Acute Effects of Fracture on Bone Markers and Vitamin K

To the Editor:

New biochemical markers provide useful information in the diagnosis and monitoring of metabolic bone disease and in the prediction of fracture risk. Vitamin K has become increasingly of interest in this field because of its role as a cofactor in the carboxylation of osteocalcin (1). Because hip fractures generally occur in severely osteoporotic patients, biochemical markers of bone metabolism and vitamin K have been studied extensively in patients with hip fractures. However, it is not clear whether a fracture itself affects the concentrations of biochemical markers of bone metabolism or, if so, how soon after or for how long after the fractures. The ideal way to study this is to obtain samples before a fracture. This is not feasible, however, because it requires a huge amount of sampling and a long follow-up. A secondary way is to do successive sampling immediately after a fracture to observe whether values change.

We studied 28 women with hip fracture, ages 64–94 years (mean age, 80.3 years). Their fractures were caused by low-energy trauma, such as a fall. They were immediately taken to an emergency room at a hospital. Serum and urine were collected from them on 3 successive days immediately after admission to the hospital (termed day 0). Most patients had surgery on day 2 after the sampling of that day. All had been ambulatory before the fracture. Exclusion criteria were: hip fractures resulting from severe trauma, admission to the hospital >24 h after the onset of fracture, blood transfusions or surgical procedures during the period of sample collection, past and present illnesses related to bone metabolism, and increased concentrations of serum creatinine. No subjects had been treated for osteoporosis, and none received medications before or during the study that might have affected calcium metabolism. Informed consent was obtained from all participants. The procedures followed were in accordance with the principles of the Declaration of Helsinki in 1975, as revised in 1983.

Serum osteocalcin was measured by RIA with a Yamasa osteocalcin kit with the use of polyclonal antibodies. Intra- and interassay CVs were <15%. Pyridinoline and deoxypyridinoline in urine were measured by HPLC after hydrolysis according to an automated analysis described by Pratt et al. (2). Before hydrolysis, urinary creatinine content was measured. The values of urinary Pyr and Dpyr were expressed per mol of urinary creatinine. The intra- and interassay CVs were <10%. Vitamin K1, menaquinone 4 (MK4), and menaquinone 7 (MK7) were measured by HPLC. The method is based on a hydrogen gas-saturated mobile phase with fluorescent detection after postcolumn derivatization with o-phthalaldehyde. The CVs were <5%. Urinary γ-carboxyglutamic acid was measured by HPLC. An aliquot of the urine was chromatographed on an anion-exchange column with a silica-based microparticulate support, and the amino acid of the eluate were detected fluorometrically by postcolumn derivatization with o-phthalaldehyde.

We report here the acute changes of vitamin K and biochemical markers of bone metabolism in patients with hip fractures. Because proteins that require vitamin K are cause proteins that require vitamin K, it was expected that vitamin K would be consumed in the process of a large fracture such as in the hip. However, the results in this
study indicate that concentrations of vitamin K were not affected by fractures in its acute phase. Bone formation markers did not change during the acute phase of hip fracture. Bone resorption markers increased on the third day. Biochemical markers of bone turnover were not affected for at least 48 h after fracture. Therefore, the values of those measurements during the first 48 h after fracture appear to reflect bone metabolism uninfluenced by the hip fracture itself.

References

Table 1. Biochemical markers and vitamin K on the three successive days immediately after fracture in patients with hip fracture.

<table>
<thead>
<tr>
<th>n</th>
<th>Day 0</th>
<th>Day 1</th>
<th>Day 2</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Calcium (mmol/L)</td>
<td>Phosphorus (mmol/L)</td>
<td>Albumin (g/L)</td>
</tr>
<tr>
<td>28</td>
<td>2.07 ± 0.17 (2.10, 1.77–2.57)</td>
<td>0.87 ± 0.26 (0.84, 0.52–1.74)</td>
<td>32 ± 5 (32, 23–42)</td>
</tr>
<tr>
<td>28</td>
<td>2.10 ± 0.15 (2.10, 1.84–2.45)</td>
<td>0.90 ± 0.19 (0.90, 0.58–1.26)</td>
<td>31 ± 5 (33, 23–41)</td>
</tr>
<tr>
<td>28</td>
<td>2.12 ± 0.15 (2.12, 1.92–2.47)</td>
<td>0.87 ± 0.19 (0.84, 0.48–1.16)</td>
<td>29 ± 5* (29, 23–39)</td>
</tr>
</tbody>
</table>

*P < 0.05 vs day 0 by Wilcoxon signed-rank test. Values are means ± SD except as noted. Values in parentheses are (median, range).

Interference with Nephelometric Assay of C-Reactive Protein by Monoclonal Immunoglobulin

To the Editor:

Various chemical laboratory methods are subject to interference by monoclonal immunoglobulins (para-proteins, e.g., those cited in references 1 and 2). This phenomenon does not depend on antibody specificity of the monoclonal immunoglobulins but on peculiarities of their physico-chemical behavior. Occasionally, similar interference has been reported with homogeneous immunoassays for C-reactive protein (CRP) determination (3–5). Yamada et al. (6) add to this list a case report of a patient with monoclonal IgM, type κ, exhibiting erroneously high results in our particle-enhanced immuno-nephelometric assays for determination of CRP and antistreptolysin O (ASO) (N Latex CRP and N Latex ASL, respectively, of Dade Behring). The mechanism of interference by monoclonal IgM with the N Latex CRP assay (product code OUSV) has been investigated in more detail by Le Carrer et al. (7). That study showed that an unspecific reaction of certain monoclonal proteins (mostly κ-type) depended on the presence of latex particles and was further affected by coating of the particles with antibody (rabbit antihuman CRP) and by reaction enhancers (polyethylene glycol, PEG).

Behring Diagnostics in 1996 launched a new generation of immuno-nephelometric CRP assay, N Latex CRP mono (product code OQIY, available in most parts of the world). This assay utilizes modified latex particles with optimized surface characteristics, mouse monoclonal antibodies, and no reaction enhancer. In our evaluation, we were unable to detect unspecific reactions with IgM paraproteins (8). Nevertheless, users should remain aware of potential interferences and should check the clinical plausibility of their results.