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Dealing with vitamin D deficiency in general practice – A Review

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Abstract

Vitamin D is the most common nutritional deficiency worldwide. It is characterized by serum 25 (OH) D< 50 nmol/L. It is usually caused by sun avoidance, using sun protection, inadequate dietary intake, malabsorption syndrome and some drug interaction. Most of the patients are asymptomatic or present with nonspecific symptoms, however severe and prolong deficiency causes rickets or growth retardation in children and osteomalacia, osteopenia or osteoporosis in adults. Vitamin D deficiencies are treated with supplementary vitamin D and sensible sunlight exposure after plasma assays.

Introduction

Vitamin D deficiency has been recognized as a worldwide health issue and common under diagnosed condition. It presents with a wide range of acute and chronic medical conditions. Several studies suggest that vitamin D reduces the risk of type 1 diabetes mellitus, certain cancers, cardiovascular disease, depression, cognitive decline, autoimmunity, pregnancy complications, allergy and frailty[1,2].

Epidemiology

It is the most common worldwide nutritional deficiency[3,4]. It is associated with various medical conditions and the strong associations are summarized in table 1.

Metabolism of vitamin D

There are two forms of vitamin D. Ergocalciferol (D2) is a plant product and cholecalciferol (D3) is an animal product1. Vitamin D is a fat-soluble vitamin and a hormone. Vitamin D3 is produced endogenously. Both vitamin D2 and vitamin D3 can be obtained from food (Figure 1).

As sunlight destroys any excess vitamin D3 produced in the skin, excessive sun exposure cannot cause vitamin D3 intoxication. Major active form of vitamin D is 1,25 (OH)D (calcitriol)[5,6,7,8].

Table 1. Medical conditions, which are strongly associated with vitamin D deficiency

Cancers	Prostate, Colon, Breast Ovarian, Pancreas
Cardiovascular system	Hypertension Heart diseases
Pregnancy	Pre-eclampsia, Low birth weight Preterm birth
Infections	Tuberculosis URTI Upper respiratory tract infection
Neuro-psychiatry	Schizophrenia, Parkinson's disease' Cognitive dysfunction, Alzheimer's diseases, Dementia, Depression
Autoimmune disease	Type1 diabetes mellitus
Rheumatology	Osteoarthritis

Vitamin D deficiency/ insufficiency

Vitamin D deficiency is defined as a serum 25 - hydroxy vitamin D level of <50 nmol/L (<20 ng/ml) and vitamin D insufficiency is defined when the 25 hydroxy vitamin D level falls between 52 and 72 nmol/L (21 and 29 ng/ml)[3,4,9,10].

Causes of vitamin D deficiency and insufficiency

Sunlight is the major source for vitamin D. Table 2 illustrates the common etiology for vitamin D deficiency or insufficiency. Ability of the skin to produce the vitamin D decreased with age. Therefore aging is considered as a risk factor[11].

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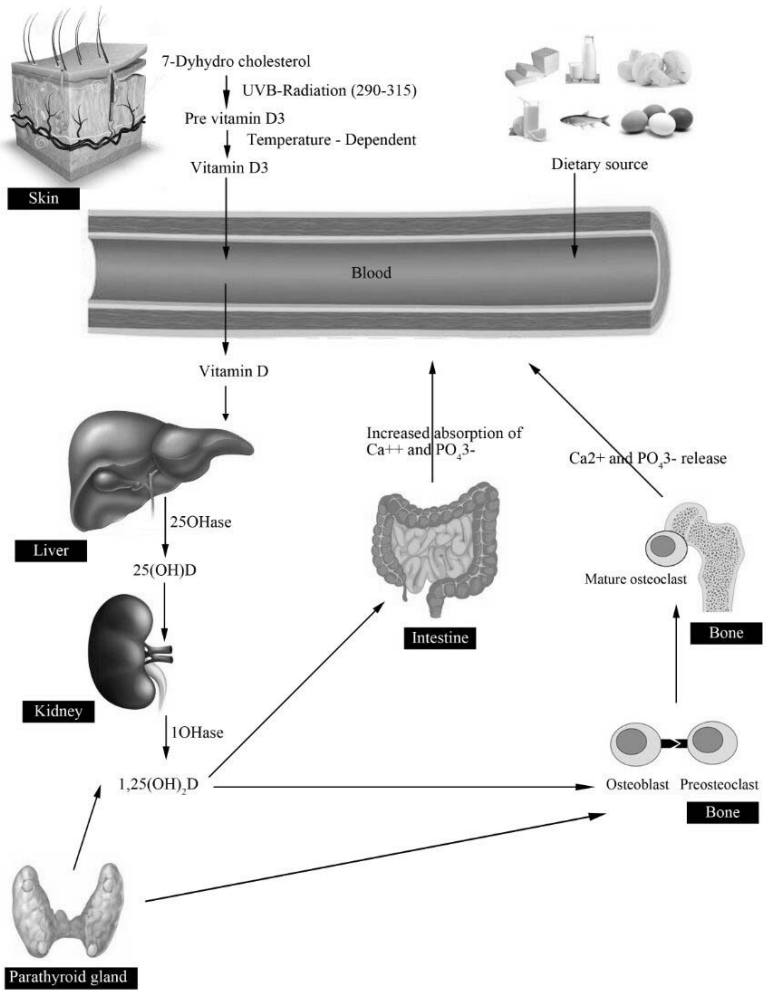

Figure 1. *The metabolism of vitamin D in human body.*

Table 2.

