POSSIBLE PLEIOTROPIC EFFECTS OF ATORVASTATIN ON BONE MARROW DERIVED MESENCHYMAL STEM CELLS

Samáková A.[1], Sabová N.[1], Valašková S.[1], Sprušanský O.[1], Gažová A.[2], Maďarič J.[3], Kyselovič J.[4]

[1]Department of Pharmacology and Toxicology, Comenius University in Bratislava, Faculty of Pharmacy, Bratislava, Slovakia
[2]Institute of Pharmacology and Clinical Pharmacology, Comenius University in Bratislava, Faculty of Medicine, Bratislava, Slovakia
[3]National Institute of Cardiovascular Diseases, Bratislava, Slovakia
[4]5th Department of Internal Medicine, Comenius University in Bratislava, Faculty of Medicine, Bratislava, Slovakia

Introduction: Critical limb ischemia together with ischemic heart disease and ischemic stroke belongs to the most serious ischemic diseases. Although both the pharmacological and surgical approaches may restore the functions of affected arteries, they are not able to promote their regeneration and functional recovery. A promising novel option represents autologous stem cell transplantation with bone marrow derived mononuclear stem cells. Statins, inhibitors of 3-hydroxy-3-methyl-glutaryl-CoA reductase, are widely used hypocholesterolemic drugs with many pleiotropic effects, which can increase the effectiveness of stem cell therapy.
Aim: To assess the pre-treatment of atorvastatin on bone marrow derived mesenchymal stem cells (BM-MSCs) characteristics, survival and mRNA expression levels *in vitro.*
Methods: Bone marrow derived mononuclear cells from patients with critical limb ischemia were characterised by flow cytometry. The third passage of BM-MSCs was used to pre-treatment with atorvastatin and the expression on mRNA levels of selected genes was assessed by quantitative RT-PCR method.
Results and conclusion: We found that atorvastatin pre-treatment of BM-MSCs significantly supressed the expression of IGF1 and cKIT, significantly increased the expression of VEGFA and HMGCR, while the expression of HGF and FGFR1 wasn't altered. These results suggest that statins are able to modulate MSCs secretome through possible mechanism PI3K/Akt pathway and thereby affect the behaviour of surrounding cells and microenvironment of implantation.
Acknowledgment: The study was approved by the ethics committee for research projects established at the National Institute of Cardiovascular Diseases in Bratislava. This project was supported by the grants MZ SR 2016/13-FAUK-1, UK/335/2019 and FaF/9/2019.