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Medication-Related Osteonecrosis of the Jaw: Risk Factors, Management and Prevention in Dental Practices

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Abstract: Medication-related osteonecrosis of the jaw (MRONJ) constitutes a considerable clinical challenge, particularly for individuals undergoing antiresorptive therapy for osseous malignancies and osteoporosis. This review seeks to investigate the risk factors, management approaches, and prophylactic strategies pertaining to MRONJ, emphasizing the implications of tooth extraction, implant therapy, oral surgical interventions, periodontitis, and inadequately fitting removable dentures. An exhaustive literature review was performed to assess the prevalence of MRONJ, concentrating on the specific drug type, method of administration, and dental interventions. Particular emphasis was placed on the hazards linked to intravenous bisphosphonate therapy, tooth extractions, dental implants, and various oral surgical procedures. Investigations examining the potential protective function of dental implants in contrast to alternative interventions were also scrutinized. Data regarding collaborative preventive strategies involving dental practitioners, medical professionals, and patients were incorporated. The review elucidated that the incidence of MRONJ is contingent upon the specific drug and procedure utilized, with intravenous bisphosphonates presenting a heightened risk. Tooth extraction is identified as a principal local risk factor for MRONJ, whereas the evidence regarding dental implants is inconsistent, with certain studies indicating a diminished risk. Prophylactic measures, encompassing pretreatment assessments, enhanced oral hygiene practices, and minimally invasive procedures, were recognized as vital for mitigating the incidence of MRONJ. The prevention and management of MRONJ necessitate a multidisciplinary framework, which includes comprehensive dental assessments, patient education initiatives, and meticulous treatment planning. Interdisciplinary collaboration among healthcare providers is imperative for optimizing clinical outcomes. Additional research is warranted to elucidate the pathophysiological mechanisms underlying MRONJ and to devise targeted therapeutic interventions that enhance safety and quality of life for patients receiving antiresorptive therapy. ©2025 NTMS.

Keywords: Medication-Related Osteonecrosis of the Jaw (MRONJ); Antiresorptive Therapy; Dental Implants; Tooth Extraction; Bisphosphonates (BPs).

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1. Introduction

Medication-related osteonecrosis of the jaw (MRONJ) is a significant clinical problem, particularly in patients receiving antiresorptive therapy for primary or metastatic bone malignancies or osteoporosis[1]. The incidence of MRONJ is reported to be between 1% and 10% in patients receiving intravenous (IV) bisphosphonates (BPs), whereas this rate is 0.001% to 0.01% in patients taking oral BPs[2]. MRONJ is considered a multifactorial disease with an incompletely defined pathophysiology. It is characterized by the complex interplay of systemic and local risk factors that sustain a continuous cycle of necrosis, leading to bone necrosis and soft tissue destruction. The disruption of soft tissue integrity exacerbates the condition, highlighting the need for ongoing preclinical and clinical research to understand the fundamental factors and modifiers of disease development, severity, progression, and healing [1].

The American Association of Oral and Maxillofacial Surgeons (AAOMS) updated the widely used definition of MRONJ in a 2022 position paper. The 2014 criterion of "current or previous treatment with antiresorptive or antiangiogenic agents" was revised to "current" or "previous treatment with antiresorptive therapy, either alone or in combination with immunomodulators or antiangiogenic drugs"[3,4]. Despite ongoing research, the underlying mechanism of MRONJ remains unknown, and systematic and targeted therapies are not yet available. Since the etiology of MRONJ is not fully understood, specific targeted treatment is currently unavailable[5].

Tooth extraction, implant treatment, oral surgery, periodontitis and poorly fitting removable dentures have been identified as triggers and associated risk factors that directly or indirectly influence the development of MRONJ[6]. Since MRONJ is mostly limited to the maxillofacial region[7], dentists have a crucial role in its prevention. They must take preventive measures to reduce the risk factors associated with drug-induced osteonecrosis. If prevention is not entirely possible, it is important to delay the start of MRONJ. Dentists are responsible for a comprehensive assessment of risk factors and developing effective strategies to mitigate or eliminate them[8].

