

# Outcomes of Placing Dental Implants in Patients Taking Oral Bisphosphonates: A Review of 115 Cases

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**Purpose:** In recent years, numerous cases of bisphosphonate-associated osteonecrosis of the jaw have been reported involving both intravenous and oral therapy regimens. The majority of these cases have involved intravenous bisphosphonates. Subsequently, drug manufacturers and the US Food and Drug Administration issued warnings about possible bisphosphonate-associated osteonecrosis of the jaw. The American Dental Association and the American Association of Oral and Maxillofacial Surgeons assembled expert panels to formulate treatment guidelines. Both panels differentiated between patients receiving bisphosphonates intravenously and those receiving the drugs orally. However, the recommendations were based on limited data, especially with regard to patients taking oral bisphosphonates. We wanted to ascertain the extent to which bisphosphonate-associated necrosis of the jaw has occurred in our dental implant patients. We also wanted to determine whether there was any indication that the bisphosphonate therapy affected the overall success of the implants as defined by Albrektsson and Zarb.

**Patients and Methods:** We identified 1,319 female patients over the age of 40 who had received dental implants at Montefiore Medical Center between January 1998 and December 2006. A survey about bisphosphonate therapy was mailed to all 1,319 patients. Responses were received from 458 patients of whom 115 reported that they had taken oral bisphosphonates. None had received intravenous bisphosphonates. All 115 patients were contacted and informed about the risk of bisphosphonate-associated osteonecrosis of the jaw. Seventy-two patients returned to the clinic for follow-up clinical and radiological evaluation.

**Results:** A total of 468 implants were placed in the 115 patients who reported that they had received oral bisphosphonate therapy. There is no evidence of bisphosphonate-associated osteonecrosis of the jaw in any of the patients evaluated in the clinic and those contacted by phone or e-mail reported no symptoms. Of the 468 implants, all but 2 integrated fully and meet criteria for establishing implant success. Implant success rates were comparable for patients receiving oral bisphosphonate therapy and those not receiving oral bisphosphonate therapy.

**Conclusions:** Guidelines for treatment of dental patients receiving intravenous bisphosphonate treatments should be different than for patients taking the oral formulations of these medications. In this study, oral bisphosphonate therapy did not appear to significantly affect implant success. Implant surgery on patients receiving bisphosphonate therapy did not result in bisphosphonate-associated osteonecrosis of the jaw. Nevertheless, sufficient evidence exists to suggest that all patients undergoing implant placement should be questioned about bisphosphonate therapy including the drug taken, the dosage, and length of treatment prior to surgery. For patients having a history of oral bisphosphonate treatment exceeding 3 years and those having concomitant treatment with prednisone, additional testing and alternate treatment options should be considered.

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**Table 1. ORAL AND INTRAVENOUS BISPHOSPHONATE MEDICATIONS AVAILABLE IN THE UNITED STATES**

Brand Name	Manufacturer	Generic Name
Actonel	Procter & Gamble	Risedronate
Boniva	Roche Pharmaceutical	Ibandronate
Didronel	Procter & Gamble	Etidronate
Fosamax	Merck & Co	Alendronate
Fosamax Plus D	Merck & Co	Alendronate
Skelid	Sanofi-Pharmaceuticals	Tiludronate
Aredia (intravenous)	Novartis	Pamidronate
Bonefos (intravenous)	Schering AG	Clodronate
Zometa (intravenous)	Novartis	Zoledronic acid

Adapted with permission from American Dental Association Council on Scientific Affairs: Dental management of patients receiving oral bisphosphonate therapy: Expert panel recommendations. *J Am Dent Assoc* 137:1144, 2006.

