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Letter to the Editor: Novel evidence on bisphosphonate related osteochemonecrosis of the jaws suggests tooth extractions and overdentures as risk factors

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Dear Editor:

We read with considerable interest the paper by Gomez Font et al. summarizing the latest information on bisphosphonate related osteochemonecrosis of the jaws (BON)(1).

The authors note that risk factors associated with osteochemonecrosis due to bisphosphonates are diverse. They report drug type, doses and means of administration, treatment duration, mucosal trauma, dentoalveolar surgery, smoking, and diabetes mellitus to be associated with the disease(1). A recent study even reports a surrogate biomarker; CTX terminal telopeptide serum levels as the authors state(1). In this regard we have carried out the first case control study addressing potential risk factors for ONJ development in breast cancer patients(2). In this study we report statistically significant risk factors for BON development among breast cancer patients under zoledronic acid (ZA) medication(2) .

An issue that remains to be elucidated is potency of BP medication. All patients included in our study (2) received ZA which is considered to be the most potent osteoclast inhibitor(3). Since our study was a matched case control we were not able to explore the potential influence of drug type, doses and administration way in the development of BON. However, we believe that other drugs, i.e. ibandronate are less effective in causing BON, also based on still unpublished data of ours(2). Further studies are needed to clarify administered drug type as a potential risk factor.

Treatment duration is probably a risk factor, which we also preferred not to explore in a matched design. It is probable that longer ZA treatment predisposes to ONJ(4). Of note we preferred not to test treatment duration as an independent risk factor since our aim was to detect prognostic factors to avoid BON and not to propose reducing ZA doses as a preventive measure(2).

The authors point out that bisphosphonates also produce an inhibitory effect on the keratinocyte cellular cycle, which hinders the habitual mucous repair mechanisms(1). A quite recent study adds to this, for the first time providing evidence that mucosal wound healing could be impaired(5). What is more these authors demonstrated that increased apoptosis –programmed cell death- is not likely to contribute to this effect(5). Mucosal trauma resulting from ill-fitting dentures could be the reason for increased risk for BON among these patients demonstrated by our study(2).

Dentoalveolar trauma is considered to influence the development of BON(1). Our study found a sixteen times higher relative risk for BON development among patients who had experienced tooth extraction during ZA treatment(2).

Smoking and endodontic treatment were not found to be independent risk factors. However smoking is a known risk factor for breast cancer(6), and the probability that it might be a confounding or effect modifying factor cannot be diminished with regard to our study(2).

The authors adopt the treatment protocol firstly proposed by Woo et al.(7). Nevertheless this protocol was argued since it was not based on knowledge about the pathobiology of ONJ, nor was it evidence based (5, 8, 9). Our study (2) provides clinical evidence that BON is associated with tooth extractions and overdentures but not with endodontic treatment, currently updating the ASCO level of evidence from V to III. In this regard we support the protocol proposed by Woo et al.(7) also adopted by Gomez Font et al.(1) with the exception of endodontic treatment which we consider to be a safe choice for these patients(2).

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