No Correlation between 25-Hydroxyvitamin D status and pro or anti-inflammatory cytokines in obese children and normal weight controls

A Carroll1, C Onwuneme1, P Mayne2, MJ McKenna3, EJ Molloy4, NP Murphy4.
1. Department of Diabetes and Endocrinology and 2. Department of Biochemistry, Children’s University Hospital; 3. Department of Endocrinology, St Vincent’s University Hospital; and 4. Trinity College Dublin, The National Children’s Hospital, Tallaght

Background

- The primary function of vitamin D relates to calcium and bone metabolism but it is now recognised that vitamin D is a potent immunomodulator.
- In vitro, 1,25(OH)2D has been shown to suppress pro-inflammatory cytokines, such as TNF-α and IL-6, while up regulating synthesis of anti-inflammatory cytokines, IL-10 and IL-4. There are no in vivo studies examining the relationship between 25-Hydroxyvitamin D (25OHD) and cytokines in healthy children.
- Obesity is recognised as a pro-inflammatory state, characterised by higher levels of TNF-α and IL-6 and lower levels of adiponectin.
- Obese individual are also more likely to be vitamin D deficient.

Aim

- To examine if vitamin D status altered the cytokine profile in different groups of children; obese children and lean healthy control children.
- The secondary aim was to determine if the cytokine profiles differed between obese and lean children.

Materials and Methods

Over a 12 month period 2 groups of children in a paediatric hospital were recruited:

- obese children (BMI > 98th centile) attending a weight management course
- healthy children attending the hospital for minor medical or surgical illnesses.

Each had 25OHD level measured along with a cytokine panel (TNF-α, IL-4, IL-6, IL-10 and adiponectin).

Results

- In the obese cohort there were 13 children (9 females) ranging in age from 7.6-15.8 years. The mean (SD) 25OHD level was 29.2 (17.0) nmol/L and 92% had 25OHD levels <50 nmol/L.
- There were 46 healthy children (28 females) ranging in age from 4.4-15.6 years. The mean (SD) for 25OHD was 44.7 (24.6) nmol/L and 54% had 25OHD levels <50 nmol/L.
- There was no correlation between the cytokines examined and 25OHD levels in either group (Table 1 and Figure 1).
- 25OHD levels and cytokine profiles differed significantly between the two groups (Table 2).

Discussion

- We believe this is the first study examining the relationship between 25OHD status and pro and anti-inflammatory cytokines in healthy children. We found no correlation. There are a number of possible explanations for this.
- Firstly, the 25OHD levels of our patients were possibly below the threshold required for 25OHD to exert its immunomodulatory effects. Zhange et al demonstrated a level of 75 nmol/L was required to successfully inhibit TNF-α and IL-6 production.
- Secondly, our patients were in good health at the time of sampling and a correlation between 25OHD and cytokines may only be evident when the immune system is stimulated through sepsis or disease.
- Thirdly, 1,25(OH)2D is the active form of vitamin D which exerts an influence on immune cells and this was not measured in our study.
- We found no correlation between 25OHD status and cytokine profiles of obese children. Previous studies have yielded inconsistent results.
- We did find a significant difference in pro-inflammatory cytokines when obese and lean controls were compared. Adipocytes possess vitamin D receptors and express 1α-hydroxylase and 1,25(OH)2D has been shown to affect cytokine expression in adipocytes making it plausible that vitamin D status may be a factor in the pro-inflammatory state seen in obesity.
- In conclusion, we found no correlation between 25OHD and either pro or anti-inflammatory cytokines in healthy or obese children. We did demonstrate a pro-inflammatory state in the obese cohort.

Table 1: Correlation between 25OHD levels and cytokines in obese children

<table>
<thead>
<tr>
<th>Cytokine</th>
<th>Mean (SD)</th>
<th>r-value</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>IL-10 (pg/ml)</td>
<td>2.4 (1.7)</td>
<td>0.065</td>
<td>0.760</td>
</tr>
<tr>
<td>IL-4 (pg/ml)</td>
<td>2.9 (2.8)</td>
<td>-0.119</td>
<td>0.579</td>
</tr>
<tr>
<td>IL-6 (pg/ml)</td>
<td>0.99 (0.70)</td>
<td>0.194</td>
<td>0.359</td>
</tr>
<tr>
<td>TNF-α (pg/ml)</td>
<td>7.6 (2.8)</td>
<td>0.199</td>
<td>0.516</td>
</tr>
<tr>
<td>Adiponectin (ug/ml)</td>
<td>70.07 (11.85)</td>
<td>0.312</td>
<td>0.299</td>
</tr>
</tbody>
</table>

Table 2: Comparison of 25OHD and cytokines levels between healthy and obese subjects

<table>
<thead>
<tr>
<th>Cytokine</th>
<th>Healthy (n=46)</th>
<th>Obese (n=13)</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>25OHD (nmol/L)</td>
<td>44.7 (24.6)</td>
<td>29.2 (17.0)</td>
<td>0.038*</td>
</tr>
<tr>
<td>IL-10 (pg/ml)</td>
<td>1.23 (2.05)</td>
<td>2.21 (2.74)</td>
<td>0.210</td>
</tr>
<tr>
<td>IL-4 (pg/ml)</td>
<td>0.51 (3.12)</td>
<td>2.90 (4.55)</td>
<td>0.106</td>
</tr>
<tr>
<td>IL-6 (pg/ml)</td>
<td>0.080 (0.43)</td>
<td>1.00 (1.17)</td>
<td>&lt;0.001*</td>
</tr>
<tr>
<td>TNF-α (pg/ml)</td>
<td>5.6 (1.8)</td>
<td>7.6 (2.8)</td>
<td>0.005*</td>
</tr>
<tr>
<td>Adiponectin (ug/ml)</td>
<td>100.1 (44.6)</td>
<td>70.0 (11.8)</td>
<td>&lt;0.001*</td>
</tr>
</tbody>
</table>

References