The expert panel encourages the development of predictive tools for the development of MRONJ, such as bone turnover markers and genetic markers[9]. These tools would help dentists identify at-risk patients and adapt preventive measures more effectively. By understanding and addressing these risk factors, dentists can significantly reduce the incidence and impact of MRONJ.

MRONJ is a potentially serious condition, and its development generally requires a combination of systemic and local oral risk factors. It is relatively common in cancer patients receiving antiresorptive therapy (2-5%) and rare in patients with osteoporosis (0.01-0.03%). Therefore, the most common systemic risk factor is the use of antiresorptive drugs [10]. The number of patients with MRONJ is expected to increase over the next decade [11]; which underscores the urgent need for further research to develop effective prevention and treatment methods.

The aim of this study is to evaluate the risk factors, management strategies, and preventive measures for MRONJ in patients receiving antiresorptive therapy, focusing on dental procedures like tooth extractions and implants to improve prevention and treatment outcomes.

Antiresorptive Agents and Risk Factors

There are several types of antiresorptive drugs including Bisphosphonates (BPs), Receptor Activator of Nuclear factor Kappa-B Ligand (RANKL)and Antiangiogenic drugs. Bisphosphonates (BPs) are classified as nitrogen-containing (zoledronic acid, pamidronate, alendronate) or non-nitrogen-containing (etidronate, clodronate, tiludronate). RANKL inhibitors include denosumab and romosozumab. Antiangiogenic drugs include bevacizumab, imatinib, and sunitinib [12]. The risk of developing MRONJ after implantation is much lower in patients with osteoporosis treated with denosumab[13].

Studies confirm that ibandronate is less effective than zoledronic acid in the treatment of MRONJ in malignancy. While the risk of alendronate is lower compared to intravenous bisphosphonates, the risk of intravenous ibandronate is lower than that of pamidronate and zoledronic acid [14]. The overall risk of MRONJ is higher in some classes of antihypertensive drugs because the total dose is higher. Drugs like alendronate can remain in circulation for up to 10 years. The risk of MRONJ is higher in those who have used these drugs for more than four years, and the risk is highest in those who have used the treatment for more than five years [3]. The AAOMS reported that the risk of developing MRONJ is highest when oral antihypertensive drugs are used for more than two years [4].

It is confirmed that malignancies increase the risk of developing MRONJ when exposed to antihypertensive, antiresorptive, or antiangiogenic drugs. Cumulative doses of intravenous drugs contribute to the development of MRONJ15. Saad and colleagues reported that the incidence of MRONJ in cancer patients treated with zoledronate or denosumab was 0.5 to 0.8 percent in one year and 1.0 to 1.8 percent in two to three years [16].

The incidence of MRONJ has been reported to be 1-25% with concurrent antiangiogenic and antiresorptive agents and 1-11% with antiresorptive agents alone. The frequency of MRONJ was found to be 6% when antiangiogenic and antiresorptive drugs were used together [17]. Compared to pamidronate or zoledronate alone, an increased incidence of MRONJ was observed with sequential pamidronate-zoledronate therapy. Similarly, patients who switched from bisphosphonates

to denosumab had a higher incidence of MRONJ compared to those who received bisphosphonates or denosumab alone [18].

The risk of MRONJ is shown to be higher with denosumab than with bisphosphonates, being 3.77% in patients treated with denosumab, compared to 2.13% in patients treated with zoledronic acid [19]. The type of antiresorptive drug leads to a higher risk with BPs compared to denosumab or antiangiogenic agents; this is due to the mechanism of action of BPs and their longer half-lives [13].

