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Chronic diabetes abolishes cyclosporine-A induced cardioprotection and nitric oxide production in rat myocardium

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Background and Aims: The interaction of cardiovascular risk factors with cardioprotection strategies in ischemia/reperfusion (I/R) injury remains unclear. The aim of this study was to investigate the interfering effects of chronic diabetes with cardioprotection by cyclosporine-A (CsA) in myocardial I/R injury and underlying mechanisms in this field.
Methods: Wistar rats (140 rats weighing 250-320g) were randomly divided into control and diabetic groups, and then further divided into four subgroups (in two series of the experiments). Diabetes, with duration of 8 weeks, was induced by single injection of streptozotocin (50 mg/kg; ip). The hearts were removed quickly, mounted on Longendorff apparatus and then subjected to 30min regional ischemia followed by 60min reperfusion. Infarct size was identified by triphenyltetrazolium chloride staining. Total amounts of nitric oxide (NO) metabolites were determined by Griess method.
Results: Administration of CsA [as a selective inhibitor of mitochondrial permeability transition pore (mPTP)] at the onset of reperfusion phase in non-diabetic animals significantly reduced the infarct size as compared with corresponding controls ($P<0.01$), but it had no positive effect in diabetic hearts. In addition, myocardial NO was significantly increased by CsA only in non-diabetic animals ($P<0.01$).
Conclusions: The present study indicated that postconditioning with CsA failed to protect the chronically diabetic myocardium against I/R injury. Impairment in the production of myocardial NO and/or further opening of mPTP may play a role in this regard.

Keywords: Cyclosporine-A; Cardioprotection; Diabetes; Reperfusion injury