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REVIEW ARTICLE

MEDICATION-RELATED OSTEONECROSIS OF THE JAW (MRONJ): CURRENT EVIDENCE ON ETIOLOGY, PATHOGENESIS, DIAGNOSIS, AND MANAGEMENT:A SCOPING REVIEW

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Abstract

Background: Medication-related osteonecrosis of the jaw (MRONJ) is a serious adverse effect associated with antiresorptive and antiangiogenic medications. Its biological mechanisms and optimal therapeutic strategies remain incompletely defined.

Objective: To synthesize current evidence regarding etiology, pathogenesis, diagnosis, risk factors, and management of MRONJ.

Methods: Following PRISMA guidelines, a search carried out in the following databases: PubMed, PMC, ScienceDirect, and Scopus using the Medical Subject Heading (MeSH). Search terms: Bisphosphonat, complication of antiresorptive therapy, osteonecrosis of the jaw, etiopathogenetic, clinical and diagnostic features.
156 articles full-text articles of high methodological quality were selected written in English. According to the review method used, the PRISMA.A structured literature review identified 80 eligible studies for qualitative synthesis. Peer-reviewed English-language articles addressing clinical and biological aspects of MRONJ were screened and qualitatively analyzed. Current evidence supports stage-adapted management ranging from conservative antimicrobial protocols to surgical resection in advanced disease. Despite progress in mechanistic understanding, uniform evidence-based treatment algorithms remain insufficiently established.

Results: MRONJ is multifactorial, involving suppressed bone remodeling, vascular compromise, microbial colonization, and immune dysregulation. Diagnosis remains primarily clinical. Conservative therapy is effective in early stages, while surgical intervention is indicated in advanced disease. Adjunctive regenerative approaches show promising but limited evidence.

Conclusions: MRONJ remains a complex clinical entity requiring interdisciplinary management. Further high-quality prospective studies are needed to establish standardized treatment protocols.

Keywords: Medication-related osteonecrosis of the jaw; MRONJ; bisphosphonates; antiresorptive therapy; osteonecrosis; oral surgery.

1. INTRODUCTION

Medication-related osteonecrosis of the jaw (MRONJ) is a severe complication associated with antiresorptive and antiangiogenic therapies, particularly bisphosphonates and denosumab. Since its first description in 2003, MRONJ has emerged as a significant interdisciplinary challenge involving dentistry, oncology, endocrinology, and maxillofacial surgery. The condition is characterized by persistent exposed necrotic bone in the maxillofacial region in patients without prior craniofacial radiation. Although its incidence remains relatively low in osteoporosis patients receiving oral bisphosphonates, it is considerably higher in oncologic populations treated with high-dose intravenous formulations. Osteonecrosis

of the jaw (ONJ) was first formally defined by the American Society for Bone and Mineral Research as exposed maxillofacial bone persisting for more than eight weeks in patients treated with bisphosphonates and without history of craniofacial radiotherapy[1].

Over time, the terminology evolved. Leading professional organizations including the American Association of Oral and Maxillofacial Surgeons (AAOMS), the Multinational Association for Supportive Care in Cancer (MASCC), the International Society of Oral Oncology (ISOO), and the American Society of Clinical Oncology (ASCO) adopted the broader term medication-related osteonecrosis of the jaw (MRONJ) to reflect cases associated not only with bisphosphonates but also with denosumab and antiangiogenic agents[2,3].

The introduction of potent aminobisphosphonates revolutionized the management of metastatic bone disease and osteoporosis; however, the emergence of jaw osteonecrosis as a treatment-related complication has substantially altered clinical practice. Bisphosphonate-associated osteonecrosis of the jaw (BRONJ), was originally described as a side effect of aminobisphosphonates by Marx in 2003[4].

The underlying pathophysiology of bisphosphonate-induced osteonecrosis remains poorly understood.

The article presents a review of the literature on the current state of the problem of BORNJ of the jaws incidence, risk factors, staging, clinical course, prevention strategies, and management.

The purpose of the study was to analyze the modern data BORNJ on the etiology pathogenesis and diagnosis and treatment.

