Vitamin D – An Overview

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Overview

- What is Vitamin D?
- Vitamin D production and metabolism
- Functions of Vitamin D
- Vitamin D, Calcium, Phosphate and PTH- interplay between them in maintaining skeletal health
- Criteria for Vitamin D deficiency and sufficiency
- Epidemiology of Vitamin D status in the population
Vitamin D is not truly a Vitamin!

- Definition of Vitamin
  - An organic compound which is an essential nutrient which body cannot synthesise in sufficient quantities and is required in diet
  - Vitamin D *can* be synthesised in the body
  - Unlike other vitamins, Vitamin D is not abundantly present in diet (fish, egg yolk and mushrooms)
Vitamin D is a Hormone!

- Endocrine system regulates and controls the synthesis of active form of Vitamin D.

- Vitamin D behaves like a hormone- produced and released by a cell or a gland, circulates in the body and affects cellular function in other parts of the body.
Two forms of Vitamin D

- Biologically equally effective
- Vitamin D$_3$ has a longer half life than Vitamin D$_2$. Relevant when large stat doses (Weekly/Monthly) are considered

Vitamin D$_2$
- Plant source
- Ergocalciferol- Irradiation of yeast

Vitamin D$_3$
- Animal source
- Colecalciferol- Irradiation of lanonin extracted from sheep wool
Vitamin D: Sources, metabolism & functions.
Sources & Metabolism of Vitamin D

**Solar UVB (280-310nm)**

**Endogenous Vitamin D**
- Skin

**Dietary source Vitamin D**
- Oily fish, eggs, fortified foods e.g:
  - Infant formulas
  - Cereals
  - Margarine

**Liver**
- 25-hydroxy vitamin D (major circulating metabolite)
- 1α hydroxylase

**Kidney**
- 1,25 Dihydroxy Vitamin D
- PTH
- ↓Ca
- ↓P
- FGF23
Endogenous Source of Vitamin D

Solar UVB (280-310nm)

Factors Controlling Vit D synthesis
- Intensity of sunlight
- Exposure of skin to sunlight
- Skin pigmentation
- Ageing

Endogenous Vitamin D

Skin

7-dehydrocholesterol

Previtamin D

(Slow conversion over 48 hours)

Colecalciferol (Vitamin D₃)

Continued sun exposure

Inactive Lumisterol & Tachysterol
Dietary Sources of Vitamin D

- Oily fish such as salmon, mackerel and herring, fish oils including cod liver oil and eggs are sources of Vitamin D.

500-1000IU/100g

100-250IU/100g

Holick et al Am J Clin Nutr 2008
Dietary Sources of Vitamin D

- Food fortification therefore, is a reliable source of Vitamin D.
- In USA all dairy products are fortified with Vitamin D.
- In UK compulsory fortification was discontinued following outbreak of hypercalcaemia in 1950’s (Except for Margarine)

40-100 IU/100 kcal
Metabolism of Vitamin D

Solar UVB (280-310nm)

Endogenous Vitamin D

Skin

Dietary source Vitamin D

Oily fish, eggs, mushrooms fortified foods e.g:
- Infant formulas
- Cereals
- Margarine

Colecaciferol + Vitamin D-binding protein (VDBP)

Liver

25-hydroxy vitamin D+ VDBP
(major circulating metabolite)

Kidney

1α hydroxylase

1,25 Dihydroxy Vitamin D + VDBP

PTH
↓Ca
↓P
FGF23
Overview of $1,25\,(\text{OH})_2\text{D}$ Regulation of Calcium and Phosphate Metabolism

- Increases Calcium & Phosphorous absorption
- Maintains serum Calcium
- Promotes Calcium re-absorption. Mediated through PTH
- Promotes mineralisation
  - Indirectly
  - Direct action

