

OVERVIEW OF BISPHOSPHONATE OSTEONECROSIS OF THE JAWS

-A course for dentists and dental auxiliary-

TUITION: \$25 per registrant or \$20 per registrant for multiple registrants from the same office.
CE Credit: 1 hour ** (Registrants must correctly answer 70% of the quiz questions to receive credit)**

INSTRUCTIONS: Read and study the narrative. Complete the quiz and registration form, and mail (along with registration fee) to: **University of Tennessee Health Science Center, Continuing Dental Education, 875 Union Avenue, Memphis, TN 38163** or fax completed quiz, registration form and credit card information to **(901) 448-1514**.

Please direct all questions to the CDE office, (901) 448-5386, fax us at (901) 448-1514, or email utcde@utmem.edu. For more information or a list of continuing education activities, visit our website at <http://cde.utmem.edu>.

COURSE OBJECTIVES:

1. Provide the dental clinician with an overview and understanding of bisphosphonate osteonecrosis of the jaws.
2. Provide the clinician with the ability to recognize bisphosphonate drug names and differentiate those administered intravenously from oral medications.
3. Enable the clinician to identify the dental profession's responsibilities concerning patients taking bisphosphonates.



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The University of the West Indies, Trinidad. He completed a second residency in Oral and Maxillofacial Pathology at The Ohio State University, Columbus, Ohio, and is a Fellow, American Academy of Oral and Maxillofacial Pathology and Diplomate, American Board of Oral and Maxillofacial Pathology. Dr. Rawal is particularly interested in soft tissue tumor pathology.

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OVERVIEW OF BISPHOSPHONATE OSTEONECROSIS OF THE JAWS

Bisphosphonate medications alter the way the body remodels bone. This results in a denser bone structure that in some cases cannot heal properly when traumatized.¹⁻⁶ The drugs incorporate themselves into the bone itself and have very long half lives.¹⁻⁴ They have antiangiogenic¹⁻⁴ and, perhaps, tumoricidal effects.¹⁻³ Unfortunately, bisphosphonates are also associated with osteonecrosis of the jaws.¹⁻⁶ Patients receiving intravenously administered bisphosphonates are at highest risk for this complication¹⁻⁶ but there are now reports of its occurrence among patients taking the much lower risk oral medications.^{1,2,4-6} These medications are deposited most in bones that remodel and repair themselves frequently.¹⁻⁵ The human jaws with their masticatory stresses and resulting microscopic fractures often remodel themselves and that may be one reason they are more prone than other bones in developing necrosis.^{1,4} Trauma is a risk factor for the development of bisphosphonate osteonecrosis¹⁻⁶ and it should be no surprise to dentists that “the most common clinical history associated with this process (of bisphosphonate osteonecrosis) is absent or delayed hard- and soft-tissue healing after dental extractions.”¹ It is interesting to note that oral surgeons were the first to recognize an association between intravenous bisphosphonate therapy and exposed bone that would not heal.⁴ Exposed bone for more than eight weeks is one of their diagnostic criteria for bisphosphonate-related osteonecrosis of the jaws.⁴ Trauma to soft tissues such as that from removable dental prostheses may also initiate bisphosphonate necrosis of the underlying bone.^{1,3,5}

PHOTOGRAPHS

The following pictures of bisphosphonate-related osteonecrosis of the jaws are used by permission from John W. Hellstein, University of Iowa College of Dentistry and Hardin MD, University of Iowa, at www.lib.uiowa.edu/hardin/md/ui/dent/osteonecrosis6.html



Figure 1, Mild Presentation of Bisphosphonate-Related Osteonecrosis

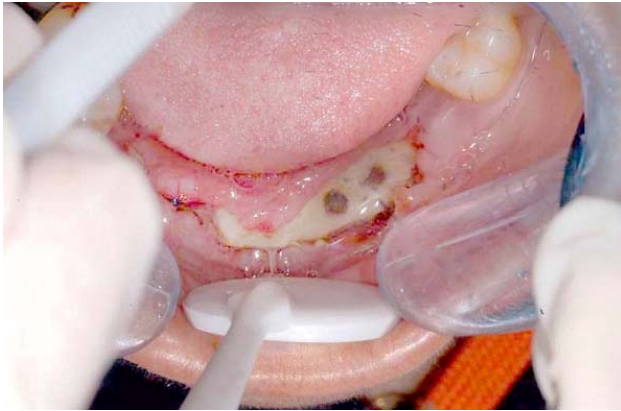


Figure 2, Presentation of Bisphosphonate-Related Osteonecrosis with Extraoral Fistula