2. MATERIALS AND METHODS

Comprehensive Search Strategy

A comprehensive electronic literature search was performed in the following databases: Google Scholar, Medline, Scopus, Web Of Sciences, and PubMed.

Search terms*:* Bisphosphonat, complication of antiresorptive therapy, osteonecrosis of the jaw, etiopathogenetic, clinical and diagnostic features. The review was conducted according to the PRISMA guidelines (PRISMA flow chart is presented in figure1.) using PICO to formulate the study objective.

Inclusion criteria: included clinical trials, considered randomized controlled trials, cross-sectional studies, case-control studies, and cohort studies in human subjects that evaluated the current literature on the Bisphosphonat, complication of antiresorptive therapy, Bisphosphonate-associated osteonecrosis of the jaw, written in English articles.There was no limitation on minimal quality, minimal sample size, or the number of patients.

Exclusion criteria:original primary studies, due to language limitations, abstracts, letters to the editor, book chapters, case reports, conference abstracts, duplicate publications, and in vitro and in vivo animal experimental studies.

Study selection

2 independent reviewers screened titles and abstracts each study to determine eligibility following the predetermined inclusion and exclusion criteria. Potentially eligible studies underwent a full-text review, and discrepancies between reviewers were resolved through discussion Reviewers identify and document the threats to validity of each study due to faulty execution or poor measurement. This information is used as a criterion for continued inclusion of the study in the body of evidence for an intervention.

Data extraction

2 reviewers extracted data from the included studies using a standardized data extraction form. Reviewers identify and document the threats to validity of each study due to faulty execution or poor measurement. Discrepancies in data extraction were resolved by discussion.

Data synthesis

The results of this review were reported following the PRISMA guidelines. A narrative synthesis of the findings was provided.

Risk of bias in included studies

In developing the data collection instrument, we considered. The form collects information needed to monitor the status of screening, reviewing and summarizing of each article by 2 reviewers. Developing that summarize the body of evidence. The form captures detailed descriptive data about the intervention and evaluation.

Classifying other key characteristics of the intervention and assessing the quality of the study's execution. Reviewers identify and document the threats to validity of each study due to faulty execution or poor measurement. This information is used as a criterion for continued inclusion of the study in the body of evidence for an intervention.

Following the study design, has identification domains rating the certainty of evidence: risk of bias, inconsistency, inconsistency, imprecision, and publication bias.

Effect measures

The analysis of currently known data on bisphosphonate osteonecrosis of the jaws presented in the article should attract the attention of dental surgeons, maxillofacial surgeons, endocrinologists, and oncologists to this problem.

3. RESULTS

156 articles full-text articles of high methodological quality were selected written in English. After analyzing the text results by two independent authors, the results

selected and corresponding to the review criteria were 80. According to the review method used, the PRISMA flow chart is presented (fig.1).