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According to the American Society of Clinical Oncology, the use of intravenous bisphosphonates for the reduction of bone pain, hypercalcemia of malignancy, and skeletal complications in patients with multiple myeloma, lung, breast and other cancers is the current standard of care.<sup>1-3</sup> The 2 drugs associated with these treatments are pamidronate (Aredia; Novartis Pharmaceuticals Corp, East Hanover, NJ) and zoledronic acid (Zometa; Novartis Pharmaceuticals Corp).<sup>4,5</sup>

Oral bisphosphonates are used to treat osteoporosis, Paget's disease, and osteogenesis imperfecta.<sup>6,7</sup> They are most widely used for treatment of osteoporosis; in the United States, some 22 million prescriptions were written for Fosamax (Merck Co, West Point, VA) between May 2003 and April 2004.<sup>8</sup> It is estimated that the number of hip fractures in the United States will triple by 2020 and that 1 of every 2 women will sustain an osteoporosis fracture in her lifetime.<sup>9</sup> Twenty-four percent of the women who fracture a hip will die within a year.<sup>10-15</sup> As the population ages, the number of people receiving bisphosphonate therapy is likely to rise. In addition, many of those treated will receive medication for an extended number of years. Oral and intravenous bisphosphonate medications available in the United States are listed in Table 1.<sup>10</sup>

In a letter to the editor of the *Journal of Oral and Maxillofacial Surgery* published in September 2003, Marx alerted the dental community to the possible relationship between intravenous bisphosphonate therapy and necrosis of the jaw.<sup>5</sup> He reported on 36 cases of bone exposure that were not responsive to surgical or medical treatments. All 36 patients were receiving intravenous bisphosphonate in the form of either Aredia or Zometa. His letter prompted others to review patient records and to make reports of similar findings.

The following year, Ruggerio et al published a review of 56 cases of osteonecrosis associated with the use of intravenous bisphosphonate therapy.<sup>1</sup> The au-

thors noted that during the 3 years covered by the study, the number of patients presenting at the medical center with necrotic lesions of the jaw had dramatically increased. The necrosis was typical of that seen in patients receiving radiation therapy. However, these patients were not being treated with radiation; rather they were receiving bisphosphonate therapy.

Soon after publication of the Ruggerio article, in September 2004, Novartis, manufacturer of Aredia and Zometa, notified health care professionals of the possible relationship between intravenous bisphosphonate therapy and necrosis of the jaws. Thereafter the US Food and Drug Administration issued an alert that included not only the intravenous bisphosphonate formulations but the oral ones as well.<sup>7</sup>

Additional articles and case studies have been published though all have limited sample sizes and all are retrospective studies. Incidence of bisphosphonate-associated osteonecrosis of the jaw is estimated to range from 0.8% to 12% for patients receiving intravenous formulations.<sup>10-15</sup> For patients taking oral medication, the incidence is estimated to be 0.7 per 100,000 person years of exposure.<sup>8</sup> Nationwide, there have been over 200 reported cases of possible bisphosphonate-associated osteonecrosis of the jaw in patients taking Fosamax or Actonel (Procter and Gamble, Cincinnati, OH). So far there are no documented cases for patients taking Boniva (Hoffman-LaRoche, Nutley, NY) although there are some anecdotal reports.<sup>7</sup> Results for patients taking other oral bisphosphonates are expected to be comparable. Risks associated with intravenous therapy appear to be substantially higher than for the oral medications.

A conclusive cause and effect relationship between bisphosphonate therapy and osteonecrosis of the jaw has not been established. But evidence suggests that such a link may in fact exist. Unfortunately there is limited data to aid in the identification of other risk factors for development of the disease. Some evi-

dence suggests that those risk factors may include the potency of the drug used, the duration of therapy, being Caucasian, being older than 65, having chronic periodontitis, ongoing corticosteroid therapy, having diabetes, smoking, and the use of alcohol.<sup>16-18</sup>

It appears important to make a distinction between osteonecrosis of the jaw induced by oral bisphosphonates versus that induced by intravenous bisphosphonates. Oral bisphosphonate-induced necrosis appears to be less frequent, less severe, more responsive to discontinuation of the drug, and curable with surgical debridement. Marx states that osteonecrosis from oral bisphosphonates differs significantly from intravenous bisphosphonate-associated osteonecrosis in 3 major ways: Patients taking oral bisphosphonates 1) require a longer period of drug therapy before bone is exposed, 2) manifest less bone exposure and symptoms are less severe, and 3) have a chance of symptoms improving or exposed bone healing after taking a drug holiday.<sup>7</sup>

