Vitamin D deficiency in patients with osteoarthritis undergoing total hip replacement

A CAUSE FOR CONCERN?

We measured the plasma 25-hydroxyvitamin D₃ (25(OH)D₃) levels in 62 consecutive Caucasian patients undergoing total hip replacement for osteoarthritis. The patients were divided into two groups based on whether they were vitamin D sufficient or deficient. The groups were matched for age, gender and the American Society of Anaesthesiologists (ASA) grade. The prevalence of vitamin D deficiency in our patients was comparable with recent population-based studies performed in the United Kingdom. Patients with vitamin D deficiency had lower pre-operative Harris hip scores (Mann-Whitney test, \(p = 0.018\)) and were significantly less likely to attain an excellent outcome from total hip replacement (chi-squared test, \(p = 0.038\)). Vitamin D levels were found to positively correlate with both pre- and post-operative Harris hip scores.

These results warrant further study of vitamin D deficiency in patients undergoing joint replacement as it is a risk factor for a suboptimal outcome which is relatively simple and cheap to correct.

Vitamin D is derived largely from cutaneous exposure to ultraviolet light, and to a lesser extent from the diet. Normal bone and cartilage metabolism depends on adequate levels of vitamin D. Suboptimal levels have adverse effects on calcium metabolism, osteoblast activity, matrix ossification, and bone density.¹

Osteoarthritis (OA) is characterised by damage to both cartilage and subchondral bone.² Vitamin D deficiency may reduce the ability of bone to respond effectively to the pathophysiological processes occurring in OA.

25-hydroxyvitamin D₃ (25(OH)D₃) is the main circulating vitamin D metabolite and its plasma level best reflects the nutritional status of vitamin D. The National Diet and Nutrition Survey³ shows a low level of vitamin D, as defined by a plasma 25(OH)D₃ concentration of < 25 nmol/l in most age groups in the United Kingdom population. One of the worst affected groups is of those over the age of 65 years living in institutions. Seasonal variations in the levels of vitamin D are observed in the United Kingdom, with the lowest concentrations between January and March. During the winter months, there is no ultraviolet light of the appropriate wavelength for the cutaneous synthesis of vitamin D, and therefore body stores and dietary intake maintain the levels of the vitamin during the winter. There is no agreed definition as to what value of 25(OH)D₃ represents a sufficient level. The levels quoted for insufficiency and deficiency vary widely in the literature.³⁻⁵ The most recent advice suggests that vitamin D insufficiency occurs at levels < 40 nmol/l.³ Vitamin D deficiency with the possibility of clinical signs or symptoms has been suggested with a plasma 25(OH)D₃ level of < 25 nmol/l.

The presence of low levels of vitamin D in patients with OA has been described as a substantial problem.⁵,⁶ A recent study found that 22% of patients with OA had a 25(OH)D₃ level of < 37.5 nmol/l.⁷ Radiological evidence of deterioration of OA of the hip in patients with low serum levels of 25(OH)D₃ has been reported.⁵,⁶ Genetic studies suggest that the vitamin D receptor allele polymorphism is correlated with aseptic loosening and possible failure of total hip replacement (THR).⁸

We are not aware of previous studies that have assessed the function of osteoarthritic patients undergoing joint replacement who are either vitamin D insufficient or deficient. This may be an important factor influencing pre-operative function and post-operative outcome. The aim of this study was therefore to investigate whether low levels of vitamin D are associated with functional deterioration in patients with OA of the hip undergoing THR.
Patients and Methods

We obtained permission to measure plasma 25(OH)D3 levels in routine blood samples taken from patients awaiting THR at their pre-admission visit for a period of three months. The levels at our institution are measured using the I125 radioimmunoassay (Diasorin, Stillwater, Minnesota). We obtained the 25(OH)D3 levels in 62 patients with OA undergoing unilateral primary THR. The operations were carried out by the same surgeon (FSH) or directly under his supervision, using a Reflection acetabular component (Smith & Nephew, Memphis, Tennessee) and an uncemented Synenergy femoral implant (Smith & Nephew) through a standard posterolateral approach.

Age, gender and the co-morbid status, as assessed by the American Society of Anaesthesiologists (ASA) grade,9 were recorded. All patients were Caucasian and none was taking vitamin D supplements (Table I).

All patients were assessed by the same observer (DHN) in a pre-admission clinic two weeks prior to surgery. The clinical state was evaluated using the Harris Hip Score (HHS),10 which was then recorded six months after the operation by the same observer.

As suggested by the definitions in the National Diet and Nutrition Survey,3 the patients were subdivided into two groups according to their vitamin D status. Those with a plasma 25(OH)D3 concentration < 40 nmol/l were deemed insufficient and deficient and those with a level > 40 nmol/l as sufficient. For each group, comparisons of age, gender, ASA grade and the pre- and post-operative HHS were made.

