

111. Osteonecrosis of the Jaw with Bisphosphonates: a Safety Review

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Introduction: Bisphosphonates are used widely in the management of bone diseases including osteoporosis, Paget's disease and hypercalcemia related to malignancy.

Method: Case-reports of osteonecrosis of the jaw associated with bisphosphonates were identified by a computer-based literature search.

Results: We identified a total of 40 publications that were relevant to our review. 545 cases were reported. The mean induction time was from one month to 77 months. 258 patients (46%) were treated for multiple myeloma, 109 (13%) for metastatic breast cancer, 21 (4%) for metastatic prostate cancer, 26 for osteoporosis and 8 for Paget's disease. 286 (53%) bone exposure occurred in the mandible alone, 94 (17%) in the maxilla and 27 (5%) in both jaws. Dental extraction was associated in 237 cases (44%), and periodontitis in 32 cases (6%). No cases recovered, the patients required surgical procedures: sequestrectomy, partial mandibulectomy.

Discussion: Osteonecrosis of the jaw closely resembles to the occupational disorder "phossy jaw" which occurred in workers in match factories using white phosphorus. In 2002, 9 cases of patients with osteonecrosis of the jaw who received intravenous bisphosphonates were reported to the Food and Drug Administration (FDA). In 2003, Marx reported 36 cases under treatment with pamidronate or zoledronate. On February 2005, FDA had collected 875 cases. Zoledronate represents 50% of the reports, pamidronate 21%, a mention of the two drugs 28% and 2% for oral bisphosphonates. Osteonecrosis of the jaw has multiple well-documented risk factors including a diagnosis of cancer, concomitant therapies (chemotherapy, radiotherapy, corticosteroids) and co-morbid conditions (anaemia, pre-existing oral disease). Over the last years, a relationship between the use of bisphosphonates and avascular osteonecrosis of the jaw has been observed. The injectable bisphosphonates appear to be more implicated. Bisphosphonates are not metabolised and have a strong binding with osteoclasts. They can persist in bone for months and several years after the drug has been discontinued. Withdrawal of bisphosphonates therapy does not appear to hasten recovery of the osteonecrosis. We should consider all varieties of bisphosphonates to have some phossy jaw risk associated with their use.

Conclusion: The majority of the reported cases are in cancer patients attendant to a dental procedure. Osteonecrosis of the jaw has also been reported in patients with osteoporosis and Paget's disease. A dental examination should be considered prior to treatment with bisphosphonates. Patient receiving bisphosphonates should avoid invasive dental procedures.