Title: Prediction of physiological responses and performance at altitude using the 6MWT in normoxia and hypoxia

Running Head: Treadmill & Outdoor 6MWT in Normoxia & Hypoxia

Submission Type: Brief Report

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Key Words
6-minute walk test; altitude sickness; hypoxia; mountaineering;

Abstract Word Count
254 (250 limit)

Manuscript Word Count
2010

Number of References
10

Number of figure and tables
2 tables, 1 figure.

Acknowledgements
The authors wish to acknowledge Cortex-Medical, MKK Sports, Mad Designs, Para-Monte and Cranlea for their support with sponsoring the expedition to Cuzco, Peru and equipment used.
Abstract

Objective. The six minute walk test (6MWT) is a reliable and valid tool for determining an individual's functional capacity, and has been used to predict summit success. The primary aim of the study was to evaluate whether a 6MWT in normobaric hypoxia could predict physiological responses and exercise performance at altitude. The secondary aim was to determine construct validity of the 6MWT for monitoring acclimatization to 3,400m (Cuzco, Peru).

Methods. Twenty nine participants performed six 6MWTs in four conditions; Normoxic Overground (NO), Normoxic Treadmill (NT), Hypoxic Treadmill (HT) all once, and Hypoxic Overground three times, 42 hours (HO1), 138 hours (HO2) and 210 hours (HO3) following arrival at Cuzco.

Results. One-way ANOVA observed no difference ($p > 0.05$) between NO and HO1 for 6MWT distance. HT and HO protocols were comparable for the measurement of $\Delta$heart rate (HR) and post-test peripheral oxygen saturation (%SpO$_2$) ($p > 0.05$). Acclimatization was evidenced by reductions ($p < 0.05$) in resting HR and respiratory rate (RR) between HO1, HO2 and HO3, and preservation of SpO$_2$ between HO1 and HO2. Post exercise HR, and RR, were not different ($p > 0.05$) with acclimatization. The duration to ascend to 4,215m on a trek was moderately correlated ($p < 0.05$) to HR during the trek and the 6MWT distance during HT, no other physiological markers predicted performance.

Conclusions. The 6MWT is a simple, time efficient tool for predicting physiological responses to simulated and actual altitude, which are comparable. The 6MWT is effective at monitoring elements of acclimatization to moderate altitude.
Introduction

Acute altitude exposure can lead to acute mountain sickness (AMS), with 48-51% of travellers to Cuzco, Peru reporting symptoms. Prolonged exposures at elevations >1,500 m are sufficient to induce AMS which is on the high altitude illness (HAI) spectrum with potential to progress to high altitude pulmonary oedema (HAPE) and high altitude cerebral oedema (HACE) if untreated. Physical exertion increases AMS with increased physiological strain placed upon cardiac, pulmonary, vascular and muscular systems. The development of a simple and efficient test for monitoring changes in physiological responses, and symptoms of AMS prior to travel and at altitude would be beneficial in aiding the identification of individuals at risk of altitude illness.

The 6MWT has been widely used in clinical and research settings to determine and monitor exercise capacity. Performance can be linked to rates of ascent and physiological responses to exercise at altitude determined. Previously, a peripheral oxygen saturation (SpO₂) >75% following a 6 minute walk test (6MWT) at a 4365m basecamp was demonstrated to be a useful screening test for predicting the outcome of successfully reaching the summit of Aconcagua (6962m). More recently however, Daniels concluded SpO₂ and 6MWT performance were unlikely to be effective in predicting summit success on Kilimanjaro (5895m). If data demonstrates a good relationship between performances in the 6MWT and physiological responses to altitude and summit success, then the 6MWT may be a useful test.

The primary aim of the study was to evaluate whether a 6MWT in normobaric hypoxia could predict physiological responses and exercise performance at altitude. Secondly, we aimed to determine construct validity of the 6MWT for monitoring acclimatization to 3,400m (Cuzco, Peru).

