Author's response to reviews

Title: No association between the aluminium content of trabecular bone and bone density, mass or size of the proximal femur in elderly men and women

Authors:

Hans-Olov Hellstrom (hans.lov.hellstrom@akademiska.se)
Bengt Mjoberg (bengt.mj@telia.com)
Hans Mallmin (hans.mallmin@akademiska.se)
Karl Michaelsson (karl.michaelsson@akademiska.se)

Version: 3 Date: 9 June 2006

Author's response to reviews: see over
Sir

We thank professor Karlsson and professor Arokoski for their reviews. Regarding the reviewers' comment on the manuscript “No association between the aluminium content of trabecular bone and bone density, mass or size of the proximal femur in elderly men and women” you can see below my clarifications point-by-point:

Magnus K Karlsson

We had several reasons not to include the DXA results in the prior publication published in Osteoporosis International. That study had a focus on hip fractures cases with and without dementia since the pilot study by Mjoberg et al published in Calcified Tissue International some years ago indicated that specifically demented hip fracture cases had high aluminium levels. There has been a debate on the importance of aluminium on the occurrence of dementia and theoretically aluminium might both cause dementia and fractures by effects on the neurons, i.e., the fractures occur by a balance disorder and not by negative effects on bone. The causes of hip fracture and low BMD/BMC/bone areas are not necessarily the same. We also, in that paper, graphically described the variation of aluminium content of bone by age. Our purpose to present some results of the association between aluminium and age in the present manuscript was to motivate for the reader why age was an important confounder since the significant association between aluminium and the DXA variables disappeared after age adjustment. This was also the explanation why we mentioned dementia and osteoarthritis as confounders in the results of the present manuscript. Nevertheless, in an order not to emphasize the age effect, we have now excluded these results from the abstract and from the last paragraph of the discussion. We also thought that it should be too many results in the same manuscript if we included data on age, hip fracture cases with and without dementia and controls, as well as the DXA-measurements. Last, we had not analyzed the DXA results when writing the hip fracture manuscript.

Jari P Arokoski

1. We think the reviewer has misunderstood the importance of selection of osteoarthritis patients as controls. It is true that some studies have shown higher BMD in OA patients, in the affected hip, than in healthy controls (Arokoski et al 2002, Dequeker et al 1995). However, it is not really relevant if the controls had similar or higher bone mineral density regarding bias possibility compared to the cases since we were examining the aluminium content of bone and its association with BMD/BMC and bone areas. In fact, selection of controls with high BMD can, by increasing the range of the dependent variable, improve our possibility to detect an association between aluminium and bone. We measured the contralateral hip in all patients, fracture cases as well as OA cases, and they had no significant OA on that side. Furthermore, aluminium is not associated with OA.

2. The aluminium content in bone is usually analysed in trabecular bone. There are very diminutive numerical data on cortical aluminium content, but the distribution seem to be uniform through out the whole skeleton, and thus the biopsy site is actually not relevant when testing associations (Pérez-Granados & Vaquero 2002, Priest, 2004, Ganrot 1986). In addition, the aluminium content is measured as mass per dry weight of bone. In an attempt to better describe the bone biopsy procedure, we have now included the following sentence: ‘During the operations in all cases, bone biopsies from the trabecular bone of the proximal femur (i.e. trochanter major, after drilling the hole for the osteosynthesis screws or after preparation for the prosthetic femur stem in cases of arthroplasty) were taken using an aluminium-free instrument. The mean weights of the samples were 300 mg (range 29-600 mg).’
3. For long term reproducibility the use of the spine phantom is an accepted method in clinical research. A phantom for CV femoral neck BMD is not available for the machine used (DPX-L™, Lunar Co, Madison, Wi, USA) but double measurements in patients, the precision error for BMD at the femoral neck site measured by DPX-L in our laboratory has been determined to be approximately 1%.

Kind regards,

Hans-Olov Hellström
Department of Orthopaedics
Uppsala University Hospital
S-751 85 Uppsala
Sweden
Phone +46 18 6114479
E-mail: hans.lov.hellstrom@akademiska.se