

Guidelines for treatment of bisphosphonate-induced avascular osteonecrosis of the jaws: A comparative literature review and 2 case reports

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Abstract

Bisphosphonates are synthetic non-metabolized analogues of the naturally occurring inorganic pyrophosphate^{1, 2} and have an elevated affinity for bone due to their R1-side chain. Despite the benefits related to the use of these medications, osteonecrosis of the jaws is a devastating complication in a subset of patients receiving these chemical drugs. Recommendations for dental management of patients undergoing bisphosphonate treatment have been developed but until today no specific guidelines exist for the management of patients taking oral and intravenous bisphosphonates.

The purpose of this article is to assess and review the available data on treatment of osteonecrosis of the jaw (ONJ), with analyzing the concept of this pathological phenomena, and proposing some new recommendations established by the Italian Society for the Study of Bisphosphonate in Oral Surgery (SISBO) that showed as follows in the two clinical cases a total healing of bisphosphonate-induced osteonecrosis of the jaw.

Key words: Bisphosphonate, affinity for bone, jaw, osteonecrosis, treatment.

Bisphosphonates are synthetic compounds with chemical structure similar to that of inorganic pyrophosphate, an endogenous regulator of bone mineralization,¹ used for the treatment of hypercalcemia in patients with bone metastasis or other disorders such as metabolic bone diseases, Paget's disease,² and have shown to alleviate many consequences associated with osteoporosis, but still are the main cause of

osteonecrosis of the jaw.

We can distinguish three generations of bisphosphonate. The first is formed of the non-aminobisphosphonate (Etidronate, Clodronate), the second correspond to the aminobisphosphonates (Pamidronate, Alendronate) that are 100 to 500 times more powerful, and the third generation (Ibandronate, Risedronate and Zoledronate) that is 10 to 20 times more powerful than the previous generations in terms of reducing skeletal-related events (SRE; defined as pathological fracture, surgery to bone and hypercalcemia).³

The addition of nitrogen increases the potency of bisphosphonates in inhibiting bone resorption than non-aminobisphosphonates.⁴

In recent years, many cases of osteonecrosis have been reported involving both oral and intravenous therapy regimens.⁵

Marx in 2003⁶ described the first case of osteonecrosis of the jaw associated with bisphosphonate therapy; since then the number of cases reported is increasing and has become a "growing epidemic.

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The expert panel recommendations should always be incorporated into clinical decision-making when facing a patient undergoing bisphosphonate treatment.

The purpose of this article is to comparatively analyse some guidelines published on the treatment of osteochemonecrosis of the jaw and to expose two clinical cases that showed a complete healing of exposed bone and a symptoms relieve, following the use of SISBO recommendations.

What is bisphosphonate-induced osteochemonecrosis of the jaws?

Osteochemonecrosis is considered as a complication showing in general terms bone exposure with an uncertain prognosis and low healing rates.

Osteochemonecrosis of the jaw also called bisphosphonate-associated osteonecrosis^{7, 8} is defined as an area of exposed bone that persists for more than eight weeks in patients undergoing or underwent bisphosphonates treatment.

ONJ can be defined according to 5 criteria:

1. Patients previously or currently treated with bisphosphonates
2. Soft tissue lesion exposing the underlying bone
3. Persistence of exposed gray-yellowish bone for more than eight weeks
4. Absence of antecedent of radiotherapy in the maxilla and mandible
5. Absence of metastatic zone in the region of osteochemonecrosis

The American Association of Oral and maxillofacial surgeons taskforce definition of ONJ is as follows: "the presence of nonhealing exposed bone in the maxilla or mandible that has persisted for more than 8 weeks in a patient who has received a systemic bisphosphonate but has not received local radiation therapy".⁸

These definitions may be correlated to many hypothesis (Table I, II).

Garcia Saenz and Taruella defined ONJ as the presence of pain, halitosis, soft-tissue swelling, gingival bleeding and infection, with or without dysesthesia of the jaw.²¹

Today a clear definition is still lacking and needs to be established.