Antiresorptive drugs alone do not cause bone necrosis; however, when combined with trauma such as tooth extraction or inflammation/infection resulting from periodontal or periapical disease, bone necrosis can occur[1] .Surgical interventions pose significant risks for patients on high-dose denosumab, especially those with cancer, periodontitis, denture use, BP history, or current BP use, as well as those who are immunosuppressed due to chemotherapy, rheumatoid arthritis, diabetes, Sjogren syndrome, or steroid treatment. Comorbidities such as diabetes and autoimmune diseases further increase the risk of MRONJ [3]. The general health status of patients also contributes to MRONJ development. Dentoalveolar surgery, particularly tooth extraction, is a major risk factor, with 52-61% of MRONJ cases reporting tooth extraction as the precipitating event [20] Low doses of antiresorptive drugs are used for osteoporosis treatment, while high doses are for cancer patients with bone metastases. It is crucial to assess antiresorptive side effects in implant therapy, including fixture installation, bone augmentation, and late complications [21]. Cancer patients typically receive a ten-fold higher cumulative antiresorptive dose than those with osteoporosis, and the addition of local oral risk factors significantly increases MRONJ incidence[10]. The mandible has a higher risk of MRONJ than the maxilla. Factors such as pre-existing inflammation, rather than just high-dose antiresorptive use before or after tooth extraction, are significant MRONJ risk factors. Key factors include root amputation, immunosuppressive therapy, extraction of mandibular teeth, teeth with pre-existing inflammation, and longer high-dose antiresorptive duration (≥ 8 months) [22]. Clinical signs like pain and infection, along with the duration of antiresorptive medication, are significantly related to early necrotic bone biopsy results[23]. Necrotic bone can cause loss of soft tissue integrity, leading to clinical MRONJ, with surgical interventions further complicating the disease. A combination of antiresorptives, trauma, and/or inflammation/infection is necessary for MRONJ development [1]. MRONJ is more common in cancer patients (1.8–5% incidence) than in those with osteoporosis (0.01–0.03% incidence). Local oral risk factors include tooth extraction, inflammatory dental disease, trauma from removable prostheses, and dental implants. Identifying and managing these risk factors is crucial to minimizing MRONJ risk in susceptible patients.(24)Other significant risk factors include chemotherapy, corticosteroids, smoking, medical conditions, cardiovascular diseases, targeted therapies, inflammatory diseases, and oral trauma[25].While bisphosphonates and denosumab are well-known causes of MRONJ, other biologic agents, notably antiangiogenics like vascular endothelial growth factor antagonists and tyrosine kinase inhibitors, have also been implicated [26]. The evidence is of very low certainty. In a study of 24 cancer types, osteoporosis was the most common non-malignant condition associated with MRONJ, accounting for 23% of cases. The primary dental risk factor was tooth extraction (45%), followed by periodontal disease (10%) [27]. Several studies have concluded that the risk of MRONJ varies among different types of cancer, with the highest incidence reported in prostate cancer patients[19].

A case study highlighted MRONJ development in a patient treated with IV zoledronate for sacral plasmacytoma, who also underwent radiotherapy and chemotherapy. The MRONJ was noted in the mandible after 13 months of orthodontic treatment [28].

Overall, recognizing and managing MRONJ risk factors such as the duration of bisphosphonate intake and local infections is crucial [29].

Radiographic tests are essential for diagnosing and staging MRONJ, with approximately 75% of cases affecting the mandible [12].

The rate of MRONJ in BP patients using glucocorticoids is higher compared to those not using them. Patients receiving corticosteroid and immunosuppressive therapy carry a risk of MRONJ even with short-term BP use [14,29]. Some results indicate that male BP patients have significantly more MRONJ cases compared to females [14]. However, MRONJ is generally reported to occur in elderly female patients [12].

Management and Treatment Strategies

Surgical interventions pose a heightened risk for patients actively receiving high-dose denosumab due to the increased trauma to the bone. In contrast, nonsurgical therapies are considered lower risk [2]. Denosumab-econdary MRONJ surgery was successful in 16 of 20 patients (80.0%). This success rate is similar to the 80-90% reported for bisphosphonates [30]. Alveoplasty is emphasized as a crucial preventive measure to minimize trauma [14]. Furthermore, understanding the pathophysiological mechanisms underlying MRONJ is vital for developing targeted interventions that can reduce its incidence and improve patient outcomes.