Nevertheless, the Council of Scientific Affairs of the American Dental Association assembled a panel of experts to provide dentists with guidelines for treating patients who are receiving bisphosphonate therapy. The American Association of Oral and Maxillofacial Surgeons convened an expert Task Force with similar goals. The resulting guidelines suggested a very cautious approach to implant surgery and extractions for patients receiving bisphosphonate therapy either intravenously or orally.<sup>8-11</sup>

The American Dental Association Expert Panel recommends that patients taking oral bisphosphonates be informed about the risks and benefits. They further recommend that nonsurgical and less invasive treatment alternatives be used when possible. The panel cautions that patients may be at increased risk when extensive implant placement or guided bone regeneration is necessary. When the treatment plan involves the medullary bone and/or periosteum in multiple sextants, the panel recommends treating 1 sextant or tooth at a time. They recommend treatment with an antimicrobial mouth rinse and a 2-month disease-free follow-up before other sextants are treated.

The Task Force appointed by the American Association of Oral and Maxillofacial Surgeons also recommends that patients taking oral bisphosphonates be informed of the small risk of compromised bone healing.<sup>11</sup> The Task Force states that elective dentoalveolar surgery does not appear to be contraindicated in patients without known risk factors who have been taking oral bisphosphonates for less than 3 years. A drug holiday of at least 3 months prior to surgery is suggested for patients who have taken an oral bisphosphonate for more than 3 years and those that have taken corticosteroids concomitantly.

If dental implants are to be placed, the panel suggests contacting the physician who prescribed the oral bisphosphonate prior to surgery to suggest an alternate dosing schedule, a drug holiday, or an alternative to bisphosphonate therapy. These recommendations were made by 2 of the Task Force members based on their clinical experience with 50 such patients.

For years dentists have routinely performed surgical procedures and placed implants in patients receiving bisphosphonate therapy. Prior to widespread awareness of the risk of bisphosphonate-associated osteonecrosis and publication of treatment guidelines, these patients were treated without modification of standard treatment procedures. Additional research is required to determine if additional diagnostic testing or treatment modifications are actually necessary. Because implant surgery is a major part of our practice, we wanted to determine the necessity of making wholesale modifications in our treatment of patients receiving oral bisphosphonate therapy based on our past clinical experience. Specifically we wanted to determine whether any patients had developed osteonecrosis of the jaw and whether there was any indication that bisphosphonate therapy affected the overall success of the implants as defined by Albrektsson and Zarb.<sup>19</sup>

## Patients and Methods

We identified 1,319 female patients over the age of 40 who had implant surgery in the Department of Oral and Maxillofacial Surgery at Montefiore Medical Center between January 1998 and December 2006. A survey (Fig 1) asking about current and past oral bisphosphonate therapy was mailed to those patients. Thirty-five percent (458) of the surveys were returned. Of those, 115 patients reported taking oral bisphosphonates before or after implant surgery. None reported receiving intravenous bisphosphonate. A total of 468 implants had been placed in these patients.

The patients who responded to our survey that reported a history of bisphosphonate use were compared with a random sample of nonresponders with regard to age and number of implants. The difference between the groups with regard to number of implants was not significant, whereas there was a significant difference in age between the groups. In addition, 115 of the 458 responders, whereas only 5 among 100 nonresponders, had a history of bisphosphonate use ( $P < .0001$ ).

The remaining 343 patients indicated that they had not received bisphosphonate therapy. A total of 1,450 implants had been placed in these patients; 1,436 implants integrated successfully.