Mechanism of action of amino- and non-amino-bisphosphonate and their effect on the biological environment of the jaw

Osteochemonecrosis of jawbones represents the main undesirable effect of treatment by nitrogen-containing

Table I: Complication of ONJ:

The most noticed complications of ONJ are:
- Aggressive evolution
- Geant sequestrum
- Bucco-nasal and cutaneous fistula
- Pathological fracture
- No concordance between mucosal evolution and bone evolution

Table II: Hypothesis concerning ethiopathology of ONJ:

- Hypothesis of hypocellularity and hypovascularization
- Infection hypothesis(Actinomyces)
- Cytotoxicity hypothesis(Toxicity to keratinocytes of the oral mucosa)

Table III: Biological effect of Bisphosphonates:

- Inhibition of soft tissue calcification
- Inhibition of bone resorption and therefore reduction in bone remodeling
- Anti-inflammatory reaction
- Anti-tumor effect
- Anti-angiogenic effect (zoledronic acid+++)

bisphosphonates, where types used for the treatment of cancer still have to be distinguish from those used for the treatment of osteoporosis.

In cases of osteoporosis, Paget's disease or cancer, bisphosphonates have, since the beginning of prescription, demonstrated many biological effects that, while solving a problem on one hand, will induce osteochemonecrosis of the jaw on the other (Table III).

The mechanism by which bisphosphonates inhibit osteoclast action appears to differ between amino- and non-aminobisphosphonates.

Aminobisphosphonates such as: Zoledronate, ibandronate, risedronate, alendronate and pamidronate, showed to inhibit the Mevalonate pathway by inhibiting the farnesyl-pyrophosphate synthase (acts in synthesizing cholesterol) which will cause apoptosis of osteoclasts (by affecting the biochemical function and morphology of the cell) and reduction in bone remodeling, while the

non-aminobisphosphonate such as: Etidronate, Clodronate and Tiludronate, which are non hydrolysable analogues of adenosine triphosphate (ATP), will lead to a lack of ATP inside the osteoclastic cell, causing immediate death of the cell. Bisphosphonates are known to inhibit differentiation of bone marrow precursors into osteoclast, inhibit osteoclast associated to an antiangiogenic effect and increase bone mass by inhibiting the resorption.²³

The importance of elucidating the mechanism of action of this complication is to establish a protocol for preventing it.

Sites of predilection of osteochemonecrosis of the jaw

Bone turnover in the mandible is ten times more critical than in the tibia region.¹⁷

The rate of alveolar bone turnover at the crest is twice the rate around mandibular canal and five times that of the inferior border of the mandible, which explains why the alveolar bone is the most predictable site for the development of ONJ.¹⁷

In cases of spontaneous exposed bone, the most common site involved appears to be the posterior lingual part of the mandible over the mylohyoid ridge area.²³

A study conducted by Senel and Duman demonstrated that inflammation of soft tissue and periapical trabecular bone in the posterior mandible is considered the region of predilection for the development of ONJ in patients undergoing zoledronic acid treatment compared to anterior mandible.²⁷

The maxilla and mandible are considered the region of predilection of ONJ due to the oral cavity environment⁹ and present the highest rate of bone remodeling.

Osteochemonecrosis of the jaw - provoked or spontaneous phenomena

The majority of reported cases of bisphosphonate-induced osteochemonecrosis of the jaw have been diagnosed after dental procedures such as tooth extraction.⁹

Some theories noted that bone osteonecrosis correlated to bisphosphonate treatment is silently in evolution and that the act of extraction will reveal it clinically.

In 2006 the American association of periodontology¹⁶ (AAP), alerted the risk of developing osteochemonecrosis associated to bisphosphonates: "The Food and Drug Administration (FDA) reclaimed a case of so-called osteonecrosis of the jaw". After the reclamation the number of cases began to increase, particularly in patients treated with intravenous bisphosphonates and who had undergone dental surgery and implant placement.

Herbozo in 2007 showed cases of severe spontaneous bone exposures related to bisphosphonates that were

correlated to a decrease in serum VEGF (vascular endothelial growth factor) levels up to 21 days after infusion.³²

Osteochemonecrosis may occur spontaneously in patients undergoing bisphosphonate treatment,⁹ but is more commonly associated with dental surgery.

Oral v/s intravenous bisphosphonates

Risks associated with intravenous therapy appear to be substantially higher than for the oral medications.⁵

The correlation between bisphosphonate and evolution of ONJ is resumed as: absence of healing of soft tissue in patients undergoing zoledronic acid treatment.

