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Title: Acute improvement of pulmonary hemodynamics does not alleviate Cheyne-Stokes respiration in chronic heart failure - a randomized, controlled, double-blind, crossover trial

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Body: Background: Studies confirmed Cheyne-Stokes respiration (CSR) to be associated with elevated pulmonary capillary wedge pressure (PCWP) in chronic heart failure (CHF). This study aimed to investigate the acute effects of lowering PCWP and pulmonary artery pressure (PAP) on CSR severity. Methods: 21 consecutive patients with CHF and CSR (apnea-hypopnea-index (AHI)≥15/h) underwent right heart catheterization, followed by infusion of glyceryltrinitrate (GTN), and inhalation of iloprost. Throughout the procedure PAP and PCWP was measured invasively. Afterwards maximum tolerable dosage of GTN and iloprost were randomly applied in 2 split-night procedures versus i.v. or inhalative NaCl 0.9% under full polysomnography monitoring. Results: Mean (m)PAP was significantly reduced by GTN (20.1±9.0 to 11.6±4.2mmHg, p<0.001; infusion rate 6.2±1.5ml/h) and iloprost (16.9±7.9 to 14.2±6.4mmHg, p<0.01; dosage: 10 mcg/ml), whereas mPCWP was lowered exclusively by GTN (14.0±5.6 to 7.2±3.9 mmHg, p<0.001; iloprost: 11.7±6.2 to 11.0±6.3mmHg, p=n.s.). Compared to placebo sleep studies revealed no significant improvement of AHI (GTN: 39.0±17.7/h vs. 35.3±16.0/h, p=n.s.; iloprost: 34.9±21.9/h vs. 33.3±19.4/h, p=n.s.) and central apnea index (GTN:14.4±16.5/h vs. 11.5±16.37h, p=n.s.; iloprost:11.0±16.3/h vs.12.5±19.1/h, p=n.s.) following GTN or iloprost treatment, respectively. Conclusion: GTN and Iloprost led to a significant reduction in PAP, whereas PCWP was lowered by GTN exclusively. However, acute improvement of pulmonary congestion had no impact on CSR severity. Extended treatment periods appear crucial for successful causal therapies.