Endothelial-to-Mesenchymal Transition and Cellular Fibrosis in Cardiac Vascular Endothelial Cells Cultured by a Novel Simulation System

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Background

Acute myocardial infarction (AMI) often leads to a variety of cardiomyopathies in human. To elucidate the pathological mechanisms and to ameliorate cardiac damage is a crucial issue for treating AMI. Our previous research disclosed that administration of paricalcitol, an active vitamin D (VD3) agonist, attenuated cardiac fibrosis induced by isoproterenol injections in a cardiomyopathic rat model. The effect was possibly involved with regulation of endothelial to mesenchymal cell transition (EndoMT). We further hypothesize that VD3 can modulate EndoMT, certain growth factors, and cell fibrosis via vitamin D receptor (VDR) dependent pathway in endothelial cell lines.

Methods

A novel simulation system (ATMS Boxer TM Dynamic Stretch Culture System) was utilized to mimic a physiological condition of dynamic heart-beating and stretching (for example, subjected to 15%, 1 Hz stretching for 6, 24 hours) and to culture cardiac microvascular endothelial cells (HMVEC) for investigation of the effects of VD3-VDR pathway on EndoMT and cell fibrosis induced by transforming growth factor- β 1 (TGF- β 1). ZK159222, a VDR antagonist, will be also utilized to study the effect of VD3-VDR pathway.

Results

HMVECs were treated with 5 ng/ml TGF- β 1 for 2, 5 days for induction of EndoMT expression and cell fibrosis. The results showed that upstream signals of cell fibrosis as SNAIL, SLUG, α -SMA (a cell marker of a mesenchymal cell), and collagen content were up-regulated, accompanied with decreased CD31 (a cell marker of an endothelial cell) on Western blot analyses. These findings were compatible with expression of TGF- β 1 evoked EndoMT and cell fibrosis using the in vitro simulation model. Investigation of the effect of VD3-VDR pathway on EndoMT and cell fibrosis is ongoing.

Conclusions

EndoMT expression and cell fibrosis can be evoked by TGF- β 1 through the in vitro simulation model. We will continue to investigate the effects and mechanisms of VD3-VDR pathway on EndoMT and cell fibrosis using the model and ZK159222.

Keywords

active vitamin D, cardiovascular disease, cell fibrosis, endothelial to mesenchymal cell transition, vitamin D receptor.