

Liraglutide and Exendin-4 postconditioning in both WKY and SHR-SP rats with left ventricular hypertrophy

Barbara Faricelli, M Salomonsson, A Consoli, T Engstroem and M Treiman
University of Copenhagen, Denmark

Introduction: Exendin-4 (exe4) postconditioning has been shown to limit reperfusion injury (RI) in experimental and clinical settings. Left ventricle hypertrophy (LVH) may be associated with increased RI. Our objective was to study exe4 and liraglutide postconditioning (PostC) in hearts with LVH, isolated from hypertensive SHR-SP (hypertensive LVH) rats.

Methods: Hearts isolated from WKY (control) and SHR-SP rats (11-15 weeks old) were subjected to 35 min LAD occlusion-2 hrs reperfusion, with exe4 0.3 nM or liraglutide 0.3 nM present during the first 15 min in treated hearts. Evans blue/TTC method was used to determine area-at-risk (AAR) and infarct size (% of AAR). Akt phosphorylation (Akt-P) was measured on western blots after 3 min of reperfusion. Arterial blood pressure (BP) was measured in conscious animals by tail cuff method. Results: BP and heart/body weight ratio were increased in SHR-SP compared to WKY rats ($p < 0.0001$ for both parameters). Infarcts were larger in SHR-SP than in WKY (65.7 ± 3.2 , $N=7$ vs 37.1 ± 3.4 , $N=12$ respectively; $P < 0.05$). Exe-4 and liraglutide PostC decreased infarct size (IS) after 35 min ischemia in WKY ($p < 0.05$). Liraglutide and preconditioning, but not Exe-4, decreased IS after 35 min in SHR-SP ($p < 0.05$). Exe4 PostC decreased IS after 15 min ischemia in SHR-SP ($p < 0.05$). In WKY hearts, exe4 treatment significantly decreased diastolic contracture and increased left ventricle developed pressure. Liraglutide, but not exe4, decreased diastolic pressure in SHR hearts. Degree of Akt phosphorylation was smaller in LVH hearts compared to normal hearts.

Conclusion: These data suggest that 0.3 nM liraglutide was more effective than 0.3 nM exe4 in limiting reperfusion injury in both WKY and SHR-SP. In both WKY and SHR-SP hearts there was a loss of response to PostC by exe4 with increasing ischemia time and infarct size. This loss of response to PostC occurs earlier in hypertrophy hearts.

b.faricelli@gmail.com