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Review Article

We Know Next to Nothing About Vitamin D in Horses!

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ABSTRACT

Very few references on vitamin D in horses exist, but the limited research available suggests that the vitamin D physiology of horses may be very different from other species. Horses can obtain vitamin D both through endogenous synthesis in the skin during sunlight exposure and through dietary sources either from synthetic vitamin D supplements or the natural vitamin D content of roughages. However, regardless of the source of vitamin D, circulating levels of vitamin D metabolites in plasma are generally reported to be very low in horses and vitamin D appears less involved in maintaining normal calcium and phosphorus homeostasis in horses than in other species. Current recommendations on the vitamin D supplementation of horses are based on a scarce amount of more or less outdated literature. Very little research has been carried out regarding the vitamin D physiology of horses and even less regarding the efficiency of different sources of vitamin D in the nutrition of horses. Furthermore, the use and management of horses has changed dramatically during the last 25 to 50 years. Hence, research in the vitamin D physiology and nutrition of modern riding horses is highly necessary, before a much needed update on the recommended vitamin D supplementation of horses can be carried out.

1. Introduction

Vitamin D has become one of the most discussed nutrients in the press and among researchers in human nutrition and physiology because it was discovered to be involved in a vast amount of physiological and immunologic processes [1,2], which stretch beyond the classically recognized effects on skeletal health and calcium and phosphorus homeostasis in the body [1,3]. How to secure a sufficient supply of vitamin D in humans has been of particular interest in parts of the world where sunlight is only a significant source of endogenous vitamin D for a limited time of the year. Hence, in Northern latitudes, advice on sun exposure and the necessity of vitamin D supplementation through the diet has been under heavy scrutiny during the later years [4]. This interest in vitamin D has found its way into the nutrition of companion and production animals. For horse owners, consultants, and so forth, a large number of computer programs, Web services, and so forth for ration formulation are now commercially available. These provide easy access to current nutrient requirements of horses under different housing and exercise conditions, including the current recommendations for covering the vitamin D requirements of horses [5,6]. But, where do these recommendations come from, when no recent experimental data on the vitamin D requirements and physiology of horses exists? It appears that the current minimum requirement of vitamin D in horses of 0.17 μg (6.6 International Unit [IU]) per kg body weight per day is mainly based on older literature and extrapolations from other species [7]. However, the limited amount of literature that does exist on the subject suggests that horses may have a very different vitamin D physiology than other species [8]. The aim of the present review was to provide an overview of the data available regarding the vitamin D status and supply of horses and point to areas of future research within vitamin D supply, nutrition, and physiology

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of horses, which can support a well-founded update of the current recommendations on the vitamin D supplementation of horses.

2. Vitamin D

Vitamin D exists in two forms important for the vitamin D status and supply of horses: vitamin D_2 (ergocalciferol, D_2), which is produced by fungi growing on plant material used as roughage for horses [9], and vitamin D_3 (cholecalciferol, D_3), which is either provided orally as synthetic additives or synthesized endogenously in the skin during exposure to sunlight (UV-B spectre 295–315 nm) [10,11]. To become physiologically active, both D_2 and D_3 must first undergo enzymatic hydroxylation in the liver to synthesize 25-hydroxyvitamin D_2 ($25OHD_2$) and 25-hydroxyvitamin D_3 ($25OHD_3$), respectively. Not all analytical methods distinguish between $25OHD_2$ and $25OHD_3$ when assessing vitamin D status in plasma but report the combined status of $25OHD_2$ and $25OHD_3$ as $25OHD_x$. In most species, $25OHD_2$ and $25OHD_3$ are the main vitamin D metabolites which circulate in plasma bound to vitamin D–binding protein (VDBP) and measured as indicators of physiological vitamin D status in the body. The second step of the physiological activation of vitamin D takes place in almost all organ systems in the body but mainly in the kidneys facilitated by the enzyme $25OHD_x$-1α-hydroxylase, which hydroxylates $25OHD_2$ and $25OHD_3$ to form 1α,25-dihydroxyvitamin D_2 ($1,25(OH)_2D_2$) and 1α,25-dihydroxyvitamin D_3 ($1,25(OH)_2D_3$), respectively. These are hormonally active metabolites of D_2 and D_3 responsible for binding to the vitamin D receptor (VDR) in different organs and carrying out the physiological functions of vitamin D in the body [1,12].

