Early and Late Integration of Biphasic Calcium Phosphate Bioceramics Mixed with Autologous Mesenchymal Cells in Osteoporotic Rabbit's Jaw

Aleksandrs Grisulonoks [1], ***Inese Cakstina*** [2], ***Vita Zalite*** [3], ***Ilze Salma*** [1], ***Andrejs Skagers*** [1], ***Vadims Klimecs*** [1]

[1] *Rīga Stradiņš University, Department of Oral and Maxillofacial Surgery, Latvia*
[2] *University of Latvia, Laboratory of Biodosimetry and Bioanalistical Methods*
[3] *Riga Technical University, Rudolfs Cimdins Riga Center for Development and Innovation of Biomaterials, Latvia*

Introduction. Formation, maintenance, and repair of bone tissue involve close interlinks between two stem cell types housed in the bone marrow: the haematologic stem cell originating osteoclasts and mesenchymal stromal cells generating osteoblasts. In osteoporosis, increased bone fragility and susceptibility to fractures results from increased osteoclastogenesis and insufficient osteoblastogenesis. Because of their ability to self-renew and differentiate, mesenchymal stem cells are the source *in vivo* for replacing lost cells in high-turnover tissues during the life of an organism.

Aim, Material and Methods. The aim of this study was to detect possible difference in reactogenicity of biphasic calcium phoshates with and without autologous mesenchymal cells after implantation in osteoporotic jaw bone. Experimental osteoporosis was induced in 2.5-year-old female rabbits by ovarioectomy and 1 mg/kg of methylprednisolone daily for 8 weeks. On the first rabbit's group the holes were created in bouth angles of lower jaw; on the left side filled with HAP/TCP 90/10 granules; on the right side – the same granules mixed with autologous fat tissue-derived mesenchymal cells.

Results. After 3 and 6 months, bone samples for Hem/Eoz staining and mBiotin-streptavidin method for immunohistochemical detection of collagen I, ON and OP were prepared. Semi-quantitative counting method was used for quantification of relative frequency of immunohistochemically detected tissue degrading collagen I, ON and OP. Morphomotric measurements were performed to notice differences between cortical and trabecular bone with and without mesenchymal stem cells. It was discovered that supplement of HAP/TCP 90/10 granules with autologous mesenchymal cells does not lead to significantly faster rates of osteoporotic bone healing controlled by methods of traditional hystology and imunohistochemistry for expression of osteonectin, osteopontin and collagen I. Such result may be based on low regenerative potency of mesenchymal cells produced in old animals. It does not exclude elucidation how cell-based therapies impact bone healing and identify autologous mesenchymal cells as an attractive candidate for cell-based skeletal regenerative therapy. Morphometric measurement of osteoporotic bone osseointegrated with Hap/TCP (90/10) granules implantated in rabbit lower jaw with and without autologous mesenchymal cells after 3 and 6-month observation period was without statisticaly significant morphological differences. Mainly healthy bone granules were embeded in the new formed bone, but in osteoporotic bone surrounded by fibrous tissue layer, more thick in samples, mesenchymal cells were added.

Conclusions. The osteoporotic old rabbit jaw bone defect with addition of autologous mesenchymal cells after immunohistochemical analysis were without significant influence on collagen I expression, osteonectin or osteopontin. Integration of HAP/TCP granules in defect of osteoporotic rabbit jaw is through encapsulation by fibrous tissue while in healthy bone occurs osseointegration. There were detected no signs of inflammation reaction in both bone types.