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Phosphodiesterase-5 inhibition delays cardiac dilation and improves myocardial function in a rat model of heart failure due to chronic volume overload

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Background

Chronic volume overload caused by insufficient cardiac valves is a well known pathomechanism to the development and progress of cardiac dilation. Recent studies suggest that PDE-5-inhibitors may have positive inotrope and cardioprotective effects. Nevertheless the long-term outcome of PDE-5 treatment in heart failure remains unknown. In this study we investigated the effects of chronic vardenafil treatment on myocardial dysfunction in rats developing heart failure on account of a surgically induced AV-shunt.

Materials and methods

In young male Sprague-Dawley rats heart failure was developed during a 3 months period after surgically inducing an AV-shunt between the inferior caval vein and abdominal aorta. In the treatment group vardenafil (10 mg/kg/d) was applied orally for 3 months. Control animals received vehicle instead. After the treatment left ventricular pressure-volume relations were measured using a microtip Millar conductance catheter. Baseline hemodynamic parameters and indexes of contractility were calculated.

Results

Treatment with vardenafil resulted in a significant increase in load independent indexes of contractility and efficiency (ESPVR: 1.07 ± 0.14 vs. 1.67 ± 0.12 mmHg/µl*; efficiency: 45.0 ± 6.0 vs. 65.0 ± 5.0%*; PRSW: 65.40 ± 15.58 vs. 81.07 ± 13.72 mmHg, dPdt/EDV: 45.11 ± 9.57 vs. 48.74 ± 14.51 mmHg; control vs. treatment; *$p < 0.05$). Furthermore a reduced left ventricular dilatation and increased ejection fraction has been proven (EDV: 295.89 ± 53.55 vs. 257.91 ± 45.77 µl; EF: 50.99 ± 3.54 vs. 56.45 ± 4.00%; control vs. treatment).

Conclusion

Our current result further support the concept that chronic downregulation of intracellular cGMP signalling may play an important role in the development of ventricular dilation and myocardial dysfunction induced by chronical volume overload. Therefore PDE-5-inhibition could represent a novel therapeutic approach in the treatment of heart failure.