

# ONJ UPDATE 2024

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### Abstract Submission FORM

**CAN PENTOXIFYLLINE AND AND TOCOPHEROLS IMPROVE THE MANAGEMENT OF PATIENTS WITH MEDICATION-RELATED OSTEONECROSIS OF THE JAW?**

SECTION: 4B

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#### **Background.**

Pentoxifylline is a methylxanthine able to inhibit inflammation and promote peripheral blood flow. Indeed, among other activities, it decreases leukocyte adhesion to endothelial cells and increases red blood cell deformability. Tocopherols include various methylated phenols that can protect cell membranes from oxidative stress and reduce inflammation and tissue fibrosis. Due to these effects, the combined use of pentoxifylline and tocopherols (PENTO-protocol) is the current standard drug-therapy in Osteoradionecrosis of the jaw. A few reports described the clinical efficacy of the PENTO-protocol also in Medication-related osteonecrosis of the jaw (MRONJ) but data are still scanty. Currently the PENTO-protocol is not included in the clinical-therapeutic recommendations published by SIPMO-SICMF (the most authoritative source at present). We report our clinical experience in 12 MRONJ patients treated with the PENTO-protocol.

#### **Patients and methods.**

In 2023, patients with a new diagnosis of MRONJ and referred to the Oral Medicine and Oral Oncology Unit of the San Luigi Gonzaga Hospital in Orbassano, were adjunctively treated with the PENTO-protocol (Pentoxifylline 400 mg twice a day and Tocopherols 800 IU once a day). The current recommendations were followed in prescribing other medical treatments (antibiotics, chlorhexidine, and painkiller) and planning surgery.

#### **Results.**

Twelve patients received the PENTO-protocol; 4 had MRONJ related to treatment for osteometabolic diseases and 8 related to treatment for bone metastases. MRONJ involved the maxilla in 4 patients and the mandible in 8 patients. All cases were classified as stage 1 or 2.

At the first evaluation pain and/or acute infection were variably present. 5 out of 12 patients complained of pain in the absence of infection; 7 had signs and symptoms of an acute infection (unrelated to pain).

Indication to surgery was given in 9 out of 12 patients, 2 spontaneous sequestrectomies were observed while preparing surgery and a wait and see approach was adopted in 3 patients, due to systemic conditions.

As PENTO-protocol results, we obtained and maintained a complete symptom remission in all the 5 patients with pain (3 also treated with antibiotics due to acute infection).

No relapse of symptoms/infections were reported neither in patients waiting for surgery nor for patients allocated in the wait and see group.

No side effects were observed.

#### **Conclusions.**

Mechanisms of action of Pentoxifylline and Tocopherols in treatment of bone necrosis (either MRONJ or Osteoradionecrosis) have not been fully elucidated yet. The present report supports a potentially positive effect of the PENTO-protocol, as an adjunctive treatment in MRONJ patients, particularly useful in pain control.

Our observation is in agreement with previous reports describing the PENTO-protocol as able to hinder bone necrosis development and to favor its delimitation by reducing inflammation and improving bone perfusion. Of interest we frequently observed a good control of pain.

In the absence of side effects PENTO-protocol can be considered a non-invasive, well tolerated, and non-expensive treatment which could be considered as valuable adjunctive treatment in MRONJ.

#### **REFERENCES:**

1. Cavalcante RC, Tomasetti G. Pentoxifylline and tocopherol protocol to treat medication-related osteonecrosis of the jaw: A systematic literature review. *J Craniomaxillofac Surg.* 2020 Nov;48(11):1080-1086. doi: 10.1016/j.jcms.2020.09.008. Epub 2020 Sep 18. PMID: 32998853.
2. Colapinto G, Goker F, Nocini R, Albanese M, Nocini PF, Sembronio S, Argenta F, Robiony M, Del Fabbro M. Outcomes of a Pharmacological Protocol with Pentoxifylline and Tocopherol for the Management of Medication-Related Osteonecrosis of the Jaws (MRONJ): A Randomized Study on 202 Osteoporosis Patients. *J Clin Med.* 2023 Jul 13;12(14):4662. doi: 10.3390/jcm12144662. PMID: 37510777; PMCID: PMC10380687.

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