

Effects of Beta-Blockade on Exercise Performance at High Altitude: A Randomized, Placebo-Controlled Trial Comparing the Efficacy of Nebivolol versus Carvedilol in Healthy Subjects

Background:

- No studies to date describe the relationship between selective and non-selective beta blockers in healthy patient's exercise tolerability experiencing hypoxia due to high altitude.

Objective:

- To determine the effects of beta blockers (selective and nonselective) on cardiopulmonary response to exercise performed under conditions of high altitude hypoxia.

Methods:

- Design: a three week, randomized, double-blind, placebo-control study took place.
- Inclusion: No inclusion criteria were listed, patients had to be healthy, non-smoking individuals taking no medications. Patients also reside at sea level.
- Exclusion: Based off of the inclusion.
- 27 patients were enrolled, 9 to each treatment group (placebo, nebivolol, carvedilol).
- Primary outcomes: a change in peak exercise oxygen consumption (VO₂) observed between sea level (SL) under no treatment and high altitude (HA) exposure under treatment.
- Secondary Outcomes: were the changes, in peak exercise minute ventilations (VE); the absolute peak values of VO₂, VE, heart rate (HR), and oxygen saturation (SpO₂), achieved in the various study conditions.
- The study was conducted as a per protocol analysis, which included a power of 90%.

Results:

- 7 placebo and 8 patients in each treatment group were included in the analysis.
- High Altitude hypoxia significantly decreased resting and peak oxygen saturation, peak workload, peak oxygen consumption (VO₂), and heart rate (HR) (P < 0.01). Changes from SL (no treatment) differed among treatments: (1) peak oxygen consumption VO₂ was better preserved with nebivolol (-22.5%) than with carvedilol (-37.6%) (P < 0.01); (2) peak HR decreased with carvedilol (-43.9 ± 11.9 beats/min) more than with nebivolol (-24.8 ± 13.6 beats/min) (P < 0.05); (3) peak minute ventilation (VE) decreased with carvedilol (-9.3%) and increased with nebivolol (+15.2%) (P= 0.053). Only peak minute ventilation (VE) changes independently predicted changes in peak oxygen consumption (VO₂) at multivariate analysis (R= 0.62, P < 0.01).
- The author's observations show that functional differences during exercise occur under conditions of HA hypoxemia in healthy subjects treated with carvedilol as compared to nebivolol. Their data might also be clinically relevant in selecting the type of β-blocker to be used in cardiac patients, especially if traveling to altitude. Based on the data, nebivolol may be preferred to carvedilol whenever hyobaric hypoxia exposure is expected. This suggestion may

also apply at SL, in the case of significant lung diffusion impairment secondary to interstitial edema, when preserving β -2 mediated alveolar fluid clearance is crucially important.

Strengths

- Randomized, placebo controlled trial

Limitations

- Small sample size
- Improper dose and titration of one of the treatment medication (carvedilol)

Conclusion:

- This study showed statistically significant advantages in some measures for nebivolol compared to carvedilol for reducing high altitude induced exercise intolerance. However due to the studies limitations, the clinical significance of the results are less obvious. Further cites should include larger sample sizes, correct dosing and titration, and different inclusion/exclusion criteria to broaden the study population range to unhealthy individuals or patients already receiving a beta blocker.

Reference: Valentini M, Revera M, Bilo G, Caldara G, Savia G, Styczkiewicz K, etc. Effects of beta-blockade on exercise performance at high altitude: a randomized, placebo-controlled trial comparing the efficacy of nebivolol versus carvedilol in healthy subjects. *Cardiovasc Ther.* 2012 Aug;30(4):240-8.

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