ATORVASTATIN INFLUENCE ON GATA4, TBX5 AND MEF2C TRANSCRIPTION FACTORS OF FIBROBLAST PHENOTYPIC REPROGRAMMING.

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Background: The heart is rich in fibroblasts after damage, so they have become a potential source of alternative heart cell therapy. Thanks to the phenotypic fibroblast plasticity, the techniques of their reprogramming and transdifferentiation are gradually revealed in the so- induced cardiomyocytes (iCM). This includes mainly the expression of transcription factors GATA4, TBX5, and MEF2C, which are known to promote cardiac development as well as proliferation and function of cardiomyocytes. It has also been demonstrated that local tissue microenvironment as well as modulation of different signaling pathways influence the success of this reprogramming. Thus, in our hypothesis we assume that statins, HMG-CoA reductase inhibitors could interfere with the expression of transcription factors GATA4, MEF2C, and TBX5 by their pleiotropic effects and thereby positively influence the possibility of fibroblast reprogramming into iCM.
Aims: The main objective of this work was to evaluate the effect of atorvastatin on the quantitative and qualitative phenotypic properties of human fibroblasts isolated from the dental pulp *in vitro*.
Methods: Fibroblasts in 6th passage of cultivation were incubated with 10 µM atorvastatin at four time intervals: 20 min, 2 h, 24 h and 96 h. By the flow cytometry method, the viability of the fibroblasts was evaluated. The relative expression of the transcription factors GATA4, TBX5 and MEF2C was measured by Western blotting.
Results and conclusion: We found that viability of fibroblasts significantly decreased directly relative to the incubation time. In the case of relative expression of the transcription factors, atorvastatin probably blocked the expression of TBX5 as compared to control samples. At the same time, a significant decrease of MEF2C expression was observed at all time intervals, as well as a decrease of GATA4 in 20 minutes and 2 hours of incubation. Based on this results, it can be said that atorvastatin under these conditions probably affected the expression of transcription factors GATA4, TBX5, and MEF2C as well as the viability of fibroblasts by a negative effect.

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