

Contributions to the prevention and understanding of pathogenic mechanisms of osteonecrosis of the jaw

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Maxillary osteonecrosis is a debilitating condition of the jaws that can significantly affect patients' quality of life. Early diagnosis and a multidisciplinary approach are two crucial elements in the management of jaw osteonecrosis. Through early diagnosis, early signs and symptoms can be identified, allowing prompt and effective treatment to be instituted. This could reduce the severity of the disease and prevent further complications.

In the first chapter, we explored the key similarities and differences between post-radiotherapy OM and bisphosphonate-induced osteonecrosis of the Jaw. It was evident that both conditions share common features, such as jaw damage and increased risk of osteonecrosis. However, there were also significant differences, including etiology, clinical presentation, and treatment options.

We have observed that the profile of the patient with osteonecrosis due to radiotherapy in the OMF sphere is more often male, and older, and frequently the manifestations are detected in the mandible, including pathological fractures. The clinical manifestations are similar, but in ORN patients there are also side effects of radiotherapy, such as xerostomia, stomatitis, and trismus. Radiographic and histopathological examinations are similar. The presence of bacterial species from the Actinomycetes group has also been identified in both categories.

In conclusion, effectively addressing these two conditions requires a thorough understanding of their similarities and differences. This requires a personalized approach in the management of patients with ORN and BRONJ, tailored to the specific etiology and clinical presentation of each condition.

In the second chapter, we highlighted the importance of multidisciplinary collaboration in the management of the oral effects of angiogenesis inhibitors. We found that a well-coordinated multidisciplinary team involving dentists, oncologists, nurses, and other specialists can provide comprehensive and personalized care to patients. This can reduce adverse oral effects, improving patients' quality of life and ensuring continuity of cancer treatment. In conclusion, optimal management of the oral effects of angiogenesis inhibitors requires an interdisciplinary approach that puts the patient at the center of their care.

In the third chapter, we examined prescribers' attitudes towards OM prevention in the context of antiresorptive and antiangiogenic drugs. We found that prescribers' attitudes can significantly influence awareness and implementation of preventive measures, playing a key role

in reducing the incidence and severity of OM. Prescriber education and awareness of these risks is essential to ensure optimal patient care.

MRONJ awareness among BMA prescribers of different specialties, including rheumatology, oncology, endocrinology, and general medicine was high. Most recommend a mandatory consultation with the dentist before starting BMA treatment. This initial consultation should become mandatory at the time of diagnosis with oncological disease, i.e. within the first 6 months of starting BMA treatment for patients with osteoporosis-type bone disease.

To facilitate communication between the prescribing physician and the dentist, it is useful to use standardized medical letters containing both information about the patient's pathology, the treatment followed, and information about the patient's dental health. For this purpose, we have developed a model communication letter.

The patient needs to be aware of the importance of oral health in MRONJ prophylaxis, which is why we have developed a leaflet that can be given to patients when they start BMA treatment.

This informative material contains information about MRONJ, risk factors that can trigger this disease, and useful tips about lifestyle, nutrition, and the importance of oral health all of which can lead to a decrease in the incidence of MRONJ.

In the chapter on dentists, we explored how dental management can help prevent OM in high-risk patients. We found that a multidisciplinary and personalized approach that integrates dentistry into the overall care of patients can have a significant impact on reducing the risk of OM and improving the quality of life of these patients. However, to successfully implement such strategies, close collaboration between dentists, oncologists, and other health professionals is required.

Dentists are aware of some drugs, especially bisphosphonates, which can have negative effects on the oral cavity, but we have observed that they are guided by the anamnestic questionnaires used in dental practices. These questionnaires need to be rapidly improved as the number of molecules that have been correlated with the occurrence of MRONJ has increased and includes different classes of antiresorptive, antiangiogenic drugs such as tyrosine kinase inhibitors or monoclonal antibodies. Also, the indications for prescribing have become increasingly broad and thus more care needs to be taken in taking the history and identifying patients at risk of OM.

Given that prophylaxis is still the best way to slow the spread of this pathology, the dentist plays a very important role in the management of osteonecrosis.

Once patients at risk of osteonecrosis are identified, they should be included in a special monitoring program, regardless of whether they are edentulous or not. The file of these patients must also include a radiological investigation such as panoramic radiography, CBCT, CT, and MRI to be compared with subsequent investigations and thus to detect early signs of bone damage that could indicate the onset of MRONJ and thus to intervene quickly.

The dentist is responsible for primary prophylaxis, which includes all the dental maneuvers that could reduce the incidence of MRONJ, brushing, scaling, periodontal treatments that could reduce the bacterial load in the oral cavity, endodontic or dental treatments that could keep the teeth on the arch longer, prosthetic treatments that remove any source of irritation of the mucous membranes. The dentist is also responsible for secondary prophylaxis and must educate the patient on ways to maintain optimal oral health, to give up certain vices, thus reducing the incidence of MRONJ.

To avoid errors in dental treatments and to facilitate optimal therapeutic decisions we have developed an Android app that calculates the risk of MRONJ and based on this risk provides the dentist with treatment indications. The degree of risk is calculated according to a score obtained by gathering information related to the pathology for which the patient receives BMA, the dose of BMA, the type of BMA, and the period of BMA administration. It also includes additional points based on the presence or absence of dental and general risk factors.

The use of such modern tools can help the dentist better understand this pathology as well as its important role in MRONJ prophylaxis.

Also, once MRONJ is established, patients should be referred to centers specialized in the treatment of MRONJ under the recommendation of the latest treatment guidelines and protocols. In this regard, we have developed a therapeutic protocol for the OMF surgery clinic that includes therapeutic methods that can be applied to patients with MRONJ according to the latest staging and recommendations of international medical associations. Creating and following such international standardized protocols can help future researchers in data collection and thus future research methods can be described.