A NEW ANGIOTENSIN II TYPE I RECEPTOR BLOCKER, BR-A-657, REDUCES REPERFUSION INJURY VIA ANTI-APOPTOTIC/ANTI-INFLAMMATORY EFFECT.

ACC Poster Contributions
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Authors: Dong-Ju Choi, Eun-Ji Kim, Min-Jung Park, Il-Yung Oh, Chang-Hwan Yun, Yung-Seok Cho, Tae-Jin Yeon, Gu-Yung Cho, Gu-Yung Cho, In-Ho Chae, Sung-Ji Park, Seoul National University Bundang Hospital, Seongnam, South Korea

Background: Angiotensin II receptor blocker (ARB) is well known as antihypertensive agent to reduce the blood pressure. In addition, inhibition of rennin-angiotensin system (RAS) is important to protect the cardiovascular system as well. We investigated the protective effect of BR-A-657, a newly developed ARB, against myocardial I/R injury and its underlying mechanisms.

Methods: In male Sprague-Dawley rats (weight of 200-230mg), 3mg/Kg of BR-A-657 or control buffer was infused intravenously over 30min before coronary occlusion. Area of necrosis (AN by TTC), the area at risk (AAR by Evans blue), and LV size were measured after 30 min of coronary occlusion and 24 hours of reperfusion. To determine the mechanisms of BR-A-657, we assessed DNA laddering, TUNEL assay and Western blot was performed with myocardial tissue and culture myocytes in ischemic/reperfusion conditions. Hemodynamic measurements and blood samples was done after ischemia/reperfusion injury for C-reactive protein, and TNF-α measurement.

Results: BR-A-657 reduced infarct size in AN/AAR by 47% (control vs. BR-A-657; 47.3±11.8 vs. 25.2±9.6 , p<0.05) and in AN/LV by 52.3% (30.4±10.5 vs. 14.5±9.6, p<0.05, respectively), while the size of AAR/LV was not different. In sham group, IR injury, DNA fragmentation and the number of apoptotic nuclei in the ischemic area were increased, and those effects were abolished by BR-A-657. The expression of Bcl-2 in the myocardium was increased, while the CRP and TNF-α was decreased by 20.9% (control vs. BR-A-657; 404.2±44.0 ug/ml vs. 320.0±47.7 ug/ml, p<0.05) and by 22.2% (control vs. BR-A-657; 164.93±18.57 pg/mg protein vs. 127.79±26.78 pg/mg protein, p <0.05 ) by treatment of BR-A-657, respectively.

Conclusions: These results suggest that BR-A-657 may have a protective effect on myocardial ischemia/reperfusion injury. This protective ability is possibly through its anti-inflammation and anti-apoptosis effect. These data imply new clinical application of BR-A-657 for myocardial protection from ischemia-reperfusion injury conjunction with reperfusion therapy during myocardial salvage.