Supine lower body negative pressure exercise maintains upright exercise capacity in male twins during 30 days of bed rest

Stuart M.C. Lee[1], Suzanne M. Schneider[2],
Wanda L. Boda[3], Donald E. Watenpaugh[4], Brandon R. Macias[5],
R. Scott Meyer[5], and Alan R. Hargens[5]

[1]Wyle Laboratories, Inc., Life Sciences Group, Houston, TX
[2]Department of Physical Performance and Development,
University of New Mexico, Albuquerque, NM
[3]Sonoma State University, Rohnert Park, CA
[4]Sleep Consultants, Inc., Fort Worth, TX
[5]Department of Orthopedic Surgery, University of California-San Diego Medical Center,
San Diego, CA

Running Title: LBNP Exercise Maintains Post-Bed Rest Exercise Capacity

Corresponding Author:
Stuart M.C. Lee, MS
Wyle Laboratories, Inc.
Life Sciences Group
1290 Hercules Blvd.
Houston, TX 77058
Telephone: (281) 483-3726
FAX: (281) 483-4181
E-mail: slee1@ems.jsc.nasa.gov

ABSTRACT

Exercise capacity is reduced following both short and long duration exposures to microgravity. We have shown previously that supine lower body negative pressure with exercise ($LBNP_{ex}$) maintains upright exercise capacity in men after 5d and 15d bed rest, as a simulation of microgravity. We hypothesized that $LBNP_{ex}$ would protect upright exercise capacity (VO_2pk) and sprint performance in eight sets of identical male twins during a 30-d bed rest. Twins within each set were randomly assigned to either a control group (CON) who performed no exercise or to an exercise group (EX) who performed a 40-min interval (40-80% pre-BR VO_2pk) $LBNP_{ex}$ (55±4 mmHg) exercise protocol, plus 5 min of resting LBNP, 6 $d \cdot wk^{-1}$. LBNP produced footward force equivalent to 1.0-1.2 times body weight. Pre- and post-bed rest, subjects completed an upright graded exercise test to volitional fatigue and sprint test of 30.5 m. After bed rest, VO_2pk was maintained in the EX subjects (-3±3%), but was significantly decreased in the CON subjects (-24±4%). Sprint time also was increased in the CON subjects (24±8%), but maintained in the EX group (8±2%). The performance of a supine, interval exercise protocol with LBNP maintains upright exercise capacity and sprint performance during 30 d of bed rest. This exercise countermeasure protocol may help prevent microgravity-induced deconditioning during long duration space flight.

Keywords: space flight, microgravity, countermeasure, LBNP, artificial gravity

INTRODUCTION

Exposure to real or simulated microgravity significantly reduces aerobic exercise capacity [Convertino, 1996; Fortney, 1996]. Self-selected exercise patterns of Space Shuttle crewmembers do not maintain peak [Levine, 1996] and submaximal exercise responses [Lee, 1995] after short duration space flight (8-16 days). However, data during short [Levine, 1996; Moore, 2001] and long duration space flight [Michel, 1977] suggest that in-flight exercise performance is maintained or even improved with in-flight exercise countermeasures, but upright exercise performance after space flight is not protected.

Previous investigators have documented that vigorous, twice-daily supine exercise maintains supine exercise capacity after bed rest, as a simulation of microgravity [Greenleaf, 1989], but maintenance of upright exercise capacity may be more problematic [Convertino, 1982]. After 10 days of bed rest, VO_2max decreases 2-2.5 times more during upright exercise (-17%) compared to supine exercise [Convertino, 1982b; Hung, 1983] and the oxygen uptake kinetics during steady-state exercise are slower during upright exercise compared to supine exercise [Convertino, 1984]. Post-bed rest exercise in the upright posture is associated with a greater reduction in stroke volume and cardiac output than supine exercise [Convertino, 1996]. Maintenance of upright exercise capacity after space flight is more important operationally than supine exercise capacity because crewmembers must be prepared to perform an emergency egress from the Space Shuttle [Lee, 1997; Watenpaugh, 2000]. Emergency egress represents a significant metabolic (>2.5 $l\bullet min^{-1}$) and cardiovascular (>160 $beats\bullet min^{-1}$) stress in normal ambulatory subjects [Bishop, 1999] and would be a much greater challenge after long-duration International Space Station missions that typically last six months or more.

