European Respiratory Society
Annual Congress 2013

Abstract Number: 1031
Publication Number: P5137

Abstract Group: 4.1. Clinical respiratory physiology, exercise and functional imaging
Keyword 1: Treatments Keyword 2: Physical activity Keyword 3: Chronic disease

Title: Effects of ivabradine on exercise endurance and VO2 kinetic in chronic ischemic heart disease

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Body: Background: Elevated heart rate (HR) represents an independent risk factor for morbidity and mortality in chronic ischemic heart disease (CIHD). Beta-blockers (βB) are considered the first choice medication to control HR in CIHD, however some patients have contraindications to their use. Ivabradine inhibits the If current of sinoatrial cells and controls HR avoiding βB collateral effects. Aim and Methods: We evaluated the short term effect of 5 mg of ivabradine b.i.d. on exercise endurance at cardiopulmonary exercise test (CPET), in 6 patients (age 59±12) with CIHD (NYHA I-II), sinus rhythm and contraindications to βB. Each patient performed an incremental workload test (IWT) and a constant workload test (CWT) at 85% of his maximal O2 consumption (VO2max) in two separate days, before and after 7 days of ivabradine. We analysed standard CPET variables at IWT. O2 kinetic and Time to limitation (TLim) were evaluated at CWT. Results: Ivabradine induced a significant reduction in rest and maximal HR (83±12 vs 69±13 bpm, 123±9 vs 106±13 bpm; p<0.001 and p=0.03, respectively), with no difference in patient exercise tolerance at IWT. Furthermore, ivabradine led to a significant improvement in exercise endurance as shown by the TLim at CWT (266±79s vs 386±144s; p<0.008). No significant changes were observed in VO2 kinetic (Tau). Conclusions: Seven days of ivabradine positively influenced baseline and maximal HR in CIHD patients. Furthermore, sub-maximal exercise tolerance was significantly improved, although no changes in VO2max were observed at IWT.