<발 표 I-3>

Effect of Diltiazem-Pretreatment on the Left Ventricular Function and Intracellular Calcium Distribution in Post-ischemic Reperfused Guinea Pig Heart.

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Background: Recent studies demonstrated that cardioprotective effect of diltiazem, a potent calcium antagonist, in a prolonged ischemia followed by reperfusion may be related to preservation of mitochondria, however, controversies still remain. In this study, the hypothesis that diltiazem may maintain the function of mitochondria during reperfusion was tested by a cytochemical method.

Methods and Results: Isolated Langendorff-perfused guinea pig hearts received 10 minutes diltiazem (7.5 μM) treatment prior to 10 minutes global ischemia followed by 20 minutes reperfusion. Functional parameters were collected and analyzed. Intracellular calcium was precipitated by potassium pyroantimonate and viewed with transmission electron microscope. Compared to the control and the ischemic hearts, the diltiazem-pretreated hearts showed significant increase in the left ventricular developed pressure (LVDP), dP/dt_{max} ($p<0.01$) and recovery rates of the LVDP ($p<0.01$ versus ischemic hearts) and dP/dt_{max} ($p<0.05$), and decrease in the heart rate ($p<0.01$) but the left ventricular end-diastolic pressure was not changed during reperfusion. In the control hearts, calcium deposits were seen along the inner aspects of sarcolemma and t-tubule membranes, and in the mitochondria. These deposits were considerably reduced in number after ischemia and reappeared in small number principally in the mitochondria by reperfusion. In contrast, in the diltiazem-pretreated hearts, the calcium deposits reappeared along the sarcolemma, t-tubule membranes, and cell junctions, and rather increased numbers were found in the mitochondria.

Conclusion: These results strongly support the hypothesis that diltiazem-pretreatment may improve cardiac function during reperfusion probably by enhancing mitochondrial function as a buffer of elevated cytosolic calcium.