Last Name: \_\_\_\_\_

First Name: \_\_\_\_\_

Address: \_\_\_\_\_

\_\_\_\_\_

Phone #: \_\_\_\_\_

1. Were you taking Fosamax, Boniva, or Actonel when your dental implants were placed?  
 No  
 Yes (Please indicate which medication you were taking)  
 Actonel  
 Boniva  
 Fosamax
2. Did you start taking one of the above medications after your dental implants were placed?  
 No  
 Yes (Please indicate which medication you began taking)  
 Actonel  
 Boniva  
 Fosamax
3. Are you taking one of these medications at this time?  
 No  
 Yes (Please indicate which medication you are taking)  
 Actonel  
 Boniva  
 Fosamax
4. What is the total number of months you have taken Actonel, Boniva, or Fosamax?  
 Months  Not Applicable
5. Have you received chemotherapy since your implants were placed?  
 No  Yes
6. Are you experiencing pain, swelling, or exposed bone around any of your implants?  
 No  Yes (Please call to schedule an exam)
7. May we contact you to get additional information? If so, what is the phone number or email address you would like us to use? \_\_\_\_\_

**Please return this questionnaire in the enclosed envelope. Thank you for your assistance.**

**FIGURE 1.** Patient survey.

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We used the criteria developed by Albrektsson and Zarb to determine implant success. Those criteria are listed in [Table 2](#).<sup>19</sup>

## Results

The 115 patients who reported having bisphosphonate therapy were contacted and informed that there was a slight risk of bisphosphonate-associated osteonecrosis of the jaw. All 115 patients had been treated using standard implant surgery techniques without modification due to the bisphosphonate therapy. Sixty-three percent of the patients (72 out of 115) were seen for a follow-up clinical and radiographic examination.

The mean duration of oral bisphosphonate therapy was 38 months. Twenty-six patients started oral bisphosphonate therapy after implant surgery and subsequent healing. The remaining 89 patients started bisphosphonate therapy before implant placement. Sixty-six patients reported taking Fosamax prior to implant placement; 21 patients were taking Actonel; and 2 patients were taking Boniva. Out of the 89 patients taking oral bisphosphonates prior to surgery, 33 patients reported taking an oral bisphosphonate for more than 3 years prior to surgery: 27 patients reported taking Fosamax, 5 patients reported taking Actonel, and 1 patient reported taking Boniva. The remaining 56 patients reported taking oral bisphos-

**Table 2. CRITERIA FOR IMPLANT SUCCESS**

An individual, unattached implant is immobile when tested clinically.
A radiograph does not show any evidence of peri-implant radiolucency.
Vertical bone loss is less than 0.2 mm annually after the implant's first year of service.
Individual implant performance is characterized by an absence of persistent and/or irreversible signs and symptoms such as pain, infection, neuropathies, paresthesia, or violation of the mandibular canal.
To be considered successful, the dental implant should provide functional service for 5 years in 75% of the cases.

Adapted with permission from Albrektsson et al.<sup>19</sup>

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phonates for less than 3 years prior to dental implant placement.

A total of 468 dental implants were placed in patients receiving bisphosphonate therapy. Four hundred sixty-six implants are in function and are successful according to criteria for success defined by Albrektsson and Zarb. Two implants failed. In the first case, the patient had 2 implants placed in the maxilla to restore the upper left first and second molars, and a simultaneous sinus lift. In the next year, an additional 2 implants were placed to restore the upper left first and second bicuspid. The following year the implant in the area of the upper left second bicuspid failed to integrate. This was discovered prior to restoration. The implant was subsequently removed and replaced several months later. This implant successfully integrated and was definitively restored 6 months later. The patient did report taking oral bisphosphonates for 3 years prior to implant placement. The patient was no longer taking the oral bisphosphonate at the time of implant placement or thereafter. To date, all implants are successful and have been in function for more than 4 years.

In the second case, the patient started taking oral bisphosphonates more than 4 years prior to implant placement. The patient had 6 implants placed in the maxilla. Two months later, 7 implants were placed in the mandible. The most posterior implant replacing the lower left second molar did not integrate and was removed 1 month later. That implant was not replaced and the area healed uneventfully. All 12 implants are integrated and in function. The patient remains on oral bisphosphonates and reports over 8 consecutive years of oral bisphosphonate therapy.

