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Title: Ivabradine prevents salbutamol-induced disturbance of cardiac autonomic regulation in patients with chronic obstructive pulmonary disease and coronary heart disease

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Body: Aim: to evaluate protective effect of If blocker ivabradine on cardiac autonomic regulation after inhalation of salbutamol in patients with COPD and coronary heart disease(CHD). Materials and methods: 23 patients with COPD stage II-IV and CHD NYHA class I-III were included in cross-over, randomized study.Spirometry test with 400 mg salbutamol inhalation was performed at two consecutive days. Patients in group I were prescribed 5 mg ivabradine per os 3 hours before salbutamol inhalation on the 1-st study day, patients of group II received 5 mg ivabradine on the 2-nd day. Cardiac autonomic regulation was assessed via heart rate variability (HRV).

HRV at baseline (b) and in folow-up(f) after salbutamol(S) inhalation alone and in combination with ivabradine(I)in patients with COPD and CHD

	S b	S f	SI b	SI f
HR,/min	80.2±3.1	83.1±3.1	77.2±2.1	74.1±2.6∗
SDNN,ms	21.3±2.6	18.4±2.1∗	22.7±2.4	19.3±1.5
LF,n.u.	55.3±4.4	56.3±5.0	55.7±4.5	46.7±4.3∗
HF,n.u.	44.7±4.4	43.7±5.0	44.4±4.5	53.3±4.3∗
LF/HF	2.04±0.43	2.51±0.67	2.02±0.41	1.16±0.17∗

∗-p<0.05, baseline vs. follow-up

Results: salbutamol decreased the standard deviation of interbeat intervals SDNN and low-frequency LF power. If salbutamol inhalation was made after ivabradine ingestion then heart rate (HR) and LF/HF ratio decreased, normalized respiratory modulation power HF increased. Salbutamol increased FEV1 by 6.0%, p <0.01. Salbutamol with ivabradine increased FEV1 by 7.7%, p<0.01, p=0.5 vs. no ivabradine. Conclusion:ivabradine 5 mg per os prevents alteration of cardiac autonomic regulation after inhalation of

400 mcg salbutamol in patients with COPD and CHD comorbidity.