Closing in on the puzzle of ONJ

Since the initial reports of osteonecrosis of the jaws (ONJ) associated with bisphosphonate therapy, several studies have tried to establish the prevalence and incidence of this lesion. Results, for both orally and intravenously administered bisphosphonates, are equivocal and vary greatly. Elucidating the epidemiologic relationship of these lesions to bisphosphonate therapy will create a sound foundation for prevention and treatment protocols for ONJ.

In this issue of JADA, Grbic and colleagues report findings from a study of 7,714 women with postmenopausal osteoporosis who were randomized into two equal groups. The treatment group received intravenous bisphosphonates (zoledronic acid 5 milligrams) once each year, while the control group received a placebo over a period of three years. Two cases of ONJ were identified, one in each group. The authors concluded that once-per-year administration of intravenous bisphosphonates was not associated with an increased risk of developing ONJ.

Zavras and colleagues used a different approach to determine the frequency of inflammatory or necrotic adverse bone conditions in the jaws. They assessed medical claims data from more than 714,000 people to determine the prevalence of jaw pathologies among patients with osteoporosis and patients with cancer—and whether that prevalence was related to the method of bisphosphonate administration used.

According to their findings, patients with conditions requiring intravenous bisphosphonates had a much higher risk of developing adverse conditions in the jaw compared with patients taking oral bisphosphonates. This finding is similar to those of previous case-controlled studies.

These two articles contribute to a growing body of knowledge that, in time, may clarify the epidemiology of an oral lesion that has puzzled scientists for the past five years. However, these studies do not help clarify the potential adverse effects of dental treatment in patients taking bisphosphonates. In the article by Grbic and colleagues, no data are available regarding how many of the participants in their study underwent traumatic dental procedures during the study period. There are similar limitations in Zavras and colleagues’ study.

The risks and benefits of any treatment protocol need to be assessed, and the decisions we make must be based on sound scientific evidence. Our patients deserve no less.

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Osteonecrosis of the jaws has been described in patients taking several different forms and brands of bisphosphonates. As very few people develop this type of lesion, it is unclear whether there are predisposing factors that influence its development beyond the presence of bisphosphonates, or whether there exist certain protective qualities. It appears likely that patients with ONJ have other underlying factors that contribute to this sometimes devastating condition.

Different risk factors for ONJ have been proposed—cancer, periodontal and other dental diseases, cancer therapy, palatal tori, glucocorticosteroid therapy, duration of bisphosphonate therapy, potency of the administered bisphosphonates, older age, female sex, and dental extractions or other dental trauma. It is not always clear how these different underlying conditions, medical treatments or dental therapies contribute to ONJ, or whether these risk factors have a synergistic effect.

On the basis of their mechanism of action, it is highly plausible that bisphosphonates may have a direct role in the development of osteonecrosis, but they also may be a marker in patients who are susceptible to osteonecrosis owing to other circumstances. For example, patients receiving chemotherapy for cancer already are highly susceptible to various oral lesions, including inadequate healing after oral trauma. It is not surprising, therefore, that we find more people with ONJ in this patient population compared with patients who have osteoporosis.

In Grbic and colleagues’ study, the two people who developed osteonecrosis had uncontrolled type 2 diabetes mellitus or were taking glucocorticosteroids. Both diabetes mellitus and glucocorticosteroids affect bone remodeling.

One major difficulty with epidemiologic research data on ONJ is the lack of standardized diagnostic criteria. An exposed bone that fails to heal after six to eight weeks in a patient taking bisphosphonates is considered bisphosphonate-associated ONJ. This is one of the major limitations of Zavras and colleagues’ study, as the researchers could not identify lesions specifically associated with bisphosphonate therapy. No histopathologic marker or other method has been validated with a high enough sensitivity and specificity to be used to establish a definitive diagnosis of bisphosphonate-associated ONJ.

JADA receives many submissions of case reports of ONJ. We cannot publish all of these reports, as they would occupy too much of The Journal, and it is uncertain whether these rejected case reports ever are published. It would be useful, of course, to compile ONJ cases from different practitioners in a large database, although it would be necessary at the outset to establish a uniform case definition. The “true” cause of bisphosphonate-associated ONJ has not been determined, but we have recognized certain epidemiologic associations. From a clinician’s standpoint, it would be helpful if specific risks and risk factors could be identified and quantified. As an example of the potential confusion that may arise, when the risk of complications cannot be assessed, some proposed protocols call for withdrawing oral bisphosphonates for a short period (three months) before performing invasive dental procedures. If all patients taking bisphosphonates are treated according to this recommendation, irrespective of their risk of developing ONJ, millions of patients will not receive appropriate and timely oral health care.

There also is an argument that discontinuing bisphosphonate therapy for patients with osteoporosis may increase their risk of experiencing hip fractures and other potentially devastating consequences. On the basis of the very low risk of developing ONJ and the potential dire complications associated with stopping oral bisphosphonate therapy, many physicians strongly oppose arbitrarily suspending a patient’s bisphosphonate therapy before dental treatment. Yet, evidence suggests that bisphosphonates, even when administered orally, are retained in a therapeutic dosage in bone for several years after the drug therapy is discontinued. This would imply that the risk of developing osteoporosis-related complications after a short drug holiday is very small, and there is no benefit from an oral health perspective to halting the use of the medication for such a short period.
As with many other circumstances in which general health and oral health are irrefutably linked, we need to establish better communications with physicians treating patients who take bisphosphonates. The risks and benefits of any treatment protocol need to be assessed, and the decisions we make must be based on sound scientific evidence. Our patients deserve no less.


**LETTERS**

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**GINGIVAL RECESSION**

The October JADA “For the Dental Patient” feature, “Gingival Recession: Causes and Treatment” (JADA 2007;138[10]:1404), is notably absent of the cause of the lesions presented in Figures A and B. One of the most notable causes of gingival recession is occlusal trauma caused by bruxism and/or clenching. While toothbrush abrasion potentiates the demineralization of the root surface, the tensile forces on the mineralized matrix of the root surface at the osseous crest are readily removed by abrasion and chemical agents. The patient is rarely aware of his or her condition, owing to its predominantly nocturnal nature.

I fully understand that the article is intended to prompt dialogue with patients. But, after having read this and being told that they may need further occlusal workup examinations, as well as possible splint therapy, equilibration or temporomandibular joint therapy, patients may be more than a little confused. These “gingival” lesions are not a periodontal phenomenon, and will return after grafting if the underlying disease is not treated. Many thanks on a generally fine publication.

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**DIAGNOSIS QUESTIONED**

I read with interest the October JADA “For the Dental Patient” feature, “Gingival Recession: Causes and Treatment” (JADA 2007;138[10]:1404). My personal feeling is that the treatment is excellent, but the diagnosis is incorrect, giving patients a misunderstanding of what actually may have happened.

None of the teeth are, as the article explains, protruded or crowded. All at one time were completely covered with healthy gingival tissue, as evidenced by the contour that remains. Other quadrants are not pictured to show whether heredity or some habit may have been involved. The enamel on the teeth, on the other hand, is completely smoothed, rounded and devoid of characteristic lines and grooves, and the root surfaces are glasslike and smooth. The cuspid that is normally prominent has the deepest grooving and the highest recession, indicating that whatever happened to it took place first.

Later on, as the grooving reached a depth where the other teeth could be affected by the process of microabrasion from