Figure 3, Severe Presentation of Bisphosphonate-Related Osteonecrosis

MEDICAL HISTORY

Patients presenting to the dental office should be thoroughly quizzed about their medical history and current medications.^{1,3,6} Oral bisphosphonates are used to treat osteoporosis and Paget's disease, while more potent, intravenous forms of the drugs are used for some osteoporosis, multiple myeloma, and metastatic cancer patients¹⁻⁶. Patients taking IV bisphosphonates are at a much higher risk for osteonecrosis.¹⁻⁶ The potency of IV bisphosphonates is up to 10 times that of oral alendronate^{1,4} and more than 50% is available for incorporation into bone.⁵ Less than 1% of alendronate, the most popular oral form of the drug, is even absorbed into the body from the gut.⁵ In one study up to 13% of patients receiving I.V. bisphosphonate developed symptoms suspicious of osteonecrosis of the jaws.¹ In contrast, alendronate related osteonecrosis occurs less than once per 100,000 person-years exposure.⁵ Table 1 shows the names of currently available bisphosphonates and their usual route of administration.

TABLE 1: Bisphosphonate Drug Names*

| Brand Name | Generic Name |
|---|-----------------|
| <i>Oral Medications:</i> | |
| Actonel | Risedronate |
| Boniva** | Ibandronate |
| Didronel ** | Etidronate |
| Fosamax | Alendronate |
| Skelid | Tiludronate |
| **IV forms now available ^{4,2} | |
| <i>Intravenous Medications:</i> | |
| Aredia | Pamidronate |
| Bonefos | Clodronate |
| Zometa | Zoledronic Acid |

**Source: Adapted from 2006 ADA Association Report⁵*

Intravenous bisphosphonates find use in the treatment of patients with metastatic cancer due to their ability to reduce pain, pathologic fractures of bone and tumor size.¹⁻⁵ They contribute so much to the patient's quality of life that physicians continue the medication when osteonecrosis of the jaw occurs.¹⁻⁴ Stopping the medication would not significantly reduce bisphosphonate levels very quickly, anyway, as their clearance from the body is very slow.¹⁻⁴ Measurable levels are present up to 12 years after bisphosphonate therapy is discontinued.²

One problem taking a current medications history in cancer patients is that intravenous bisphosphonates are part of their cancer therapy.¹⁻⁶ Patients should be questioned thoroughly regarding bisphosphonates³ because they may not realize dentists need to know of their use.^{2,3}

The dentist should ask how long the patient has been taking bisphosphonates.¹ There is a low incidence of intravenous bisphosphonate patients developing necrosis prior to 6 months from the onset of therapy.¹ The risk then rises quickly for the stronger agents. In one study, the average onset of osteonecrosis in patients taking I.V. zoledronic acid was 18 months while those taking pamidronate, a weaker I.V. agent, was 6 years.¹ Oral bisphosphonate complications are more likely after 3 years of therapy.⁴ Remember that the effects of these medications last for long periods of time even if discontinued so it is wise to ask patients if they have had these medications in the past.³ Also, asking patients taking bisphosphonates if they have symptoms that might indicate osteonecrosis may be useful.^{3,4} The bone lesions may cause pain if infected but may otherwise be painless.^{1,3,4} The exposed bone¹⁻⁶ and tissue margins may feel rough to the patient.¹ Other symptoms include loose teeth, swelling, discharge and mouth odor.¹⁻⁵ Trauma¹⁻⁶ and, perhaps, infection^{1,6} are local risk factors for developing bisphosphonate osteonecrosis so at risk patients might benefit from questions concerning recent dental infections, tooth extractions, and the atraumatic function of any removable dental prostheses they might wear.

