WHAT IS OSTEOPOROSIS AND WHAT ARE ITS COMPLICATIONS?

Osteoporosis is a major non-communicable disease characterised by reduced bone mass and disruption of bone architecture, resulting in increased bone fragility and fracture risk. The condition has long been identified as a significant healthcare issue worldwide, especially in countries with an ageing population such as Singapore. It was forecast that by 2030, one out of five persons residing in Singapore will be 65 years old and above. Therefore, the incidence of osteoporosis with its associated fractures is likely to increase over the coming decades.

Worldwide, the lifetime risk for hip, vertebral and forearm (wrist) fractures has been estimated to be approximately 40%, similar to that for coronary heart disease. Fractures are of particular concern in the elderly osteoporotic patient. According to the Asian Osteoporosis Study published in 2001, by the next century, 50% of all hip fractures in the world will occur in Asia. The Singapore Ministry of Health (MOH) Clinical Practice Guidelines on Osteoporosis have reported that since the 1960s, hip fractures have increased by 1.5 times in men and five times in women. The incidence of hip fracture in Singapore is estimated to be 402 out of 100,000 women and 152 out of 100,000 men, making it one of the highest incidences in Asia. Apart from resulting in fractures, osteoporosis may also cause patients to become bedridden with secondary complications that may be life-threatening.

Numerous factors contribute to the risk of osteoporosis and fractures. To aid in treatment decision-making, fracture risk can be assessed using the WHO Fracture Risk Assessment (FRAX) tool, which takes into account the morbidity and economic burden. It was reported by MOH that the mortality rate one year after experiencing a hip fracture is approximately 20%–27%. One-fifth of patients who survive the fracture either become semi- or fully-dependent, and 39% are affected by reduced mobility. Patients who survive the event but are left with residual impairment to mobility and self-care require long-term nursing care and rehabilitation. This contributes to economic costs for the patients and society.

WHAT IS MEDICATION-RELATED OSTEONECROSIS OF THE JAW?

Osteonecrosis of the jaw is a rare adverse effect that may occur in patients being treated for osteoporosis with antiresorptive medications. A position paper issued by the American Association of Oral and Maxillofacial Surgeons (AAOMS) in 2014 suggested the term medication-related osteonecrosis of the jaw (MRONJ). This was in recognition of the potential for other antiresorptive and antiangiogenic medications, apart from bisphosphonates, to cause osteonecrosis of the jaw, such as the human monoclonal antibody, denosumab. This article provides advice on the possible risks of developing MRONJ in these patients, as well as the recommended preventive and management strategies for such patients, from a multidisciplinary team perspective.

HOW RELEVANT IS THIS TO MY PRACTICE?

Management of osteoporosis

Osteoporosis management aims to reduce the impact of the condition and its associated complications. Each fragility fracture incured increases the risk of future fractures: research has shown that 50% of those who break their hip previously presented with a minimal trauma (fragility) fracture and that a prior fracture is associated with an 86% increased risk of any fracture in the future. The risk of a future fracture can be reduced by up to 80% if the root causes (i.e. osteoporosis and...
Risk of MRONJ from intravenous bisphosphonate/denosumab therapy

According to the AAOMS position paper, osteoporotic patients receiving yearly administration of bisphosphonate therapy via the IV route were found to have a 0.017% risk of developing MRONJ. This percentage did not appear to increase even when the duration of therapy was longer than four years. Other studies reported a risk of up to 0.35% in patients on IV bisphosphonate. The risk of developing MRONJ while on denosumab was reported to be around 0.04%, although research conducted in the United Kingdom reported a risk of up to 0.3%. Osteoporotic patients on IV bisphosphonate or denosumab therapy are generally given much lower dosages and frequencies of medication, as compared to oncology patients on therapy for prevention of skeletal-related events and metastases in cancer.

Other medical factors were found to increase the risk of developing MRONJ. These include: duration of therapy, chemotherapy, erythropoietin therapy, renal dialysis, hypothyroidism, corticosteroid therapy and diabetes mellitus. The patient’s age, smoking habit and obesity are also significant contributing factors. It is important to emphasise good dental hygiene and practices in these patients to avoid the rare side effect of MRONJ.

Box 1 summarises the risk of developing MRONJ associated with various types of therapy.

WHAT CAN I DO IN MY PRACTICE?

Fig. 1 summarises the recommended management of osteoporotic patients, including those with MRONJ.

