No association between vitamin D deficiency and parathyroid hormone, bone density and bone turnover in a large cohort of HIV-infected men on tenofovir

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Vitamin D deficiency (VDD)

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25-hydroxyvitamin D [25(OH)D] < 50 nmol/L

Decreased whole-body calcium

Increased parathyroid hormone (PTH)

Increased reabsorption of calcium
Increased excretion of phosphate

Decreased bone mineral density (BMD)
Increased bone turnover

Low serum phosphate and osteomalacia
VDD and HIV infection

• High rates of VDD have been reported in HIV-positive patients\(^1\)

• Factors associated with VDD are similar to those in general population\(^2\)
  – Black/Hispanic ethnicity
  – Reduced sunlight exposure
  – Increased body mass index (BMI)
  – Low exercise level

1. Childs K et al. AIDS 2012, 26:253–262
VDD and antiretroviral therapy

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Efavirenz

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VDD and antiretroviral therapy

Vitamin D deficiency (VDD)
25-hydroxyvitamin D [25(OH)D] < 50 nmol/L

- Efavirenz

- Tenofovir

- Decreased whole-body calcium

- Increased parathyroid hormone (PTH)
  - Kidney damage (Renal tubular dysfunction/Fanconi syndrome)
  - Increased reabsorption of calcium
  - Increased excretion of phosphate
  - Increased excretion of phosphate
  - Low serum phosphate and osteomalacia

- Decreased bone mineral density (BMD)
- Increased bone turnover
Aims

• Prevalence of VDD

• Factors associated with VDD

• Associations of VDD and tenofovir with PTH, bone turnover and BMD
Methods

• Cross-sectional cohort of randomly selected HIV-positive men

• Demographic and HIV factors

• Risk factors for low BMD (self-reported questionnaire)

• Fasting blood samples:
  – 25(OH)D
  – PTH
  – Bone resorption: C-terminal telopeptide crosslinks (CTX)
  – Bone formation: N-terminal propeptide of type I collagen (P1NP)

• Dual-energy x-ray absorptiometry (DXA): BMD (g/cm²) at lumbar spine, non-dominant total hip and femoral neck
## Demographics

<table>
<thead>
<tr>
<th>Demographic</th>
<th>Total N=422</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Age</strong> years, mean (SD)</td>
<td>47 (10)</td>
</tr>
<tr>
<td>White ethnicity n (%)</td>
<td>398 (94)</td>
</tr>
<tr>
<td>MSM n (%)</td>
<td>392 (93)</td>
</tr>
<tr>
<td>Years since HIV diagnosis median (IQR)</td>
<td>9.6 (5.0, 15.5)</td>
</tr>
<tr>
<td><strong>cART On cART</strong> n (%)</td>
<td>381 (90)</td>
</tr>
<tr>
<td><strong>Duration on cART</strong> median (IQR)</td>
<td>6.1 (2.2, 11.7)</td>
</tr>
<tr>
<td><strong>VL &lt; 40 copies/mL</strong> n (%)</td>
<td>365 (87)</td>
</tr>
<tr>
<td><strong>Current tenofovir</strong> n (%)</td>
<td>292 (69)</td>
</tr>
<tr>
<td><strong>Current efavirenz</strong> n (%)</td>
<td>135 (32)</td>
</tr>
</tbody>
</table>

MSM: men who have sex with men, cART: combination antiretroviral therapy, VL: viral load
Prevalence of VDD

- Overall prevalence of VDD was 56%
- Of 381 men on cART, VDD occurred in 215 (56%)
- Of 292 men on tenofovir, VDD occurred in 166 (57%)

<table>
<thead>
<tr>
<th></th>
<th>Total (%) (n=421*)</th>
<th>Patients on tenofovir (%) (n=292)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Normal (&gt; 75 nmol/L)</td>
<td>60 (14)</td>
<td>37 (13)</td>
</tr>
<tr>
<td>Insufficiency (50 - 75 nmol/L)</td>
<td>127 (30)</td>
<td>89 (30)</td>
</tr>
<tr>
<td>Deficiency (25 - 50 nmol/L)</td>
<td>204 (49)</td>
<td>144 (49)</td>
</tr>
<tr>
<td>Severe deficiency (&lt; 25 nmol/L)</td>
<td>30 (7)</td>
<td>22 (8)</td>
</tr>
</tbody>
</table>

