

Synergistic cardioprotective effects of rAAV9-CyclinA2 combined with fibrin glue in rats after myocardial infarction.

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Abstract:

The present study aimed to investigate the protective effects of rAAV9-CyclinA2 combined with fibrin glue (FG) in vivo in rats after myocardial infarction (MI). Ninety male Sprague-Dawley rats were randomized into 6 groups (15 in each group): sham, MI, rAAV9-green fluorescent protein (GFP) + MI, rAAV9-CyclinA2 + MI, FG + MI, and rAAV9-CyclinA2 + FG + MI. Packed virus (5×10^{11} vg/ml) in 150 μ l of normal saline or FG was injected into the infarcted myocardium at five locations in rAAV9-GFP + MI, rAAV9-CyclinA2 + MI, and rAAV9-CyclinA2 + FG + MI groups. The sham, MI, and FG + MI groups were injected with an equal volume of normal saline or FG at the same sites. Five weeks after injection, echocardiography was performed to evaluate the left ventricular function. The expressions of CyclinA2, proliferating cell nuclear antigen (PCNA), and phospho-histone-H3 (H3P), vascular density, and infarct area were assessed by Western blot, immunohistochemistry, immunofluorescence, and Masson staining. As a result, the combination of rAAV9-CyclinA2 and FG increased ejection fraction and fractional shortening compared with FG or rAAV9-CyclinA2 alone. The expression level of CyclinA2 was significantly higher in the rAAV9-CyclinA2 + FG + MI group compared with the rAAV9-CyclinA2 + MI and FG + MI groups ($70.1 \pm 1.86\%$ vs. $14.74 \pm 2.02\%$, $P < 0.01$; or vs. $50.13 \pm 3.80\%$; $P < 0.01$). A higher expression level of PCNA and H3P was found in the rAAV9-CyclinA2 + FG + MI group compared with other groups. Comparing with other experiment groups, collagen deposition and the infarct size significantly decreased in rAAV9-CyclinA2 + Fibrin + MI group. The vascular density was much higher in the rAAV9-CyclinA2 + FG + MI group compared with the rAAV9-CyclinA2 + MI group. We

concluded that fibrin glue combined with rAAV9-CyclinA2 was found to be effective in cardiac remodeling and improving myocardial protection.

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