A study for Merigo and Manfredi¹⁵ described the necessity of interruption and replacing intravenous bisphosphonate by non-aminobisphosphonate such as Clodronate. While Marx in 2007¹⁰ described a study on 17 patients with ONJ where the interruption of Oral bisphosphonate with medical treatment and CTX testing proved to lead to total healing with augmentation of CTX (C-terminal telopeptide) of 26 pg/ml/month with a satisfactory bone remodeling.

The American Association of Oral and Maxillofacial Surgery has published an official paper concerning ONJ. They mentioned that the treatment duration and the route of administration of bisphosphonate have an important role in the proliferation of the lesion. The intravenous form of bisphosphonate is especially concerned but also the oral form associated to invasive dental surgery that can contribute as a risk factor.⁸

Oral bisphosphonate-induced osteochemonecrosis revealed to be a less severe, less frequent, more predictable and more responsive to treatment entity than intravenous forms of osteochemonecrosis.¹⁰

Woo incriminated the zoledronic acid in 35% of ONJ and pamidronate with 31%, the association zoledronate –pamidronate revealed 28%.²⁰

Brooks in 2007 described two cases of ONJ correlated to a treatment with orally administrated risedronate.¹²

Fournier and Boissier have shown that pamidronate and zoledronate inhibit angiogenesis, decrease capillary tube formation, and inhibit vascular endothelial growth factor,²⁶ which may constitute an essential cause for bone exposure in this type of bisphosphonate and explains why the exposed bone does not bleed.

A study conducted by Mavrokokki in 2007 noted that the incidence of ONJ obtained in patients treated with intravenous bisphosphonates is 70% following invasive dental treatment and 30% occurred spontaneously. On the other hand, 50% was obtained after surgical treatment in patients undergoing oral bisphosphonate and 50% of ONJ cases were spontaneously obtained.²⁹

In many studies, Zoledronic acid showed to cause delays in wound healing of the tooth extraction socket, inhibit oral epithelial cell migration and promote proliferation and adhesion to hydroxiapatite of oral bacteria without causing osteocyte death neither osteonecrosis of the jaw in mice.^{30,31}

Oral surgery, implantology and bisphosphonates

Although oral bisphosphonate therapy is not considered an absolute contra-indication in patients who require oral surgery, informed consent is important, especially in patients who are still undergoing bisphosphonate treatment and necessitating dento-alveolar surgery.

Jeffcoat in 2006 showed no correlation between orally administrated bisphosphonate and implant failure,²⁴ while Savoldelli in 2006 described a case of implant failure due to bisphosphonate-associated osteochemonecrosis of the jaw with bone sequestration in patients undergoing intravenous zoledronic acid treatment.²⁵

Berardi in 2007 described the necessity of covering implants with a layer of non-aminobisphosphonate (Clodronate) that proved to enhance the differentiation of osteoblasts.³³ Another study on rabbits by Chacon in 2006 after administration of alendronate showed no effect on osseointegration of implants.³⁴

Hypotheses are still ambiguous and further investigations are needed.

Weak point theory

The complete cycle of bone remodeling is 160 days in means of 3 to 4 months in normal cases without bisphosphonate treatment. Thus surgery to be conducted on a patient undergoing bisphosphonate treatment, who has a systemic metabolic condition, should be delayed until the end of the bone remodeling in order to minimize the risk of developing ONJ, due to reduction of bone remodeling and inhibition of bone resorption. The region of bone remodeling will be recognized by bisphosphonates as a weak area which may lead to exposed bone. Bisphosphonates will reduce the rate of bone remodeling and so removal of microdamaged regions of bone may be impaired. Since non-invasive extraction site healing involves osteoclastic and osteoblastic activity to remodel the tooth socket, the action of bisphosphonate in the region with bacterial infested saliva in the socket may result in the alteration of the wound healing and therefore inducing ONJ.

Adjuvant and alternative treatments used nowadays

Today many adjuvant therapies are used in order to treat ONJ.

A study conducted by Vescovi and Merigo in 2008¹¹ on

14 cases, showed the ability of the Nd-YAG laser to enhance the medical and surgical treatment of exposed necrotic bone areas. On the other hand two studies conducted in 2007 by Petrucci¹⁴ demonstrated ozone therapy combined with surgical intervention as a possible option with 54% healing rate. This may be due to the antibacterial and healing potentials of ozone therapy. (Table IV).

Some alternative treatments are used nowadays to replace bisphosphonate treatment and prevent ONJ such as: Teliparatide, strontium ranelate (Protelos), Denosumab human monoclonal antibodies.