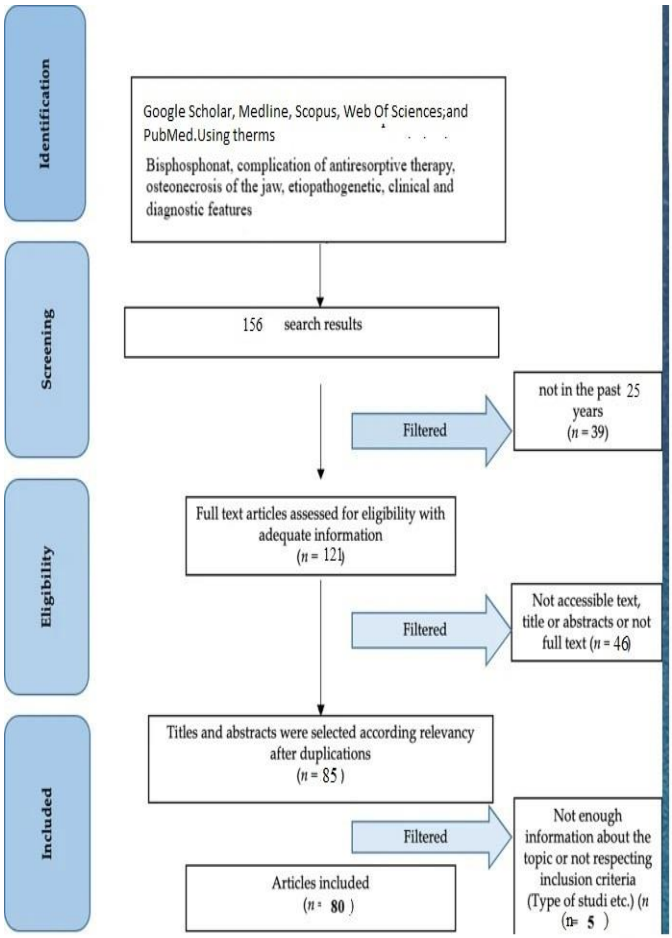

Fig.1 PRISMA flow chart is presented

3.1. Epidemiology and Clinical Distribution

The incidence of MRONJ varies according to indication and route of drug administration.

- In oncology patients receiving high-dose intravenous bisphosphonates, prevalence ranges between 1% and 10%[5].
- In individuals treated with oral bisphosphonates for osteoporosis, annual risk is extremely low (approximately 0.0004–0.04%).
- The mandible accounts for nearly two-thirds of cases, the maxilla approximately one-quarter, while combined involvement is less common.
- Clinical manifestation typically occurs between 6 and 60 months after therapy initiation.

This discrepancy in incidence is likely related to cumulative drug dose, potency, duration of therapy, and underlying systemic disease

3.2 Risk Factors

MRONJ development is multifactorial and influenced by both local and systemic determinants[6].

3.2.1 Local Risk Factors

- Tooth extraction
- Dental implant placement
- Periodontal disease
- Ill-fitting dentures
- Mandibular exostoses
- Chronic mucosal trauma

Approximately 60% of cases follow invasive dental procedures.

3.2.2 Systemic Risk Factors

- High cumulative antiresorptive dose
- Intravenous administration
- Advanced malignancy
- Diabetes mellitus
- Corticosteroid therapy
- Immunosuppression
- Advanced age
- Tobacco and alcohol use

The interaction between impaired bone remodeling and microbial contamination appears central to disease initiation.

4. Pathophysiological Mechanisms

The pathogenesis of MRONJ remains incompletely elucidated and is likely multifactorial, involves suppression of bone remodeling, impaired angiogenesis, immune dysregulation, and microbial colonization. Antiresorptive agents suppress osteoclast-mediated bone turnover, leading to accumulation of microstructural damage. Concurrent inhibition of angiogenesis and altered inflammatory signaling further compromises tissue viability. Bacterial biofilms may exacerbate local necrosis through persistent inflammatory stimulation.

BORNJ is characterized by unique etiopathogenetic, clinical and diagnostic features that distinguish it from other inflammatory, dystrophic diseases of the orofacial region[7-9].

Bisphosphonates inhibit endothelial proliferation, interrupt intraosseous circulation, and bone blood flow, promoting osteonecrosis. It is unclear whether patients receiving intravenous bisphosphonates are at greater risk than those receiving oral bisphosphonates[10].
The negative effects of bisphosphonates on bone

physiology are concentrated on impaired osteoclast function and are also associated with depressed bone blood flow, and bisphosphonates exhibit antiangiogenic properties and have the ability to inhibit endothelial cell function[11].

Most authors agree that the trigger for the process is also infection of the bone by oral microflora with the slightest trauma. Most often, bisphosphonate radionecrosis occurs during tooth extraction and oral surgery, damage to the mucous membrane by irrationally made removable dentures and artificial crowns, and exposure of bone as a result of periodontal disease[12].

It also remains unclear whether bisphosphonates have affinity for the jaws. It is believed that bones are subject to constant trauma (for example, invasive dental procedures in the jaws), while their regeneration is slow, all this can lead to necrosis[13].

