Sterile gel based on sodium hyaluronate and amino acids: bone healing biological mechanism in patients treated for third stage bisphosphonates-related osteonecrosis of the jaws (BRONJ)

Massimo Corsolini¹, Daniela Di Venere¹, Simonetta Franco², Simona Miccoli², Eugenio Maiorano³, Gianfranco Favia⁴

¹Assistant Professor – Dental School, University of Bari, Italy
²Student – Dental School, University of Bari, Italy
³Full Professor – Pathological Anatomy, University of Bari, Italy
⁴Full Professor – Dental School, University of Bari, Italy

Objectives: The aim of this study was to carry out clinical and radiographic outcomes of bone healing using a new medical device, a sterile gel formulation of sodium hyaluronate and amino acids Gly-Leu-Pro-Lys (AMINOGAM®) in treatment of third stage bisphosphonates-related osteonecrosis of the jaws (BRONJ).

Materials and methods: We selected 52 third stage BRONJ patients divided in two groups according to systemic pathology: Neoplastic diseases group that includes 21 patients; Non-neoplastic diseases group of 11 patients. According to AAOMS guidelines, all patients suspended bisphosphonate therapy three-six months before the surgery and were subjected to antibiotic therapy: three courses of 1g ceftriaxone intramuscular injection/die and 250mg metronidazole oral tablet two times/die for 8 days with 10 days rest between each course. Surgical treatment provides local anesthesia without vasoconstrictor, segmental resection, Piezosurgery osteoplasty, intracavitary intraoperative use of gel to fill up residual bone defect and a first application upon the stitches (sandwich technique). Our procedure includes using of gel 4 times/die till to complete mucosal healing. Finally a clinical and radiographic follow-up by orthopantomograph and CT examinations at 3, 6, 12 and 24 months was carried out.

Results: Clinical outcomes showed complete hard and soft tissue healing in all post-surgical sites, with a difference between two groups: neoplastic diseases group needed a longer soft wound healing time of 5 days compared to non-neo-plastic diseases group. Radiographic outcomes show radiolucency areas decreasing due to gel direct osteoinductive effect with a faster osteo regeneration time in non-neoplastic diseases group: 15% difference between ossification level at 3 and 6 months. Gel preparation of sodium hyaluronate and amino acids enhances angiogenesis, fibroblast and osteoblast proliferation, collagen biosynthesis and production of growth factors as evidenced by MTT test and alkaline phosphatase histochemical staining. In vivo and in vitro studies have suggested that hyaluronic acid plays important roles in bone wound healing by enhancement of osteoblast differentiation through the down-regulation of BMP-2 antagonists. Lysine and proline regulate collagen matrix synthesis during osteogenesis.

Conclusions: Sodium hyaluronate and amino acids gel formulation decreases postoperative pain, swelling and infective complications after surgery by surgical wound mechanical protection. This new medical device is biocompatible, extremely cheap, safe and useful in all surgical procedure in order to obtain a faster healing of oral hard and soft tissues, specially in BRONJ that are often prone to difficult, slow and complicated recovery.