None of the 458 patients who responded to the survey reported symptoms of bisphosphonate-associated osteonecrosis of the jaw. If it is assumed that none of the 115 responders treated with bisphosphonates had os-

teonecrosis, then the upper bound of a 1-sided confidence interval for 0 events for  $N = 115$  is 0.026. Thus, we would not expect that the rate of osteonecrosis is greater than 2.6%. However, none of the 72 patients who were examined in the clinic after reporting a history of bisphosphonate therapy had evidence of osteonecrosis. We have no reports of osteonecrosis from any of the 861 patients who did not return the survey. Nor do we have reports of osteonecrosis from any of the referring restorative dentists. We cannot say definitively that none of these patients has developed bisphosphonate-associated necrosis. However, it is our experience that we hear rather quickly from implant patients who have problems such as losing an implant or development of oral lesions.

Patients taking bisphosphonates who reported to the clinic or who contacted us by phone or e-mail were asked about known risk factors such as age over 65, having diabetes or taking prednisone concomitantly with bisphosphonate therapy. The mean age of the patients who had bisphosphonate therapy was 67.4 years; 51 of the 115 were over the age of 65. Three of the patients reported taking prednisone concomitantly with bisphosphonate therapy; 2 patients had diabetes.

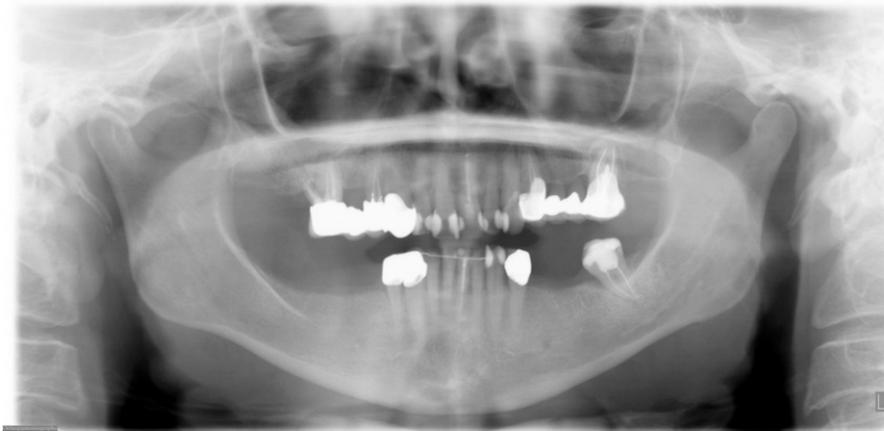
More invasive surgical procedures have been identified as risk factors for developing bisphosphonate-associated osteonecrosis. In the group of 115 patients, 32 had maxillary sinus augmentation. Six of the 32 were taking an oral bisphosphonate for at least 3 years prior to sinus augmentation.

The ADA panel recommended that surgical treatments be limited to a single sextant with a substantial interval for healing before proceeding to treatment of another sextant.<sup>4</sup> At Montefiore, single session, multiple sextant surgery was performed on 29 patients who had been taking oral bisphosphonates prior to surgery.

The most interesting of these patients is a 67-year-old female who had been taking Actonel for more than 5 years prior to dental implant placement. Two implants were placed into the upper right quadrant with a simultaneous maxillary bone graft. The following year, 5 additional implants were placed in the right and left mandible. To date, the patient is still taking Actonel. All 7 dental implants are in function and show no evidence of osteonecrosis (Figs 2-5).

