The effects of empagliflozin on right ventricular adaptation to pressure overload

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Background: Right ventricular (RV) failure is the prime cause of death in patients with pulmonary arterial hypertension. Novel treatment strategies that protect the RV are needed. Empagliflozin, a member of the new anti-diabetic sodium-glucose co-transporter-2 inhibitors, shows a cardioprotective effect on the left ventricle in clinical and preclinical studies, but its direct cardiac effects on the RV remain elusive.

Purpose: To investigate the effects of empagliflozin on RV dysfunction induced by pulmonary trunk banding (PTB).

Methods: Male Wistar rat weanlings (116±10 g) were randomized to PTB or sham surgery. One week after surgery, PTB animals were randomized to empagliflozin 20 mg/kg/day mixed in the chow (300 mg empagliflozin/kg chow) (PTB-empa, n=10) or standard chow (PTB-control, n=10). Sham rats (Sham, n=6) received standard chow. After five weeks, RV function was evaluated by clinically relevant methods including echocardiography, cardiac MRI, and invasive pressure-volume measurements.

Results: PTB increased RV end-systolic pressures four-fold and caused RV hypertrophy with a 55 % increase in RV/(left ventricle + septum) weight ratio in PTB-control rats compared with sham. RV failure was evident by a decrease in cardiac output (PTB-control: 1.07±0.06 mL/s vs sham: 2.06±0.24 mL/s, p=0.0136). PTB-empa rats had a slight but non-significant weight reduction and a 33 % increase in water intake compared with PTB-control, yet no differences in hematocrit or blood glucose were observed. Treatment with empagliflozin decreased RV end-systolic pressures by 11 % (PTB-empa: 81±3 mmHg vs PTB-control: 91±2 mmHg, p=0.0091) without any effects on RV cardiac output. This decrease in RV end-systolic pressure in PTB-empa rats was complemented by less decreased minimum dp/dt and less increased maximum dp/dt compared with PTB-control without changes in the ventriculo-arterial coupling (Ees/Ea) (PTB-empa: 0.58±0.08 vs PTB-control: 0.67±0.14, p=0.8170). Load-independent measures of RV systolic and diastolic function were not affected in PTB-empa rats compared with PTB-control.

Conclusion: PTB caused RV failure in all rats subjected to the procedure. Empagliflozin treatment showed promising effects in pressure overload induced RV failure by reducing end-systolic pressure. Our study supports that treatment with empagliflozin has no toxic or adverse effects on the failing RV. Further studies are needed to explore empagliflozin’s potential beneficial role against RV failure.