Proceedings of the closed round table and *Italian Consensus* on the Medication-Related OsteoNecrosis of Jaws (MRONJ) at the Symposium of Italian Society of Oral Pathology and Medicine (SIPMO) Ancona, 20 October 2018 – Part II

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C. Practices at risk of inappropriateness in prevention of MRONJ and good practices

Very recently, some Italian experts of the SIPMO ONJ board have defined in an open-access peer-reviewed document the new paradigms by SIPMO

on preventive dental management in patients at risk of MRONJ, prior to and during/after the administration of the aforementioned ONJ-related drugs [1]. The MRONJ Italian Consensus has confirmed the principles declared by the SIPMO ONJ board in terms of prevention. Briefly, they believe that, for reducing the risk of MRONJ, key figures are prescribers, dentists and oral hygienists by applying correct protocols of 1) primary prevention for both pre-treatment and in-treatment patients, and 2) secondary prevention (i.e. early diagnosis of MRONJ).

1) Primary prevention for MRONJ mainly means elimination/reduction of oral and dental risk factors, it is targeted at restoring and/or maintaining good oral health and reducing the risk of an onset of pathological conditions or any other negative event. This approach has the greatest impact when aimed at protecting constantly the oral health of patient at risk of MRONJ.

   Initially, about fifteen years ago, MRONJ (at that time labeled BRONJ) has been thought to be associated to dental extraction in patients already being treated with bisphosphonates. More recently, the presence of infection at dental-periodontal and peri-implant locations has been underlined as being one of the main local risk factors of developing MRONJ, often being the main reason of surgical procedures of dental extraction or implant removal. It is advisable to consult the full text by SIPMO ONJ board for the division by risk categories, for a complete listing of systemic and local risk factors.

   A new emerging aspect is that primary prevention should be performed not only prior to taking the ONJ-related drugs, but also during and after the treatment with those drugs, in order to eliminate any infective outbreaks of MRONJ. It is the responsibility of the dentist to accurately assess risk factors leading to the development of MRONJ and suggest a strategy for removing these factors. The dentist must also stress the importance of maintaining effective dental hygiene (together with dental hygienist), including regular check-ups, for the patient. Both are necessary for maintaining oral health, reducing the outbreak of MRONJ, and/or detecting possible signs of the early symptoms of this disease.

   Finally, dental procedures for the patient (both cancer and non-cancer) in pre-treatment and in-treatment phases can be divided in invasive and non-invasive ones, all indicated in these patients when related to the control

of local risk factors. Of great assistance in this regard is the use of leaflets, such as those which can be free downloaded, https://www.unipa.it/dipartimenti/di.chir.on.s./. content/documenti/ONJ-Leaflet-_SIPMO-by-Di-Fede-Campisi20-02-17.pdf. The app DoctOral® provides an open-access consultation of guided paths and recommendations regarding the dental management of patients at risk of MRONJ; it is free available both for Android, https://play.google.com/store/apps/details?id=com.olgadifede.olgapp&hl=it and iOS system [2], https://itunes.apple.com/it/app/doctoral/id1232326837?mt=8.

2) Secondary prevention or early diagnosis is the second pillar in the strategy against MRONJ, since we know that the earlier the MRONJ stage is, its prognosis will be better. With respect to the diagnostic work-up, the main problem is the possible under-diagnosing of MRONJ cases without bone exposure. A recent multicenter study [3] has demonstrated that the use of the traditional AAOMS [4,5] and ASBMR case definition [6] induces clinicians up to a quarter of undiagnosed BRONJ cases. Thus, in order to avoid any underestimation of MRONJ, care should be taken with respect to the definition adopted and to the use of the imaging studies in cancer and osteometabolic patients, who are already receiving MRONJ-associated therapies in combination or alone [7].

Practices at risk of inappropriateness

#1 keeping teeth with endodontic and/or periodontal diseases at uncertain prognosis only for avoiding, in patients at risk of MRONJ, extractive invasive procedures.

