Sildenafil improves established right ventricular dysfunction via enhancement of diastolic function

Poster Contributions
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Authors: Marinus Alexander Borgdorff, Beatrijs Bartelds, Michael Dickinson, Paul Steendijk, Maartje de Vroomen, Rolf Berger, Center for Congenital Heart Diseases, University Medical Center Groningen, Groningen, The Netherlands, Leiden University Medical Center, Leiden, The Netherlands

Background: Right ventricular (RV) failure is a major determinant of mortality in pulmonary hypertension or congenital heart diseases. Sildenafil (SIL) benefits the RV when started at the onset of pressure load (prevention). However, it is unknown whether SIL is effective in established RV dysfunction (therapeutic strategy). We assessed the effects of SIL on RV function and fibrosis in a rat model of established RV dysfunction that is not amenable to pulmonary vasodilatory therapy.

Methods: Wistar rats were subjected to pulmonary artery banding (PAB), which results in pressure load-induced RV dysfunction in 4 wks. From week 4 onward, PAB rats were treated with SIL (100mg/kg/d) or placebo (VEH). After 4 (baseline) and 8 wks (end) invasive RV pressure-volume analysis was performed. RV fibrosis was measured as % surface area using Masson-Trichrome staining.

Results: PAB induced RV dysfunction after 4 wks, characterized by decreased ejection fraction (EF: 27±2 vs 47±3%, PAB vs CON, p<0.05). Subsequently started SIL improved EF at 8 wks (43±5 vs 33±3%, SIL vs VEH, p<0.05). This was due to improved diastolic function (end diastolic elastance, end diastolic pressure, see figure) rather than improved contractility (end systolic elastance unchanged). The improvement was accompanied by attenuated fibrosis.

Conclusion: Sildenafil is useful in treating established RV dysfunction via improving diastolic dysfunction. This is clinically important, as many patients present in a progressed stage of RV dysfunction.