Pressure-controlled Intermittent Coronary Sinus Occlusion (PICSO) study on mechanical control of cardiac tissue morphogenesis

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Abstract

Background:

Despite improved heart failure therapy, there remains a lack of clinically relevant concepts for structural regeneration of the diseased heart muscle. We have previously reported that Pressure controlled Intermittent Sinus Coronary Occlusion (PICSO) - a coronary sinus intervention, reduces infarct size clinically and induces washout clearing the ischemic/reperfused microcirculation. There is experimental and clinical evidence that besides the hemodynamic “mechanistic” effect another molecular pathway may exist influencing myocardial regeneration thus improving clinical outcome. We hypothesize that PICSO is a clinically feasible form activating coronary venous endothelium and its underlying mode of action is similar to the common understanding of stem cell research.

Objective:

We analyzed the regenerative potential of hitherto unknown molecules released in the Coronary venous blood of heart failure patients after 20 minutes of PICSO to confirm our hypothesis of reactivating developmental processes (“embryonic recall”) by inducing proliferation in cell cultures as surrogate for regenerative pathways.

Design: Serum from healthy volunteers and Cardiomyopathy patients enrolled during the surgical intervention of resynchronization therapy, was collected pre and post 20 minutes of PICSO and compared to controls (n>10). Serum levels of interleukin-6 (IL-6) and N-terminal pro-brain natriuretic peptide (NT-PreBNP) levels were analyzed. In addition, in vitro cellular proliferative and migrative evaluations were also measured.

Results:

Levels of NT-proBNP and IL-6 were seen in serum samples from cardiomyopathy patients increased after PICSO therapy. Serum IL-6 levels were associated with NT-ProBNP levels. Interestingly, 3 of 5 test serum samples showed also a significant increase in the capability of proliferation of human fibroblast cells compared to both control groups. In addition, cell scratch test showed increase migration capability (P>0.05) for test serum samples.

Conclusions:

Levels of established cardiovascular biomarkers (IL-6 and NT-ProBNP) could indicate an induction of the SAFE-pathway, leading to mitochondrial integrity and explaining reduction in infarct size. The in vitro data on proliferation and cell migration indicate that, besides the hemodynamic mechanistic effect also molecular pathways recapitalizing developmental processes may exist and that these effects are responsible for the beneficial effects of PICSO clinically. Based on our results we have to scrutinize the hitherto unknown molecules in further experiments to elucidate the conundrum of clinical relevant structural regeneration.