Spontaneous ONJ is possible, trigger events are tooth extraction or other surgical interventions in the oral cavity in 61.5% of cases. Bisphosphonates (BP) are a class of drugs that prevent bone loss and are used in oncology to treat bone metastases, myeloma, and secondary hypercalcemia in patients with malignant neoplasms. They are also used in osteoporosis, Paget's disease, pediatric osteogenesis imperfecta, and other diseases that cause bone fragility[14].

Given the prevalence of these diseases, bisphosphonates are among the most prescribed drugs in the world, especially in patients with a high incidence of cancer and frequent bone metastases. Bisphosphonates are resistant to enzymatic degradation, so high concentrations of them remain in the bone for a long time. The addition of an amine radical increases the activity of bisphosphonate drugs. Only with the use of a newer generation of bisphosphonate drugs - aminobenzophosphonates (alendronate, ibandronate, risedronate, pamidronate, zoledronate) have side effects such as osteonecrosis of the jaws been described[15].

4.1 Suppression of Bone Remodeling

Bisphosphonates bind to hydroxyapatite and accumulate in bone. Nitrogen-containing bisphosphonates inhibit farnesyl pyrophosphate synthase within the mevalonate pathway, leading to osteoclast apoptosis and profound suppression of bone turnover.

4.2 Impaired Angiogenesis

Antiresorptive and antiangiogenic agents inhibit endothelial cell proliferation and reduce intraosseous blood flow, predisposing bone to ischemia.

4.3 Immune and Inflammatory Mechanisms

Altered neutrophil and macrophage activity, dysregulated cytokine release, and persistent infection contribute to chronic inflammation and delayed healing.

4.4 Microbial Colonization

Oral microbiota invade exposed bone following mucosal disruption. Secondary infection accelerates necrosis progression. The combination of suppressed remodeling, vascular compromise, and microbial contamination explains the jaw predilection, given its high turnover rate and frequent exposure to trauma.

BP are potent inhibitors of bone resorption, pyrophosphate analogs that differ from it by a central carbon atom instead of an oxygen atom (P-C-P- instead of P-O-P-bond)[16].

Types of BP:

1) unsubstituted BP (clodronic acid, sodium etidronate, disodium tiludronate);

2) aminobisphosphonates:

2.1) with one nitrogen atom (pamidronic acid, alendronic acid, ibandronic acid);

2.2) with nitrogen-containing basic heterocyclic compounds (risedronic acid, zoledronic acid).

Attempts to influence osteoclasts in order to prevent their activation, maturation and recruitment of their precursors have become the main direction of research in the treatment of bone metastases.

Among the drugs that inhibit osteoclast activity (calcitonin, gallium nitrate, bisphosphonates), bisphosphonates (BP) have proven to be the most active[17-19].

According to the 2011 ASCO recommendations, bisphosphonate therapy is indicated for patients with proven bone metastases [20,21].

Bisphosphonates are potent inhibitors of bone resorption, pyrophosphate analogs that differ from it by a central carbon atom instead of an oxygen atom (P–C–P- instead of P–O–P-bond)[22].

Currently, BPs are one of the most widely used groups of drugs for the treatment of Paget disease, osteoporosis, breast cancer and neoplastic bone metastases, multiple myeloma, some other rare bone diseases, neurodegenerative diseases, and also in dentistry[23-29].

The mechanism of action of all BP is similar: penetration into bone tissue and interaction with hydroxyapatite crystals; concentration around osteoclasts, creation of a high concentration in resorption lacunae; disruption of the formation of the osteoclast cytoskeleton; reduction of secretion of lysosomal enzymes by osteoclasts; suppression of transmission of intercellular signals; inhibition of osteoclast migration and their resorptive capacity; inhibition of tumor cell adhesion. Thus, due to increased strength, the ability to regenerate decreases [30,31].

Bisphosphonate penetrate bone tissue, concentrate around osteoclasts, creating a high concentration in the

resorption lacunae, and bind to the mineral matrix of the bone[32].

The migration of osteoclasts slows down, and their resorption capacity decreases. BPs also cause osteoclast apoptosis in the bone resorption zone[33].

