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**Title:** Effect of nocturnal oxygen and acetazolamide on exercise performance in patients with precapillary pulmonary hypertension and sleep disturbed breathing. Randomized, double-blind, cross-over trial

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**Body:** Background: Sleep disturbed breathing (SDB) is common in patients with precapillary pulmonary hypertension (PH) and impairs well-being. We tested whether nocturnal oxygen therapy (NOT) or acetazolamide improve exercise performance, quality of life and pulmonary hemodynamics in patients with precapillary PH and SDB. Methods and results: This was a randomized, placebo-controlled, double-blind, cross-over trial. Participants received NOT (3l/min), acetazolamide tablets (2x250mg), and sham-NOT/placebo tablets each during 1 week with one-week washout between treatments periods. The trial included 23 patients (15 females, 16 with pulmonary arterial, 7 with chronic thromboembolic PH) on optimized pharmacological therapy, daytime PaO2 ≥7.2 kPa but either mean nocturnal oxygen saturation <90% or oxygen saturation dips >10/h. Medians (quartiles) of the 6 minute walk distance on NOT, acetazolamide and placebo were 480m (390;528), 440m (368;468), 454m (367;510), respectively, mean difference (95% CI) NOT vs. placebo +25 m (3 to 46, p=.027); mean difference acetazolamide vs. placebo -9 m (-34 to 17, p=.23). SF-36 quality of life was similar on NOT, acetazolamide and placebo. Right ventricular fractional area change was greater on NOT compared to placebo (p=.042). Conclusion: In patients with precapillary PH and SDB on optimized pharmacological therapy, NOT but not acetazolamide improved the 6 min walk distance compared to placebo already after one week. Therefore, NOT is promising as a long-term treatment for PH patients with SDB. Trial Registration: Clinical trial.gov, NCT01427192.