Physicians and dentists should prioritize the prevention of MRONJ in patients with malignancies receiving antiresorptive therapies [15]. The importance of a collaborative approach involving dentists, physicians, and pharmacists cannot be overstated, as it is critical for preventing MRONJ development [31]. Increased awareness of MRONJ among dental professionals has led to a rise in cases where extractions were avoided, potentially allowing MRONJ to develop despite the

need for intervention [32]. Therefore, there is a critical imperative to enhance the awareness, education, and training of dentists in effectively managing patients prescribed antiresorptive drugs [33].

Optimizing oral and dental health before starting treatment with antiresorptive medications is mandatory. Patients should be strongly reminded to promptly report any early signs and symptoms of MRONJ. When infection is detected, treatment should begin immediately with less traumatic procedures [29]. Evidence from a 2022 Cochrane review suggests that various preventive strategies, including regular dental checkups, oral care instructions, antibiotics, and special wound closure techniques, can reduce the risk of MRONJ in cancer patients receiving antiresorptive drugs [7]. One retrospective study found a significantly higher risk of MRONJ in antibiotic-naïve patients. The QUIPS tool showed a moderately high risk of bias. The validity of antibiotics remains to be determined [34].

Development of management recommendations using algorithms to guide healthcare professionals in the prevention, diagnosis and treatment of MRONJ in different clinical scenarios. Preventive strategies should be adopted to avoid MRONJ, which is a rare but important complication that can compromise patients' quality of life. These strategies must also take into account the prevention of fragility fractures associated with untreated osteoporosis, which not only affects the quality of life but also increases mortality [35].

During treatment with antiresorptive medications, close follow-ups and meticulous oral hygiene routines should be maintained by patients. The management of MRONJ is generally challenging, and a well-established treatment strategy is yet to be developed. Therefore, prevention remains more effective than management [12]. According to the 2022 position papers of the American Association of Oral and Maxillofacial Surgeons (AAOMS), nonoperative therapy is effective for treating any stage of MRONJ [3], while surgery also plays a crucial role in its management, as indicated by a multicenter study conducted in Europe [36].

Among patients with osteoporosis treated with antiresorptive medications and undergoing tooth extraction, radiographic signs of chronic dental infection can predict MRONJ onset. Greater pathology development has been observed in sites with furcation involvement, root remnants, or untreated dentinal or pulpal caries lesions. ARDs induce bony changes visible in diagnostic images commonly used in dental practice. Postoperatively, these bony changes, such as the persistence of the alveolar socket and lamina dura, are noteworthy [37].

Development of MRONJ in Pediatric Populations

While much is known about the risks and prevalence in adult populations, particularly the elderly, It is well-documented that increased age is a significant risk factor for the development of MRONJ. Patients over the age of 65 are particularly vulnerable [3,4]. The incidence and implications in pediatric populations remain relatively understudied. There are compelling reasons to believe that MRONJ may not significantly affect children, particularly those with genetic conditions that influence bone formation. To date, no cases of MRONJ have been reported in children or adolescents in the literature, suggesting that the risk of developing MRONJ in this demographic is negligible. For instance, patients with secondary osteoporosis undergoing long-term bisphosphonate treatment should be closely monitored from adolescence into adulthood, as the risk becomes more pertinent with age [38]. The presence of MRONJ in the child and youth population treated with antiresorptive drugs has been noted to be very low, further supporting this observation [39]. A position paper has stated that there have been no reports of MRONJ or Drug-Related Osteonecrosis of the Jaw (DRONJ) in bisphosphonate-treated children with conditions like osteogenesis imperfecta [40]. This lack of evidence highlights the rarity of such occurrences in pediatric patients. However, there has been a notable case report, which is, as far as the authors are aware, the first known instance of MRONJ in a child following dental extractions. This case underscores the importance of recognizing the unusual and slow presentation of MRONJ in younger patients, which necessitates careful follow-up and monitoring [41]. Given the current evidence, longitudinal studies are required to assess the long-term implications for children treated with bisphosphonates as they transition into adulthood. These studies are crucial to evaluate the potential risks posed by the cumulative doses of past bisphosphonate therapy on the development of MRONJ later in life. Until more data is available, primary prevention of oral and dental pathologies in adulthood remains a critical strategy. Pediatric dentists play a pivotal role in maintaining the oral health of these patients during their growth, thus potentially mitigating the future risk of MRONJ [42].

