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Inflammation mitigation improves post-infarction functional recovery of the heart

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Aim: The in vitro evaluation of the cardiac functional effects of TNF-α antagonist administration in rats after isoproterenol induced myocardial infarction.

Material and methods: Myocardial infarction was reproduced using a proven model based on isoproterenol i/p administration in rats in 2 consecutive days in a similar dose, 150 mg/kg. In another group the animals after isoproterenol induced myocardial infarction (series IMI) have received daily TNF-α antagonist, a specific monoclonal antibody (ma-TNF-α) i/p in dose of 50 mg/kg during 8 days (series IMI+ma-TNF-α). In both series the animals were sacrificed after 10 days from the 1st injection and their isolated hearts ware perfused with Krebs solution according to Langendorff and Neely-Rovetto models.

Results: The most remarkable traits of left ventricle dysfunction in IMI in comparison to control were following: (1) diminution of cardiac output (CO), systolic pressure (SP) and +dP/dT max by respectively 28,7 and 34,7 and 23,3%; (2) negative inotropic effect to action of endothelin-1 manifested by decrease of SP and aortic jet during stimulation up to 13,9%; (3) increased cardiac arrhythmogenic activity in response to calcium overload; (4) increasing by 45,2% of ischemia induced contracture as well as decreasing by 37,5% of SP during reperfusion. The ma-TNF-α administration in post-infarction period led to noticeable benefits such as: significant enhancement of SP and CO respectively by 17,3 and 18,6% as well as positive inotropic effect developing to ET-1 action as well as significant increase of time regarding the appearance of ventricular extrasystole and ventricular tachyarrhythmia by respectively 12,9 and 11,7% as well as perceptible improvement of ischemia-reperfusion syndrome.

Conclusion: A sustained inflammation inhibition by ma-TNF-α administration in post-infarction period improves tangibly the cardiac functioning that proves the role of inflammatory response in myocardial infarction induced functional and structural myocardial remodeling and underlines the inflammation as a therapeutic target.