CYCLOSPORINE AFTER MI

Cyclosporine is a cyclic nonribosomal peptide commonly used as an immunosuppressant after organ transplantation. An early clinical trial by Michel Ovize's group demonstrated that cyclosporine can also reduce infarct size when given during reperfusion therapy for acute myocardial infarction (MI). However, data from animal studies have raised concerns that this drug could be associated with attenuation of beneficial cardiac remodeling. Ovize and colleagues have now shown that cyclosporine has no detrimental effect on post-MI remodeling in patients who underwent percutaneous coronary intervention (PCI).

The investigators performed a cardiac MRI substudy of 28 patients from the cohort of 58 individuals enrolled in their original cyclosporine pilot trial. Patients received a single intravenous dose (2.5 mg/kg) of cyclosporine or placebo immediately before PCI. Cardiac MRI revealed that infarct size was significantly reduced in the cyclosporine group at 5 days and 6 months after reperfusion when compared with the control group. There were no significant differences between the two groups in left ventricular mass or wall thickness at either of these follow-up points.

The beneficial effects of cyclosporine on infarct size are thought to be related to "the inhibition ... of the opening of the mitochondrial permeability transition pore, which has been involved in cardiomyocyte death after a prolonged ischemic insult," explains Ovize. However, cyclosporine also inhibits the calcineurin-dependent pathway that is essential for the healing process of cardiac remodeling. The lack of effect on remodeling in this study, which is discordant with some results from preclinical research, could be related to the dose of cyclosporine, which was much higher and given repeatedly in animal studies. This finding "opens up a new area of investigation, since there is currently no treatment for lethal reperfusion injury," concludes Ovize.

Alexandra King

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