

Kongress: 11th Int. Congress of Cardiothoracic and Vascular Anesthesia
Name: Jun Yin
Abstract Nr.: 32
Kategorie: Heart failure
Vortragssprache: E
Vortragsart: P
Erstautor: Dr. Jun Yin, Deutsches Herzzentrum Berlin, Berlin
Coautoren: Dr. Marian Kukucka, Deutsches Herzzentrum Berlin, Berlin
Dr. Julia Hoffmann, Charite-Universitaetsmedizin Berlin, Berlin
Prof.Dr. Hermann Kuppe, Deutsches Herzzentrum Berlin, Berlin
Prof.Dr. Wolfgang Kuebler, Deutsches Herzzentrum Berlin, Berlin
Abstracttitel: SILDENAIL PREVENTS SECONDARY PULMONARY HYPERTENSION IN
CHRONIC HEART FAILURE

Purpose: Due to the relaxant effect on smooth muscle cells, the phosphodiesterase (PDE) 5 inhibitor sildenafil has proven beneficial in the treatment of pulmonary arterial hypertension. Yet, in secondary pulmonary hypertension (SPH), a common complication of chronic heart failure (CHF), the therapeutic effects of sildenafil has not been addressed. Here, we studied the effects of long-term (10 weeks) sildenafil treatment on pulmonary vascular endothelial dysfunction and pulmonary vascular remodeling, which have been implicated with the development of SPH.

Methods: CHF experimental model was induced in juvenile Sprague-Dawley rats (102±8 g, bw) by supracoronary aortic banding. Sildenafil was administered (60 mg/kg bw/day po) via drinking water from postoperative day 5 till day 75. In combining real-time optical imaging of endothelial NO production and lung vascular filtration coefficient (K_f) measurements in the isolated-perfused lung, with echocardiography examination and histological analysis, the effects of sildenafil in SPH were evaluated.

Results: Data are means±SEM, n=5 each, * p<0.05 vs. baseline, # p<0.05 vs. sham, †p<0.05 vs. untreated CHF. In sham operated control lungs, acute elevation of left atrial pressure (P_{LA}) from 5 to 15 cmH₂O increased endothelial NO-production (239±18% of baseline) and K_f (665±24% of baseline). In CHF, depleted EC NO production in response to both pressure elevation (98±2%[#]) and acetylcholine (Ach, 10⁻⁵ mol/L) (97±11%[#] vs. 447±23% sham) were found, indicating impaired EC function. As measures of pulmonary hypertension, increased mean pulmonary vascular wall thickness (VWT) (157±13%[#] of sham) and right ventricle end diastolic diameter (RVEDD) (175±21%[#] of sham) were demonstrated in CHF. Sildenafil treatment re-established the EC NO production in response to both mechanical stimulation (114±3%[†]) and Ach (337±17%[†]), attenuated vascular remodeling (VWT, 95±16%[†] of sham) and right ventricular hypertrophy (RVEDD, 112±21%[†] of sham). Although K_f increase at elevated P_{LA} was blunt in CHF (73±11% of sham[#]), this effect was even more intense in sildenafil treated lungs (32±11%^{#†} of sham), suggesting the adaptive enhanced endothelial barrier function in CHF was further strengthened. Concomitantly, sildenafil increased plasma cGMP levels to 38±3^{#†} pmol/ml as compared to 15±1 and 21±1 pmol/ml in untreated CHF and sham-operated rats, respectively.

Conclusion: By reducing degradation of cGMP, long-term sildenafil treatment restores endothelial function, limits vascular and ventricular remodeling, and prevents secondary pulmonary hypertension in CHF. Therefore, it may present a new therapeutic strategy not only in pulmonary arterial hypertension, but also in pulmonary hypertension secondary to CHF, and to improve the therapeutic outcome of CHF.

Sponsored by Kaiserin-Friedrich Foundation and Pfizer GmbH.