Acquired

- Lack of sun exposure.
- Application of sun block creams.
- Inadequate dietary and supplemental vitamin D.
- Intestinal malabsorption (celiac diseases, crohn's disease).
- Renal failure.
- Severe liver failure.
- Drugs (antiepileptic, glucocorticoids, Rifampicin,
- Primary hyperparathyroidism.
- Hypothyroidism.
- Obesity.

Inheritance

- Vitamin D- Dependent rickets (Type 1, Type 2, Type 3)
- X-linked hypophosphatemic rickets
- Autosomal – dominant hypophosphatemic rickets.

Table 3. Symptoms of vitamin D deficiency

Adults	• Bone pain (localized/generalized)
	• Easy fatigability
	• Malaise
	• Difficulty in rising from a sitting position
	• Muscle cramps
	• Parasthesia
Children	• Failure to thrive
	• Delayed achievement of motor milestones

History and clinical examination

History and clinical examination are essential for the diagnosis and screening. In mild or early disease, patient can be asymptomatic[12,13,14,15].

Table 4. Signs of vitamin D deficiency in children and adults

In children (rickets)

- Bone deformity of forearm
- Posterior bowing of distal tibia
- Genu varus
- Valgus deformity of legs
- Rachitic rosary
- Frontal bossing
- Pectuscarinatum
- Head sweating

In adults

- Bone tenderness
- Waddling gait
- Proximal myopathy

Laboratory investigation

Serum level of 25 (OH) D is the best method to determine. Although 1,25 (OH) 2D is the biologically active form, it provides no information about vitamin D status, because it is often normal or even elevated in children and adults who have vitamin D deficiency, 1000 times lower than 25-(OH) D and has a low half-life -4 hours.

Measurement of plasma calcium, phosphate, intact PTH and alkaline phosphatase can help to determine the etiology for vitamin D deficiency.

Table 5. Typical biochemical profile of vitamin D deficiency

Biochemical profile	*Results*
Serum 25 (OH) D_2	Low
Serum Ca^{2}+	Normal
Phosphate	Low-normal
Intact PTH	High-normal/ elevated

Table 6. Expected radiological finding of patients with rickets, osteomalacia and osteoporosis

Rickets	Widening of epiphyseal plate
Osteomalacia	Looser's pseudo fracture
Dual X-ray absorptiometry	Osteoporosis, osteopenia

Diagnostic criteria

Vitamin D deficiency

It is defined as serum 25-hydroxyvitamin D level of <50 nmol/L (<20 ng/ml).

Vitamin D insufficiency

It is defined as serum 25-hydroxyvitamin D level between 52-72nmol/L (21-29ng/ml).

In children, a serum 25- (OH)D level of <37nmol/L in usually associated with skeletal manifestation of vitamin D deficiency rickets[1,2].

Management

Vitamin D replacement

Vitamin D replacement is the mainstay of treatment. Target level of vitamin D in both children and adults is serum 25(OH)D3 between 75 and 250 nmol/L. The correction can be with vitamin D2 (ergocalciferol) or vitamin D3 (colecalciferol). Both can be given orally for 6 to 8 weeks followed by a lower maintenance dose. Ongoing maintenance therapy is recommended for those with documented vitamin D deficiency and where the underlying cause for this cannot be rectified.

Higher daily oral dose is required in patient with intestinal or fat malabsorption syndromes and history of gastric bypass surgery. Pregnant or lactating women with vitamin D deficiency should be treated as for non pregnant adults[3].

Insufficiency

Ergocalciferol/Colecalciferol

Children are treated with a dose of 1000-2000 IU/day for 8weeks or 50,000 IU given orally once weekly for 6 weeks followed by a maintenance dose of 400 – 1000 IU/ day . For an adult, 50000 IU is given orally once weekly for 8 weeks followed by a maintenance dose of 50000 IU twice monthly[16,17].

Deficiency

Ergocalciferol

In children – It is treated with 1000-2000 IU/day or 50 000 IU orally once weekly for 6 weeks and then followed by a maintenance dose of 400-1000IU/day. Adult are treated with 50 000IU orally once weekly for 8 weeks and then followed by 50 000 IU twice monthly as maintenance[16,17,18,19].

Colecalciferol

Children are treated with 1000-2000IU/day orally for 8 weeks or 50 000IU orally once weekly for 6 weeks. Maintenance dose is 400-1000IU/day. Adults are treated with 50 000 IU orally once weekly for 8 weeks and 50 000 IU is given twice monthly as maintenance[16,17,18,19].

UVB radiation exposure

UVB radiation exposure is an excellent source of vitamin D and it should be recommended to all patients for both treatment and prevention.

Exposing the arm and legs (with sun protection of the face) for about 5 to 30 minutes between 10 am and 3 pm twice a week is recommended. Darker skinned people require longer exposure (3-6 times)[20].

Calcium and phosphate replacement

Patients who do not meet the daily requirements of calcium from dietary source alone should be given supplementation. Recommended dietary intake of calcium is between 1000-1300 mg/day depending on age and sex.

For children, calcium carbonate is given 45-65 mg/kg/day orally in 4 divided doses. Adults are given 1-2g/day orally in 3-4 divided doses for both vitamin D deficiency and insufficiency. Supplementation of phosphate is not orally needed unless there is acquired or inherited disorder-causing phosphate wasting in the kidney[21].

Conclusion

Vitamin D deficiency should be considered as a differential diagnosis for patients presented with non specific symptoms. However diagnosis of vitamin D deficiency is only possible by assessing the plasma Vitamin D level. Unfortunately high cost of plasma vitamin D assays is a big challenge. There is no enough evidence to prescribe vitamin D and then periodic monitoring of any symptomatic improvement without plasma assays.

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