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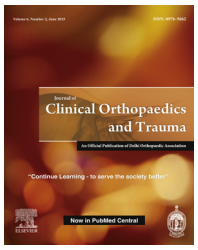

Review Article

Resurgence of vitamin D: Old wine in new bottle

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ABSTRACT

There are early references of it in ancient text and physicians have discussed its importance and features of its deficiency in the past. Vitamin D has again regained interest with recent dramatic rise in the incidence of deficiency in the developing as well as developing world. In this review article, we discuss the biochemical and role of vitamin D in the skeletal system. We also discuss the recommended dietary requirements and features of skeletal deficiency. Extra-skeletal roles of vitamin D deficiency have been a matter of debate lately and it has also been discussed in detail in this article. In conclusion, it would not be wrong to label vitamin D as one of the most important vitamin involved in the metabolism of the musculoskeletal system and any clinician, especially the orthopaedician, should be well versed with its overall mechanism and roles in the human body.

1. Introduction

Although Vitamin D Deficiency disorder (VDD), namely Rickets was known for centuries, but its causative factor was known only after the discovery of Vitamin D (VD) by E.V. McCollum and his associates in 1913. But it attained a new interest in recent years as VDD has been found to be pandemic worldwide and its association with others diseases.[1,2] **Vitamin D** is a group of fat-soluble secosteroids (a steroid with a "broken" ring) plays an important role in bone metabolism and seems to have some anti-inflammatory and immune-modulating properties. Several forms (vitamers) of VD exist namely, VD_1 (ergocalciferol with lumisterol), VD_2 (ergocalciferol), VD_3 (cholecalciferol) VD_4 (dihydroergocalciferol), VD_5 (sitacalciferol). The most important compounds in this group are VD_3 and VD_2.[3–5] In this review article we discuss vitamin D metabolism and functions in the human body. The common causes of vitamin D deficiency along with daily requirements and prevalence of vitamin D deficiency in the world and India have been discussed along with the extra-skeletal manifestations of vitamin D.

2. Vitamin D metabolism and functions

Ultra Violet (UV)-B irradiation of skin triggers photolysis of 7-dehydrocholesterol ($proVD_3$) to $preVD_3$ in the plasma membrane of human skin keratinocytes.[6–8] Once formed in the skin, cell plasma membrane $preVD_3$ is rapidly converted to VD_3 by

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the skin's temperature VD_3 from the skin and VD from the diet undergo two sequential hydroxylations, first in the liver to 25 (OH)D and then in the kidney to its biologically active form, 1,25-dihydroxyVD (1,25[OH]2D) (Fig. 1).

3. Mechanism of action

VD acts in 2 ways:

I) *Genomic action of VD*: VD Receptor (VDR) is a member of the superfamily of nuclear receptors for steroid hormones, which can be categorized as a ligand activated transcription factor.[9] VDR is also thought to play an important role in engendering to rapid action of 1, 25 (OH)2D3.[10]

II) *Non genomic action of VD*: There exist rapid response non-genomic actions of VD, which are mediated through cell surface receptors, known as 1, 25 D3 MARRS (membrane associated rapid response steroid binding proteins).[11]

4. Bioactions of VD

On Intestine: 1, 25 (OH)2D3 enhances the efficacy of small intestine to absorb calcium and phosphorus, iron, magnesium, zinc.[10]

On Skeleton: VD is essential for the development and maintenance of mineralized skeleton.