## Discussion

Ruggerio's study that included 7 patients taking oral bisphosphonates for treatment of osteoporosis contains the single most compelling evidence of a link between oral bisphosphonate treatment and osteonecrosis.<sup>1</sup> None of the 7 patients had a history of malignant disease or chemotherapy. He did not report on the duration of the bisphosphonate therapy. The re-



**FIGURE 2.** Preoperative panoramic x-ray taken in September 2005.

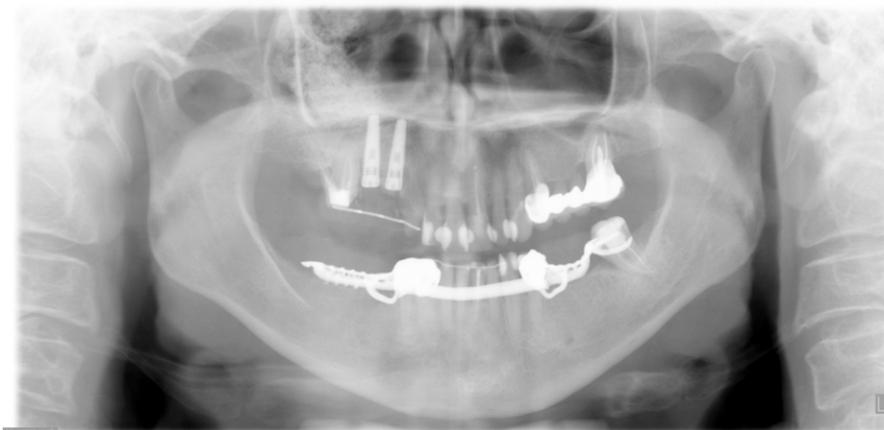
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maining 56 patients in the study were all taking intravenous bisphosphonate in conjunction with treatment for multiple myeloma, breast cancer, or some other form of malignant disease.

Despite the widespread use of oral bisphosphonates, a review of the literature found only 1 case of dental implant failure associated specifically with oral bisphosphonate use. A case report from 1995 suggested that failure of 5 implants was caused by bisphosphonate therapy.<sup>20</sup> The drug discussed in this case report was etidronate disodium (Didronel; Procter and Gamble), a non-nitrogen containing bisphosphonate that is not the drug of choice for treatment of osteoporosis. Didronel is 1,000 times less potent than alendronate (Fosamax) and is used to treat fibrous dysplasia and Paget's disease.<sup>21</sup> Didronel does not contain nitrogen. Other than this report, only nitrogen containing bisphosphonates have been found to produce bisphosphonate-associated osteonecrosis of

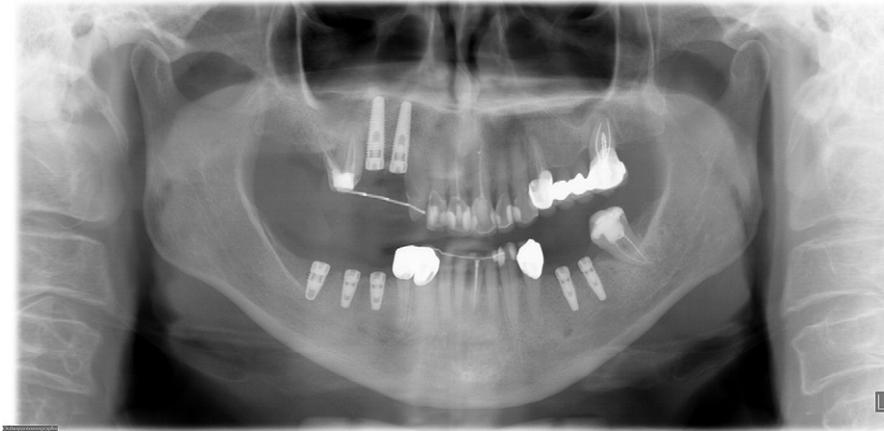
the jaw. Marx speculates that Didronel does not cause osteonecrosis because it contains no nitrogen and therapy is not constant; patients are treated with a cycle of on-off doses.<sup>7</sup>

According to the case report, 5 implants were placed and successfully integrated in the anterior mandible. The patient was restored and had an uneventful postoperative course. The patient began etidronate disodium (Didronel) therapy 28 months after implant placement. This drug can be administered intravenously or orally; however, the route of drug administration for the patient was not specified by the authors. After taking the drug for 4 months, the patient presented with pain in the mandible. A panoramic radiograph revealed extensive osteolysis around all implants and all 5 implants were removed 1 month later. The bisphosphonate treatment was discontinued. The authors make no mention of poor or delayed healing fol-



**FIGURE 3.** Postoperative panoramic x-ray after 2 dental implants were placed in the upper right quadrant with a simultaneous maxillary sinus lift in October 2005.