Method

Twenty nine (14 female) healthy participants (Age 22.2 ± 5.4 years; No prior history of AMS, No exposure to simulated or actual altitude for 8 weeks prior to commencement of study. For day of test descriptive data, see table 1) volunteered to participate in an 18 day project in Eastbourne, UK and Cuzco, Peru. Following full description of experimental procedures the protocol was approved by the University of Brighton ethics committee. All participants completed medical questionnaires and provided written informed consent following the principles outlined by the Declaration of Helsinki of 1975, as revised in 2008.

Preliminary Testing

Anthropometric data were collected for height (cm; Detecto Physicians Scales; Cranlea & Co., Birmingham, UK), body mass (kg; ADAM GFK 150, USA) and percentage body fat obtained following multi-frequency bioelectrical impedance analysis (Xitron 4000, San Diego, CA) after 20 min of supine rest. Hydration status was confirmed in accordance with established guidelines to reduce the potential for fluid dependent changes in AMS.

6-minute walk testing
Each participant completed testing on six occasions where a first familiarisation, and then experimental 6MWT were performed to permit habituation to the method and environment, and ensure reliability on each day. Ten minutes seated rest was provided between familiarisation and experimental trials. Only data from the experimental 6MWT were analysed. Participants performed a normoxic treadmill (NT) test, normoxic outdoor (NO) test, and a hypoxic treadmill test (HT) within a 7 day period (all sea level, 760mmHg) separated with 24 hours of rest. After arrival in Cuzco, Peru (altitude ~3,400m, 460mmHg), three additional hypoxic outdoor tests were performed at 42 (HO1), 138 (HO2), and 210 (HO3) hours post arrival. Participants performed all 6MWTs in identical athletic attire between 09.00 and 12.00; data were collected during the month of April. Environmental conditions are presented in table 1. Standardised instructions were provided before each test as follows: "walk as far as possible in 6 minutes without running or jogging", and every 60s duration was communicated until the final 60s where 30s remaining was also communicated. During the treadmill familiarisation trials, participants were asked to self-select a treadmill start speed they could maintain for 6 minutes. Participants began each experimental trial at 50% of their self-selected start speed, which was doubled within 5s and then obscured from the view of the participant. Participants signalled to increase speed, decrease speed, or stop the treadmill as needed.

The NT 6MWT was performed on a treadmill (Woodway, ELG2, Germany) in temperate (20°C, 40% relative humidity (RH)) laboratory conditions (FiO₂ = 0.2093). The HT 6MWT was performed on treadmill (Woodway PPS 55sport, Germany) in a purpose built hypoxic chamber (The Altitude Centre, UK) set at FiO₂ = 0.137; ~3,400m and 20°C to simulate field-testing location (Cuzco, Peru). The NO 6MWT was performed outside on level concrete tennis courts and the HO 6MWT was performed in Cuzco, Peru on a stadium tartan athletic track, for each trial a measured distance of 40 m, with 5m intervals was demarcated. Temperature and humidity were monitored by a portable heat stress meter (Extech HT30, USA) and wind speed via a wind anemometer (Technoline EA3010, USA) for both outdoor trials (environmental data are presented in table 1). Prior to all trials, a Lake Louise Score (LLS) was self-reported as an indicator of AMS. During all trials, heart rate (HR) and peripheral arterial saturation (SpO₂) were measured before and immediately after the test in a seated position using a pulse oximeter (Nonin 2500, Nonin Medical Inc, USA) affixed to the right index finger. Respiratory rate (RR) was counted over a 30s period commencing upon sitting.

In addition to 6MWTs in Cuzco, participants also performed a 4 day trek carrying day packs and dressed in typical trekking attire commencing 24 hours after HO3. Prior to departure LLS was recorded to determine AMS symptoms. The duration taken to reach the summit (Dead Woman’s Pass, Peru - 4,215m, 48hr after HO3) from the camp (3,459m) was recorded for each participant with HR and SpO₂ taken immediately upon reaching the pass.