Impact of Dental Implants on (MRONJ) Risk in Patients with Antiresorptive Therapy

Recent studies have explored the relationship between dental implants and the risk of Osteonecrosis of the Jaw (ONJ) in patients undergoing antiresorptive therapy, such as bisphosphonates (BPs) and denosumab, with varying results. In a systematic review of 31 failed implants due to MRONJ, 36% were in the maxilla and 65% were in the mandible, mostly posteriorly (85%). 23% of implants failed after postresorptive therapy, and 83% of these failures were due to MRONJ. The average time from the start of antiresorptive medications to the start of MRONJ was 34 months. 65% of the implants that received MRONJ were in the mandible, mainly in the posterior part. 80% of MRONJ cases were stage 2 and limited to the alveolar bone 43. Contrary to initial concerns, dental implants did not increase the risk of ONJ. In fact, they may reduce the risk even in patients with a history of bisphosphonates, steroids, periodontitis, or tooth extraction. Implant surgery did not show a higher MRONJ risk compared to those

without implants, suggesting implants might lower the MRONJ risk [44]. Ryu et al. [45] found that osteoporosis patients with dental implants had a lower risk of MRONJcompared to those without implants, suggesting that dental implants may be safely considered in patients with a history of antiresorptive therapy.

A recent systematic review Despite some limitations, implant-assisted rehabilitation in patients with previous surgical treatment of MRONJ showed a low incidence of biological complications, reduced disease recurrence for implants, and satisfactory implant survival. However, the strength of the evidence supporting these results is considered "very low"[46]. Despite these encouraging findings, other studies present a more nuanced picture. Pichardo et al. [47] reported an increased risk of MRONJ in patients with dental implants taking antiresorptive medications, including bisphosphonates. They observed that short-term (<2 years), low-dose oral bisphosphonate therapy for osteoporosis did not significantly impact implant success rates. Gelazius et al. [48] conducted a systematic review revealing a higher success rate for implants in patients receiving oral bisphosphonate therapy (98.8%) compared to those receiving intravenous treatment (91%). This underscores the potential for favorable outcomes in bisphosphonate-treated patients, offering reassurance to clinicians and patients. Conversely, Sulaiman et al. [49] showed that implants in bisphosphonate-treated patients had a higher failure risk compared to non-treated patients. Papadakis et al. [50] introduced a critical caveat, noting the challenges in making definitive claims about the impact of antiresorptive medication on dental implant success rates due to limitations in many studies, such as small sample sizes, absence of control groups, and short follow-up periods. Consequently, establishing the precise success rate of dental implants in patients undergoing antiresorptive medication remains challenging. Sher et al. [13] found that patients with a history of bisphosphonates were not at increased risk of implant failure compared to healthy patients but emphasized the risk of developing MRONJafter implant placement. Systematic reviews have also reported mixed results, with some indicating high success rates for implants in patients receiving bisphosphonate therapy, while others highlighted an elevated risk of bisphosphonate-related osteonecrosis of the jaw (MRONJ) and implant failure [51]. Specifically, Granate-Marques et al. [51] identified an increased risk of MRONJ associated with dental implants placed in the posterior jaw of patients on long-term bisphosphonate therapy, particularly those concurrently receiving systemic corticosteroids. Close collaboration between oral surgeons and prescribing physicians, individualized treatment planning, regular post-implant maintenance, and vigilant monitoring are essential for achieving successful outcomes in bisphosphonate-treated patients [52]. Evidence suggests that low-dose oral bisphosphonate intake for osteoporosis generally does not compromise implant therapy [13]. These patients do not lose more implants nor experience more implant-related complications or failures compared to implant patients without bisphosphonate intake. However, high-dose bisphosphonate intake for managing malignancies, long-term oral bisphosphonate