A new effective treatment protocol for bisphosphonate associated osteonecrosis of the jaws by using Low-level-laser therapy combined with conservative dentoalveolar surgery

Hafner S., Otto S., Schiel S., Breitfeld M., Mast G., Ehrenfeld M.
Department of Oral and Maxillofacial Surgery (Ludwig-Maximilians-University), Munich

Figure 1. Patient (66a, D: prostatic carcinoma) with osteonecrosis in the upper jaw (17-18) after bisphosphonate therapy (Zometa).

Osteonecrosis of the jaws is a well known issue adverse side effect of bisphosphonate therapy. Bisphosphonates are used to treat patients with osteolytic bone metastasis (e.g. mammary or prostatic carcinoma), multiple myeloma, osteoporosis, Paget´s disease of bone and hypercalcemia syndrom. Their primary mechanism of action is inhibition of osteoclastic resorption of bone. Within the past 4 years many papers reported that bisphosphonate use, especially intravenous nitrogen-containing preparations, may be associated with osteonecrosis of the jaws. Oversuppression of bone turnover is probably the primary mechanism for the development of this condition, although there may be contributing comorbid factors. There are no sufficient current treatment strategies to manage these osteonecrosis. Extensive resection has not consistently resulted in wound closure and may lead to worsening or progression of disease. Sufficient therapy should reduce the local oversuppression of bone turnover by stimulating and inducing the invasion of osteoclasts.

Low-level laser therapy (LLLT) is being used in many countries to speed up the healing of wounds (1, 2, 5, 6). This therapy seems to be effective in the regeneration of soft tissue, modulating inflammation and accelerating cell proliferation and bone healing process (3, 4, 5, 6). Some studies analysed the effect at wavelengths of 633 nm and 660 nm on bone structure and cell activity. It was shown that irradiation increased the number of osteoclasts and stimulated the growth of the trabecular bone area and the concomitant invasion of active osteoclasts (3, 6). Increasing hydroxyapatite concentration and osteoblast activity with improvements in the organic matrix formation and mineralization was also found (3, 6).

Methods: In our study we performed a treatment protocol by preferring a conservative débridement of necrotic bone combined with Low-level laser therapy (diode-softlaser/200mW/685nm, Physiolaser Olympic) including n=42 patients (49-83a, 32 female, 10 male) with bisphosphonate associated osteonecrosis of the jaws. We used softlaser application before and after surgery at the locations of osteonecrosis directly on the bone and the environing tissue. Bisphosphonate-treatment was discontinued if it was medically sustainable and supported our therapy by prescripting antibiotics (amoxicillin/clavulanic acid or clindamycin). Low-level laser therapy was started in short intervals (2-3 a week, 4-6 Joule/cm²). If we saw a good progress in healing we reduced the treatment to once a week until healing was completed.

LLLT

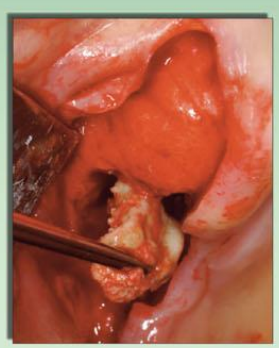

Figure 2. Sequestrotomy after one week of Low-level laser therapy.

LLLT

Figure 3. Softlaser application after surgery (4-6 J/cm²) on the environing tissue.

LLLT

Figure 4. Wound dehiscence 6 days after surgery, healing by granulation.

LLLT

Figure 5. Wound healing is completed 4 weeks after surgery and in a staple condition 10 weeks after surgery

Figure 6. Physiolaser Olympic (Reimers & Janssen). Any configuration between 635 to 904 nm is possible. We used a 200mW/685nm probe.

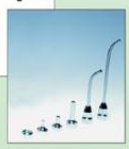

Figure 7. Special applicators

Results: This new regenerative therapy concept – used in 42 cases with one or more sites of osteonecrosis - showed good clinical results with an effective infection management (no major complications such as mandibulectomy, abscess or systemic inflammation although some of the patients were in chemotherapeutical treatment during the LLLT, occurred). In addition an effective pain control was reported by the patients. Healing or significant improve of the local condition could be seen in 20 patients within the first weeks after starting the treatment. The other n=22 patients are still in therapy while a major part of these patients shows continuing progress in wound healing. Low-level laser therapy seemed to be most effective if the treatment is carried out immediately after surgery.

Conclusions: In our study we determined a effective treatment protocol for bisphosphonate associated osteonecrosis of the jaws by using softlaser combined with dentoalveolar surgery. The key of therapy could be the local reduction of oversuppression of bone turnover by stimulating osteoclasts using Low-level laser therapy (LLLT). The removal of the antiangiogenic effects of the drug on the soft tissues and periosteum combined with the angiogenetic and osteogenetic effect of the softlaser therapy may play a role in healing (3, 4, 6). Some studies indicate that bone irradiated with softlaser shows increased osteoclastic and osteoblastic proliferation, collagen deposition, and bone neoformation (3, 6). Vascular responses to softlaser phototherapy were also suggested as one of the possible mechanisms responsible for the positive clinical results observed following LLLT (6). More clinical studies are needed to evaluate and optimize the mode of softlaser application and to improve the success of this regenerative therapy concept.

References

1. Herascu N, Velciu B, Calin M, Savastru D, Talianu C. Low-level laser therapy (LLLT) efficacy in post-operative wounds. Photomed Laser Surg. 2005; 23(1): 70-73

2. Simunovic Z, Ivankovich AD, Depolo A. Wound healing of animal and human body sport and traffic accident injuries using low-level laser therapy treatment: a randomized clinical study of seventy-four patients with control group. J Clin Laser Med Surg. 2000;18(2): 67-73

3. Nicola RA, Jorgetti V, Rigau J, Pacheco MT, dos Reis LM, Zangaro RA. Effect of Low-Power GaAlAs Laser (660 Nm) on bone structure and cell activity: an experimental animal study. Lasers Med Sci. 2003; 18(2): 89-94

4. Silva Júnior AN, Pinheiro AL, Oliveira MG, Weismann R, Ramalho LM, Nicolau RA. Computerized Morphometric Assessment of the Effect of Low-Level Laser Therapy on Bone Repair: An Experimental Animal Study. J Clin Laser Med Surg. 2002; 20: 83-87

5. Karu T. Molecular mechanism of the therapeutic effect of low-intensity laser radiation. Lasers Life Sci. 1988; 2: 53-74

6. Barushka O, Yaakobi T, Oron U. Effects of low energy-laser (He-Ne) irradiation on the process of bone repair in the rat tibia. Bone 1995; 16: 47-55

LMU KLINIKUM DER UNIVERSITÄT MÜNCHEN

LMU KLINIKUM DER UNIVERSITÄT MÜNCHEN