Effect of calcium and cholecalciferol supplement on bone mass accrual among perinatally HIV-infected adolescents with osteopenia


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Background

• Prevalence of low bone mineral density (BMD) among HIV-infected adolescents\(^1\): range 4-32%

• **Factors associated with low BMD**
  
  – Nutrition factors\(^2\)
    
    • Only 17% had calcium intake > 1000 mg/day
    • Only 25% had 25-OH vitamin D > 30 ng/ml
  
  – HIV infection esp. advanced stage
  
  – Antiretroviral drugs e.g. TDF, PIs

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\(^1\)Puthanakit T, Siberry GK 2013, JIAS;16:18575
Bone mineral density in adolescents

- **BMD** = Bone mineral content (g/cm²) per area
- **BMD** is increased by age
- **BMD z-score** is a comparison with age, gender, ethnicity

N=174
N=193
Study Objective

To describe changes in bone mineral density (BMD) among perinatally HIV-infected adolescents with osteopenia (< -2 Z-score) before and after calcium + cholecalciferol supplement

Dual-energy X-ray absorptiometry (DXA)
At Lumber spine (L2-L4)
Study design

Population*: Perinatally HIV-infected aged 12-20 yrs
L2-L4 BMD < -2 Z-score

Intervention: 1.2 g of calcium + Vit D3 400 IU/d * 6 mos

1st BMD

2nd BMD 3rd BMD

Dietary & Exercise Education & Counselling

6 months Calcium + D3 supplement

21 months

Study procedure

• **Without vitamin D deficiency**
  – Calcium 600 mg+ D3 200 IU (Oskept) 1 tab bid

• **With vitamin D deficiency (< 20 ng/mL)**
  – Vitamin D2 60,000 IU/week * 8 weeks then every 4 weeks **PLUS**
    Oskept 1 tab twice daily until 25-OHD > 30 mg/mL

• **Parameters of interest**
  – L2-L4 BMD by DEXA scan: BMD, BMD z-score
  – Vitamin D, Calcium, Parathyroid hormone (PTH)
Statistical Methods

• BMD z-score was calculated using age and sex-matched Thai adolescent norms (Lunar prodigy)\textsuperscript{1}

• Comparison of changes in BMD and BMDz-score pre and post supplementation using signed-rank test

### Result: Baseline characteristics

<table>
<thead>
<tr>
<th></th>
<th>Total (N=24)</th>
<th>Persistent (N=13)</th>
<th>New (N=11)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Age (years)</strong></td>
<td>14.1 (13.0-14.9)</td>
<td>13.8 (12.9-15.1)</td>
<td>14.5 (13.3-14.8)</td>
</tr>
<tr>
<td><strong>Male (%)</strong></td>
<td>15 (63%)</td>
<td>6 (46%)</td>
<td>9 (82%)</td>
</tr>
<tr>
<td><strong>CD4 cell (cell/mm³)</strong></td>
<td>706 (540-789)</td>
<td>738 (614-807)</td>
<td>610 (472-769)</td>
</tr>
<tr>
<td><strong>% HIV RNA &lt; 50 c/ml</strong></td>
<td>21 (88%)</td>
<td>11 (85%)</td>
<td>10 (91%)</td>
</tr>
<tr>
<td><strong>Tanner stage</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>1-2</td>
<td>15 (63%)</td>
<td>9 (69%)</td>
<td>6 (55%)</td>
</tr>
<tr>
<td>3-5</td>
<td>9 (37%)</td>
<td>4 (31%)</td>
<td>5 (45%)</td>
</tr>
</tbody>
</table>
### Result: Pre and post supplement

<table>
<thead>
<tr>
<th>Data of 24 adolescents</th>
<th>Pre-supplement</th>
<th>Post-Supplement</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>BMD (g/cm²)</td>
<td>0.76 (0.70-0.86)</td>
<td>0.82 (0.78-0.92)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>BMD z-score</td>
<td>-2.59 (-3.02 to -2.35)</td>
<td>-1.70 (-2.76 to -1.10)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>BMD &gt; -2z-score</td>
<td>0(0%)</td>
<td>14(58%)</td>
<td>-</td>
</tr>
<tr>
<td>25-OH vitamin D</td>
<td>31.2 (23.6-37.3)</td>
<td>28.7 (24.2-35.8)</td>
<td>0.573</td>
</tr>
<tr>
<td>Calcium</td>
<td>9.3 (9.0-9.5)</td>
<td>9.5 (9.2-9.9)</td>
<td>0.036</td>
</tr>
<tr>
<td>PTH level</td>
<td>58.2 (35.7-84.0)</td>
<td>42.8 (33.3-51.7)</td>
<td>0.055</td>
</tr>
</tbody>
</table>
### Result: Change pre vs post supplement

<table>
<thead>
<tr>
<th>Data of 13 adolescents</th>
<th>Change Pre-Supplement</th>
<th>Change Post-supplement</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Interval (month)</td>
<td>20.9 (20.5-21.6)</td>
<td>6.0 (5.8-6.7)</td>
<td>N/A</td>
</tr>
<tr>
<td>BMD gain (g/cm²)</td>
<td>0.063 (0.047-0.096)</td>
<td>0.057 (0.040-0.066)</td>
<td>0.133</td>
</tr>
<tr>
<td>BMD z-score change</td>
<td>-0.50 (-1.00 to 0.06)</td>
<td>0.65 (0.13 to 1.20)</td>
<td>0.028</td>
</tr>
<tr>
<td>25-OH vitamin D change</td>
<td>5.51 (2.02 to 11.95)</td>
<td>0.10 (-4.80 to 3.31)</td>
<td>0.075</td>
</tr>
<tr>
<td>Calcium change</td>
<td>-0.5 (-0.7 to -0.1)</td>
<td>0.45 (-0.2 to 0.9)</td>
<td>0.047</td>
</tr>
<tr>
<td>PTH level change</td>
<td>11.57 (-11.87 to 22.87)</td>
<td>-3.33 (-42.45 to 0.36)</td>
<td>0.314</td>
</tr>
</tbody>
</table>
Discussions (I)

• Improvement of bone mass accrual after 6 months of calcium and vit D supplement in pt. with low BMD

1 No improvement after 2 yrs of supplement among 30 HIV-infected children with baseline BMD 50th percentile

2 Improvement of BMD after 1 yr of supplement in 24 adult on TDF-based ART with baseline vit D or calcium deficiency (BMD change +2.4%, Low baseline BMD group +3.4%)

3 Improvement of BMD among 10-12 yrs old girls in Beijing Vitamin D-fortified milk supplement for 2 yrs versus control (change in BMD 8.9% versus 3.9%)

1 Arpardi SM. Am J Clin Nutr 2012; 95: 678-85
3 Du X. Br J Nutr 2004;92:159-68
Discussions (II)

**Strength**
- Longitudinal cohort comparing PRE-POST supplement
- Selected patient with low baseline BMD

**Limitations**
- Pilot study (N=24)
- Short term supplement for 6 months
- Whether the effect last after stop supplement

3. Du X. Br J Nutr 2004;92:159-68
Conclusions

- Improvement of bone mass accrual after 6 months of calcium and vitamin D supplement in HIV-infected adolescents who had low BMD.
  - In context of inadequate nutrition intake of calcium and vitamin D.

- Additional research is needed e.g.
  - Randomized placebo controlled trial
  - Duration of supplement
  - Long term effect after stop supplement
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