Dental treatment in patients on antiresorptive therapy

Dental infections and invasive treatments are the most common factors that result in the development of MRONJ. Teeth that require extraction are often associated with periapical and periodontal infections. Infection and inflammation, dental extractions, irritation and trauma to the oral mucosa from ill-fitting oral appliances can result in a increased risk of developing MRONJ. However, it should be noted that MRONJ can also occur spontaneously even without any obvious pre-existing dental infections or treatment, and the risk of MRONJ in patients undergoing dental treatment should be assessed with this in mind. Studies have shown that 20%–33% of cases of MRONJ occur spontaneously in patients on antiresorptive therapy.

The incidence of MRONJ in patients treated with antiresorptive therapies was reported to be as high as 0.1% to 0.21%, if they were on oral bisphosphonates therapy for more than four years.
medications was reported to be comparable to the risk of MRONJ developing spontaneously in patients only exposed to placebo medications (0.017%–0.04% vs. 0%–0.02%, respectively). Box 2 provides useful information for physicians with patients on antiresorptive therapy who require dental treatment.

**Prevention of MRONJ**

General practitioners should optimise patients’ medical condition prior to commencement of antiresorptive therapy. Modifiable medical conditions and factors that increase the risk of MRONJ should be properly managed. Physicians should advise their patients to stop smoking and reduce alcohol intake. Patients should be referred to a dental practitioner for dental clearance to rule out and treat any dental diseases before starting antiresorptive therapy. Adequate time of approximately one month or more should be provided for the dentist to complete treatment of acute conditions, as well as to put in place a preventive oral hygiene plan. Management of any chronic dental conditions can be started concurrently while managing the acute problems.

A thorough dental clearance includes a thorough clinical and radiographic examination. Proper oral hygiene and preventive practices must be instituted. Dietary modifications to reduce sugar intake should be done to prevent dental caries (tooth decay) and the need for dental extractions. A study by Dimopoulos et al demonstrated a significant reduction in MRONJ occurrence in patients who received preventive dental treatment prior to commencing therapy. These findings were further supported by Bonacina et al and Vandone et al, who discovered no new cases of MRONJ in patients who underwent dental clearance, and that the overall risk of developing MRONJ was halved.

Acute infections such as abscesses of pulpal or periodontal origin must be treated to remove the source of infection. This treatment should be carried out prior to or even during antiresorptive therapy, as the presence of infection and inflammation is a well-recognised risk factor for development of MRONJ. Chronic periodontal conditions must also be managed to avoid further bony and gingival recession and subsequent tooth loss. Dental therapy aimed at removing infection and inflammation can be done in a primary dental care setting and as part of a preventive treatment strategy against MRONJ. It has been reported that dental extraction is a major factor in the development of MRONJ, such as in Filleul et al, where 67% of cases of bisphosphonate-related osteonecrosis of the jaw were precipitated by dental extractions. This was similar to the range reported by AAOMS of 52%–61%, which corresponded to a risk of 0.09%–0.34%. However, it is still necessary to actively treat or remove teeth that can be a source of infection and inflammation, in order to avoid an

---

**Box 2. Dental treatment for patients on antiresorptive therapy**

- Risk of developing MRONJ in patients on oral bisphosphonates is low.
- Slightly higher risk of developing MRONJ in patients on > 4 years of oral bisphosphonates, IV bisphosphonates or denosumab.
- Routine dental treatment, including extractions and implant placement, can be carried out in patients with ≤ 4 years of oral bisphosphonates.
- Discussion of risks and benefits must be done if invasive dental treatment is needed in patients on > 4 years of oral bisphosphonates, IV bisphosphonates and denosumab. Alternative treatment options should be considered.
- Following extraction or surgical treatment, close monitoring is needed to observe for mucosal healing. Prompt referral to a specialist is recommended if MRONJ is detected.
is dependent on the stage of the condition, as well as the corresponding symptoms and effects on the patient’s daily life and functioning. Prompt referral to an oral and maxillofacial surgeon for further management is warranted. Treatment of MRONJ ranges from observation, local debridement or sequestrectomy, to resection of necrotic bone with or without reconstruction with vascularised free flap.  