TREATMENT OF BISPHOSPHONATE OSTEONECROSIS

Bisphosphonate-associated osteonecrosis of the jaws has a poor prognosis in patients taking the drug intravenously. Many types of treatment have been tried including hyperbaric oxygen, debridement to more vascular bone, sequestrectomy, mandibular resections, and even maxillectomies but none have proved dependably curative.¹⁻³ Indeed, one study treating 63 patients using some of the treatment modalities mentioned found “no healing occurred in any of the patients treated.”¹ Currently, “the goals of therapy...are to eliminate pain and infection and minimize the progression of necrosis.”⁴ This involves close monitoring of the patient and the appropriate use of antibiotics, antibacterial rinses, pain control, superficial debridement, surgical debridement and resection.⁴ Removable appliances designed to protect the exposed bone and tissues from insult have also been suggested.¹ “If systemic conditions permit, long-term discontinuation (of I.V. bisphosphonates) may be beneficial in stabilizing established sites of (osteonecrosis), reducing the risk of new site development and reducing clinical symptoms.”⁴ In some cases, bisphosphonate-related osteonecrosis may be a sequela of cancer treatment that must be managed for the remainder of the patient’s life.²

Patients with osteonecrosis from oral bisphosphonate therapy have less severe presentations of the condition and respond better to treatment.^{4,6} They have a much better prognosis for improvement and eventual healing.^{4,6}

PREVENTION OF BISPHOSPHONATE OSTEONECROSIS

Since bisphosphonate osteonecrosis is relatively refractory to treatment, emphasis should be placed on its prevention.¹⁻⁵ Good oral health should be established and maintained before the institution of oral or intravenous bisphosphonate therapy, if possible.¹⁻⁵ For patients who will start intravenous medications, a protocol similar to that for chemotherapy or radiation therapy is suggested.¹⁻⁴ All extractions and other surgical procedures should be accomplished at this time and potential infection sites eliminated.¹⁻³ Once I.V. therapy is ongoing, tooth extractions,

implants and other surgical procedures should be avoided when possible, and alternative treatments like endodontia should be recommended instead.³ When extractions are unavoidable, referral to an oral and maxillofacial surgeon is recommended for even the most routine extraction.² Gentle soft tissue management and atraumatic scaling and prophylaxis are recommended for patients with bisphosphonate osteonecrosis,¹ and that would also seem a common sense precaution for patients at high risk for developing jaw necrosis. Soft liners for dentures are also recommended for patients taking I.V. bisphosphonates³ especially if they have osteonecrotic lesions.¹

The prevention of osteonecrosis in patients taking oral bisphosphonates is addressed by an expert panel's recommendations in JADA.⁵ They recommend a comprehensive dental evaluation prior to the initiation of these medications when possible and state that "routine dental treatment generally should not be modified solely on the basis of oral bisphosphonate therapy."⁵ Patients taking the oral medications should be informed of the very small risk of necrosis in general and, specifically, when invasive procedures involving bone are to be performed. Alternatives to the invasive procedures should be discussed. Examples include endodontic treatments instead of extractions, and fixed or removable prostheses instead of implants. This is not to say that more invasive procedures should be avoided, but to document that the patient acknowledged and accepted the risks involved, and consented to the treatment. The panel recommended that extensive invasive treatments be performed in trial increments. For example, treating one tooth or sextant of teeth first, allowing a two month or longer healing period to pass, and then treating other sextants or multiple sextants based on successful outcome of the trial site. Similarly, periodontal disease treatment should not utilize surgical procedures during a prolonged initial phase of care that provides an observation period in which resolution of the disease is evaluated. Poor resolution may be an effect of bisphosphonates as they decrease tissue vascularity which may also have a negative effect on grafted sites. Other recommendations by the panel include the use of chlorhexidine rinses pre- and post-operatively when extracting teeth or encountering bone, use of primary tissue closure when possible, and avoiding endodontic manipulation beyond the apex. Prosthodontic appliances should be "adjusted for fit as needed."⁵ There were no recommendations or precautions for restorative dentistry.