A study published in 2009 by Anastasilakis, demonstrated, in cases of osteoporosis, that the use of antibodies specific to the Receptor Activator of Nuclear Receptor Factor-Kappa B (RANKL) inhibitor, Denosumab, can be effective in such pathology in order to replace the usage of bisphosphonate and obtain a satisfactory bone anti-resorption activity.¹³ Another study published by Body 2006³⁵ showed Denosumab to have a fast anti-resorption activity and to have an effect in the prevention of bone complication compared to bisphosphonates prescribed in breast cancer and multiple myeloma cases.

Today the use of antiangiogenic molecules (anti-VEGF) Bevacisumab (Avastin) showed cases of exposed bone that was repaired after interrupting the medication.

More research is still necessary to elucidate these theories.

Recommendations for prevention of osteochemonecrosis

Prevention by ensuring adequate oral health before treatment is indicated, particularly if high doses of bisphosphonates are employed.

Recommendations for dental management of patients taking bisphosphonate have developed. Marx in 2007 established some recommendations for the prevention of ONJ (Table V).¹⁰

The American Dental Association established some recommendations for the prevention of ONJ by establishing measures to optimize dental health in patients who will be treated with bisphosphonate. Invasive dento-alveolar surgery should be considered cautiously and should be performed with minimal soft and hard tissue trauma, with separate treatment of each sextant. If all 4 sextants are concerned, a waiting period of 2 months is recommended before treatment of the other sextant associated to chlorhexidine 0.12% mouth wash⁸.

As it is imperative that we establish predictive and preventive dental metrics for prevention of ONJ, accurate examination and treatment planning should be established.

Until more is known, measures should be taken to prevent osteochemonecrosis of the jaw especially in patients who are still undergoing oral and intravenous bisphosphonate treatment.

Table IV: Adjuvant treatments:

<ul style="list-style-type: none"> - Hyperbaric Oxygenotherapy - Concentrated platelets - Phototherapy laser ND-YAG - Ozone therapy

Table V: Prevention of ONJ:Marx 2007.¹⁰

<ul style="list-style-type: none"> - Patients diagnosed with osteoporosis and are prescribed a bisphosphonate: Non restorable teeth should be removed, followed by periodontal therapy and a recall schedule. - Patients who have been taking an oral bisphosphonate and present for dental treatment: If less than 3 years, CTX testing is not necessary, the healing will be uncomplicated. - If more than 3 years, CTX testing is highly recommended, if more than 150pg/ml oral surgery can be done without complications and a drug holiday with or without a substitute drug approved for osteoporosis can be established.

Table VI: Recommendations for the treatment of ONJ: Longobardi 2007:¹⁸

<ul style="list-style-type: none"> - Surgical treatment like debridement, removing all the osteonecrotic tissue and covering the lesion with sliding flap. - Pharmacological therapy using antibiotics and chlorhexidine-based mouth wash. - Hyperbaric therapy.

Guidelines for the treatment of osteochemonecrosis

Treatment of osteochemonecrosis may be difficult to achieve and it can be presented by medical or surgical interventions. Marx does not recommend surgery in treatment of bone osteonecrosis as it will only lead to more exposed bone.^{10, 28}

Marx established a protocol for the treatment of oral bisphosphonate-induced osteonecrosis where he uses a mouth wash with 0,12% chlorhexidine in cases of painless exposed bone. If the patient reports pain, antibiotic therapy should be prescribed (PenicillinV-K 500mg), 4 times daily for 14 days or when pain is controlled. No surgery of debridement should be conducted in these cases as it will lead to more exposed bone.¹⁰

Table VII: Treatment of ONJ according to SISBO recommendations:

<ul style="list-style-type: none"> - Stage 1: Interruption of bisphosphonate? Chlorhexidine 0.12%, norma saline and bicarbonate based mouth wash Control each 15 to 20 days Oral hygiene - Stage 2: Antibiotic(Amoxicillin 2g/day associated to Metronidazol 1g/day)for 2 to 3 months Amphotericin B (Fungizone) 80mg daily for 2 to 3 months Chlorhexidine 0.12%, norma saline and bicarbonate mouth wash Minor Analgesic (Tramadol) with antiinflammatory medications (Mefenamic acid) A minimal invasive bone curettage Enoxaparin(Lovenox) ,30mg daily Cholecalciferol (VitD) 5000 UI/day Monadiol(VitK)10mg/day Pentoxifyline 400mg (Vasodilatator) twice daily associated to tocopherol(VitE)1000UI/day for 2 to 3 months PTH(1-34) 400UI/day for 2 weeks Replacement of aminobisphosphonate by clodronate - Stage 3: Antibiotic prescribed after culture and study of infested bacterias Amphotericin B(Fungizone) 80mg daily for 2 to 3 months Chlorhexidine 0.12% mouth wash, norma saline and bicarbonate Minor Analgesic (Tramadol) with antiinflammatory medications (Mefenamic acid) PTH(1-34) 400UI/day for 2 weeks Enoxaparin(Lovenox),30 mg daily Pentoxifyline 400mg (Vasodilatator) twice daily associated to tocopherol(VitE)1000UI/day for 2 to 3 months Cholecalciferol (VitD) 5000 UI/day Monadiol(VitK)10mg/day Replacement of aminobisphosphonate by clodronate

Longobardi in 2007 recommended a management of ONJ using a surgical treatment and indicating that the " not friable limit " represents the clinical limit for debridement (Table VI).¹⁸

In cases of osteochemonecrosis Marx noted that the entire bone is affected therefore cannot be debrided.²⁸ Treatment of exposed bone using hyperbaric oxygen therapy may not offer an additional benefit.²³

Two treatment modalities exist today:

1. Medical treatment: Can or cannot be associated to the surgical treatment where the surgeon can control the case with adequate medications until he obtains a spontaneous removal of the sequestrum and wound healing with an epithelialization of the underlying soft tissue.

2. Surgical treatment: This consists of eliminating the sequestrum and curettage of affected bone after elevation of soft tissue flap, the medical treatment will follow.

The evolution will be either "stabilization" with good bone and soft tissue healing or "aggravation" with exposed bone and sequestrum formation. Some measures were established by the SISBO concerning treatment of ONJ cases (Table VII).

The aim of these recommendations is to provide comprehensive care with minimal risk and a satisfying stabilization of the osteochemonecrosis pathology.

Clinical cases according to SISBO recommendations

Case 1

A 67 year-old male patient consulted our private clinic, for an asymptomatic bone exposure causing halitosis and difficulty in masticatory functions. The patient mentioned that since starting treatment for osteoporosis 6 months previously, he had experienced spontaneous loss of all his teeth (Figure 1). Detailed questioning revealed that was undergoing intravenous bisphosphonate treatment based on zoledronate (Zometa 4mg/month).

An extraoral examination showed a facial asymmetry with a fistula draining pus. (Figure 2). The panoramic examination showed an extended sequestrum of the alveolar crest with remaining fractured basal bone (Figure 3). The intraoral examination revealed a yellowish, exposed bone extending from the right to the left molar region (Figure 4). The case was classified as a stage 3 osteochemonecrosis of the jaw related to bisphosphonates.

The patient was operated on under general anesthesia, and the sequestrum was removed (Figure 5). No osteosynthesis device was placed to prevent trauma to the remaining fractured basal bone. A partial flap ensured covering of the remaining bone and Polyglactin 910 ensured stabilization of the mucosa (Figure 6). The fistula pathway was removed and an artificial drainage was placed for 3 weeks (Figure 7). Post operative medication was prescribed.

A 4 months post operative control showed clinically a total healing of the wound and an acceptable jaw function.

Case 2

A 62 year-old female patient consulted our private clinic for a spontaneous loss of teeth. On intraoral examination, she showed absence of the 35 and 37 teeth, with exposed

fluctuant yellowish bone (Figure 9). The patient mentioned irradiated pain in the mandibular bone region, with spontaneous loss of teeth 1 month previously.

After questioning, the patient revealed undergoing zoledronate (Zometa 4mg/ month) treatment intravenously, for the past 8 years, associated to chemotherapy and surgical ablation of the left breast following cancer of the same region. The treatment was interrupted 2 years ago but she was still undergoing chemotherapy every 6 months.

Panoramic and Cone Beam examination detected an osteolytic region in the left mandible region and an intimate contact with the lower alveolar nerve, although no paraesthesia was noticed (Figures 10 - 12). The osteolytic region extended from the 35 to 37 site. The case was classified as a stage 2 osteochemonecrosis of the jaw.