**TAKE HOME MESSAGES**

1. Osteoporosis and its associated risk of fractures is a major, growing healthcare issue in Singapore’s ageing population.
2. Osteoporotic fractures are associated with increased morbidity and mortality.
3. Antiresorptive therapies (e.g. bisphosphonates and denosumab) are proven to reduce fracture risk in osteoporotic patients.
4. The risk of MRONJ formation in osteoporotic patients on antiresorptive therapy is real but low.
5. Routine dental treatment and invasive dental treatment such as extractions and implants can be carried out for the majority of osteoporotic patients on antiresorptive therapy.

---

**ABSTRACT**

Osteoporosis is a major, growing healthcare issue. This is especially of concern in an ageing population like that of Singapore. Osteoporotic patients are at risk of fractures, which can result in increased morbidity and mortality. The use of antiresorptive therapy with bisphosphonates or denosumab has been proven to reduce fracture risk. However, the use of these medications has rarely been associated with the development of osteonecrosis of the jaw. A potentially debilitating condition affecting one or both jaws. Appropriate understanding of the patient’s antiresorptive therapy regime, as well as early institution of preventive dental measures, can play an important role in preventing medication-related osteonecrosis of the jaw (MRONJ). Regular monitoring and prompt referral to specialist care is warranted for patients with established MRONJ.

**Keywords:** bisphosphonates, osteonecrosis, osteoporosis, MRONJ
REFERENCES


SINGAPORE MEDICAL COUNCIL CATEGORY 3B CME PROGRAMME
(Code SMJ 201802A)

1. Osteoporosis is a major healthcare issue worldwide.
2. The estimated mortality rate one year after experiencing a hip fracture is less than 5%.
3. Men are at a higher risk for hip fracture compared to women.
4. Singapore has one of the highest incidence rates of hip fractures in Asia.
5. Antiresorptive medications such as bisphosphonates have been proven to reduce fracture risk in osteoporotic patients.
6. Medication-related osteonecrosis of the jaw (MRONJ) is a reported side effect of antiresorptive therapy.
7. Patients should be referred for dental clearance prior to starting antiresorptive therapy.
8. General dental practitioners should not manage patients on antiresorptive therapy.
9. The risk of developing MRONJ in osteoporotic patients on antiresorptive therapy is higher than the chance of sustaining an injury from a road traffic accident in Singapore.
10. Proper informed consent, including discussion of the risks of developing MRONJ, must be obtained from patients on antiresorptive therapy prior to doing any invasive dental treatment.
11. Close monitoring must be done to observe for healing after invasive dental treatment.
12. Patients who received dental clearance have a lower risk of developing MRONJ.
13. Acute dental infections must be treated to remove the infectious source, so as to avoid development of MRONJ.
14. All acute dental infections in patients on antiresorptive therapy for osteoporosis must be referred for specialist management.
15. Patients on intravenous bisphosphonate for oncology treatment have a higher risk of developing MRONJ.
16. Elective dental treatment should not be carried out on patients with diagnosed MRONJ. Referral to specialist care is needed.
17. Patients on concurrent corticosteroid and antiresorptive therapy are at a higher risk of developing MRONJ.
18. Development of MRONJ is a potential side effect of denosumab therapy.
19. The management of MRONJ is dependent on the stage, symptoms and effects of the condition on the patient.
20. Using minimally traumatic techniques when doing invasive dental procedures on patients on antiresorptive therapy is not necessary.

Doctor’s particulars:
Name in full: __________________________________________ MCR no.: ____________________________________________
Specialty: ___________________________ Email: _____________________________________________________________

SUBMISSION INSTRUCTIONS:
Visit the SMJ website: http://www.smj.org.sg/current-issue and select the appropriate quiz. You will be redirected to the SMA login page.
For SMA member: (1) Log in with your username and password (if you do not know your password, please click on ‘Forgot your password?’). (2) Select your answers for each quiz and click ‘Submit’.
For non-SMA member: (1) Create an SMJ CME account, or login with your SMJ CME username and password (for returning users). (2) Make payment of SGD 21.40 (inclusive of 7% GST) via PayPal to access this month’s quizzes. (3) Select your answers for each quiz and click ‘Submit’.

RESULTS:
(1) Answers will be published online in the SMJ April 2018 issue. (2) The MCR numbers of successful candidates will be posted online at the SMJ website by 4 April 2018. (3) Passing mark is 60%. No mark will be deducted for incorrect answers. (4) The SMJ editorial office will submit the list of successful candidates to the Singapore Medical Council. (5) One CME point is awarded for successful candidates.