Reliability of parathyroid hormone measurements in the period immediately following hip fracture

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Abstract

Aim: as it is unclear whether parathyroid hormone (PTH) measurements performed immediately after hip fracture are reliable indicators of pre-fracture metabolic status, we set out to define how PTH levels are affected by hip fracture and its surgical repair.

Method: in two longitudinal projects, we studied 12 patients presenting with hip fracture and eight patients undergoing elective hip replacement. PTH, calcium and 25-hydroxyvitamin D (25OHD) levels were measured on admission, 2 days and 1 week later and after recovery at least 2 months after initial admission.

Findings: in the subjects presenting with hip fracture, PTH levels during inpatient care were no different from those subsequently measured during the recovery period. In subjects undergoing elective hip surgery, PTH levels did not change following surgery and again remained unchanged into the recovery period.

Conclusions: measurements of PTH performed during inpatient care of those with hip fracture appear sufficiently reliable for use in assessment of metabolic status.

Keywords: elderly patients, hip fracture, parathyroid hormone

Introduction

Patients presenting with hip fracture frequently have a poor dietary calcium intake and may have vitamin D deficiency, although histologically defined osteomalacia is uncommon [1]. Calcium and vitamin D deficiency contribute to the pathogenesis of hip fracture through an effect on bone mineral density, inducing osteoporosis by stimulating the increased production of parathyroid hormone (PTH). This secondary hyperparathyroidism is found in up to half of those admitted with hip fracture [2, 3].

Calcium and vitamin D supplementation has been shown to be effective in reducing secondary hyperparathyroidism [4, 5] and in reducing the incidence of hip and other non-vertebral fractures in elderly women [5, 6].

In selecting hip fracture patients who might be offered such supplementation as secondary fracture prevention, it is useful to characterize PTH, calcium and vitamin D status. However, the timing of PTH measurements may be important. It has been suggested that measurements performed in the first weeks after hip fracture are an unreliable indicator of pre-fracture metabolic status and that PTH may be transiently elevated as a consequence of the stress associated with the injury [3, 7].

In this project, we investigated how fracture and surgery at the hip affect PTH status. Since we could not know a patient’s PTH status immediately before hip fracture, we were unable to measure the consequences of fracture directly. Instead we followed up patients undergoing elective hip surgery, to define the change in PTH levels before and after the acute stress of hip surgery. These patients and those presenting with hip fracture were also followed into the recovery period, when PTH results should have returned to the ‘unstressed’ pre-fracture values.

Methods

Firstly, we studied a group of eight ‘fit’ elderly [8] patients undergoing elective total hip replacement for osteoarthritis of the hip. Blood samples were taken on admission (day 1) to give baseline pre-operative status and were repeated 2 days and 1 week after operation.
Table 1. Corrected calcium, 25-hydroxyvitamin D (25OHD) and parathyroid hormone (PTH) in elective hip replacement patients (mean ± SEM)

<table>
<thead>
<tr>
<th></th>
<th>Corrected Ca²⁺ (mmol/l)</th>
<th>25OHD (ng/ml)</th>
<th>PTH (pmol/l)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Normal values</td>
<td>2.2–2.6</td>
<td>8–50</td>
<td>0.9–5.4</td>
</tr>
<tr>
<td>Values in patients undergoing elective hip replacement</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Pre-operative</td>
<td>2.49 ± 0.03</td>
<td>25.10 ± 7.99</td>
<td>3.75 ± 0.39</td>
</tr>
<tr>
<td>Day 3</td>
<td>2.45 ± 0.03</td>
<td>–</td>
<td>3.58 ± 0.57</td>
</tr>
<tr>
<td>Day 8</td>
<td>2.50 ± 0.06</td>
<td>–</td>
<td>3.84 ± 0.58</td>
</tr>
<tr>
<td>Recovery</td>
<td>2.47 ± 0.04</td>
<td>26.74 ± 8.41</td>
<td>4.29 ± 0.62</td>
</tr>
</tbody>
</table>

(days 3 and 8). Finally, community follow-up allowed measurement of PTH in the recovery period, 2–6 months after surgery.

Secondly, we studied 12 patients presenting with hip fracture after a fall from standing height or less. PTH levels were measured within 24 h of admission (day 1) to define the stressed post-fracture state and repeated 2 days and 1 week later (days 3 and 8) to define the changes during the post-operative period. Again, community follow-up provided blood samples from the recovery period, 2–6 months after surgery. The operation performed was the insertion of AO screws, or of a Thompson hemiarthroplasty, depending on the type of fracture.