SUMMARY AND ADDITIONAL READING

This has been a very brief overview of bisphosphonate osteonecrosis of the jaws and the dental profession's responsibilities in its management. Please refer to the original articles and/or the ADA website for more detailed information. In addition, a second set of guidelines for prevention and treatment of osteonecrosis of the jaws in cancer patients published in the *Journal of Oncology Practice* can be accessed from the ADA site:

www.ada.org/prof/resources/topics/osteonecrosis.asp

References

1. Managing the care of patients with bisphosphonate-associated osteonecrosis: An American Academy of Oral Medicine position paper. Migliorati CA, Casiglia J, Epstein J, Jacobsen PL, Siegel MA, Woo S-K. JADA 2005; 136:1658-68.
2. Bisphosphonate-associated osteonecrosis of the jaws: A review of current knowledge. Markiewicz MR, Margarone JE, Campbell JH, Aguirre A. JADA 2005; 136:1669-74.
3. Osteonecrosis of the jaws in patients with a history of receiving bisphosphonate therapy: Strategies for prevention and early recognition. Melo MD, Obeid G. JADA 2005; 136:1675-81.
4. Bisphosphonate-Related Osteonecrosis of the Jaw. American Association of Oral and Maxillofacial Surgeons Surgical Update; volume 20, issue 2.
5. Dental Management of patients on oral bisphosphonate therapy: Expert panel recommendations. American Dental Association Report of the Council of Scientific Affairs. JADA 2006; 137:1144-50.
6. Osteonecrosis of the jaw and oral bisphosphonate treatment. Nase JB, Suzuki JB. JADA 2006; 137:1115-19.

Test on Next Page

Test

****Please duplicate and complete one form for each registrant****

Name: _____

Instructions: Choose the best possible answer. Registrants must correctly answer 70% of the test questions to receive CE credit.

OVERVIEW OF BISPHOSPHONATE OSTEONECROSIS OF THE JAWS

1. Bisphosphonate osteonecrosis of the jaws is most often associated with which of the following dental treatments?
 - a. Endodontic therapy
 - b. Tooth extraction
 - c. Wearing removable dental appliances
 - d. Restorative dentistry
2. Which form of bisphosphonate therapy is associated with the highest number of cases of osteonecrosis of the jaw?
 - a. Oral
 - b. Intravenous
3. According to this course, how many patients receiving intravenous bisphosphonate will develop symptoms of osteonecrosis?
 - a. Less than 1%
 - b. Up to 13%
 - c. Up to 36%
 - d. Up to 79%
4. Which of the following bisphosphonates is usually not administered intravenously?
 - a. Pamidronate (Aredia)
 - b. Clodronate (Bonafos)
 - c. Alendronate (Fosamax)
 - d. Zoledronate (Zometa)
5. Signs and symptoms of bisphosphonate osteonecrosis of the jaw may include:
 - a. Exposed bone
 - b. Loose teeth
 - c. Mouth odor
 - d. All of the above
6. Stopping I.V. bisphosphonate therapy usually results in healing of osteonecrotic lesions of the jaws within two months.
 - a. True
 - b. False
7. The majority of osteonecrotic lesions of the jaws in patients receiving I.V. bisphosphonate heal completely within two months with appropriate therapy.
 - a. True
 - b. False
8. Soft liners for dentures are recommended for patients taking I.V. bisphosphonate.
 - a. True
 - b. False
9. For patients taking I.V. bisphosphonate, which of the following dental treatments should be avoided, when possible?
 - a. Extractions
 - b. Implant placement
 - c. Removal of tori
 - d. All of the above
10. For dental patients taking an oral bisphosphonate and requiring invasive treatment involving bone, the A.D.A. panel of experts recommended:
 - a. Chlorhexidine rinses pre- and post-operatively
 - b. Periodontal surgery should be performed as early in the treatment sequence as possible
 - c. Initial simultaneous treatment of multiple quadrants, whenever possible
 - d. All of the above