No extraoral findings were depicted. The SISBO recommendations were prescribed for 2 months. Isolation with mobility of the 38 tooth was obtained followed by removal of the tooth and sequestrum (Figure 13).

2 months later, the patient underwent further chemotherapy treatment, which resulted in recurrent osteochemonecrosis of the jaw in the mandible region. Exposed bone, mobility and fluctuation with localized pain were the evolving symptoms. The SISBO recommendations were prescribed for another 1 month. After 5 weeks, total healing was obtained with no involvement of vital structures (Figure 14).

Discussion

Bisphosphonates are prescribed to stabilize bone loss caused by osteoporosis and to inhibit the resorption of trabecular bone by osteoclasts in order to preserve its density. Osteonecrosis is considered as a complication with uncertain prognosis and a low healing rate.

The clinical aspects of the presentation of bone osteochemonecrosis associated with bisphosphonates described in literature are diverse, some very extensive and others limited to the extraction socket.

Typical presentation is a non-healing extraction socket or exposed bone with progression to sequestrum, swelling and purulent discharge.²¹ The site of predilection of ONJ showed to be the posterior region of the mandible, due to the high rate of remodeling in this region.

The precautionary measures still include comprehensive interrogation to detect all the existing risk factors.

Osteochemonecrosis is reported as being a spontaneous and provoked process depending on the molecule used and the existing risk factors such as trauma (tooth extraction).

Some co-morbidity factors should be considered such as corticosteroids, chemotherapy, trauma and infection, when

Case 1

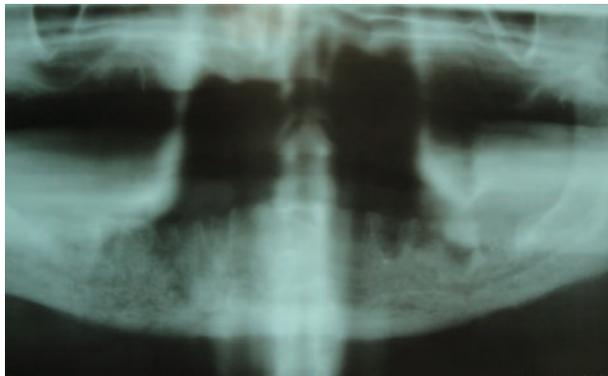


Figure 1: Panoramic radiograph showing empty sockets after spontaneous loss of teeth.



Figure 2: Extraoral view, showing the fistula circumscribed by granulation tissues.



Figure 3: Panoramic view showing the extended mandibular sequestrum, with fracture of basal bone.



Figure 4: Intraoral view showing the extended bone exposure.

faced with a patient undergoing a bisphosphonate treatment and necessitating a surgical intervention³⁶. Dose cumulated factor which is the dose absorbed modified by the bioavailability of each bisphosphonate may be another theory determining the predilection of bisphosphonate to cause ONJ.

CTX testing showed to be an interesting indicator of recovery of bone remodeling.¹⁰

The type of bisphosphonates showed to play an important role in the development of ONJ are associated with pamidronate and zoledronate.^{20-22,27} The data demonstrates that the duration of bisphosphonate treatment constitutes a risk factor due to its accumulation in bone.²³

The non-aminobisphosphonate (Clodronate) promotes the neoformation of bone seen in peri-implant tissues and stimulates the neoformation of bone around implants compared to other bisphosphonate.³³

Surgical debridement of the lesion appeared to lead to more complications and exposed bone with no biological reactivation,¹⁸ supporting the theory that ONJ is a silent phenomenon and that surgical intervention will reveal it clinically.

Drug holidays were also found to be insufficient in many ways, as bisphosphonate was found in bone many years

later.¹⁹

Conservative medical treatment showed to be more efficient in cases of ONJ. Medical treatment of ONJ using Penicillin is recommended due to its wide action, especially if associated to Metronidazole, which will act on anaerobic germs. Some cases can be treated using Quinolone (Ciprofloxacin) due to its bactericide effect, which can be prescribed until the end of clinical symptoms (pain, infection).