$1,25\,(\text{OH})_2\text{D}$
Role of $1,25\,(OH)_2D$ in Calcium Homeostasis

From AJCN. 2004; 80,(6) 1689-96.
Physiological response to Vitamin D deficiency

Low 1,25 (OH)_2D

Ca absorption from gut

Serum Ca

If Ca intake is high

Serum Ca is maintained

Mobilisation of Ca & PO_4

Ca absorption from gut

Conversion of 25(OH)D to 1,25 (OH)_2D

Serum Ca Normalises

Biochemistry

Normal Ca

Vit D

1,25 (OH)2D

PTH

PO_4

PTH normal

If Ca intake is high
## Low Calcium Diet & Vitamin D Deficiency

<table>
<thead>
<tr>
<th></th>
<th>Pune (18.34°N) N = 50</th>
<th>Manchester (54.4°N) N=51</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years)</td>
<td>14.7 ± 0.7</td>
<td>15.3 ± 0.4</td>
</tr>
<tr>
<td>Serum 25OHD concentrations &lt; 12 ng/ml</td>
<td>70%</td>
<td>73%</td>
</tr>
<tr>
<td>PTH &gt; upper end of the reference range</td>
<td>48%</td>
<td>6%</td>
</tr>
<tr>
<td>Serum calcium concentration &lt; 2.2 mmol/l (%)</td>
<td>74%</td>
<td>0%</td>
</tr>
<tr>
<td>Non-specific aches and pains (%)</td>
<td>76%</td>
<td>26%</td>
</tr>
<tr>
<td>Genu Varum or Genu Valgum (%)</td>
<td>44%</td>
<td>0%</td>
</tr>
<tr>
<td>Dietary vitamin D intake (µg/day)</td>
<td>0.17</td>
<td>1.3</td>
</tr>
<tr>
<td>% Ca intake (mg/day) - dairy products</td>
<td>65 (31-76)</td>
<td>401 (195 - 594)</td>
</tr>
<tr>
<td>Total Ca intake (mg/day)</td>
<td>449 (356 - 538)</td>
<td>Data not available</td>
</tr>
</tbody>
</table>

Khadilkar, Das, Sayyad, Sanwalka, Bhandari, Khadilkar, Mughal. Low Calcium intake & Hypovitaminosis D in Adolescent Girls. Archives of Disease in Childhood. 2007 ;92(11):1045
Vitamin D Deficiency & Insufficiency

Definition of vitamin D deficiency & sufficiency based on serum 25(OH)D concentrations

Table 1: Management of vitamin D status

<table>
<thead>
<tr>
<th>Vitamin D status</th>
<th>Serum 25-OHD (nmol/l)</th>
<th>Serum 25-OHD (ng/ml)</th>
<th>Intervention</th>
</tr>
</thead>
<tbody>
<tr>
<td>Severe deficiency</td>
<td>&lt;25</td>
<td>&lt;10</td>
<td>Treatment dose</td>
</tr>
<tr>
<td>Insufficiency</td>
<td>25–50</td>
<td>10–20</td>
<td>Supplementation</td>
</tr>
<tr>
<td>Sufficiency</td>
<td>51–75</td>
<td>20–30</td>
<td>Lifestyle advice</td>
</tr>
<tr>
<td>Excess</td>
<td>&gt;250</td>
<td>&gt;100</td>
<td>Stop treatment</td>
</tr>
</tbody>
</table>

25-OHD, 25-hydroxyvitamin D.

Vitamin D & PTH concentrations

Thomas et al NEJM 1998
Vitamin D Deficiency & Insufficiency

Sai et al. JCEM, March 2011
Vitamin D Deficiency & Insufficiency

Rosen et al JCEM, April 2012.
Institute of Medicine Committee Members Response to Vitamin D Guidelines
Vitamin D and Evolution

Luxwolda et al *Br J Nutr.*, 2012 Nov 14

Traditional living in East Africa- mean serum 25-OHD of 115 nmol/l

Fig. 1. Serum 25-hydroxyvitamin D (25(OH)D) frequency distributions for Maasai (■) and Hadzabe (□). The numbers in the bars refer to the absolute number of subjects.
Vitamin D Concentration and Mortality

Durup et al. JCEM 2012 Aug
All-cause mortality with serum 25OHD
Vitamin D deficiency is now recognised as a worldwide pandemic.

Cross sectional survey of 1102 children aged 4-18 years
- Insufficiency in 35%
- Increased risk in
  - Adolescents
  - Non white
  - On income support
  - Overweight

Plos One July 2012
Epidemiology of Vitamin D Deficiency

Cross sectional survey of 7560 children - mean age of 9 years
Insufficiency in 29% (<50nmol/l; <20ng/ml)
Increased risk in
  ▪ Winter season
  ▪ Time spent indoors
  ▪ Low socioeconomic
  ▪ Non white
  ▪ Advanced pubertal status

JCEM April 2012
Factors which contribute to development of Vitamin D deficiency

- Residence in Northern or Southern Latitudes
- Pigmented skin
- Sun blocking creams – *Factor 8 ↓ Vit D synthesis by >95%*
- Sunshine avoidance for religious or cultural reasons
- Cloud Cover & Atmospheric Pollution
- Obesity
- Genetic propensity
- Low dietary Calcium & High Fibre diets
Low Calcium & High Fibre Diet and Vitamin D Status

- High fibre & phytic acid reduce dietary Ca intake
- High Phosphate diet reduces Ca/P ratio, reducing serum Ca
- Low Ca intake leads to secondary hyperparathyroidism & raised serum $1,25(\text{OH})_2\text{D}$ concentration
- Raised serum $1,25(\text{OH})_2\text{D}$ concentration degrades 25OHD to inactive $24,25(\text{OH})_2\text{D}$, thereby depleting body stores of vitamin D
Summary

- Two forms of Vitamin D- Ergocalciferol, D$_2$ from plant source and Colecalciferol, D$_3$ from animal source
- 80-90% of Vitamin D requirement can be synthesised by exposure to sunlight
- Changes in demography and lifestyle necessitates food supplementation as an important source of Vitamin D
Summary

- 1,25 (OH)$_2$ D is important for calcium homeostasis
- Physiological response of Vitamin D deficiency is dependent on dietary calcium intake
- Optimal serum concentration of Vitamin D is controversial, aim for 51-75nmol/l (20-30ng/ml)
Thank You