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**FIGURE 4.** Panoramic x-ray after mandibular dental implants were placed in May 2006.

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lowing removal of the implants as might be expected with bisphosphonate-induced necrosis.

The authors reported that the patient developed a parafunctional clenching habit subsequent to implant placement and loading. It is possible that increased physiologic loads were the cause of implant failure. Nevertheless, the authors concluded

that the implant failure and osteolysis were caused by the Didronel therapy.<sup>20</sup> They recommend that patients who have previously undergone implant placement forego bisphosphonate therapy. They further recommend that dentists avoid implant placement in patients who require bisphosphonate therapy.



**FIGURE 5.** Clinical photos show no evidence of bisphosphonate-associated osteonecrosis.

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In 2006, Jeffcoat reported the results of a single-blind controlled study of 50 postmenopausal female dental implant patients, all of whom had bone mineral density scores indicative of osteoporosis.<sup>22</sup> Twenty-five patients had taken oral bisphosphonates (alendronate or risendronate) for 1 to 4 years prior to inclusion in the study. The mean duration of bisphosphonate therapy prior to the study was 3 years. The other 25 patients did not take oral bisphosphonates prior to or during the study. One patient in each group smoked. A total of 102 implants were placed in the group taking bisphosphonates; 108 dental implants were placed in the nonbisphosphonate group. After 3 years, there was a 100% success rate with no clinical evidence of infection, pain, or necrosis in the patients who received oral bisphosphonates. There was a 99.2% success rate in the group who did not receive oral bisphosphonates.

We found similar results in our study. Of the 115 patients taking oral bisphosphonates, none show evidence or have symptoms of necrosis. All have had successful implant restorations. Had recommendations of the ADA and AAOMS panels been followed, treatment for at least 30 of these patients would have been modified. Possible treatment modifications include a drug holiday, obtaining a C-terminal cross-linking telopeptide serum test, treating individual quadrants separately, or even use of nonimplant-supported prostheses.<sup>7,8,23</sup> Management of patients receiving oral bisphosphonates should be separated and distinguished from the management of patients receiving intravenous bisphosphonates. All patients considering surgical treatments should be asked about bisphosphonate use and should be advised of possible risks. Dental records should be revised to include this information. Additional research is required to guide the management of patients taking oral bisphosphonates. Some evidence suggests that duration of oral bisphosphonate therapy correlates with the development and severity of osteonecrosis. More data are needed to determine at what point invasive dental treatment should be routinely modified. In addition, more data is needed to determine whether the serum C-terminal cross-linking telopeptide serum test is valid for assessing risk.<sup>7</sup> There is insufficient evidence to suggest that implant placement, tooth extraction, and other surgical treatments should be routinely avoided for patients receiving oral bisphosphonate therapy. Instead, evidence suggests that frequent clinical and radiological examinations with prompt treatment of problems will minimize potential risks.