A special group of patients who are indicated for antiresorptive therapy are cancer patients with identified bone metastases. Against the background of taking BF, the number of metastases decreases, bone strength increases, pain syndrome disappears, the risk of pathological fractures decreases, and the level of hypercalcemia decreases [34,35].

According to a number of authors, the pathogenesis of the disease is based on bisphosphonate suppression of osteoclast differentiation from monocytes, increased osteoclast apoptosis, stimulation of osteoclast-suppressing factor and decreased osteoclast activity, as well as the antiangiogenic properties of phosphorus [36].

As a result, deep suppression of bone metabolism occurs, which can lead to its necrosis and significantly, and sometimes irreversibly, reduces the chances of recovery. Thus, due to increased strength, the bone loses its ability to regenerate.

Currently, the most common classification of, Bisphosphonate-related osteonecrosis is the one proposed by the American Association of Oral and Maxillofacial Surgeons (2009) [37].

5.Clinical Presentation and Staging

AAOMS staging remains the most widely used classification.

- **Stage0:**Non-specific symptoms without exposed bone
- **Stage I:** Exposed necrotic bone, asymptomatic
- **Stage II:** Exposed bone with pain and infection
- **Stage III:** Extensive necrosis with pathologic fracture, fistula, or oroantral communication

The hallmark clinical feature is persistent non-healing exposed bone, often yellowish to dark brown.

In describing the typical picture of bisphosphonate-related osteonecrosis the authors agree that most often the only reliable clinical sign is the presence of non-healing necrosis of the mucous membrane in the mouth with an area of exposed bone from yellowish or greenish to dark brown. The lower jaw is affected more often than the upper, and combined damage to the jaws is even less common.

In some patients, the process of osteonecrosis occurs with a pronounced inflammatory reaction, accompanied by abscess formation and the formation of intra- and extraoral fistulas, while in others, complaints are limited to a section of exposed bone in the mouth and the impossibility of prosthetics for this reason[38].

A special category consists of patients in whom the inflammatory processes complicating osteonecrosis take a sluggish form with frequent exacerbations that do not tend to lastingly heal.

6. Diagnostic Evaluation

Diagnosis is primarily clinical and requires:

1. Current or prior antiresorptive or antiangiogenic therapy
2. Exposed bone persisting longer than eight weeks
3. No history of radiation therapy to the jaws

Although it is necessary to exclude other processes such as neoplastic bone infiltration and osteomyelitis, bone biopsy is not usually performed because it may further damage and progression of BORNJ. The appearance of BORNJ on radiography, CT, and MRI is not specific. Imaging may play a role in determining the severity of the disease, is relevant in the early diagnosis of BORNJ, in the differential diagnosis between jaw metastases and, and in excluding other jaw diseases, and may also play a role in the diagnosis of jaw fractures.

The American Association of Oral and Maxillofacial Surgeons has stated that for a clinical diagnosis bisphosphonate-related osteonecrosis to be made, patients must meet three criteria[39,40]:

- current or previous treatment with bisphosphonates;
- exposed, necrotic bone in the maxillofacial region that persists for more than 8 weeks;
- there is no history of radiation therapy.

6.1 Radiographic appearance

Radiographic findings are variable and non-specific:

- Sclerosis of lamina dura
- Osteolysis
- Sequestration
- Periosteal reaction
- Pathological fracture

Cone beam CT is particularly valuable for assessing cortical involvement and sequestra. MRI may assist in evaluating soft tissue inflammation.

Radiographic features along the alveolar bone may include widening of the periodontal ligament space and sclerosis of the lamina dura.

Altered bone morphology, periosteal bone formation, increased bone density, or sequestration may be radiographic features of BRONJ.

Cone beam CT reveals osteosclerotic and osteolytic areas and can also evaluate sequestration, periosteal reaction, and integrity of vital adjacent structures, potential sinus tract, cortical erosion, and incomplete healing of the extraction socket.

To define stage characteristics and guide treatment, Ruggiero et al (2014)developed and adopted the American Association of Oral and Maxillofacial Surgeons (AAOMS) Staging System[37].