* Data missing in 1 patient
## Associations with VDD

<table>
<thead>
<tr>
<th></th>
<th>Crude OR (95% CI)</th>
<th>P</th>
<th>Adjusted OR (95% CI)</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sampling date*</td>
<td>1.27 (1.09, 1.47)</td>
<td>0.002</td>
<td>1.29 (1.10, 1.51)</td>
<td>0.001</td>
</tr>
<tr>
<td>Nadir CD4 count, cells/µL</td>
<td>0.93 (0.86, 1.00)</td>
<td>0.06</td>
<td>0.92 (0.84, 1.00)</td>
<td>0.05</td>
</tr>
<tr>
<td>Current tenofovir</td>
<td>1.05 (0.65, 1.69)</td>
<td>0.85</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Current efavirenz</td>
<td>1.71 (1.11, 2.63)</td>
<td>0.02</td>
<td>1.94 (1.21, 3.13)</td>
<td>0.01</td>
</tr>
</tbody>
</table>

*Sampling away from August, which was considered to be month with maximum sun exposure

Other factors inserted into model: age, body mass index, skin colour, kidney disease, duration of HIV infection, HIV clinical stage, HIV RNA viral load, current protease inhibitor use, vitamin D supplementation
Vitamin D and PTH

<table>
<thead>
<tr>
<th></th>
<th>25(OH)D &gt; 50 nmol/L (n=166)</th>
<th>VDD (&lt; 50 nmol/L) (n=215)</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>High PTH (&gt; 65 ng/L), n (%)</td>
<td>45 (27)</td>
<td>46 (21)</td>
<td>0.18</td>
</tr>
<tr>
<td>PTH, median (IQR)</td>
<td>53 (39, 66)</td>
<td>47 (36, 63)</td>
<td>0.07</td>
</tr>
</tbody>
</table>

- Significant but weak correlation between vitamin D and PTH (r=0.11, p=0.03)
- Proportion of patients with high PTH did not differ with vitamin D status (p=0.18)
Vitamin D, PTH and tenofovir

- No association between vitamin D and PTH according to tenofovir ($r=0.11$, $p=0.06$) or non-tenofovir ($r=0.12$, $p=0.29$) cART

- No interaction effect between vitamin D and tenofovir use ($p=0.94$)
**Bone turnover and tenofovir**

<table>
<thead>
<tr>
<th>Median (IQR)</th>
<th>All patients (n=381)</th>
<th>VDD (n=215)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Tenofovir (n=293)</td>
<td>Tenofovir (n=166)</td>
</tr>
<tr>
<td><strong>CTX</strong></td>
<td>1.94 (0.85, 4.84)</td>
<td>2.02 (1.03, 4.84)</td>
</tr>
<tr>
<td><strong>P1NP</strong></td>
<td>13.6 (5.6, 32.4)</td>
<td>14.5 (5.8, 40.7)</td>
</tr>
</tbody>
</table>

P: statistical significance

VDD: vitamin D deficiency; CTX: C-terminal telopeptide crosslinks, ng/mL; P1NP: N-terminal propeptide of type I collagen, ng/mL
## BMD and tenofovir

<table>
<thead>
<tr>
<th>Mean (SD)</th>
<th>All patients (n=381)</th>
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<th>VDD (n=215)</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Tenofovir (n=293)</td>
<td>Non-tenofovir (n=88)</td>
<td>P</td>
<td>Tenofovir (n=166)</td>
</tr>
<tr>
<td>Lumbar spine BMD</td>
<td>1.13 (0.15)</td>
<td>1.15 (0.17)</td>
<td>0.41</td>
<td>1.13 (0.15)</td>
</tr>
<tr>
<td>Total hip BMD</td>
<td>1.00 (0.13)</td>
<td>0.99 (0.14)</td>
<td>0.61</td>
<td>0.99 (0.14)</td>
</tr>
<tr>
<td>Femoral neck BMD</td>
<td>0.94 (0.12)</td>
<td>0.94 (0.18)</td>
<td>0.96</td>
<td>0.94 (0.13)</td>
</tr>
</tbody>
</table>

VDD: vitamin D deficiency; BMD: bone mineral density, g/cm²
Summary

• Majority of patients were vitamin D-deficient

• Factors associated with VDD similar to reports in other studies in HIV-positive patients

• No association between vitamin D and PTH, bone turnover or BMD

• Results did not alter with tenofovir use
Discussion

• No evidence to support additional monitoring of bone status in patients on tenofovir, regardless of vitamin D status

• No association between VDD and tenofovir use

• No association between tenofovir use and BMD

• Longitudinal data are required
Acknowledgements

- Professor Martin Fisher

- Patients in Brighton who participated in the study