LETTER

New evidence on bisphosphonate related osteonecrosis of the jaws suggests dental referral prior to commencement of treatment

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Bisphosphonates (BP) reduce excessive bone turnover, resulting in preservation of structure and mineralization of the bone. Based on these properties, BP have become the treatment of choice for preventing skeletal complications in cancer patients with bone metastases as well as in patients suffering from osteoporosis, Paget's disease and rheumatoid arthritis[1,2]. Adverse effects associated with intravenous administration of bisphosphonates are rare and consist of pyrexia, renal function impairment, and hypocalcaemia. Over the last years, a new complication associated with the use of BP has been described: avascular osteonecrosis of the jaw (ONJ)[3]. It has been suggested that oncologists use intravenous bisphosphonates in much higher doses and this has been postulated to be responsible for the development of ONJ[4]. Nonetheless, recent good quality evidence suggests that ONJ is also frequent among patients receiving BP (per os or intravenous) for non malignant indications[1].

The hallmark of ONJ is the finding of exposed bone in the oral cavity[3,4]. In many cases, the precipitating event appears to be a dental extraction or other dental invasive procedure[4]. Recently, a study from our institution provided solid evidence that ONJ is associated with dental extraction and use of dentures[3]. In this study we reported statistically significant risk factors for ONJ development among breast cancer patients under zoledronic acid (ZA) treatment[3] .Mucosal trauma resulting from dental extraction or ill–fitting dentures could be the reason for increased risk for ONJ among these patients[3]. Our study found a sixteen times higher relative risk for ONJ development among patients who had experienced tooth extraction during ZA treatment[3]. Smoking and endodontic treatment were not found to be independent risk factors[3]. However smoking is a known risk factor for breast cancer and the probability that it might be a confounding or effect modifying factor cannot be diminished with regard to our study[3].

Furthermore, a recent study provides more evidence that mucosal wound healing could be impaired in patients receiving BP[5]. These authors demonstrated that increased apoptosis is not likely to contribute to this effect[5]. We believe that BP could be impairing molecular signaling not only of osteoblasts and osteoclasts but also of fibroblasts and keratinocytes, via cell to cell endocrine and paracrine interactions in a double manner. However, only scattered evidence supporting this hypothesis exists to date.

An interesting point addressed in the literature, concerns the difference in the incidence of ONJ among the Greek and US populations[6,7]. One should anticipate that this is attributable to more tooth extractions in the Greek population probably resulting from poorer hygiene, but based on WHO data such a difference does not exist[6]. Thus, the incidence differences could be attributable to differential susceptibility to ONJ. Such susceptibility differences could exist, and we have previously reported decreased susceptibility to adenocarcinoma among Greek patients with Barrett's oesophagus and inflammatory bowel disease, perhaps attributable to Bax-protein over-expression[6,8]. A recent well designed study from Germany, also reports on a higher incidence of ONJ in German patients compared to the US reported incidence[7].

Proposed protocols for ONJ treatment to date have not been based on knowledge about the pathobiology of ONJ, neither have been evidence based[5]. Nevertheless it has been suggested that until solid evidence is available patients receiving BP should have regular inspection of the mouth, undergo dental check-ups every 6–12 months and avoid invasive dental surgery unless no alternative is available[9]. Our study[3] provides clinical evidence that ONJ is associated with tooth extractions and use of dentures but not with endodontic treatment, currently updating the American Society of Clinical Oncology (ASCO) level of evidence from V to III[3]. We concluded that practitioners should refer patients for baseline dental evaluation and treatment prior to commencement of BP treatment. Also additional dental and medical attention should be paid to BP patients using removable dentition to avoid mucosal breaches caused by dentures[3].

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