Although radiographic findings bisphosphonate-related osteonecrosis are not part of the diagnostic criteria, they provide valuable information to the clinician[41].

Radiographic findings BORNJ of the jaw are not specific and can be found in other conditions such as osteomyelitis, osteoradionecrosis, and cancer metastasis[42.]

CT is very useful in being able to visualize and characterize the bisphosphonate-related osteonecrosis, in detecting cortical involvement, while MRI should be reserved for patients who have lesions with soft tissue swelling, since soft tissue changes are better detected on X-ray, CT MRI: osteolysis, sclerotic lesions, periosteal reaction, decreased marrow space volume, mandibular canal involvement, fractures, sequestrum formation[43,44].

A large variability of radiographic signs of jaw damage is noted: large extent, no clear boundaries of destruction zones, multifocality with different localization, alternation of zones of osteosclerosis and osteoporosis ("soap suds"), absence of a demarcation line along the edges of the process, presence of radiographic pathological fracture of the jaw, involvement of the walls of the maxillary sinuses, tubercles of the upper jaw, pterygopalatine processes of the sphenoid bone, sequestration [45].

There is no doubt about the need to use high-tech examination methods with minimal radiation exposure in these patients - magnetic resonance imaging, cone beam computed tomography and ultrasound examination.

The histopathologic appearance of BORNJ is variable. Specimens obtained from areas of destroyed bone are characterized by extensive necrosis[46].

In the description of the histological picture of the surgical material obtained for BORNJ, there is a description of both aseptic necrosis and necrosis with a pronounced inflammatory nature of changes in the jaw tissues due to infiltration by lymphocytes and granulocytes. Typical histological results are a picture of non-viable bone with surrounding bacterial colonies and an inflammatory cellular infiltrate[47].

Specimens from areas adjacent to BORNJ sites are characterized by hypervascular fibrous tissue and inflammatory infiltration filling large intertrabecular spaces, making the picture similar to chronic osteomyelitis[48,49].

6.2 Blood Test

Markers determined in the patient's fasting blood serum are predominantly specific and accurate. Osteocalcin, amino-terminal propeptide of type I procollagen, bone-specific alkaline phosphatase are among the most accessible and widespread indicators of bone formation, and C-terminal telopeptide - in CrossLaps (CTX) and tartrate-resistant acid phosphatase - markers of bone resorption[50].

C-terminal telopeptide (CTX) levels are associated with the number of osteonecrotic lesions, stage of disease, and bone turnover index.

C-terminal telopeptide (CTX) levels represent an octapeptide fragment released by osteoclastic bone resorption from bone collagen type I.

C-terminal telopeptide less than 100 pg/mL indicates high risk, 100 to 150 pg/mL indicates moderate risk, and greater than 150 pg/mL indicates minimal or no risk.

Bone biomarkers have been suggested for the risk assessment for osteonecrosis of the jaw, a serious complication associated with BORNJ use; however, no consensus has been reached[51].

Non-invasive biochemical methods for diagnosing and monitoring bisphosphonate-induced osteonecrosis of the jaw on determining the ratio and intensity of bone tissue formation and destruction processes have recently become popular due to their simplicity and availability.

6.3 Histopathology

Histological examination typically demonstrates necrotic bone devoid of osteocytes, bacterial colonies, and surrounding inflammatory infiltrate.

7.Treatment methods BORNJ

The goal of treatment is to relieve pain, control infection, and stabilize the progression of exposed bone. Treatment plan is based on the stage of the disease, the size of the lesion, comorbidities, and is dependent on age, gender, and medications.

BRONJ is a multifactorial disease and it is therefore difficult to develop an aetiological therapy.

The management of bisphosphonate-related osteonecrosis of the jaw is multi-level and includes dental assessment prior to the initiation of intravenous bisphosphonates, increasing patient education, and maintaining good oral hygiene[52,53].

There is currently no single approach to the treatment of choice for stage I BRONJ, and no effective unique therapy has yet been developed. Currently two main approaches to the treatment of bisphosphonate-related osteonecrosis of the jaw (BRONJ) can be distinguished: conservative and surgical[54,55.]