Previous investigations consistently demonstrate that plasma volume is rapidly reduced during exposure to space flight and bed rest. Convertino [Convertino, 1997] found that 70% of the variability in VO_2max following bed rest can be explained by a decreased plasma volume. Reduced circulating plasma volume may negatively affect exercise stroke volume, the delivery of oxygen and nutrients to working muscle, and the removal of metabolic waste products. Thus, preservation of plasma volume may be an important factor in the maintenance of exercise capacity during bed rest. Post-bed rest relative hypovolemia is more problematic during upright than supine exercise because of the gravitational shift of blood to the lower extremities with the addition of orthostatic stress.

The combination of a gravity-like stress during exercise training probably is necessary to maintain upright exercise responses after space flight and bed rest [Convertino, 1982]. Supine exercise may maintain plasma volume [Greenleaf, 1992], but a gravitational component, real or simulated, may be required to maintain venous return and stroke volume during post-flight exercise and work. The present study is one of a series to investigate the use of lower body negative pressure (LBNP) during exercise ($LBNP_{ex}$) as a countermeasure to space flight-induced deconditioning. Previous investigations from our group demonstrate that supine $LBNP_{ex}$ (Figure 1) produces exercise responses similar to upright exercise [Boda, 2000], maintains upright exercise responses after five days of bed rest [Lee, 1997], and protects upright exercise capacity during 15 days of bed rest [Watenpaugh, 2000]. The purpose of this investigation is to determine whether $LBNP_{ex}$

maintains upright exercise responses following a longer bed rest study, 30 days of 6° head-down tilt. Specifically, we hypothesized that subjects who exercised for 40 minutes against LBNP, with five minutes of post-exercise resting LBNP, would maintain upright submaximal and peak exercise responses following 30 days of bed rest, while a group of non-exercising control subjects would not. A unique aspect of this study was that identical twins were used as subjects, one as control and one as countermeasure subjects, to reduce the overall effect of genetic variability in these comparisons.

METHODS

Overall Protocol

Eight pairs of healthy male twins (27±5 yr, 174.6±12.9 cm; 68.0±11.0 kg, mean ±SD) volunteered to participate in this 30-day bed rest study. Monozygosity was confirmed using DNA polymorphism analysis for STR markers, D3 S1358, vWA, D16 S539, D2 S1338, D8 S1179, D21S11, D18 S51, D19 S433, Thol, and FGA. The subject's DNA was obtained using a cheek swab kit. Protocols were reviewed and approved by the Institutional Review Boards of University of California-San Diego (UCSD) and NASA-Johnson Space Center (JSC). Subjects received verbal and written explanation of all procedures and signed statements of informed consent prior to participation.

Subjects received complete physical examinations from qualified physicians and were admitted to the General Clinical Research Center (GCRC) at UCSD for the duration of the study. Subjects were hospitalized six days prior to bed rest for a period of ambulatory control during which they underwent familiarization and pre-bed rest testing sessions. Subjects completed a period of 30 days of strict 6° head-down tilt bed rest and were not allowed to be in the upright posture at any time during the bed rest. Urination, defecation, showering, and transport to and from all testing and countermeasure sessions were conducted in the head-down posture.

Within each twin pair, one twin was randomly assigned to the non-exercise control (CON) group and his brother to the exercise countermeasure group (EX). Six days per week during bed rest, the EX subjects performed 40-minutes of supine treadmill exercise against LBNP, followed by 5 minutes of resting lower body negative pressure (without exercise). LBNP was adjusted during these sessions such that subjects experienced between 1.0 and 1.2 times body weight during the countermeasure, similar to our previous work [Lee, 1997; Watenpaugh, 2000].

Subjects were prescribed a diet consisting of 55% carbohydrate, 15% protein, and 30% fat. The dietary staff of the GCRC prepared the food, and diet records were maintained to insure consistency. Initial caloric consumption was prescribed for each subject using the Harris-Benedict equations, adjusting for self-reported activity level (correction factor: 1.4-1.5) prior to hospitalization [Harris, 1919]. Thereafter, caloric consumption was adjusted such that subjects maintained their body weight within ±1.0 kg. Body weight was measured each morning at 0700 hrs, prior to breakfast, in the supine position using a bedside scale (Century CC894, Hill-Rom Co., Inc., Batesville, IN). Additionally, sodium consumption was maintained at 3,500 mg/day, calcium consumption was targeted at 800-1200 mg/day, and dietary fiber was prescribed at 25 g/day. Fluid intakes and output were measured daily. Fluid intake was *ad libitum*, but no caffeinated or alcohol beverages were allowed.