Growth plate development requires coordinated calcium and 1, 25 (OH)2D3 actions and VDR, where as optimal osteoblastic bone formation and osteoclastic bone resorption demand both 1, 25(OH)2D3 and VDR.1, 25(OH)2D3 regulates osteoclastogenesis in reciprocal regulation of receptor

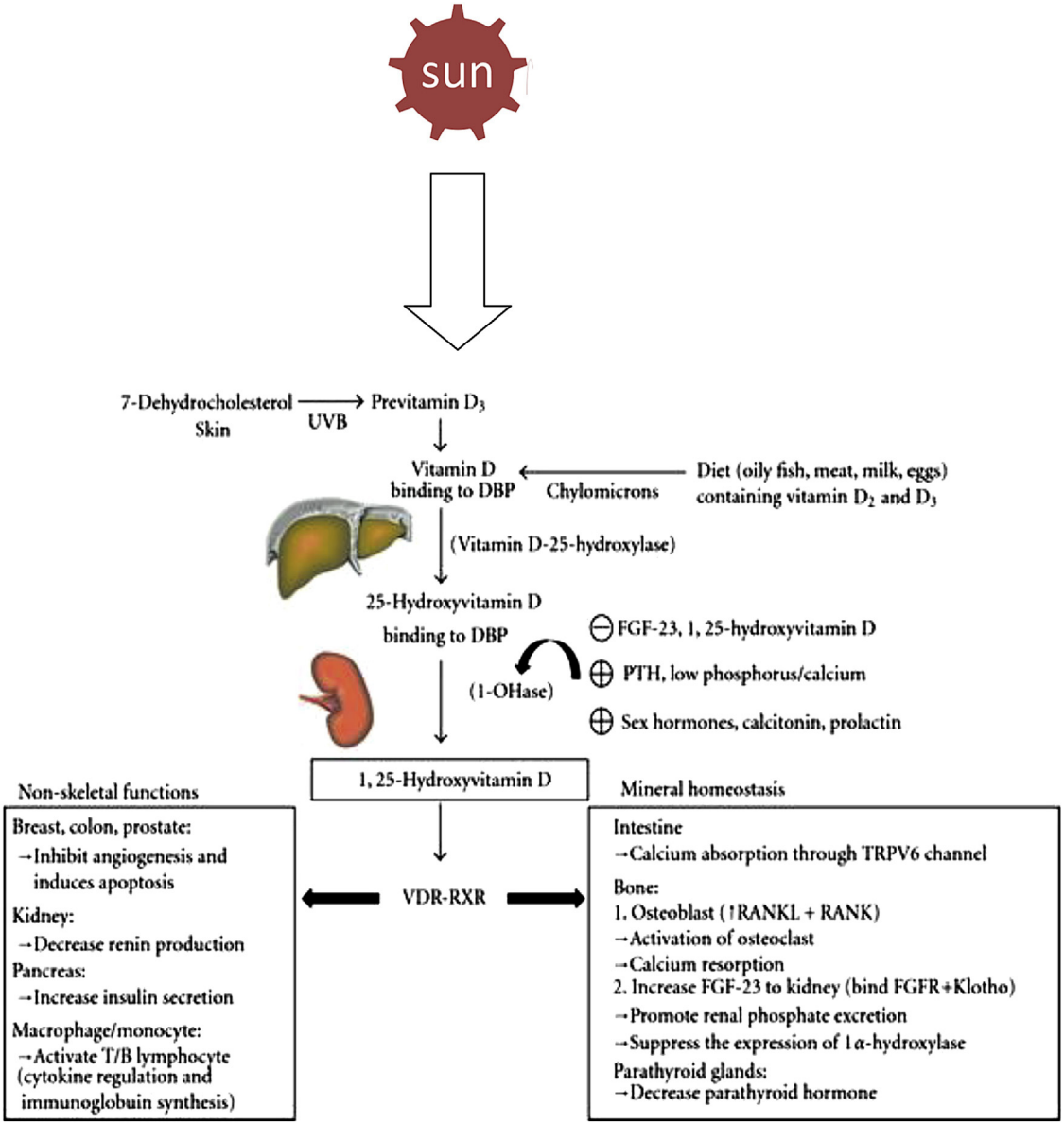

Fig. 1 – Biosynthesis and metabolism of vitamin D (*UVB* = Ultraviolet ray B, *DBP* = VD Binding Protein, *FGF* = Fibroblast Growth Factor, *PTH* = Parathormone, *VDR* = VD Receptor).