use, and the presence of comorbidities may increase the risk of MRONJ [21]. Studies by Abtahi et al. [53] evaluated patients over a five-year follow-up period and reported that marginal bone loss increased over time in both bisphosphonate-coated and uncoated implant groups. However, results were satisfactory, with the bisphosphonate-coated implants showing 0.20 mm of marginal bone loss compared to 0.70 mm for the control group. There was a significant decrease in the incidence of MRONJin the dental implants group compared with the no dental implants group. Inserting dental implants before intravenous BP administration was not a risk factor. Dental implants were not risk factors; they were associated with lower MRONJratios [45]. Holzinger et al. [54] noted that the development of osteonecrosis in conjunction with dental implants might be a side effect of treatment with oral or intravenous BPs. Conversely, javed and Almas [55] showed that the incidence of implant failure was minimal in patients using oral and intravenous bisphosphonates, concluding that dental implants in patients undergoing bisphosphonate therapy can osseointegrate and remain functionally stable. In general, the majority of reported implant losses in antiresorptive patients occur within a short time post-installation/post-loading (i.e. early losses), Low-dose oral BP intake for osteoporosis treatment does not compromise implant therapy, indicating these patients do not lose more implants or experience more complications compared to those without BP intake [21]. Nisi et al. [56] included 90 patients with MRONJ caused by various reasons, with only 9 cases attributed to implant placement. Indicating that implant surgery might trigger MRONJ development. The presence of peri-implantitis during surgery was found to potentially affect implantation success adversely [45].

Systematic review suggested that patients with a history of bisphosphonates for osteoporosis treatment are not at increased risk of implant failure in terms of osseointegration compared to those without such medications [13]. However, studies reported significant differences in success and survival rates of dental implants between bisphosphonate-treated and control patients [57]. The overall evidence from the systematic review suggests that patients taking BPs present a higher risk of implant failure than patients not taking BPs [49]. This evidence has prompted new research suggesting that long-term use of antiresorptive drugs is contraindicated for implant treatment [58].

In a related case report, a patient with a history of bisphosphonate use for osteoporosis underwent dental implants. Follow-up visits were scheduled at 1-month intervals, during which no pathology was detected. After prosthesis placement, the patient was evaluated clinically and radiographically at 1, 3, and 6 months.

During this evaluation, no complications were observed in the jaw or in the implant [59].

Tooth extraction

Tooth extraction has been identified as a major risk factor for the development of MRONJ, particularly in patients receiving antiresorptive and antiangiogenic agents. It is reported that among patients with MRONJ, 52 to 61% attribute tooth extraction as the precipitating event [20]. The most reported dental risk factor was tooth extraction (45%), followed by periodontal disease (10%) [27].

The extraction of a tooth with preexisting infection has been suggested as one of the risk factors for antiangiogenesis agents [2]. The risk is especially pronounced in those undergoing high-dose bisphosphonate therapy for cancer treatment [22], with the duration of intravenous bisphosphonate therapy exceeding 11 months being a significant risk factor [60].

The risk of MRONJ after tooth extraction is influenced by several factors, including the duration of medication use, the presence of pre-existing inflammation, and the patient's overall health status. Furthermore, root amputation, immunosuppressive therapy, extraction of mandibular teeth, extraction of teeth with pre-existing inflammation, and longer duration of high-dose BMA (≥ 8 months) were all significantly associated with the development of MRONJ. Additionally, extractions in patients with pre-existing inflammation, such as periodontal disease or infection, are more likely to lead to MRONJ. A study found that 90.2% of all MRONJ cases had pre-existing inflammation, underscoring the importance of addressing infection before extraction [22].

