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Title: Strength Training in Hypoxia to Improve Bone and Cardiovascular Health of Elderly

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Brief Summary

Due to age-related effects, the bone and cardiovascular health are damaged. Physical exercise and in particular the strength training has been proposed as a fundamental tool to these pathologies, especially in the elderly. On the other hand, the use of normobaric hypoxia combined with exercise could have a beneficial synergistic effect on disease prevention and the quality of life of the elderly.
Therefore, the general objective of this project is to analyze the effects of different methods of strength training combined with conditions of normobaric hypoxia on the bone and cardiovascular health of the elderly. This general objective is specified in the following specific objectives:

- To analyze the effects of resistance circuit training on bone mineral density and bone remodelling markers of elderly, under normoxic and normobaric hypoxic conditions.
- To analyze the effects of resistance circuit training on biochemical parameters, inflammatory, endothelial and clinical markers just like cardiovascular risk level of elderly, under normoxic and normobaric hypoxic conditions.
- To analyze the effects of resistance circuit training on body composition and functional capacity of elderly, under normoxic and normobaric hypoxic conditions.
- To analyze the effects of whole-body vibration training on bone mineral density and bone remodelling markers of elderly, under normoxic and normobaric hypoxic conditions.
- To analyze the effects of whole-body vibration training on biochemical parameters, inflammatory, endothelial and clinical markers just like cardiovascular risk level of elderly, under normoxic and normobaric hypoxic conditions.
- To analyze the effects of whole-body vibration training on body composition and functional capacity of elderly, under normoxic and normobaric hypoxic conditions.
- To compare the effects of resistance circuit versus whole-body vibration training on bone and cardiovascular health of elderly, under normoxic and normobaric hypoxic conditions.
- To value the normobaric hypoxic environment efficacy on bone and cardiovascular health of elderly subjected to resistance circuit and whole-body vibration training.

We hypothesize that bone and cardiovascular health will improve in the participants subjected to both resistance training, but greater improved may be found when these protocol are combined with normobaric hypoxia.

Methodology

Participants

Various associations of pensioners will be contacted as well as the university of seniors of the University of Extremadura to recruit volunteer participants. Total sample size will be 120 people, being this calculated to obtaining a statistical power of 90%, calculated with a margin of error of 5% and a mean difference of 10% in the study variables.

Inclusion criteria will be: (1) women and men aged 65 years or older; (2) no current medical condition not compatible with planned exercise; (3) free of illness or medication potentially affecting the bone and cardiovascular system; (4) estimated daily calcium intake of 1200-2000 mg/day; (5) consumption of no more than two alcoholic beverages per day. Exclusion criteria will be: (1) participation in any other type of intervention based on physical exercise in the last 6 months in order to avoid interactions with the previous practice; (2) subjects have been above 1500 m during the last 3 months; (3) contra indications for whole-body vibration training: severe cardiovascular diseases, ocular diseases that affect the retina, neuromuscular and heart diseases, stroke, implant, bypass, stent, arthritis and other joint disease or epilepsy.

Participants will be assigned to 6 different groups: (1) Normoxia Control Group (NCON), who will be instructed to continue with their normal daily activities for the entire duration of the study; (2) Hypoxia Control Group (HCON); who will perform an intellectual activity while they will be exposed to normobaric hypoxic conditions (16.0% FiO2); (3) Normoxia Circuit Training (NCIR); who will perform a circuit training with elastic bands in normoxic conditions (20.9% FiO2); (4) Hypoxia Circuit Training (HCIR); who will perform a circuit training with elastic bands in hypoxic conditions (16.0% FiO2); (5) Normoxia Vibration (NVIB); who will perform whole-body vibration training in normoxic conditions (20.9% FiO2); (6) Hypoxia Vibration (HVIB); who will perform whole-body vibration training in hypoxic conditions (16.0% FiO2).

All procedures will be performed in studies involving human participants will be in accordance with the 1964 Helsinki declaration and its later amendments or comparable ethical standards and the study design was approved by the Bioethical and Biosecurity Commission of the University of Extremadura (65/2018).