Conservative medical therapy with prescription of antibiotics and mouth wash and a non surgical approach is advocated.⁸

The effect of bisphosphonates is a reduction in bone turnover, resulting in the preservation of the bone mineralization. This treatment can lead to a destruction of osteoclasts with maintenance of osteocytes that are responsible for mineralization of bone. This causes sclerosis of the lamina dura, which is considered a region of predilection for remodeling. Bisphosphonates will be highly concentrated in this region and will be unable to remodel, leading to spontaneous loss of teeth and development of osteonecrosis of the jaw. Radiographic changes are not evident in the first stages of ONJ.



Figure 5: View of the extended mandibular bony sequestrum.



Figure 6: Intraoral view of the wound after removal of sequestrum.



Figure 7: Artificial drainage placed after enucleation of granulation tissue.



Figure 8: 4 months later, a total healing of mucosa was obtained.

It has been demonstrated that bisphosphonates inhibit endothelial cell functions and that pamidronate inhibits not only bone resorption but also bone blood flow.²

We have accumulated some recommendations concerning the treatment of ONJ, and which, based on the clinical cases the SISBO protocol, have so far proved efficient.

Conclusion

Osteochemonecrosis of the jaw associated to bisphosphonate is a severe complication for patients undergoing bisphosphonate treatment. Until now no consensus was established for the prevention or treatment of osteochemonecrosis, and the main objective remains the control of pain and inflectional symptoms.

This article supports the need to establish preventive measures in all patients treated with bisphosphonates in order to prevent osteochemonecrosis pathology of the jaws. It further needs to alert surgeons about the potential complication of maxillary and mandibular bone in patients receiving bisphosphonate therapy with proposing

guidelines established by SISBO for the treatment of bone osteochemonecrosis of the jaw.

As more data becomes available, the guidelines will need to be updated.

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Case 2



Figure 9: Intraoral view of the yellowish exposed bone in lower left mandible.

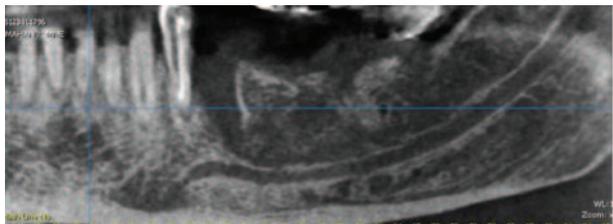


Figure 11: Frontal cut of cone beam showing the sequestrum in intimate contact with the lower alveolar nerve.



Figure 13: Macroscopic view of the 7 cm sequestrum after osteochemonecrosis of the lower left alveolar bone, with the extracted 3.8 tooth.

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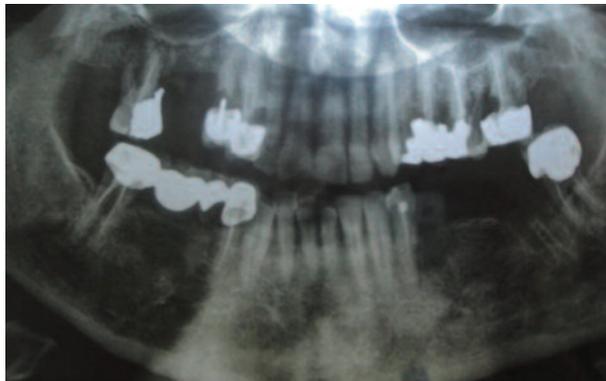


Figure 10: Panoramic view, showing absence of 1.6, 3.5 and 3.7 teeth with a sequestration of bone in both right maxillary and left mandible regions.

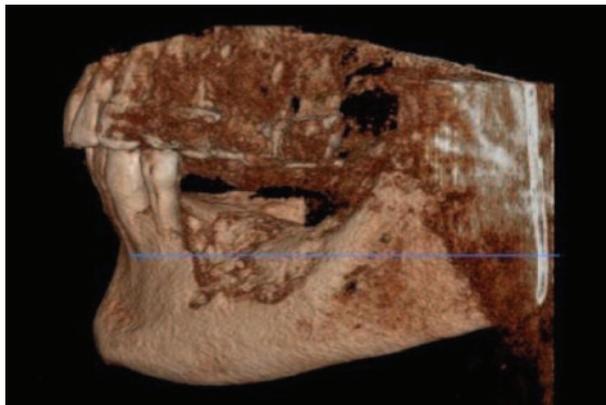


Figure 12: 3D cone beam radiography showing the amount of bone undergoing sequestration and its contact with lower alveolar nerve.



Figure 14: Intraoral view 4 months post-operatively, note the total healing in the region with absence of exposed bone.

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