Statistical Analysis
All statistical calculations were performed using PASW software version 20.0 (SPSS, Chicago, IL, US). All outcome variables were assessed for normality of distribution and sphericity prior to further analysis and met these criteria in all instances unless otherwise stated. Data are reported as mean (95% CI), with two
tailed significance accepted at \( p < 0.05 \). One-way Analysis of Variance (ANOVA) with repeated measures was used to compare NT, NO, HT, HO1, HO2 and HO3 data. Bonferroni pairwise comparisons compared between trials to determine the differences between tests. Pearson’s correlations \( (r) \) were used to examine the relationships between dependent variables in HT and HO1, and for comparisons of the trek data with HT, HO1 and HO3.

**Results**

Twenty-four of the twenty-nine participants completed all tests. One participant was unable to complete the NO trial due to an acute musculoskeletal injury. Three people were excluded from the HO2 dataset for as a result of diarrhoea and vomiting \( (n=2) \) and severe AMS symptoms \( (n=1) \). Two different individuals were excluded from the HO3 data set as a result of diarrhoea and vomiting. Each of the ill participant’s data were within the mean ± SD for six minute walk distance \( (6MWD) \) and post-trial physiological responses during HO1 and are therefore considered unremarkable.

**Hypoxic Treadmill 6MWT vs. Hypoxic Outdoor 6MWT**

A difference \( (p < 0.05) \) was observed between HT and HO1 \( (\text{Table 2}) \) for 6MWD, LLS, HR\(_{\text{pre}}\), HR\(_{\text{post}}\), SpO\(_{2\text{pre}}\), change in \( (\Delta) \) SpO\(_2\), RR\(_{\text{pre}}\), RR\(_{\text{post}}\) and \( \Delta RR \). No correlation \( (p > 0.05) \) was observed for SpO\(_{2\text{pre}}\), ΔSpO\(_2\), RR\(_{\text{pre}}\), RR\(_{\text{post}}\) or \( \Delta RR \) \( (\text{figure 1}) \). No difference \( (p > 0.05) \) was observed between HT and HO1 for \( \Delta HR \) and SpO\(_{2\text{post}}\) with significant \( (p < 0.05) \) relationships observed between HT and HO1 trials for HR\(_{\text{pre}}\) \( (r = 0.753) \), HR\(_{\text{post}}\) \( (r = 0.721) \), \( \Delta HR \) \( (r = 0.538) \), SpO\(_{2\text{post}}\) \( (r = 0.545) \) and 6MWD \( (r= 0.614) \).

**Normoxic Treadmill 6MWT vs. Normoxic Outdoor 6MWT**

No differences \( (p > 0.05) \) were observed between NT and NO for 6MWD, LLS, HR\(_{\text{pre}}\), HR\(_{\text{post}}\), ΔHR, SpO\(_{2\text{pre}}\), SpO\(_{2\text{post}}\), ΔSpO\(_2\), RR\(_{\text{pre}}\), RR\(_{\text{post}}\) and \( \Delta RR \) \( (\text{table 2}) \).

**Normoxic Outdoor 6MWT vs. Hypoxic Outdoor 6MWT**

Differences \( (p < 0.05) \) were observed between NO and HO1 for LLS, HR\(_{\text{pre}}\), HR\(_{\text{post}}\), ΔHR, SpO\(_{2\text{pre}}\), SpO\(_{2\text{post}}\), ΔSpO\(_2\), RR\(_{\text{pre}}\), RR\(_{\text{post}}\) and \( \Delta RR \). No difference \( (p > 0.05) \) was observed between NO and HO1 for 6MWD.

**Hypobaric Hypoxic comparisons – The effect of acclimatisation**

Performance and physiological variables 6MWD, LLS, HR\(_{\text{pre}}\), HR\(_{\text{post}}\), ΔHR, SpO\(_{2\text{pre}}\), SpO\(_{2\text{post}}\), ΔSpO\(_2\), RR\(_{\text{pre}}\), RR\(_{\text{post}}\), ΔRR reported differences \( (p < 0.05) \) between NO, HT, HO1, HO2 and HO3; post hoc analysis is detailed in Table 2.