In horses, the vitamin D status in the body, measured as plasma content of both $25OHD_2$ and $25OHD_3$, is generally reported to be very low (<10 ng/mL regardless of season and latitude) (Table 1) compared with other species, for example, cattle (~30 ng/mL during summer in Scandinavia) [27], but the VDBP circulating in horses has the same binding affinity for $25OHD_x$ as in other species [19]. Rickets, a disease caused by vitamin D deficiency, is, however, rare in horses and difficult to induce experimentally [28], and horses have high serum calcium (2.75–3.25 mmol/L) and low serum phosphorus levels (0.7–1.7 mmol/L) compared with other species. Serum levels of these minerals do appear regulated, but vitamin D control of the calcium uptake is not as effective as in other species and VDR expression is low in target organs [19,29]. In vitro studies on $25OHD_x$-1α-hydroxylase activity revealed no enzyme activity in the kidneys of horses, but it is unknown if this was due to down regulation of the enzyme due to high serum calcium levels or a lack of $25OHD_x$-1α-hydroxylase enzyme all together [19].

Vitamin D has many important functions in the body, best known are probably the classical functions of maintaining calcium and phosphorus homeostasis through controlling their uptake from the gastrointestinal tract and excretion through the kidneys together with the kinetics of bone mineralization of the skeleton [3] described in many species, whereas some more recently discovered nonclassical functions of vitamin D are regulation of inflammatory markers, immune system control, and antiproliferative effects [1,2]. Although the effect of vitamin D on the calcium and phosphorus metabolism of horses appears limited, its effect on other physiological processes is unknown. Traditionally, the biological response variables measured in animals when determining quantitative requirements of vitamins have been clear cut signs of deficiency and physical performance, for example, osteomalacia and rickets in case of vitamin D. However, currently measuring immunocompetence has become the method of choice when assessing vitamin requirements which usually gives rise to greater requirements than the traditional biological measures [30].

3. Endogenous Synthesis of Vitamin D_3 in Horses

Endogenous synthesis of D_3 is facilitated by UV-light in the UV-B spectre of sunlight, which penetrates the skin and cleaves 7-dehydrocholesterol (7DHC) in the epithelial cells rendering pre-D_3, which at body temperature spontaneously isomerizes into D_3 [10] and enters the blood stream bound to VDBP. The efficiency of the endogenous D_3 synthesis depends on the intensity of the sunlight and is therefore affected by latitude and time of year. This is because the zenith angle between the sun and the earth increases during winter, causing sunlight with wavelengths in the UV-B spectre, to be reflected away from the earth in the atmosphere [31,32]. Hence, above 51°N, the conversion of 7DHC to pre-D_3 in the skin is not possible during winter months [23], that is, between September and April in the Northern Hemisphere, even in horses that are not covered with rugs.

This endogenous route of obtaining D_3 is considered the natural way of obtaining D_3 in humans and most other mammals. However, not all species are able to obtain D_3 from endogenous synthesis. For instance, the 7DHC levels in the skin of polar bears are only 10% of the levels found in humans, probably due to evolutionary adaptation to heavy fur coverage and a life at very northern latitudes lacking in sunlight [33]. Mole rats have no access to sunlight due to their subterranean life [34]. Hence, the natural source of vitamin D in species like these appears to be through dietary sources either as D_2 or D_3. It has been heavily debated whether hair-coated animals, for example, horses and cattle, are able to synthesize D_3 in the skin or if their hair coating prevents sunlight from reaching the skin surface [35] like clothes in humans [36]. However, in cattle, a direct positive correlation between the percentage of the body area exposed to sunlight and the $25OHD_3$ status in plasma has recently been established [27] and the amount of time cattle are exposed to sunlight during the day correlates directly to their $25OHD_3$ status in plasma [37], but it is unknown if these direct positive correlations can also be applied in horses.

In studies on horses and ponies, limited response in $25OHD_3$ status to sunlight exposure has generally been reported. In Finland, Mäenpää et al [14] found all over very low $25OHD_x$ levels in mares with very small seasonal variation. In January, the plasma concentration of $25OHD_x$ was 4.20 ± 0.34 ng/mL and in June 6.20 ± 0.36 ng/mL,