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DOCTORAL THESIS

CLINICAL AND THERAPEUTICAL ASPECTS IN MAXILLARY OSTEONECROSIS

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Introduction

Iatrogen-induced maxillary osteonecrosis is a clinical entity with an increasing frequency in clinical activity.

The evolution of these conditions is serious, with an unfavorable prognosis. The results obtained usually consist in the improvement of the symptomatology, temporary remissions, the cure being difficult to obtain. Due to the increased frequency, the complexity of the treatment, the cases of osteonecrosis are very time and resources consuming.

The definition of maxillary osteonecrosis has undergone changes in recent years, which has led to a significant variation in the number of cases and the incidence of the disease between various clinical studies published in the literature.

A significant change in the number of cases was recorded by increasing the frequency of osteonecrosis in patients who underwent osteoporosis treatment compared to patients receiving antiosteoclastic agents for the treatment of oncological conditions.

The treatment of osteonecrosis of the maxillary bones is also continually being improved, new treatment methods being recently introduced in medical practice. These new acquisitions have led to a lack of standardization of treatment, the lack of unanimously accepted protocols.

The purpose of the present research is to perform the analysis of the specific parameters of the epidemiology, diagnosis and treatment of bisphosphonate-induced jaw osteonecrosis related to the population in the Dobrogea area and to develop a therapeutic algorithm according to the evolutionary stage of the bisphosphonate-induced osteonecrosis..

General part

I. CURRENT STATUS OF KNOWLEDGE

The first reports on bisphosphonate-induced jaw osteonecrosis appeared in 2003, but similar cases of workers were observed in white phosphorus mines and match factories described as early as 1899.

Biphosphonates are widely used in diseases that develop with bone destruction through increased osteoclast-mediated resorption (osteoporosis, bone metastases secondary to neoplasms)..

II. CLINICAL THERAPY WITH PHOSPHONES

Bisphosphonates are a class of drugs with anti-osteoclastic effect used in the therapy of osteoporosis, bone metastases and bone diseases with tissue destruction (multiple myeloma, Paget's disease, etc.).

The first medical use was recorded in 1968, when sodium ethidronate was used in the treatment of a child with progressive ossifying myositis (progressive ossifying fibrodysplasia).

One of the most serious adverse effects of bisphosphonates is osteonecrosis of the maxilla, defined as an exposed area of the bone in the maxillofacial region that persists for at least 8 weeks..

III. ETIOPATHOGENY OF BISPHOSPHONATE INDUCED JAW OSTEONECROSIS

The etiopathogenesis of bisphosphonate-induced maxillary bone osteonecrosis is incompletely elucidated, with four theories regarding the prevalence of this condition; none of the theories can explain why the jaw tissue is the exclusive target of osteonecrosis.

The generally accepted theory regarding the etiopathogenesis of bisphosphonate-induced maxillary bone osteonecrosis argues as a cause for suppression of bisphosphonate-induced bone remodeling. The premises of this theory are represented

by: the high rate of bone remodeling of the bones of the jaw compared with other bones and the suppression of the bone remodeling by bisphosphonates.

IV. DIAGNOSIS OF MAXILLARY OSTEONECROSIS BOSPHOSPHONES INDUCED

Standardization of diagnostic criteria for bisphosphonate-induced maxillary bone necrosis is important in order to facilitate future clinical and epidemiological research.

The uniform definition of the necrosis of the maxillary bones induced by bisphosphonates serves to distinguish this clinical entity from other conditions underlying the delayed healing of various wounds in the oral cavity. The American Association of Oral and Maxillofacial Surgery (AAOMS) has established a working definition for bisphosphonate-induced maxillary bone necrosis, which is quite concise and specific.

The imaging diagnosis - OPG, CT, CB-CT, MRI - is a real help in diagnosing the disease and especially in making a treatment plan as efficient as possible. The information obtained is complementary, combining several imaging methods increasing the accuracy of the diagnosis.

V. TREATMENT OF OSTEONECROSIS OF MAXILARY INDUCED BY PHOSPHONATES

The treatment varies according to the stage of the disease, the prevention of the onset of osteonecrosis being of essential importance.

Management of the treatment of evolving osteonecrosis is still a topic under debate, without a unanimously accepted therapeutic protocol.

Improving symptomatology, pain and local infection is the most accessible objective, healing being a difficult task to achieve, especially in oncology patients.

Special part

I. ARGUMENT

At present, there is a significant increase in the percentage of osteonecrosis cases in non-oncological patients, especially in patients with osteoporosis and even osteopenia. This aspect is favored by the introduction into the clinical use of the increasingly powerful bisphosphonates, the decrease of the age from which they are administered and the inclusion in the category of prescribing doctors of several medical specialties, including family doctors. Given that patients with osteoporosis have a higher life expectancy than oncologic patients with metastases, a longer duration of administration results and, consequently, an increased risk of osteonecrosis of the maxilla.

II. OBJECTIVES

1. Primary

1. Identification of iatrogen-induced maxillary osteonecrosis cases in patients from Constanța county.
2. Development of a therapeutic algorithm specific for bisphosphonate-induced jaw osteonecrosis.

The treatment of osteonecrosis of the maxillary bones represents the work of a multidisciplinary team (oncologists, rheumatologists, surgeons of Oral and Maxillofacial Surgery or Oral Surgery, dentists, family doctors).

