Serum 25-hydroxy-vitamin D levels in malnourished children with rickets

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SUMMARY Serum levels of calcium, phosphorus, alkaline phosphatase, and 25 hydroxy-vitamin D (25-OH-D$_3$) were measured in normal and malnourished children with and without rickets. Children with rickets had clinical, biochemical, and x-ray evidence of the disease; most of them were malnourished. 25-OH-D$_3$ levels were lower than in normal children. After treatment with vitamin D their condition improved. 25-OH-D$_3$ levels were also found to be reduced in malnourished children without rickets.

These studies show that rickets is common in malnourished children. Inadequate exposure to sunlight appears to be the factor mainly responsible for the high incidence of the disease. In addition, malnutrition perhaps contributes to the development of rickets.

Nutritional rickets is not rare among children in India, despite abundant sunshine. The reported incidence varies from 0·8 to 20% depending on the criteria.1-4 Rickets is usually described as a disease of rapidly growing children, yet many children who come to our hospitals with clinically overt rickets are found to be malnourished.5-7 The factors responsible for this are not clearly understood.

Alterations in serum calcium, phosphorus, and alkaline phosphatase are conventional criteria used in the diagnosis of rickets. However, these parameters have been shown to be of limited value in the case of malnourished children with rickets.8 6 Direct assessment of vitamin D status is now possible using a highly sensitive assay for 25-hydroxy-vitamin D (25-OH-D) which is the main circulating form of the vitamin. Using this criterion, vitamin D deficiency has been shown to be widely prevalent among Indian immigrants in Britain.9-11 There is however no information on this aspect in our own population. The present study was undertaken to determine serum 25-OH-D$_3$ levels in normal and malnourished children with and without rickets in India.

Subjects and methods

54 children aged between 1 and 6 years were investigated. They were divided into 3 groups according to their nutritional status.

Group 1 ($n=13$). These were apparently healthy children whose weights were above the 80th centile of the local standard.12

Group 2 ($n=19$). These were malnourished children whose weights were below the 80th centile of the standard. Six children had clinical signs of kwashiorkor.

Group 3 ($n=22$). These were children with clinical and x-ray evidence of active rickets. Four children had weights above the 80th centile of the standard. The other 18 children were malnourished as judged by weight for age; they showed varying degrees of wasting but no oedema. None of them had a complaint which could be attributed directly to rickets. The presenting features were mainly diarrhoea or respiratory symptoms.

Children with protein-energy malnutrition and those with rickets were admitted to hospital, while the normal children were investigated as outpatients.

Fasting blood samples were analysed for serum calcium,13 phosphorus,14 and alkaline phosphatase.15 Serum 25-OH-D$_3$ was measured by the competitive protein-binding assay using rat serum.16

Children with rickets were treated with a single intramuscular dose of 600 000 IU vitamin D$_2$. Appropriate treatment was also given for infections. Biochemical studies and x-rays were repeated 2-3 weeks after treatment.
Table 1  Serum biochemical parameters (mean ± SE) in children

<table>
<thead>
<tr>
<th>Group</th>
<th>Alkaline phosphatase (Bodansky units)</th>
<th>Inorganic phosphorus (mg/100 ml)</th>
<th>Calcium (mg/100 ml)</th>
<th>25-OH-D₃ (ng/ml)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Normal (n = 13)</td>
<td>10.2 ± 0.73</td>
<td>5.1 ± 0.28</td>
<td>10.1 ± 0.46</td>
<td>34.1 ± 3.43</td>
</tr>
<tr>
<td>Malnourished (n = 19)</td>
<td>8.8 ± 0.83</td>
<td>4.3 ± 0.31</td>
<td>9.7 ± 0.38</td>
<td>21.1 ± 1.58***</td>
</tr>
<tr>
<td>Rickets (n = 22)</td>
<td>29.3 ± 9.06***</td>
<td>2.8 ± 0.29***</td>
<td>8.2 ± 0.62*</td>
<td>7.1 ± 2.67***</td>
</tr>
<tr>
<td>Well nourished (n = 4)</td>
<td>20.5 ± 2.56***</td>
<td>2.6 ± 0.21***</td>
<td>8.9 ± 0.26*</td>
<td>4.8 ± 0.68***</td>
</tr>
<tr>
<td>Malnourished (n = 18)</td>
<td>20.5 ± 2.56***</td>
<td>2.6 ± 0.21***</td>
<td>8.9 ± 0.26*</td>
<td>4.8 ± 0.68***</td>
</tr>
</tbody>
</table>

*** P<0.001; * P<0.05 compared with normal children.

Conversion: traditional units to SI—Inorganic phosphorus: 1 mg/100 ml ≈ 0.323 mmol/l. Calcium: 1 mg/100 ml ≈ 0.250 mmol/l. Serum 25-OH-D₃: 1 ng/ml ≈ 2.4962 nmol/l.