Therapeutic Strategies

Management is stage-dependent and aims to:

- Control pain

- Reduce infection
- Prevent disease progression

7.1 Conservative Management

- Antimicrobial mouth rinses
- Systemic antibiotics
- Analgesics
- Strict oral hygiene

Adjunctive therapies include:

- Teriparatide (limited duration use)
- Pentoxifylline and tocopherol
- Hyperbaric oxygen therapy
- Ozone therapy
- Low-level laser therapy

Laser debridement using Er:YAG systems has demonstrated promising results in early stages due to bactericidal and biostimulatory effects.

Could a long break from taking medications be the cause of the Osteonecrosis site condition or could it improve healing after surgical procedures? it is still unclear. Whether stopping bisphosphonate therapy can lead to recurrence of bone pain, progression of metastases or osteolytic lesions, or development of skeletal-related events (RSE)[56,57].

Most of the authors privilege a noninvasive approach especially for asymptomatic stages of BRONJ (stage I in Ruggiero'staging system)[37].

The main purposes of each treatment are to reduce pain and infection and slow the progression of the disease.

Conservative therapy primarily involves prescribing patients a course of antibacterial, symptomatic therapy, daily treatment of bone lesions with antiseptic solutions, as well as careful oral hygiene. Treatment of established BORNJ includes oral antimicrobial rinses and systemic antibacterial therapy[58-60].

The effective use of teriparatide (the N-terminal 34 amino acids of recombinant human parathyroid hormone) is a compound that increases bone density by stimulating osteoblastic bone formation and bone remodeling [61,62].

However, treatment with such a drug should be limited to 2 years, since preclinical studies have shown an increased risk of osteosarcoma with long-term exposure[63].

A study has shown the effectiveness of Pentoxifylline and α-tocopherol in addition to antimicrobial therapy, which caused a 74% reduction in bone exposure and symptoms in patients with BRONJ, also in the early stages of the disease[64].

Ozone therapy, hyperbaric oxygen therapy, and Low-level laser therapy are generally recommended in addition to medical or surgical therapy: good clinical results.

Studies confirm that local OT and HBO can stimulate cell proliferation and soft tissue healing, reducing pain [65-67].

The role of hyperbaric oxygenation is unclear, and the need to discontinue bisphosphonate treatment in these patients is a matter of debate.

LLLT for the treatment of BRONJ improves the reparative process, increases the inorganic bone matrix and the mitotic index of osteoblasts, and stimulates the growth of lymphatic and blood capillaries[68-70].

The literature describes works on the use of bone marrow and stem cell transplantation into necrotic foci, the use of platelet-rich plasma the addition of tocopherol and pentoxifylline to the standard antibiotic therapy regimen as well as teriparatide - recombinant human parathyroid hormone in patients with bisphosphonate-induced osteonecrosis[71,72].

7.2 Surgical Treatment

Surgery is reserved for refractory or advanced stages:

- Sequestrectomy
- Debridement to bleeding bone
- Resection with flap reconstruction
- Tension-free mucosal closure

Radical surgery should be carefully balanced against systemic disease status.

Surgical treatment with platelet rich plasma has been used to manage medication-related osteonecrosis of the jaw, PRP failed to show any benefit in the prevention of osteoradionecrosis[73-75].

Non-invasive treatment is effective in the early stages, many authors have reported better results with surgical treatment than with medical treatment alone, and have suggested performing surgical procedures in cases that are not controlled by local or systemic therapy to limit the risk of progression to stage III[76].

Areas of bone necrosis that are the source of soft tissue inflammation should be eliminated within viable tissue, but more radical surgical treatment should be postponed. Surgical procedure begins after oral cavity ablation and antibacterial preparation. Surgical methods osteonecrosis of the jaw include curettage of sockets of extracted teeth, sequestrectomy, jaw resection, including palliative treatment - opening and drainage of purulent foci, immobilization in case of pathological fractures of the jaws. Operation is performed under general anesthesia. Radical resection of the affected area is performed to viable bone, free flap reconstruction and hermetic closure of the wound, leaving no sharp edges. Soft tissue closure is performed without tension and which can lead to rupture of the mucous membrane[77,78].