For patients exposed to oral bisphosphonates, the risk is approximately 0.5%, whereas intravenous bisphosphonates elevate this risk to about 14.8% [52]. For cancer patients exposed to BPs, the risk of developing MRONJ after tooth extraction ranges from 1.6 percent to 14.8 percent (3), with some studies reporting rates as high as 51.9% [62]. The risk is directly proportional to the duration of medication use and the patient's age [62].

A significant relationship between tooth extraction frequency and increased MRONJ risk has been observed in various studies. For example, the incidence of MRONJ after tooth extraction was found to be lower in the group of osteoporotic patients with dental implants compared to those without implants [45].

The control of inflammation should be the first step, and wound-healing-compromising diseases and medications should be considered for osteoporotic patients. The older osteoporotic Korean patients who underwent tooth extraction had a six times higher risk of developing MRONJ, with rheumatoid arthritis and bisphosphonates also associated with a significantly higher risk [45]. This suggests that pre-existing inflammation is a significant risk factor for MRONJ development post-extraction.

Invasive dental procedures, such as tooth extraction, can disrupt the delicate mucosal and periosteal barrier between the teeth and bones, increasing the susceptibility to the development of MRONJ [52].

To minimize the risk of MRONJ, several preventive measures and surgical techniques have been recommended. These include minimally traumatic extraction techniques, removal of any bone edges, and mucosal wound closure [63]. The SPP muco-periosteal flap has been demonstrated to be markedly superior to the EPP mucosa flap for primary wound closure after surgical tooth extractions in cancer and osteoporosis patients undergoing or after antiresorptive treatment [23].

In terms of clinical management, it is advised that infected teeth, which cannot be salvaged through nonsurgical endodontic therapy, be extracted to prevent the progression of the infection and potential MRONJ development [2]. Prophylactic antibiotics before tooth extraction may be necessary despite their limited efficacy in reducing MRONJ risk (63). Experts have noted that the risk of developing MRONJ after a periodontal surgical procedure that requires bone manipulation is comparable with the risk associated with a dental extraction. Nonsurgical therapy should not be considered high risk because of the relatively lower level of trauma to the bone [2]. Furthermore, early dental examinations and preventive care are recommended to decrease the risk of MRONJ, especially in older osteoporotic patients [45].

Tooth extraction may also be attributable to the success of dental implants. The dental implant is closely related to tooth extraction, which happens before the surgery in most cases. Patients who had complications after extraction should be excluded from dental implantation. Only patients with insignificant problems can undergo this surgery. The incidence of MRONJ after tooth extraction was lower in the group of osteoporotic patients with dental implants than in the no-implants group [45].

Despite the high risk associated with tooth extraction, successful outcomes have been reported with the use of atraumatic surgical protocols and careful postoperative management. For example, no postoperative bisphosphonate-associated osteonecrosis of the jaw was observed in a study group of 700 patients who underwent 1,480 extractions using minimally traumatic techniques. No patients with steroid therapy had problems during healing time or developed MRONJ, and all OPTs performed showed normal alveolar bone healing following the extractions. At the last visit of the follow-up, all patients had intact mucosa and displayed no additional signs of inflammation [64].

Additionally, factors such as root amputation, the extraction of a single tooth, the presence of bone loss or severe tooth mobility, and an unclosed wound were all significantly associated with the development of MRONJ. Therefore, it is essential to consider these factors and adopt minimally traumatic extraction techniques to minimize the risk of MRONJ [63].

Tooth extraction in patients undergoing or after antiresorptive treatment cannot be considered the major risk factor for MRONJ; however, it might be the major

triggering event when not performed with preventive measures [23].

