Abstract

Osteoporosis is a disease of the bone metabolism which is characterised with a decrease of bone substance. The cause of this disease is the imbalance between the creation of a new bone substance by osteoblasts and the resorption of a bone tissue by osteoclasts, in favour of the bone resorption. The risk group of the development of this disease are women after menopause, who naturally register a decline of the estrogen hormone. Estrogen operates as an inhibitor of proosteoclastic factors such as receptor activator of NFκB ligand (RANKL), interleukin (IL)-1, IL-6 or TNF-α. The imbalance of the bone metabolism can also be caused by a disbalance in the production of Prostaglandin E2 (PGE2) and 1α,25-dihydroxyvitamin D_3. They are strong mediators which can both stimulate and inhibit an osteoclastogenesis *in vitro* in concordance with the conditions of the culture/co-culture. This thesis focuses on the examination of an influence of those mediators (PGE2 in the concentration of 10^{-6} M and 10^{-8} M; 1α,25-dihydroxyvitamin D_3 in the concentration of 10^{-8} M and 10^{-9} M) on the osteoclastogenesis from the rat PBMC at the presence of osteoblasts, with or without the combination of proosteoclastic factors macrophage colony-stimulating factor (M-CSF) and RANKL. Osteoclastogenesis was stimulated if PGE2 and 1α,25-dihydroxyvitamin D_3 were combined with M-CSF and RANKL with the exception of PGE2 10^{-6} M, which recorded the inhibitory effect. The exclusive addition of PGE2 or 1α,25-dihydroxyvitamin D_3, without the combination of M-CSF and RANKL, was not sufficient enough for the initiation of the osteogenesis. A potential of the osteoclastogenesis was tested within the cells isolated from rats with osteoporosis induced by ovariectomy. PBMC isolated from these individuals presented the ability of the differentiation in osteoclasts at the presence of osteoblasts with no other added supplementation. In addition, the effect of PGE2 and 1α,25-dihydroxyvitamin D_3 was observed on the production of inflammatory cytokines IL1-β, IL-6 and TNF-α, which level is increased in the blood of the osteoporotic individuals. The highest levels were recorded on 14th day of the co-culture. TNF-α was increased mainly during the supplementation of M-CSF, RANKL. IL-6 was the highest during the combination of M-CSF and RANKL with 1α,25-dihydroxyvitamin D_3 10^{-8} M. IL-1β was not detected at any of the monitored group.

Key words: osteoblasts, PBMCs, osteoclastogenesis, osteoclasts, M-CSF, RANKL, PGE2, 1α,25-dihydroxyvitamin D_3, osteoporosis, ovariectomy, cytokines IL-1β, IL-6, TNF-α