Subjects completed two graded exercise tests (GXT) to volitional fatigue before and one immediately after bed rest to determine the effectiveness of the $LBNP_{ex}$ countermeasure to prevent losses in maximal and submaximal exercise responses. On the same day prior to the GXT, subjects also participated in an orthostatic tolerance test to presyncope, sprint trials, and balance testing. These tests were performed in the same order at the same time of day during familiarization, pre-bed rest, and post-bed rest testing sessions. All tests were at least two hours postprandial. Orthostatic tolerance and balance results will be reported elsewhere. Plasma volume was measured the day before pre- and post-bed rest GXT.

Exercise Countermeasure

The exercise device used for this study (FIGURE 1) was the same as used in our previous 5-day [Lee, 1997] and 15-day bed rest studies [Watenpaugh, 2000]. The device consists of a vacuum chamber in which subjects ran comfortably on a vertically oriented treadmill (PaceMaster SX-Pro, Aerobics, Little Falls, NJ). Chamber pressure was reduced using a high capacity vacuum cleaner. A small amount of leakage was allowed in the chamber such that airflow through the system minimized heat accumulation caused by the treadmill motor and the exercising subject. Interchangeable wooden plates were used to allow the adjustment of the opening size through which the subject's legs and lower torso projected into the chamber. The size of the elliptical opening was chosen to be approximately twice the subject's waist cross-sectional area. In this way, the negative pressure required to produce 1.0 times body weight was approximately 50 to 60 mmHg.

INSERT FIGURE 1 HERE

Each subject wore a neoprene waist seal, with shoulder straps attached to prevent the seal from sliding down the subject's body and to provide 60-65% of BW through axial loading [Cao, 2005]. A sling supported the subject's upper body with a solid back support outside the chamber, and the hips were supported with a soft sling inside the chamber. Cuffs were placed around the knees and ankles. A bungee cord connected the cuffs at their respective positions through pulleys suspended from the ceiling of the chamber. In this way, the legs counterbalanced each other and minimized the work required to move against gravity. The distance between the treadmill and the chamber opening was adjusted such that the iliac crest was positioned at the level of the opening when the subject was flat-footed against the treadmill with their legs fully extended.

EX subjects performed 40 minutes of exercise 6 days per week using the same protocol that successfully preserved upright exercise capacity during 15-day bed rest [Watenpaugh, 2000]. Target exercise intensities for this protocol consisted of 7 minutes at 40%, 3 minutes at 60%, 2 minutes at 40%, 3 minutes at 70%, 2 minutes at 50%, 3 minutes at 80%, 2 minutes at 60%, 3 minutes at 80%, 2 minutes at 50%, 3 minutes at 70%, 2 minutes at 40%, 3 minutes at 60%, and 5 minutes at 40% pre-bed rest VO_2pk [Figure 2]. Target speeds to achieve these exercise intensities were prescribed based upon a linear relationship between treadmill speed and VO_2 determined during the pre-bed rest GXT. Lower body negative pressure was used to produce footward force of 1.0 times body weight at the start of bed rest and was increased up to 1.2 times body weight based upon subject tolerance to the exercise countermeasure. At the conclusion of the exercise period, LBNP was maintained for five minutes while the subjects rested with their legs outstretched to the treadmill belt.

EX subjects participated in the complete countermeasure session each day that exercise was prescribed (**FIGURE 2**), but two sessions were shortened in one subject (25 and 35 out of 40 minutes of exercise) due to treadmill malfunction. Most EX subjects completed their exercise at an LBNP that produced one body weight for the first two weeks. Thereafter, as their tolerance to exercise increased, six of eight subjects exercised at least three sessions at 1.05-1.1 times body weight, and three completed some of their exercise sessions at 1.2 times body weight. In one subject, three of the exercise sessions were performed at less than one body weight (90%) as he acclimated to the exercise at the start of bed rest, but he later exercised at 1.2 times body weight at the end of bed rest. EX subjects underwent LBNP 44.8±1.6 min per session and walked and ran for an average distance of 4.9±0.7 km (3.0±0.4 miles) per exercise session. Across all exercise sessions, the average LBNP was 55.4±3.4 mmHg, which corresponded to a mean loading of 1.0±0.1 times body weight.

INSERT FIGURE 2 HERE

Graded Exercise Test

Subjects performed two upright GXT's prior to bed rest and one GXT on the last day of bed rest. The first test served as a familiarization session and consisted of one five-minute stage of level walking at 4.8 km·h^{-1} (3 mph) followed by three-minute stages of increasing treadmill speeds (8.0, 9.7, and 11.3 km·h^{-1} [5, 6, and 7 mph]) at 0% grade.