Figure 1. Parathyroid hormone (PTH) results during follow-up of individual subjects.
PTH measurements immediately after hip fracture

Table 2. Corrected calcium, 25-hydroxyvitamin D (25OHD) and parathyroid hormone (PTH) in hip fracture patients (mean ± SEM)

<table>
<thead>
<tr>
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<th>PTH (pmol/l)</th>
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<td>2.2-2.6</td>
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<td>0.9-5.4</td>
</tr>
<tr>
<td>Values in patients with hip fractures</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Admission</td>
<td>2.40 ± 0.02</td>
<td>13.44 ± 3.34</td>
<td>6.28 ± 1.06</td>
</tr>
<tr>
<td>Day 3</td>
<td>2.41 ± 0.02</td>
<td>-</td>
<td>5.61 ± 0.77</td>
</tr>
<tr>
<td>Day 8</td>
<td>2.49 ± 0.02</td>
<td>-</td>
<td>5.73 ± 0.65</td>
</tr>
<tr>
<td>Recovery</td>
<td>2.47 ± 0.03</td>
<td>10.24 ± 2.27</td>
<td>6.06 ± 0.85</td>
</tr>
</tbody>
</table>

In both projects the blood samples were taken without prior fasting. Samples from all four different time-points were run in the same assay. Serum electrolytes, urea, creatinine, calcium and albumin were measured. Serum calcium was corrected for the albumin level. Plasma PTH was measured using a two-site assay for the intact molecule (Ciba-Corning Diagnostics, Halstead, UK) as described previously [9, 10], with a reference range of 0.9-5.4 pmol/l. The inter- and intra-assay variations at 2.9 pmol/l are 9% and 7.2% respectively, and at 39.2 pmol/l are 5.4% and 3.4% respectively [10]. In addition, samples taken on initial admission and during recovery were analysed to measure 25-hydroxyvitamin D (25OHD) using a competitive protein binding assay (Medgenex, 6220 Floris, Belgium) with a reference range of 8-50 ng/ml [10, 11].

For one of the hip replacement patients PTH results were only available pre-operatively and at 2 days after surgery, but PTH data were complete for all other subjects. Data were analysed by ANOVA, using the ARCUS statistical package.

Results

The eight patients receiving total hip replacements were aged 70 ± 0.8 years (mean ± SE); five were women. All had normal corrected calcium and PTH on admission, although two (25%) had low 25OHD levels. The mean corrected calcium, 25OHD and PTH at the four time-points are shown in Table 1. ANOVA showed no significant change in any of these measurements during follow-up. PTH results appeared unaffected by hip surgery (Figure 1).

The 12 patients presenting with hip fracture were 84 ± 2.1 years old (mean ± SE); 11 were women. On admission six subjects (50%) had low 25OHD and two others had results at the lower limit of normal. Five of these are included in a total of seven (58%) who showed an elevation of PTH; findings similar to those of other studies of hip fracture sufferers [2, 3].

On admission one subject had a very slightly elevated corrected calcium (2.61 mmol/l), but all others were normocalcaemic. None was commenced on calcium or vitamin D supplementation during the follow-up period. Mean corrected calcium, 25OHD and PTH results did not change significantly between the initial tests following admission with fracture and those performed in the unstressed, recovery period (Table 2). PTH results can be affected by renal function [10], but urea and creatinine levels showed no significant change during the peri-operative period, and variation in renal function will not have influenced our findings.

Individual patients showed little variation in PTH values during the follow-up period (Figure 1). One patient with a hip fracture had mild renal impairment which improved following admission and low-normal 25OHD levels at both time-points, and these factors may have contributed to the large fluctuations seen in the PTH results. Despite this fluctuation, the four results for this individual were consistent in that all were above the normal range.

Discussion

Although PTH levels have been reported to rise in response to acute myocardial infarction [12] and other sources of adrenergic stress [13], only one study has previously addressed the effects of elective orthopaedic surgery [14]. This small study showed a significant rise of PTH in young patients (13-33 years of age) undergoing spinal or hip surgery. Our study used a more modern PTH assay and found no such change accompanying elective hip replacement in patients aged 67-73 years; an age-range more consistent with that at which hip fracture commonly occurs.

Similarly, our follow-up of elderly trauma patients found nothing to suggest a rise of PTH levels in the period following hip fracture and its surgical repair. A previous study [3, 7] demonstrated PTH levels on admission to be higher than those measured 3 months later, in the recovery phase. This led the authors to conclude that initial PTH measurements were artificially elevated in response to stress and they suggested that measurements in the first weeks after hip fracture were unreliable as an indicator of pre-fracture parathyroid status. An alternative
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exploration of their findings might be that better diet following hospital admission improved calcium balance, so allowing resolution of previous secondary hyperparathyroidism.

Both of our studies thus suggest that measurements of PTH performed following hip fracture are sufficiently reliable to be used as indicators of pre-fracture metabolic status. PTH results can thus form a component of the inpatient assessment of osteoporosis following hip fracture. Secondary prevention has received very little attention in the published literature and future work should consider how the identification of secondary hyperparathyroidism might affect the choice of calcium or vitamin D supplements offered to those recovering from hip fracture.

Key points
- Parathyroid hormone measurements made after hip fracture in older people appear to be unaffected by the injury or subsequent surgery.
- These measurements are sufficiently reliable to be used as indicators of pre-fracture metabolic status.

References

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