Drug holiday

The effectiveness of a drug holiday in reducing the incidence of Medication-Related Osteonecrosis of the Jaw (MRONJ) remains inconclusive; since bisphosphonate (BP) therapy has a long-term effect due to its incorporation into bone, a drug holiday of a few months is unlikely to significantly alter this risk (22, 63), although recent systematic reviews support the benefits of a drug holiday [65].

For patients undergoing procedures involving bone tissue, such as tooth extractions or dental implant installations, there is a consensus to suspend BP medication three months before and after the intervention. However, evidence supporting the efficacy of this short-term pharmacological interruption in reducing osteonecrosis risk is lacking [23]. Some studies have suggested that a preoperative drug holiday, combined with serum CTx level control, could allow safe osseointegrated implant installation without MRONJ development [66]. Despite these isolated findings, new guidelines highlight the lack of high-quality evidence supporting the effectiveness of interrupting antiresorptive drug therapy to mitigate MRONJ risk [3.9.35.67]. Overall, current evidence does not support the routine implementation of drug holidays to minimize MRONJ risk. Larger, well-designed prospective studies and randomized controlled trials are needed to draw definitive conclusions [68, 69]. A two-month holiday period did not show significant differences in osteonecrosis development [37], although some animal studies reported a 50% reduction in MRONJ incidence with a drug holiday [70].

2. Conclusion

In conclusion, the management of patients on antiresorptive therapy represents a significant challenge in dentistry, especially in relation tooth extraction, implant treatment, oral surgery, periodontitis and poorly fitting removable dentures. The development of MRONJ remains critical due to the multifactorial nature of the disease, which includes both systemic and local risk factors. Dental implants have historically been considered a risk factor for MRONJ, but recent studies have shown conflicting results. Some evidence suggests that dental implants may not significantly increase the risk of MRONJ and may even decrease it compared to other dental procedures. However, the success rate of implants in patients receiving antiresorptive therapy can vary, and factors such as duration and dose of medication play a critical role. Tooth extraction remains an important local risk factor for MRONJ, with a significant proportion of MRONJ cases attributable to this procedure. Extraction-related trauma, especially in patients with underlying disease such as periodontitis or high-dose antiresorptive therapy, requires careful planning and preventive measures. Preventive strategies including careful oral hygiene, regular dental checkups and the use of less traumatic dental procedures are important to minimize the risk of MRONJ. Collaboration between dentists and other healthcare providers is essential to optimize patient outcomes and develop effective treatment strategies for those at risk for MRONJ. Increasing awareness of MRONJ among dentists and patients is essential. A better understanding of risk factors, early signs and appropriate treatment strategies can significantly reduce the incidence of MRONJ. Continuing education and research in this area allows dentists to implement better preventive measures and improve patient care. Future research should continue to focus on understanding the pathophysiology of MRONJ, developing targeted therapies, and improving preventive strategies to improve the quality of life of patients receiving antiresorptive therapy. In addition, it is very important to implement oral measures as soon as antiresorptive therapy begins. Before starting treatment, patients should receive a thorough dental evaluation and appropriate treatment. To reduce the risk of developing MRONJ, continuous oral care and preventive measures such as maintaining excellent oral hygiene and scheduling regular dental checkups should be prioritized. Dentists must work closely with other healthcare providers to ensure a holistic approach to a patient's overall health and treatment plan.

Limitations of the Study

The limitations of this study warrant careful consideration. Variability in data sources and methodologies introduces inconsistencies, while the lack of large-scale, high-quality studies restricts the generalizability of the findings. Additionally, the incomplete understanding of MRONJ's multifactorial etiology and pathophysiology presents challenges in establishing definitive prevention and management strategies. The study’s focus on cancer and osteoporosis patients receiving antiresorptive therapy may overlook other at-risk groups. Lastly, the potential for publication bias and the evolving nature of research in this field could limit the broader applicability of the conclusions.

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None.

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Consent to participate
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