2. Secondary

1. Clinical evaluation of bisphosphonate-induced jaw osteonecrosis.
2. Analysis of the relationships between osteonecrosis of the jaws and bisphosphonate therapy.
3. Protecting the post-extraction cell with A-PRF and monitoring the post-operative evolution.

4. Application of different surgical treatment techniques in bisphosphonate-induced jaw osteonecrosis and evaluation of results.

III. MATERIAL AND METHOD

The studied group included 88 patients, of both sexes, who appeared in the Oral and Maxillofacial Surgery Department of the County Emergency Clinical Hospital „Sf. Apostol Andrei ”Constanta from January 2013 to December 2018 and who were diagnosed with osteonecrosis of the jaw in different stages.

IV. RESULTS

The distribution by sex of the studied group is as follows:

78.4% - female patients (highest share);

21.6% - male patients

Analyzing the age distribution of the patients participating in the study the highest weight - 42% was recorded in 37 cases (42%) corresponding to the age group of 60-69 years, at the opposite pole, the fewest cases, respectively 2 (2.3%) were related to the age group over 80 years.

DISCUSSIONS

In recent years, the incidence of iatrogen-induced maxillary osteonecrosis has seen a steep increase, especially due to the number of new cases treated for osteoporosis and even osteopenia.

Establishing a stable definition, taking into account clinical but also imaging criteria, will lead to comparable studies and a more accurate assessment of the incidence of this condition.

The multitude of new therapeutic options requires further studies to organize, systematize and verify a current therapeutic algorithm..

Evaluation of the efficiency of alveolar bone protection with A-PRF

In the study performed, the evaluation of the efficiency of the protection of the alveolar bone with A-PRF was performed in a group of 34 patients diagnosed with osteonecrosis in stage 0. Following the data collection, the comparison between the two groups in terms of healing and presence was performed. of postextraction complications, observing the decrease of complications in the group of patients to whom A-PRF was applied compared to the percentage registered in the group in which no A-PRF was used.

Value of surgical treatment in bisphosphonate-induced maxillary osteonecrosis

The disease evolved favorably in 21 cases, with the reduction of the symptoms and the passage to a lower and unfavorable evolutionary stage in 5 cases, in which the disease progressed, with the increase of the osteonecrosis surfaces and their denudation, and in 11.54% after performing radical resections with reconstruction evolution was unfavorable.

CONCLUSIONS

Osteonecrosis of the maxillary bones is a serious, debilitating condition with a significant negative effect on quality of life.

Facial skin fistulas, marked facial asymmetries, unpleasant odor due to recurrent suppurations affect the patient's social life with a psychic already weakened by a serious diagnosis, by the side effects of chemotherapy and radiotherapy.

Improving the quality of life is an essential goal in patients with bifosonate-induced maxillary osteonecrosis, and healing is difficult to achieve.

Prevention of osteonecrosis of the bisphosphonate-induced maxillary bones is the essential element for improving the quality of life of patients undergoing bisphosphonate treatment.

The management of patients receiving bisphosphonate treatment must be performed by a multidisciplinary team (oncologists, rheumatologists, oral and maxillofacial surgeons), as well as oral health assessment, treatment of all infectious and irritant outbreaks before the initiation of most anti-osseous treatments.

Discontinuation of bisphosphonate treatment prior to surgery was not an effective solution in preventing the onset of osteonecrosis, according to our experience; the discontinuation of bisphosphonate therapy led in all cases to the extension of the metastases, with accompanying clinical manifestations and to high intensity bone pain.

The study shows that, in more than half of cases, osteonecrosis of the jaw has occurred after a period of administration of bisphosphonates greater than three years.

Osteonecrosis of the jaw is more common in women (78.40%), both due to the prevalence of osteoporosis and bone metastases after breast cancer.

The most common condition in our study for which bisphosphonates were administered was breast cancer with bone metastases 34.01%, followed by osteoporosis 31.81%, and in men, bone metastases after prostate cancer 14 77%.

As a condition associated with osteonecrosis, in our group, the major prevalence was 31% hypertension, followed by diabetes in 14.8% of cases.

Depending on the location of the osteonecrosis lesions, 65.91% were found in the mandible, 25% in the maxilla and 9.09% in both jaws, the unique lesions accounting for 77.3% of the cases.

The use of A-PRF and local flaps, although the toxic effect of bisphosphonates also manifests on the gingiva-mucosa with direct implications on wound healing, increases the chances of primary wound healing after surgery on the maxillary bones.

Fluorescence marking of the maxillary bones is a real help in establishing the limits of osteotomy, but the surgeon's experience is essential to achieve a unitary integration of the imaging information with the intraoperative aspect in natural and ultraviolet light.

The surgical treatment is indispensable in the advanced phases, the fractures on the pathological bone, the appearance of massive convulsions of the maxillary bones with oro-antral and oro-nasal communications being a common evolution.

Following the evaluation of the postoperative evolution, we found that, in 11.54% of cases, the evolution was unfavorable after performing radical reconstructions with reconstruction, and in the case of limited sequestrectomy, the evolution was favorable in most cases, as in the case of radical convulsions. In the situation of radical resections with reconstruction, in 15.38% of cases the evolution was favorable; the five cases of unfavorable evolution were completely correlated with the existence of associated risk factors (smoking).

The study shows that in 4 patients (4.54%) we observed the appearance of periosteal neoosteogenesis confirmed, in addition to the clinical aspect, by CT examinations.

As a perspective, we believe that further studies are needed to determine the factors that induce this particular (favorable) evolution in such a small percentage of the patients studied.

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