## References

- Ruggerio SI, Mekrotra B, Engroff SL: Osteonecrosis of the jaws associated with the use of bisphosphonates. A review of 63 cases. *J Oral Maxillofac Surg* 62:527, 2004
- Hillner BE, Ingle JN, Berenson JR, et al: American Society of Clinical Oncology guideline on the role of bisphosphonates in breast cancer. *J Clin Oncol* 18:1378, 2000
- Berenson JR, Hillner BE, Kyle RA, et al: American Society of Clinical Oncology clinical practice guidelines: The role of bisphosphonates in multiple myeloma. *J Clin Oncol* 20:3719, 2002
- Migliorati CA. Bisphosphonates and oral cavity avascular bone necrosis. *J Clin Oncol* 21:4253, 2003
- Marx RE. Pamidromate (Aredia) and zoledronate (Zometa) induced avascular necrosis of the jaws: A growing epidemic. *J Oral Maxillofac Surg* 61:1115, 2003
- Glorieux FH, Bishop NJ, Plotkin H, et al: Cyclic administration of pamidronate in children with severe osteogenesis imperfecta. *N Engl J Med* 339:947, 1998
- Marx RE: Oral and Intravenous Bisphosphonate-Induced Osteonecrosis of the Jaws. Hanover Park, IL, Quintessence, 2007
- American Dental Association Council on Scientific Affairs: Dental management of patients receiving oral bisphosphonate therapy: Expert panel recommendations. *J Am Dent Assoc* 137:1144, 2006
- US Department of Health and Human Services. Bone health and osteoporosis: A report of the Surgeon General. Rockville, MD: US Department of Health and Human Services, Office of the Surgeon General, 2004
- American Dental Association Council on Scientific Affairs: Dental management of patients receiving oral bisphosphonate therapy: Expert panel recommendations. *J Am Dent Assoc* 137:1144, 2006
- Advisory Task Force on Bisphosphonate-Related Osteonecrosis of the Jaws, American Association of Oral and Maxillofacial Surgeons: American Association of Oral and Maxillofacial Surgeons position paper on bisphosphonate-related osteonecrosis of the jaws. *J Oral Maxillofac Surg* 65:369, 2007
- Durie BGM, Katz M, Crowley J: Osteonecrosis of the jaws and bisphosphonates. *N Engl J Med* 353:99, 2005
- Bamias A, Kastiris E, Bania C, et al: Osteonecrosis of the jaw in cancer after treatment with bisphosphonates: Incidence and risk factors. *J Clin Oncol* 23:8580, 2005
- Dimopoulos MA, Kastiris E, Anagnostopoulos A, et al: Osteonecrosis of the jaw in patients with multiple myeloma treated with bisphosphonates: Evidence of increased risk after treatment with zoledronic acid. *Haematologica* 91:968, 2006
- Zavras AI, Zhu S: Bisphosphonates are associated with increased risk for jaw surgery in medical claims data; Is it osteonecrosis? *J Oral Maxillofac Surg* 64:917, 2006
- Marx RE, Sawatari Y, Fortin M, et al: Bisphosphonate-induced exposed bone (osteonecrosis/osteopetrosis) of the jaws. Risk factors, recognition, prevention, and treatment. *J Oral Maxillofac Surg* 63:1567, 2005
- Ruggiero SL, Mehrotra B: Ten years of alendronate treatment for osteoporosis in postmenopausal women. *N Engl J Med* 350:1189, 2004
- Schwartz HC: Osteonecrosis and bisphosphonates: Correlation versus causation. *J Oral Maxillofac Surg* 62:763, 2004
- Albrektsson T, Zarb G, Worthington P, et al: The long-term efficacy of currently used dental implants: A review and proposed criteria of success. *Int J Oral Maxillofac Implants* 1:11, 1986
- Stark WJ, Epker BN: Failure of osteointegrated dental implants after diphosphonate therapy for osteoporosis: A case report. *Int J Oral Maxillofac Implants* 10:74, 1995
- Chapurlat R, Meunier PJ: Bisphosphonates and bone remodeling: Effectiveness in Paget's disease, fibrous dysplasia, and osteoporosis [in French]. *Rev Chir Orthop Reparatrice Appar Mot* 84:743, 1998
- Jeffcoat MK: Safety of oral bisphosphonates: Controlled studies on alveolar bone. *Int J Oral Maxillofac Implants* 21:349, 2006
- Rosen HN, Moses AC, Garber J, et al: Serum CTX. A new marker of bone resorption that shows treatment effect more often than other markers because of low coefficient of variability and large changes with bisphosphonate therapy. *Calcif Tissue Int* 66:100, 2000