The latest recommendations are effective local

application of hyperbaric oxygen, low-level laser therapy to the affected area platelet-rich plasma.

For conservative surgery, the Erbium laser can be used, which penetrates hard tissue by 0.1 mm. Gradual evaporation of necrotic bone can be performed until healthy bleeding bone is visible. Additional benefits minimally invasive laser surgery are the bactericidal and biostimulating effects of the laser beam with better postoperative recovery[79].

The literature shows that the efficiency of laser surgery is very high compared to traditional surgery and allows for minimally invasive treatment of early stages of the disease. Less invasive surgery can determine complete healing of the mucosa containing microbial infection and the risk of disease dissemination[80].

In the prevention of this pathology, the main emphasis is on oral sanitation and an attempt to prevent the need for treatment and tooth extraction during subsequent BF intake.

There is much that remains unclear in the clinical, diagnostic and treatment issues of BORNJ and with the increase in cancer incidence, it can be argued that the number of patients with such a pathology will grow. At present, effective measures for the prevention and prognosis of the clinical course of BORNJ have not been developed. The regulatory framework and algorithm for joint patient management by doctors of various specialties have not been approved, and the continuity between oncologists, endocrinologists and dentists is very weak, resulting in a situation where the patient is faced with the fact of an already developed complication. No single effective treatment method has been approved, because much in the issues of the pathogenesis of osteonecrosis still remains unclear.

In general, despite the large number of reports on individual aspects of the pathogenesis, clinical picture, diagnostics, treatment and prevention of BORNJ and the enormous amount of research that has been done, this disease remains a pressing problem for scientists and clinicians today and requires further study.

The analysis of currently known data on bisphosphonate osteonecrosis of the jaws presented in the article should attract the attention of dental surgeons, maxillofacial surgeons, endocrinologists, and oncologists to this problem.

8. Prevention

Preventive measures are critical and include:

- Comprehensive dental examination before initiating antiresorptive therapy
- Completion of invasive dental treatment prior to therapy
- Regular dental follow-up
- Patient education regarding oral hygiene

Interdisciplinary coordination between oncologists, endocrinologists, and dental professionals remains essential.

In the prevention of this pathology, the main emphasis is on oral sanitation and an attempt to prevent the need for treatment and tooth extraction during subsequent BF intake.

There is much that remains unclear in the clinical, diagnostic and treatment issues of BORNJ and with the increase in cancer incidence, it can be argued that the number of patients with such a pathology will grow. At present, effective measures for the prevention and prognosis of the clinical course of BORNJ have not been developed. The regulatory framework and algorithm for joint patient management by doctors of various specialties have not been approved, and the continuity between oncologists, endocrinologists and dentists is very weak, resulting in a situation where the patient is faced with the fact of an already developed complication. No single effective treatment method has been approved, because much in the issues of the pathogenesis of osteonecrosis still remains unclear.

9.DISCUSSION

Despite two decades of research, MRONJ continues to pose diagnostic and therapeutic challenges. The absence of a universally effective treatment protocol reflects incomplete understanding of pathogenesis. The increasing global use of antiresorptive agents suggests that MRONJ prevalence will rise.

Early detection, risk stratification, and minimally invasive intervention remain the cornerstone of management. Emerging regenerative approaches and biologic adjuncts require further high-quality randomized clinical trials. In general, despite the large number of reports on individual aspects of the pathogenesis, clinical picture, diagnostics, treatment and prevention of BORNJ and the enormous amount of research that has been done, this disease remains a pressing problem for scientists and clinicians today and requires further study.

The analysis of currently known data on bisphosphonate osteonecrosis of the jaws presented in the article should attract the attention of dental surgeons, maxillofacial surgeons, endocrinologists, and oncologists to this problem.

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Competing interests

The authors have no competing interests to declare.

Ethical Approval

The study was approved by the appropriate ethics committee and conducted according to relevant guidelines and regulations.

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