Table 2  Effect of vitamin D administration on serum biochemical parameters (mean ± SE) in rickets

<table>
<thead>
<tr>
<th>Serum biochemical parameter</th>
<th>Before treatment</th>
<th>After vitamin D treatment</th>
</tr>
</thead>
<tbody>
<tr>
<td>Alkaline phosphatase (Bu)</td>
<td>33.6 ± 4.22</td>
<td>16.0 ± 1.73***</td>
</tr>
<tr>
<td>Inorganic phosphorus (mg/100 ml)</td>
<td>2.5 ± 0.56</td>
<td>4.8 ± 0.41***</td>
</tr>
<tr>
<td>Calcium (mg/100 ml)</td>
<td>8.2 ± 0.67</td>
<td>9.3 ± 0.37*</td>
</tr>
<tr>
<td>25-OH-D₃ (ng/ml)</td>
<td>6.5 ± 1.65</td>
<td>31.8 ± 5.7***</td>
</tr>
</tbody>
</table>

***P<0.001; **P<0.02 compared with values before treatment. Conversions are given in footnote to Table 1.

Results

In children with rickets, serum calcium and phosphorus concentrations were significantly low, while alkaline phosphatase activity was increased compared with that of normal children (Table 1). The mean level of alkaline phosphatase was higher in well nourished children than in malnourished ones with rickets.

In normal children, serum 25-OH-D₃ levels ranged from 20 to 60 ng/ml (49.9 to 149.8 nmol/l) with a mean of 34.1 ng/ml (85.1 nmol/l). The mean levels of 25-OH-D₃ were significantly low in children with rickets (group 3) and also in malnourished children without rickets (group 2) compared with levels in normal children. The reduction was very pronounced in children with rickets.

After vitamin D administration, children with rickets showed improvement in all the biochemical parameters (Table 2). Serum 25-OH-D₃ showed a significant increase from a mean level of 6.5 to 31.8 ng/ml (16.2 to 79.4 nmol/l). X-rays gave evidence of healing.

Discussion

In the present series about 5% of patients admitted to hospital had rickets. Although this may not convey the true incidence of the disease, it shows that rickets is a fairly common disorder in children. All the children came from families in the low socio-economic group and many of them were malnourished. Other reports also show that rickets is common in malnourished children. It is not clear whether these two factors merely coexist because of poverty and poor living conditions, or whether malnutrition is causally related to rickets.

All our patients had clear clinical and x-ray evidence of rickets. Serum alkaline phosphatase activity was raised to a greater extent in well nourished children with rickets than in malnourished children with rickets. These results are in line with our earlier observations. Other workers have also reported that malnutrition can modify the biochemical changes which are characteristic of rickets, and therefore that serum biochemistry is not always a reliable diagnostic tool in such cases.

Serum 25-OH-D₃ is now recognised as a sensitive indicator of vitamin D status. In the normal children studied here, 25-OH-D₃ levels ranged from 20 to 60 ng/ml. These levels are higher than those reported in Asian immigrants in Britain, among whom rickets is reported to be a problem. This is probably because children in the UK lack the protective effect of sunlight of their home countries.

In children with rickets serum 25-OH-D₃ levels were significantly low, ranging from 0 to 10 ng/ml (0 to 25 nmol/l). After treatment with vitamin D₃ there was a significant increase from a mean level of 6.5 ng/ml to 31.8 ng/ml. Other biochemical parameters were also restored to normal. These observations indicate that the children studied here were suffering from vitamin D deficiency.

It is interesting to note that serum 25-OH-D₃ levels were also reduced in malnourished children without rickets. Although the levels were not low enough to cause symptoms, they were significantly lower than those of well nourished children. These findings suggest that in protein-energy malnutrition, cutaneous synthesis of vitamin D may be impaired, or there may be a defective conversion of the vitamin to its active metabolites. However, it can also be argued that malnourished children, being inactive, may not be exposed to sunlight to the same extent as normal children.

There may be several factors that could contribute to the wide prevalence of rickets in poor communities.
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The dietary intake of vitamin D is low. Apart from this, other factors such as high phytate content and low levels of calcium and phosphorus in the diet have been implicated. However, our earlier studies suggest that these factors may not play a significant role in the aetiology of rickets. As the diet provides very little vitamin D, we in India rely heavily on sunshine as the natural source. Unfortunately, rickets is a problem in our country, despite abundant sunshine all the year. The incidence has been found to be higher in cities than in rural communities. Most of the patients studied here came from urban slums, where the houses are congested and situated in narrow lanes. Young children living in such homes may not have enough sunlight. This, perhaps, is the most important factor responsible for the high incidence of rickets in poor undernourished communities. In addition, it is possible that protein-energy malnutrition may interfere with the metabolism of vitamin D and thus contribute to the development of rickets. Studies are now in progress to investigate this possibility.

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References


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