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New Myocardial Protection Therapies

Alburquerque-Béjar JJ, Barba I, Inserte J, Miró-Casas E, Ruiz-Meana M, Poncelas M, et al. Combination therapy with remote ischaemic conditioning and insulin or exenatide enhances infarct size limitation in pigs. **Cardiovasc Res. 2015;107:246-54. http://doi.org/72h**

The incorporation of reperfusion therapies has reduced morbidity and mortality of patients with ST-segment elevation acute myocardial infarction (STEMI). However, extensive areas of myocardial necrosis still persist in a significant percentage of these patients, leading to elevated mortality, heart failure and presence of arrhythmias. This is mainly due to the difficulty in shortening the total ischemic time to which the heart is submitted until tissue reperfusion, but also because part of the beneficial effect of reperfusion is lost due to myocardial reperfusion injury. In this regard, a series of therapeutic strategies, potentially able of attenuating reperfusion injury, have been identified during the last years, some of which have limited infarct size (ischemic postconditioning) with encouraging results even in humans. Yet, none of these strategies has been successfully implemented in clinical practice.

Remote ischemic conditioning (RIC), induced by brief ischemia-reperfusion episodes applied to an arm or leg, seems to be a promising cardioprotective strategy. Remote ischemic conditioning can be easily extrapolated to the clinical setting, and a series of studies have shown evidence of its beneficial effects in STEMI patients and during coronary artery bypass graft surgery. However, its protective effect may be attenuated in patients with diabetes or metabolic syndrome. This type of protocol may be applied before myocardial ischemia (remote preconditioning), during myocardial ischemia(remote perconditioning) and simultaneously with myocardial reperfusion (remote postconditioning), the last two being of great clinical interest since they are applicable once the ischemic event has occurred.

On the other hand, reduction of reperfusion injury has also been attempted administering different pharmacological agents such as cyclosporine (mitochondrial permeability transition pore inhibitor), compounds activating the cGMP-PKG pathway, drugs used in the treatment of diabetes (exenatide) and solutions with the ability of increasing glucose uptake as the glucose-insulin-potassium solution (GIK).

In the present work, the group directed by Dr. David García Dorado evaluates the effect of the combined therapy: RIC + GIK or RIC + exenatide on myocardial infarction in a porcine model of coronary occlusion followed by reperfusion. In this study, all the cardioprotective strategies were applied during myocardial ischemia. The research showed that RIC, GIK and exenatide have a different impact on the pathways involved in myocardial protection. RIC reduces the oxidative stress that increases at the onset of reperfusion, which is responsible for the nitration of different proteins, whereas GIK solution shares with exenatide an effect on cardiac glucose metabolism and an important impact on the Akt-eNOS pathway. Thus, the combined therapy (RIC, either with GIK or exenatide) by activating different intracellular mechanisms was more efficient than single treatments to limit infarct size.

The application of therapies at the onset of reperfusion is more feasible in the clinical setting and particularly in STEMI patients. In this sense, various studies performed in patients have tested the application of RIC during transfer to the hospital. Similarly, in the IMMEDIATE trial, GIK was administered in the ambulance. Finally, the authors cannot rule out the possible beneficial effect of these interventions on ischemic injury, as they were all performed at that moment.