優秀賞

26. Progression of ventricular dysfunction after myocardial infarction is prevented by anti-Alzheimer's disease drug, donepezil.

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Introduction: We have previously demonstrated that the vagal nerve stimulation improved survival of rats with both acute and chronic heart failure through release of the neurotransmitter acetylcholine. Recently donepezil (Aricept), an acetylcholinesterase inhibitor, was also found to improve survival rate in rats with chronic heart failure. However the protective effects of donepezil against progression of cardiac dysfunction have not yet been elucidated. In this study, we investigated whether donepezil prevents progression of left ventricular dysfunction in ischemic chronic heart failure rats.

Methods: Myocardial infarction was constructed by left coronary artery occlusion. The survived rats were thereafter divided into sham, untreated (control) and donepezil-treated (5 mg/kg/day in drinking water) groups. Six weeks after surgery, left ventricular pressure-volume relationships were determined in Langendorff perfused heart preparation.

Results: Compared to the sham group (Ees=1.03 mmHg/µl, ESV=60 µl estimated from linear regression analysis at ESP=100 mmHg), the control group showed severe depression of left ventricular function (Ees=0.23 mmHg/µl, ESV=320 µl). In contrast, compared with the control group, donepezil-treated group exhibited significant improvement of especially left ventricular contractility (Ees=0.36 mmHg/µl, ESV=210 µl), but with no differences in an EDP-volume relationship and a heart/body weight ratio between control and donepezil-treated groups.

Conclusions: The present results showed that donepezil has a preventive effect on left ventricular dysfunction of ischemic failing hearts, suggesting that donepezil can be a new potential candidate for a clinically useful drug for chronic heart failure therapy.