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Antiresorptive Therapy: Roles and Responsibilities of Dental Professionals

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As the population ages, the incidence of diseases that may require antiresorptive therapy will also increase. The term "antiresorptive therapy" refers to the administration of oral or parenteral medications to reduce or stop the loss of bone mass. Bone mass-loss ailments include osteoporosis, osteopenia, metastatic cancer to the bone, and hypercalcemia, to name a few. In the case of osteoporosis, the homeostasis of bone remodeling is disrupted. This can lead to reduced bone mineralization and increase in bone fragility.

Patients with metastatic cancer to the bone also suffer from a higher incidence of bone fracture or "skeletal related events." The tumor cell infiltration to the medullary bone cavity leads to osteoblastic and/or osteolytic processes.[1]

The potential side effects of antiresorptive therapy treatment on the jawbone is of particular interest to the dental field. It may cause osteonecrosis of the jaw, also called avascular necrosis, which is also called medication-related osteonecrosis of the jaw (MRONJ). Avascular necrosis of the jaw may also be caused by radiation to the jawbone or other medications including high dose, long term use of corticosteroids or other immunosuppressants like chemotherapeutic drugs. It is therefore important to be able to establish proper causation based on specific diagnostic criteria. As reported on the position paper by American Academy of Oral and Maxillofacial Surgery, to positively identify MRONJ in a patient, the following findings must be present:

1. Current or previous treatment with antiresorptive therapy alone or in combination with immune modulators or antiangiogenic medications.
2. Exposed bone or bone that can be probed through an intraoral or extraoral fistula(e) in the maxillofacial region that has persisted for more than 8 weeks.
3. No history of radiation therapy to the jaws or metastatic disease to the jaws."[2]

The incidence of MRONJ is approximately 5-19 percent, depending on single or sequential antiresorptive therapy.[3] This is an alarmingly high number, which underscores the importance of proper dental supervision in this population.

There are two main class of drugs used to combat bone fractures and skeletal-related events — Denosumab and Bisphosphonate. Bisphosphonates are the original class of antiresorptive medications used to prevent osteoclastic activity and to interfere with bone remodeling. The half-life of bisphosphonates is quite long, often greater than 10 years.[4] This is due to the high affinity of its inherent chemical compounds for the surface of the osteoclasts. The efficacy of bisphosphonates is directly related to the concentration and the duration of treatment. By the same token, the longer the treatment, the more intimately the drug will have incorporated itself within the bone matrix.

Denosumab is a natural monoclonal antibody (IGg2), which is administered subcutaneously as an antiresorptive medication. It is produced and marketed under two different brand names, Prolia and Xgeva. Prolia is a low dose, longer term denosumab recommended once every 6 months for treatment of osteoporosis. Xgeva is a higher-dose drug administered to patients with metastatic bone cancer every 4 weeks. [5]

Unlike its bisphosphonate counterpart, Denosumab's mode of action as an antiresorptive therapeutic is at the biochemical level and not the bone matrix. It inhibits the formation of osteoclasts by interfering with chemical pathways. Additionally, since it does not bind to bone, its bioavailability is diminished within 6 months of treatment cessation.

Protocol:

Irrespective of which antiresorptive medication is being administered or contemplated, it is important to follow a standard preventive protocol.

Prior to antiresorptive administration:

- A complete head and neck evaluation, including a thorough intra-oral examination with recent imagining is required.
- Completion of prophylaxis and any restorative procedures.
- Completion of any oral surgical procedures on the dentition with fair to poor prognosis, with high probability of future infection. Allow 6-8 weeks of post operative healing prior to initiation of antiresorptive therapy.
- Close communication and coordination with the rest of the medical team is important to avoid complications.

During or post antiresorptive administration:

- Routine recall maintenance, 3-6 months.
- Avoid any elective surgical procedures that involve exposure of the periosteum, i.e, scaling and root planning, dental extractions, endosseous dental implant surgery, etc.
- Urgent oral surgical procedures may require consultation with the medical team and cessation of the use of Denosumab (drug holiday) for a minimum of 3-4 months prior to surgery. It is also important to allow 6-8 weeks of post-operative healing prior to resumption of Denosumab. [4]

Factors that contribute to a higher incidence of and poorer recovery from MRONJ include drug dosage and frequency and other comorbidities (e.g., diabetes, immune suppression, etc.)

The use of antibiotics is highly recommended if there is evidence of infection or for patients with a suppressed immune system or uncontrolled diabetes.

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About The Author

Reza Radmand, DMD, FAAOM is a Diplomate of the American Board of Dental Sleep Medicine with offices in Boston, MA and CT. He actively contributes to study design and data for research efforts between hospitals, academic institutions, and private practices for the treatment of sleep related disorders, including obstructive sleep apnea.

Dr. Radmand graduated from Tufts University School of Dental Medicine in 1989. He then went on to complete a Hospital Dentistry Residency Program at UCLA, after which he continued to spend the next 20 years of his dental career, teaching as a part time faculty at UCLA School of Dentistry.

In 2010, Dr. Radmand accepted a position at Yale New Haven Hospital, as Section Chief in Hospital Dentistry and the postgraduate dental faculty, in their dental residency program. In 2018 he joined Harvard's Brigham and Women's Hospital staff as a Research Collaborator in the Division of Sleep Medicine. In July 2022, Dr. Radmand received an academic appointment as a lecturer in the Department of Medicine at Harvard University Medical School. First board certified dental sleep medicine practitioner to receive such an appointment.

Dr. Radmand is a current Diplomate of American Board of Dental Sleep Medicine, "Academic Fellow" of the American Academy of Oral Medicine. Dr. Radmand is vastly involved with oral appliance therapy, in monitoring, and treatment of patients with obstructive sleep apnea. He is a strong advocate for a multi-disciplinary approach to prevention and treatment of systemic diseases and sleep disorders, working closely with academic physicians, including those at Harvard's Brigham and Women's section of Sleep Medicine, Yale School of Medicine, Yale New Haven Hospital and Bridgeport Hospital.

Dr. Radmand is an inventor and the founder of Achaemenid LLC, a start up medical device company. Achaemenid has over 19 IP medical concepts and prototypes. A number of these concepts are published, granted full patents or are in patent pending status.

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