Statistical analysis. The Mann-Whitney U test was used to analyse the difference between mean hip scores in the two groups. The relationship between vitamin D levels and hip scores were analysed using the non-parametric Spearman's correlation. The figures were adjusted for age, gender and ASA grade by a multivariate linear analysis. A p-value of < 0.05 was considered statistically significant. All analyses were undertaken using the statistical package SPSS for Windows (version 13.0; SPSS Inc., Chicago, Illinois).

Results

All 62 patients included in this study attended for their follow-up appointment at six months. There were no complications related to the surgery. The mean vitamin D level was 58.0 nmol/l (SD 25.4).

There were 15 patients who were vitamin D insufficient / deficient (< 40 nmol/l) and 47 patients who were vitamin D sufficient (> 40 nmol/l). These two groups were matched for age, gender and ASA grade (Table II).

On breaking down the post-operative scores into categories, the vitamin D sufficient group had a significantly higher number of patients attaining excellent scores. The patients in both groups were similar demographically and undergoing a procedure with a high likelihood of yielding an excellent outcome in terms of HHS. In an attempt to reduce the impact of any potential ceiling effect of the HHS, we also analysed the difference in mean vitamin D

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**Table I.** Patient demographics

<table>
<thead>
<tr>
<th>Mean age in yrs (range)</th>
<th>71 (45 to 89)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Gender M:F</td>
<td>39:23</td>
</tr>
<tr>
<td>ASA* grade I</td>
<td>13</td>
</tr>
<tr>
<td>ASA* grade II</td>
<td>39</td>
</tr>
<tr>
<td>ASA* grade III</td>
<td>10</td>
</tr>
</tbody>
</table>

* ASA, American Society of Anaesthesiologists

**Table II.** Characteristics of the vitamin D study groups

<table>
<thead>
<tr>
<th>25(OH)D3*&lt; 40 nmol/l</th>
<th>25(OH)D3* &gt; 40 nmol/l</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Number of patients (%)</td>
<td>15 (24)</td>
<td>47 (76)</td>
</tr>
<tr>
<td>Mean age in yrs (range)</td>
<td>72 (52 to 89)</td>
<td>71 (45 to 87)</td>
</tr>
<tr>
<td>Gender M:F</td>
<td>4:11</td>
<td>19:28</td>
</tr>
<tr>
<td>ASA† grade I</td>
<td>2</td>
<td>11</td>
</tr>
<tr>
<td>ASA† grade II</td>
<td>10</td>
<td>29</td>
</tr>
<tr>
<td>ASA† grade III</td>
<td>3</td>
<td>7</td>
</tr>
</tbody>
</table>

* 25(OH)D3, 25 hydroxyvitamin D3
† ASA, American Society of Anaesthesiologists
‡ Mann-Whitney U test
§ chi-squared test

**Table III.** Pre- and post-operative Harris hip scores (HHS) for the vitamin D study groups

<table>
<thead>
<tr>
<th>25(OH)D3* &lt; 40 nmol/l</th>
<th>25(OH)D3* &gt; 40 nmol/l</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mean pre-operative HHS (sd)</td>
<td>32.0 (11.0)</td>
<td>42.0 (13.0)</td>
</tr>
<tr>
<td>Mean post-operative HHS (sd)</td>
<td>85.0 (9.0)</td>
<td>89.0 (11.0)</td>
</tr>
</tbody>
</table>

Post-operative HHS (number)

| Excellent | 5 | 30 | 0.038‡ |
| Good      | 7 | 8  | |
| Fair      | 2 | 5  | |
| Poor      | 1 | 4  | |

* 25(OH)D3, 25 hydroxyvitamin D3
† Mann-Whitney U test
‡ chi-squared test
levels in those patients who attained an excellent HHS (90 to 100) post-operatively with those who did not (< 90). A total of 31 patients had a post-operative HHS of > 90 and the mean 25(OH)D$_3$ level in this group was 67.5 nmol/l (SD 27.5); 31 patients had a post-operative HHS of < 90 with a mean 25(OH)D$_3$ level of 48.6 nmol/l (SD 19.2). The higher vitamin D level in the excellent post-operative HHS group was statistically significant (p = 0.003).

The plasma 25(OH)D$_3$ levels correlated positively with both the pre- and post-operative HHS's yielding Spearman's correlation coefficients of +0.347 (p = 0.006) and +0.332 (p = 0.008), respectively. The correlations were adjusted for age, gender and ASA grade with a multivariate linear analysis.

Discussion
We have shown that vitamin D insufficiency and deficiency is prevalent in a sample of patients with OA of the hip with 24% (15 of 62) of patients having plasma 25(OH)D$_3$ levels of < 40 nmol/l. This result is similar to a previous study in which the prevalence of low vitamin D levels in patients with OA of the hip was 22%.7 A low level of vitamin D in patients with OA of the knee has been reported in 66%4 in a study of 228 patients, a number far in excess of our sample of 62 patients and the 68 patients investigated by Glowacki et al.7

A report recently published by the Scientific Advisory Committee on Nutrition1 provides evidence of low vitamin D levels in most age groups in the United Kingdom and the levels in patients over the age of 65 matches the prevalence of low vitamin D levels in our patients. The report5 shows that 28% of patients aged between 65 and 74 are vitamin D insufficient and that this rises sharply with increasing age, reaching 85% in the 85+ age group.

