Malden N, Lopes V. An epidemiological study of alendronate-related osteonecrosis of the jaws. A case series from the south-east of Scotland with attention given to case definition and prevalence. J Bone Miner Metab. 2011. [Epub ahead of print]

This article presents a close case study series of alendronate-associated osteonecrosis of the jaws (AONJ). From their study the authors draw epidemiologic conclusion regarding AONJ as well as comment on clinical considerations and treatment protocol. Alendronate is the most common bisphosphonate prescribed in the world. Since the first cases of ONJ started to emerge a task force of the American Society of Bone and Mineral Research (ASBMR) proposed recommendations to address key issues with ONJ and bisphosphonates. These include case definition and clinical management as well as epidemiology. In this study, to confirm and stage AONJ, the authors used the definition proposed by American Association of Oral and Maxillofacial Surgeons 2009 position papers on BONJ. The specific details for case definition, as described by ASBMR, fall in to 7 categories of information (A–G): A, patient details—for this article all were white Caucasian except for one, and 82% were female; B, diagnosis/staging of disease—mild to moderate pain, presence of nonvital bone; C, local site and clinical history—64% included a history of dental extraction preceding the condition; D, alendronate dose and duration of presentation—70 mg daily dose; the duration of administration to first ONJ recognition had a mean of 3 years; E, indication for bisphosphonate use—64% were receiving alendronate to counteract the osteoporotic affects of glucocorticosteroids; 36% were receiving the drug for age-related or hormone/menopause-related osteoporosis; an estimate mean of 4.7 years of "disease onset" prior to ONJ onset; F, co-morbidity and duration of ONJ—55% were ASA III; duration of comorbidity to diagnosis of ONJ was difficult to assess, but in 64% it was considered between 5 and 10 years; G, co-medications and duration of ONJ—prednisolone was prescribed in 55% of the cases. Three patients were taking immunosuppressant leflunomide or methotrexate. A known complication of immunosuppressive drugs is oral ulcerations and 27% of patients had concomitant administration of those with alendronate. Four patients with cardiovascular disease were taking statins and two were taking nicorandil. Nicorandil is a drug used in the management of persistent angina pectoris. It has been associated with oral ulcerations, occasionally affecting the alveolar ridges. Thus the authors suggest that drug associated ulcerations, if occurring over bone in the presence of alendronate could initiate the development of ONJ. Thus these drugs should be considered risk factors. 55% of patients who developed ONJ were taking prednisolon and alendronate.

Management of ONJ included mild analgesics (64%), antimicrobials in various combinations (73%) that ranged from 1 to 11 weeks, one surgical debridement (64%), chlorhexidine was prescribed to all patients, and 45% of patients discontinued alendronate use at the diagnosis of ONJ. It was decided that the risk associated with discontinuation of alendronate are less then the risks associated with continuation of alendronate. However a case-by-case review with multispecialist discussion is suggested when discontinuation of bisphosphonate therapy is considered as a treatment adjunct to management of AONJ. In this study the duration from diagnosis to resolution ranged from 2 weeks to 20 months (mean of 6.5 months). By tracking alendronate prescriptions the drug patient year (DPY) was calculated. Thus epidemiology could be approximated. In the population studied, the incidence of AONJ as a spontaneous event or in response to a traumatic oral insult is between 0.03% and 0.017% respectively. Where alendronate is prescribed alone or for age-related or hormone-related osteoporosis the prevalence is 0.004%. The presence of comorbidity where

comedications are being prescribed with alendronate significantly increases the risk of developing AONJ. It is suggested that rheumatoid arthritis patients receiving alendronate, glucocorticosteroids, and often an immunosuppressant are at an increased risk of ONJ with an incidence of 0.1% of AONJ. This study of 11 patients and an extrapolation to a population of 900 000 with DPY calculations brings our attention to AONJ from another clinical perspective that should benefit our patients and our considerations in their care.

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