Effect of acetazolamide on incremental cycling exercise in precapillary pulmonary hypertension. A randomized placebo-controlled, double blind, cross-over trial

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Aims: Acetazolamide (AZA) improves nocturnal and daytime blood oxygenation in patients with pulmonary arterial and distal chronic thromboembolic pulmonary hypertension (PH, PAH/CTEPH), which may result in improved exercise performance.

Methods: We investigated the effect of AZA (250mg capsules bid for 5 weeks) vs placebo on cardiopulmonary physiology and maximal load during incremental ramp cycling exercise in patients with PH was assessed in a double-blind randomized controlled cross-over study (wash-out > 2 weeks).

Results: 25 patients (12 PAH, 13 CTEPH, 10 women, age 62±15y) completed the trial per protocol. Maximum workload did not significantly differ between AZA vs. placebo (mean±SE) 113±9 vs 117±9 watts, mean difference -4 watts, 95%CI -9 to 1, p=0.138). With AZA, end-exercise PaO2 was higher (9.3 vs 8.2kPa, mean difference, 1.10kPa (0.5 to 1.8), p=0.003) while arterial pH and PaCO2 were significantly lower. The anaerobic threshold was reached at a higher load on AZA (108±8 vs 97±8 watts, mean difference 11 watts (3 to 19), p=0.013) while the breathing equivalent for O2 and CO2 were significantly higher at end-exercise and AT. AZA showed notably more side effects than placebo (26% of the patients reported dyspnea vs. 0% in placebo).

Conclusion: Five weeks of AZA therapy did not affect maximal load in PH-patients despite a higher PaO2. Beneficial effects of the increased blood oxygenation could be mitigated through the increased perception of dyspnea associated with hyperventilation.