Summary of: A study of 225 patients on bisphosphonates presenting to the bisphosphonate clinic at King's College Hospital

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VERIFIABLE CPD PAPER

FULL PAPER DETAILS

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Aim The aim of this retrospective study was to examine the outcome of patients referred to a dedicated clinic for dental extractions while they were prescribed either oral or intra-venous (IV) bisphosphonates (BPs). The following parameters were assessed: mode of BP administration, indication for BP prescription, incidence of BRONJ, concomitant risk factors for development of bisphosphonate-related osteonecrosis of the jaws (BRONJ) and demographic details. **Material and methods** The clinical records of 225 patients who underwent dental extraction while receiving oral or intravenous bisphosphonates were reviewed. Their clinical outcome, specifically the development of BRONJ was determined. **Results** Of the 225 patients, 202 were prescribed oral and 23 IV BPs. 34.8% (8/23) of patients prescribed IV BPs developed BRONJ following dental extraction, which was a significantly ($p < 0.001$) higher proportion than that of the oral BP group, which was 2.5% (5/202 patients). 12.3% (8/65) patients taking BPs with steroids were at a significantly increased risk of a BRONJ ($p < 0.003$). 12.3% (7/57) males developed a BRONJ compared with 3.6% (6/168) females where $p = 0.015$. All of the patients who developed a BRONJ as a result of oral BP prescription had been taking this medication for three years or more. **Conclusion** In our patient cohort the risk of developing a BRONJ following dental extractions was greatest in those patients receiving IV BPs and those on oral BPs with concomitant steroid medication.

EDITOR'S SUMMARY

The number of patients prescribed bisphosphonates (BPs) has increased significantly in the last 15 years. This is not surprising considering that BPs are the drugs most commonly used to treat osteoporosis and are also administered for the management of hypercalcaemia and the treatment of bone lesions associated with metastatic cancers, amongst others. But we know this already, don't we? Since bisphosphonate-related osteonecrosis of the jaw (BRONJ) was recognised as a side effect of BP treatment, dental publications, including this journal, consistently feature the topic on their pages.

However, BRONJ must be considered in context: it is a rare condition, as recently determined by a two-year UK study based on patient case records.[1] Nevertheless, if you are one of these 'rare' cases then BRONJ matters to you very much; so research that will help to inform treatment of such patients is essential. This study, by Talli Taylor and co-workers from King's College Hospital, examined the outcomes of dental extraction for a cohort of 225 patients on IV and oral BPs. They determined that there was a highly significant risk of developing a BRONJ if you are a patient on IV BPs undergoing a dental extraction as opposed to a patient taking oral BPs. The authors also note that the prescription of IV infusion has increased since the FDA approved the use of an annual infusion of zoledronate for osteoporosis in 2007. IV infusion is associated with reduced oesophageal irritation and so the method of choice for many patients.

Interestingly and unlike previous studies, this article also reports a significantly greater proportion of male patients developed a BRONJ compared to females. However, the authors note that the reason for prescription for males in the study, ie mainly IV BPs for metastatic prostate cancer, may have been more of a determinant than gender.

According to Wikipedia (and the many websites that appear to have used this Wikipedia fact!), the main non-medical use of BPs was to soften water in irrigation systems used in orange groves. This conjures a pretty picture and perhaps describes a more romantic use for BPs. Hopefully, the picture for those patients on BPs at risk of a BRONJ will continue to improve with the advent of further research such as this study.

The full paper can be accessed from the *BDJ* website (www.bdj.co.uk), under 'Research' in the table of contents for Volume 214 issue 7.

Ruth Doherty
Managing Editor

1. K. Maynard. Bisphosphonate-related osteonecrosis of the jaw is rare. Br Dent J 2012; 213: 594.

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IN BRIEF

- Highlights the clinical outcomes of patients prescribed bisphosphonates following dento-alveolar procedures.
- Assesses the parameters and risks of developing a bisphosphonate-related osteonecrosis of the jaws (BRONJ).
- Compares the risk factors of developing a BRONJ to previously published data.

RESEARCH

COMMENTARY

This retrospective study, covering a period of three and a half years, examined the outcomes of 225 subjects who had received bisphosphonates (BP) via the oral or intravenous route and were undergoing tooth extraction. A standardised extraction and/or surgical technique including an antimicrobial postoperative regime were adopted. Informed consent was obtained with reference to a number of accepted risk factors for bisphosphonate related osteonecrosis of the jaw (BRONJ). The following general factors were included, BP potency, period of administration, age, concomitant drugs, co-morbidities and tobacco habit. Only those teeth deemed unrestorable were selected for removal (the option of endodontic treatment of retained roots was not considered in this study). A follow-up period of one year was applied and on the appearance of BRONJ the disease was categorised into stage 0-3 and managed using a standardised protocol.

Results: 2.5% of the oral BPs group developed BRONJ compared to an incidence of 35% in the intravenous (IV) group ($p < 0.001$). Further analysis of the oral BP group demonstrated an increased incidence in subjects receiving BPs for >3 years and also in those receiving concomitant corticosteroids. A slight predominance of male sufferers was also suggested. Other suspected risk factors for BRONJ, age, co-morbidity and tobacco habit were not statistically evidenced.

The discussion attempted to clarify the differing risks associated with IV *versus* oral administration. It was acknowledged that the most recently introduced IV regimes using zolendronic acid in the management of osteoporosis were likely to carry a similar risk of BRONJ to the established oral regimes (using alendronic acid).

I suggest that, conversely, the management of metastatic disease utilising oral ibandronic acid may carry as high a risk of BRONJ as the standard IV regimes.

Conclusion: The study was of sufficient size to demonstrate a significant increased risk of BRONJ in IV treated subjects compared to those treated with oral regimes. Within the oral administration group an increased risk of BRONJ was suggested when concurrent corticosteroids were prescribed. It was accepted that the study was of insufficient size to demonstrate any significant relationship between other risk factors and an increased incidence of BRONJ.

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AUTHOR QUESTIONS AND ANSWERS

1. Why did you undertake this research?

Treatment protocols for performing dento-alveolar procedures for patients on bisphosphonates vary significantly. The risk of BRONJ is a recognised side effect. This study was undertaken as there was a significant cohort of patients on both intravenous and oral bisphosphonates that required dento-alveolar procedures and the risks contributing to a BRONJ could be assessed statistically. We wanted to determine whether patients with known risk factors were at a higher risk of developing a BRONJ. Classification of patients into low, medium and high risk categories for BRONJ development could aid development of an appropriate treatment protocol for this cohort of patients.

2. What would you like to do next in this area to follow on from this work?

We would like to carry out a further study on the cohort of patients since 2011 as the size of the cohort would be significantly higher and other significant factors can be identified with the aim of eventually publishing a national protocol for treatment of these patients undergoing dento-alveolar procedures.

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