#2 extracting, only for preventive purposes, teeth in partial or total inclusion in patients pre-treatment with drugs at risk of ONJ.

#3 scheduling in cancer patients the first dental check-up only after diagnosis of bone metastases.

#4 omitting in osteometabolic patients dental check-ups for oral health status assessment and relative preventive dentistry actions.

#5 omitting periodic dental check-ups for edentulous patients or wearing removable prostheses, if they are at risk of MRONJ.

#6 underestimating the usefulness of imaging performed for monitoring neoplastic status with respect to ONJ diagnosis.

Good practices

#1 extract teeth with endodontic and/or periodontal diseases, in patients at risk of MRONJ, when conservative approach is not possible and a good prognosis is not guaranteed.

#2 maintain teeth in partial or total inclusion, if no signs and/or symptoms of inflammation/infection are presents (e.g. dysodontiasis, pericoronaritis, decay, periodontal disease, caries and /or root resorption of the second molar, mechanical trauma on the surrounding mucous membranes).

#3 schedule in cancer patients the first dental check-up as soon as possible, preferably during the tumour staging process in the pre-treatment phase.

#4 consider in osteometabolic patients a potential gradient of MRONJ risk according to

a) Administration and duration of treatment with ONJ-related drugs [8–11] and

b) Eventual presence of comorbidities and further medical therapies indirectly associated; assess, during the prescription of the ONJ-associated drugs, the oral health status even by a questionnaire (bypassing the preliminary dental check-up); schedule semi-annual dental visits (the first within 6 months from the first assumption of anti-resorptive drugs).

#5 schedule preventive dental check-ups even in patients at risk of MRONJ but edentulous with or without removable dentures, in order to intercept and correct any injury on the oral mucosa.

#6 consider useful, in cancer patients, the imaging investigations of II level (e.g. PET, bone scintigraphy) already performed for detecting early radiological signs of MRONJ, especially before prescribing further specific imaging.

D. Practices at risk of inappropriateness in dental management and good practices for patients at risk of MRONJ

As before illustrated, the SIPMO ONJ board has defined in an open-access peer-reviewed shared protocols for dental management in patients at risk of MRONJ, prior to and during/after the administration of the aforementioned ONJ-related drugs [1]. The MRONJ Italian Consensus has adopted the principles and good practices stated by the SIPMO ONJ board with respect to dental management. In particular, as follows, some hot points were here emphasized: implants in cancer and osteometabolic patients, antibiotic prophylaxis, healing for I vs II intention.

Practices at risk of inappropriateness

#1 following an implant rehabilitation in cancer patients who have to take or are taking MRONJ-associated drugs.

#2 considering as contraindicated, in an absolute sense, implant rehabilitation in ostometabolic patients taking MRONJ-associated drugs.

#3 prescribing antibiotic prophylaxis before dental therapies as non-invasive for bone.

#4 practicing extractive procedures without removing, even if necessary, alveolar bone, and plan healing for second intention (especially with cortisone administration).

Good practices

#1 do not perform in cancer patients implant rehabilitation and plan non-surgical rehabilitation.

#2 practice in osteometabolic patients implant rehabilitation taking into account the cumulative dose of drug already taken, the periodontal status, any smoking, comorbidities and other drugs. Sharing with the patient a hypothetical medium-long term risk of MRONJ related to peri-implantitis and bone mini-cracks. Plan informed consent and six months follow-up.

#3 recommend always, in patients at MRONJ risk, antibiotic prophylaxis when surgical procedures involving dento-alveolar process or maxillary bones

are planned (e.g. extractions, periodontal/endodontic surgery, implants, pre-implant surgery).

#4 practice extractive or surgical procedures planning the healing for first intent with the clot maintenance.

Keywords: MRONJ, ONJ (osteonecrosis of the jaws), BRONJ (Bisphosphonate-Related Osteonecrosis of the Jaw), risk of inappropriateness, MRONJ Italian Consensus, SIPMO, SIdCO

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