Abstract: P5994

Role of BGP-15 treatment in hypertensive heart failure progression and mitochondrial protection

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Introduction: The deterioration of mitochondrial quality control greatly contributes to the hypertension induced cardiac remodeling and progression of heart failure. Our previous in vitro results demonstrated the mitochondrial protective effect of antioxidant BGP-15 compound in the presence of cellular stress.

Purpose: In our recent study we investigated the effect of BGP-15 on cardiac remodeling in spontaneously hypertensive rats (SHR) with manifested heart failure and on mitochondrial dynamics and function in cell culture model.

Methods: 15-month-old male SHR received 25 mg/kg/day BGP-15 (SHR-B) or placebo (SHR-C) for 18 weeks. Age matched Wistar rats (WKY) were used as normotensive control. The heart function was monitored by echocardiography. Histological preparations were made from cardiac tissue. Neonatal rat cardiomyocytes (NRCMs) were used as in vitro model. 150 μM H2O2 stress and 50 μM BGP-15 treatment was applied. Mitochondrial network was stained with MitoTracker Red. Mitochondrial membrane potential was detected using JC-1 dye, while mitochondrial function was monitored by the Agilent Seahorse XFp, Cell Mito Stress Test. In both model the cellular levels of mitochondrial dynamics proteins were measured in Western blot. To study the ultrastructure we used electron microscopy in our in vivo and in vitro model.

Results: Left ventricular (LV) mass and LV wall thickness were increased significantly in SHR-C group compared to the initial values (p<0.05). These parameters were decreased considerably in the SHR-B group. Ejection fraction (EF%) decreased in both SHR group although this downturn was minimal because of the treatment. Chronic high blood pressure caused higher collagen deposition in SHR-C rats that was significantly diminished in the SHR-B group. Regarding the mitochondrial function decrease in the levels of fusion proteins OPA1 and MFN2 was observed in the SHR-C group. These differences were significantly reduced by BGP-15 treatment (p<0.05). Mitigation of the level of fission protein DRP1 was however reduced by BGP-15 (p<0.05). In our cellular model, we observed that the H2O2-induced mitochondrial fragmentation was decreased by BGP-15 treatment (p<0.05). BGP-15 treatment prevented mitochondrial membrane potential fall in H2O2 stress (p<0.05). There was no significant difference in basal respiration among groups by monitoring the mitochondrial function. The maximal respiration capacity and ATP production were significantly higher in the BGP-15 treated group in comparison to the stressed group (p<0.05).

Conclusion: BGP-15 treatment has beneficial effects on mitochondrial dynamics and structure by promoting fusion processes. It also supports the maintenance of mitochondrial function through the preservation of the mitochondrial structure. The mitigation of remodeling processes and the preserved EF in the treated group are results at least partly of the comprehensible effects of BGP-15 on mitochondrial structure and function.
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