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LETTER

Bisphosphonate-associated atypical femoral fractures and one-year mortality

MOHAMMAD KHARAZMI[1,2] & PÄR HALLBERG[3]

[1]*Central Hospital, Department of Oral and Maxillofacial Surgery, Västerås, Sweden,* [2]*Uppsala University, Section of Orthopaedics, Department of Surgical Sciences, Uppsala, Sweden, and* [3]*Uppsala University, Department of Medical Sciences, Uppsala, Sweden*

Dear Editor,

It is well known that osteoporotic fractures (OF) of the hip are associated with increased mortality, in particular immediately after the fracture (1). Although several theories have been proposed, the cause of the increase is not fully understood. In the past few years there have been an increasing number of reports of femoral fractures associated with bisphosphonate use (2). The pattern of these fractures differs from the typical OFs, and hence they are referred to as atypical fractures (AF). One of the differences between the two is the fact that OFs are secondary to a disease, while AFs is the result of an adverse drug reaction (ADR). However, both affect patients with osteoporosis, and the end result is fracture of the same bone (femur). Whether or not AFs are associated with a similar increase in mortality as OFs is unknown. We aimed to investigate this question.

The Medical Products Agency (MPA) is the Swedish regulatory authority registering spontaneous reports of ADRs from health care professionals. We reviewed all reports of AF received by the MPA, from January 2006 through September 2013, associated with use of oral bisphosphonates or once-yearly intravenous zoledronic acid, prescribed with osteoporosis as the indication. Reports not fulfilling diagnostic criteria for AF were excluded (3). Diagnostic accuracy (3) was confirmed in all patients consenting to have their medical records and radiographs reviewed. The one-year mortality rate was determined by using data from the national population register of the Swedish tax authority. For all cases, survival or mortality was determined at least one year after the fracture.

A total of 48 reports had been received from January 2006 through September 2013. Forty-four reports (2 men, 42 women) fulfilled the diagnostic criteria for AF (3). Twenty-seven patients consented to complete a structured interview about their medical history and drug therapies, and to have their medical records and radiographs reviewed. Diagnostic accuracy (3) could be confirmed in each case. Data on co-morbidities were collected based on either interviews and medical records, or on information from case narratives.

The mean age of the 44 patients at the time of the AF was 73 years. During the mean follow-up time (from fracture to determination of mortality) of four years, five (all women) of the included 44 patients had died (11.4%), of which one (2.3%) had done so within one year after the fracture.

Like patients who experience OFs, the great majority of the patients in the current study were women. Based on the results of a previously published Swedish nation-wide study, the one-year mortality rate among women aged 70–75 years who experience a hip fracture has been estimated to be 9.6% (4). In comparison, based on the results of the present study, the one-year mortality rate following AF of the hip appears significantly lower (2.4% for the 42 women). As frequencies of co-morbidities were similar (cardiovascular disease 21.4% versus 28.6%; obstructive lung disease/pneumonia 14.3% versus 5.0%; diabetes

Correspondence: Mohammad Kharazmi, Central Hospital, Department of Oral and Maxillofacial Surgery, Västerås, Sweden.
E-mail: kharazmi.mohammad@gmail.com

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4.8% versus 5.0%; cancer 7.1% versus 8.3%; psychiatric disease 4.8% versus 12.5%), the difference in mortality rate is unlikely to be explained by differences in patient characteristics.

In conclusion, although AF is often associated with delayed healing (3), our results reveal no evidence of a high mortality rate. In this respect, AF appears less hazardous compared to OF, which should be of importance when assessing the benefit risk ratio of bisphosphonate therapy. Since both AF and OF affect the same category of patients and the same bone, it is reasonable to assume that the higher mortality rate associated with OF is not entirely due to the fracture (5), but rather the overall systemic effects of the disease, and possibly genetic factors.

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