca requirements increase approximately three-fold to support colostrum and milk production. Sun-exposed skin and diet are the two sources of Vitamin D for dairy cattle. Due to its importance on Ca metabolism, it is a standard practice to add supplemental Vitamin D in prepartum diets. Once Vitamin D is absorbed, it needs to pass through a metabolic pathway in the liver and kidneys to be activated and perform its biological functions.

Figure 3: Role of Vitamin D on Bone Resorption

(Sigl et al., 2016 - <https://royalsocietypublishing.org/doi/10.1098/rsob.160230>)



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This information has been prepared for industry technical professionals.