The rheumatological literature has a number of studies reporting the association of low vitamin D levels with the radiological severity of OA.11 Lane et al5 studied baseline and follow-up radiographs of the hip of 237 subjects obtained an average of eight years apart. Low levels of plasma 25(OH)D$_3$ increased the risk of developing narrowing of the joint space by approximately threefold. No association was found with osteophyte formation. McAlindon et al11 found a similar association for the radiological progression of OA in patients with low levels of 25(OH)D$_3$ in the knee. Conversely, however, Felson et al6 found that the risk of narrowing of the joint space in OA of the knee is unrelated to the levels of vitamin D. OA of the hip and knee have different risk factors and it would not be surprising if the association between vitamin D status in these two conditions differed.

The association between levels of vitamin D and OA has been postulated to occur because of effects on the metabolism of both cartilage and bone. The results of the radiological studies suggest an effect on cartilage metabolism, as indicated by narrowing of the joint space. OA results from a loss of balance between synthesis of the matrix of articular cartilage and its degradation by metalloproteinases. Vitamin D has been shown to modulate the activity of metalloproteinase enzymes, with low levels of 25(OH)D$_3$ increasing the production of degradative enzymes.12 The theory behind the changes in the bone is that low levels of vitamin D slow the remodelling response of subarticular bone, resulting in thickening of the subchondral bone, osteophyte formation and resultant cartilage damage.13

Since low levels of vitamin D are associated with radiological deterioration of OA of the hip, functional deterioration in patients would also be expected. No previous study has investigated this hypothesis. In patients
undergoing THR, we found a statistically significantly lower pre-operative HHS in patients with plasma 25(OH)D3 levels < 40 nmol/l. We also found a statistically significant positive correlation between vitamin D status and the pre-operative HHS.

The level of vitamin D also seems to be related to the outcome after THR. We found significantly more patients with excellent scores post-operatively in the vitamin D sufficient group and patients attaining excellent scores also had a significantly higher mean level of vitamin D. The positive correlation between the level of vitamin D and the post-operative HHS was statistically significant. It is known that pre-operative function is a good predictor of outcome.14,15 The relationship between the level of vitamin D and outcome may therefore simply reflect the association already demonstrated between vitamin D levels and the pre-operative status.

The relationship between the level of vitamin D and THR has been investigated in animal studies. In an ovariectomised rat model, Nakamura et al16 demonstrated that alendronic acid and vitamin D supplements improve the cancellous bone mineral density and the stability of hydroxyapatite-coated hip implants. Malik et al8 have shown that the T-allele and the TT genotype of the vitamin D receptor are significantly associated with osteolysis caused by deep infection.

This study was intended to be a pilot. Our aim was to look at an aspect of OA of the hip and arthroplasty which has not previously been investigated in any detail. There are, however, a number of limitations. The number of patients in this study is small as we were limited in the number of patients that could be recruited in the three months available to us. These results have allowed us to perform a sample size calculation for a future prospective study. Based on the SD of hip scores for our study group (SD 13.5), the sample size required to show a difference of 10 points in the SD of hip scores for our study group (SD 13.5), the sample size calculation for a future prospective study. Based on the SD of hip scores for our study group (SD 13.5), the sample size required to show a difference of 10 points in the SD of hip scores for our study group.

The follow-up in this study is short compared with the radiological studies which we have quoted and continued follow-up will be required. We chose a simple joint-specific outcome measure in the HHS, thus not looking at general quality of life (e.g. SF-36) or disease-specific (e.g. Western Ontario Mcmaster University) outcome measures. We decided to use a simple, clinician-based score to reduce the number of patients who would be potential non-responders. Several factors are known to have an effect on the levels of vitamin D. These include seasonal variation, use of vitamin D supplements, osteoporosis and ethnic background. These factors were not strictly accounted for but our groups were adequately matched demographically. None of our patients were taking vitamin D supplements and they were all Caucasians. All the vitamin D measurements were performed during the winter.

This pilot study has shown that Vitamin D insufficiency and deficiency is prevalent in patients undergoing THR in the United Kingdom. It is also the first study to show that a low vitamin D level may be a predictor of poor pre-operative function in patients with OA of the hip and worse outcome from THR. It may be that trials of vitamin D supplementation in patients with OA undergoing THR should be subsequently undertaken. Vitamin D supplementation is simple, safe, well tolerated and inexpensive.17 If a beneficial effect can be demonstrated, an important change could be advocated in the management regime of patients undergoing THR through the simple addition of vitamin D supplements.

No benefits in any form have been received or will be received from a commercial party related directly or indirectly to the subject of this article.

References