**Trek Data**

Time taken to complete the ascent to Dead Woman’s Pass \( (157 \text{ min}; \text{CI 144 - 171}) \) was weakly correlated with HR \( (r = 0.420, p < 0.05) \) and the HT 6MWD \( (r = 0.407, p < 0.05) \). Additionally, SpO\(_2\) following the ascent \( (78.2 \% \text{ CI 76.4 – 79.9}) \) was weakly correlated with the ΔRR during HO3 \( (r = 0.391, p < 0.05) \) \( (\text{Table 3}) \); no relationships were observed for the LLS \( (0.9 \text{ CI 0.4 – 1.31}) \) prior to the ascent.
Discussion

Our data demonstrate that ∆HR and post-test %SpO₂ were correlated between hypoxic treadmill and overground 6MWT protocols. Other physiological or performance markers are not correlated. In accordance with our primary aim, these variables are therefore appropriate for use to determine physiological responses to simulated altitude prior to travel and upon immediate arrival at altitude. AMS symptoms were not clinically relevant or related to performance of any 6MWT.

In comparison to the normoxic outdoor baseline trial, no differences were observed in the distance walked during hypoxic outdoor trials. Acclimatization was evidenced by reductions in resting HR and RR, although post exercise HR, SpO₂ and RR, and the change in variables were not different with acclimatization. This might suggest that the physiological challenge of exercising in hypoxia in comparison to normoxia is too great to overcome, or the sensitivity / construct validity of the test is inadequate. Our hypoxic outdoor trial data suggests participants were able to walk a greater distance, and consequently, elicited more favourable physiological responses (increased HR, decreased RR and preserved SpO₂ post-test) at 3,400m in Cuzco, in comparison to a similar study performed at 4,365m. This is unsurprising due to the differences in PO₂ at these locations.

The duration taken to reach the peak ascent (Dead Woman’s Pass), a field based performance indicator, was moderately related to the 6MWD in the HT trial suggesting that the exercise capacity of an individual is important in governing the speed of ascent. The relationship between ascent time and the HR during the ascent also provides a useful performance indicator. The lack of relationship between the duration taken to ascend, and any other physiological or AMS marker suggest that SpO₂ and 6MWD are unlikely to be effective tools for predicting successful ascent. It has been suggested that with AMS symptoms likely amongst climbers, psychological factors would more likely dictate peak or summit success. The success of reaching a pass or summit of a peak is dependent upon a number of variables including acclimatization, psychological factors, weather, impaired sleep, inflammation, fluid shifts, and haematopoiesis thus success, cannot be fully elucidated with vital signs in a small group alone.

Limitations

The severity of AMS symptoms peak between days 1 and 3 of arrival at altitude, and acclimatization tends to occur during the first week. Therefore, the identification of no differences between HO2 and HO3 is unsurprising, and future studies should implement earlier and more frequent analysis. The authors acknowledge that differences in participant approach to overland and treadmill walking e.g. pacing may have affected findings. Further, deceleration and acceleration associated with turning during overland walking may have reduced strain. Finally, the rate of ascent, and physiological data may have been affected by pacing e.g. additional rest breaks or faster walking at the end of the ascent, continuous monitoring of HR and O₂, and walking velocity, via GPS would be more beneficial.
Conclusion

The 6MWT is a useful and simple tool for determining performance and physiological responses to self-paced exercise in hypoxia that can be administered using a treadmill and over level ground. The implementation of the 6MWT warrants further investigation as a means for predicting for responses to acute exposures, and altitude acclimatization, via the post exercise changes in physiological responses to, but not performance during the 6MWT. Preliminary data suggests the 6MWT may be useful to determine acclimatization to altitude as attenuation of physiological responses (change in HR and post-test SpO$_2$) from baseline tests.

References