10.1136/heartjnl-2011-300867.56

Introduction Switched myocardial substrate uptake from fatty acids to carbohydrate has been proposed to resist ischemia/reperfusion injury. We hypothesised that altered myocardial substrate uptake during early reperfusion may contribute to IPC-afforded cardioprotection.

Methods Adult male rats were subjected to 30 min of myocardial ischemia and 3 h of reperfusion (MI/R). IPC was achieved by two cycles of 5 min ischemia and 5 min reperfusion. Myocardial glucose and fatty acid (FA) uptake were assessed at the end of 1 h reperfusion by determining fluorodeoxyglucose uptake and fatty acid translocase (FAT)/CD36 translocation, respectively.

Results IPC significantly improved cardiac functions, reduced myocardial infarction, apoptotic cell death and blood CK/LDH levels following MI/R (all $p<0.05$). Myocardial glucose uptake was markedly elevated after IPC treatment (17.0±1.5 vs 12.4±1.0 in MI/R group, $p<0.05$, n=10-12), as well as translocation of glucose transporter 4 (GLUT4) to plasma membrane (PM) ($p<0.01$). Meanwhile, myocardial PI3K expression and Akt phosphorylation were significantly enhanced in IPC group ($p<0.05$). Interestingly, IPC also increased CD36 translocation to PM and AMPK phosphorylation (both $p<0.05$). Wortmannin not only abrogated the cardioprotective effect of IPC, but also inhibited IPC-induced Akt/AMPK phosphorylation and subsequent GLUT4/CD36 translocation. Furthermore, the cardioprotection of IPC was markedly blunted in STZ-induced insulin-deficient diabetic hearts with failure of increase in glucose/FA uptake and impaired IPC-stimulated PI3K-Akt and AMPK signalling ($p<0.05$, n=6).

Conclusions IPC increased both glucose and FA uptake during early reperfusion to resist myocardial injury via insulin/PI3K-dependent Akt and AMPK activation. Therefore, augmenting insulin signaling may be a potential therapy to improve myocardial substrate uptake and restore the cardioprotection of IPC in the diabetic hearts.

[gw22-e0591]

INCREASED MYOCARDIAL SUBSTRATE UPTAKE CONTRIBUTES TO THE PROTECTION OF ISCHEMIC PRECONDITIONING: ROLE OF INSULIN-DEPENDENT AKT AND AMPK ACTIVATION

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