The K_{ATP} channel opener diazoxide attenuates mitochondrial Ca^{2+} overload in rat ventricular myocytes

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Background : Mitochondrial K_{ATP} channel protects the heart from ischemia-reperfusion injury and mediatesischemic preconditioning (IPC). In this study, we intended to characterize the cardiac protection effect of mitochondrial K_{ATP} channel opening.

Methods and results : Single rat ventricular myocytes were isolated using enzymatic method. Mitochondrial Ca^{2+} and inner membrane potential ($\Delta\Psi_m$) were measured with rhod-2 AM and JC-1, respectively, under laser scanning confocal microscope (LSCM). When rhod-2 AM loaded cells were administrated with ouabain (1 mM), a Na^+/K^+ ATPase inhibitor, the fluorescence intensity of rhod-2 AM increased by about 120 % of the baseline. The increased rhod-2 AM fluorescence intensity was attenuated when a mitochondrial KATP channel opener, diazoxide (100 □M) was added again. However, the mitochondrial Ca^{2+} decrease by diazoxide was blocked by 5-Hydroxydecanoate (5-HD, 500□M), mitochondria K_{APT} channel antagonist. Furthermore, in the presence of ouabain, diazoxide depolarized m and reduced the JC-1 fluorescence intensity by about 50 % of the baseline.

Conclusion : These data suggest that the opening of mitochondrial KATP channel leads to depolarization of $\Delta\Psi_m$, which attenuates mitochondrial Ca^{2+} overload. Diazoxide might be a useful candidate for the protection from cardiac ischemia /reperfusion injury (I/R).

Key words : Mitochondrial KATP channel, ouabain, diazoxide, JC-1, Rhod-2 AM, 5-HD.