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Title: The effects of beta-blocker therapy on heart rate, symptoms and exercise in pulmonary arterial hypertension

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Body: Experimental studies have suggested potential benefit of beta-blocker therapy in pulmonary hypertension. However, it is uncertain whether a reduction in heart rate can be achieved without impairing exercise testing and at the costs of little side effects. Therefore we analyzed side effects, heart rate and exercise capacity in the first 13 patients (6/7 NYHA II/III; age 46,0 years±14,8) who received beta-blocker therapy in an escalating dose as part of the ongoing randomized placebo controlled cross-over trial assessing safety and efficacy of bisoprolol in iPAH-patients (NCT01246037). An average dose of 4 mg (0 -7,5mg) of bisoprolol was achieved. None of the patients collapsed during the treatment period. One patient developed fluid retention after the start of bisoprolol despite oral diuretics and she had to be treated with IV diuretics for several days. Heart rate was significantly reduced by bisoprolol (baseline 78/min± 3,3 vs. bisoprolol 68/min±3,7) with only a small, clinically not relevant decrease in exercise capacity (6MWD baseline 463m±27vs. bisoprolol 441m±31; VO₂/kg baseline 15,5 ml/kg/min±1,1 vs. bisoprolol 14,7 ml/kg/min ±1,2). Bisoprolol treatment didn't influence the quality of life (Minnesota quality of life questionnaire baseline 27,5 ± 6,8vs bisoprolol 28±6,4). **Conclusions** This preliminary study demonstrates that heart rate reduction by beta-blocker therapy could be achieved with minimal side-effects and only a small, decrease in exercise capacity.