Design

This will be a randomised double-blind controlled study. There were separate intervention and assessment teams. We will try to blind the study for participants, as they will be trained/tested separately. Training sessions will be supervised by an experienced member of the research group.

All interventions will be performed during 24 weeks, with a frequency training of 3 days per weeks; sessions will be scheduled with at least one day of rest in between for optimal recovery. All patients were assessed at two time points: at baseline before the 24 weeks of intervention (Pre) and reassessed 7 days after the last session (Post). Participants will be instructed to continue with their normal daily activities, diet and caloric and calicium intake for the entire duration of the study.

Interventions

During several times of the session in each intervention, oxygen saturation (SpO_2) will be controlled using a finger pulse-oximeter (Konica Minolta, Japan) and heart rate (HR) using a heart rate monitor (Polar team 2, Polar, Finland) to know the physiological challenge posed on the participants during the exposure.

Passive hypoxia

During 30 minutes of session, the participants will be performed an intellectual activity while they will be exposed to normobaric hypoxic conditions in a hypoxic chamber (CAT 310, Lousiville, Colorado). They will inspire oxygen fraction (FiO2) set to 16.1% (0.16) in order to simulate an altitude of 2500m above sea level.

Normoxia circuit training

Each training sessions will consist of a circuit training with elastic bands, where different muscle groups will be involved (pectoral, shoulders, back, arms, thighs, legs and abdominals). Duration of the session will be about 30 minutes, which will include 10 minutes warm-up consisting of slight movements, and 5 minutes of static stretching for the muscles at the end of the sessions. Main section of the sessions will be a circuit that will be composed by 3 sets of 12-15 repetitions of nine different exercises. Six exercises will be performed using elastic resistance bands (ERS; TheraBand®): chest press, row, glute kickbacks, front and side raises, standing bíceps curls and tríceps kickbacks. To provide resistance with ERB, elastic bands with resistance ranging from light to very heavy loading (colors: yellow-gold) were used. ERBs were 2 meters, but the actual length used (grip on ERBs and distance to anchor point) was fine tuned for each subject in each exercise to find the correct resistance. When necessary to increase loading, two or more bands were combined. Bands were prestretched and never elongated more than 300% of resting length, as recommended by the manufacturer. Two additional exercise will be developed with kettlebell (KB): squat with 6 kg or increase loading until 10 kg; and hip trust, increase loading with support of a foot alone or with additional loading (KB of 5 or 10 kg). Finally, the subjects will keep a plank position during 15-20 seconds.

Training will take place in a hypoxia chamber (CAT 310, Lousiville, Colorado, United States) will place in the laboratory. In order to blind subjects to altitude, the system will be run with normoxic airflow into the chamber (up to 1000 l/min) and will produce the same audible noise as in the hypoxic condition. Subjects will inspire FiO2 of 21.0% (0.21) to simulate an altitude of 459 m above sea level. Furthermore, all systems will be covered with fabric to prevent participants from visually identifying the normoxic or hypoxic conditions. FiO2 will be controlled regularly with an electronic device (HANDIC,Maxtec, Salt Lake City, Utah, United States).

Hypoxia circuit training

Each training sessions will consist of a circuit training with elastic bands, where different muscle groups will be involved (pectoral, shoulders, back, arms, thighs, legs and abdominals). Duration of the session will be about 30 minutes, which will include 10 minutes warm-up consisting of slight movements, and 5 minutes of static stretching for the muscles at the end of the sessions. Main section of the sessions will be a circuit, that will be composed by 3 sets of 12-15 repetitions of nine different exercises. Six exercises will be performed using elastic resistance bands (ERS; TheraBand®): chest press, row, glute kickbacks, front and side raises, standing bíceps curls and tríceps kickbacks. To provide resistance with ERB, elastic bands with resistance ranging from light to very heavy loading (colors: yellow-gold) were used. ERBs were 2 meters, but the actual length used (grip on ERBs and distance to anchor point) was fine tuned for each subject in each exercise to find the correct resistance. When necessary to increase loading, two or more bands were combined. Bands were prestretched and never elongated more than 300% of resting length, as recommended by the manufacturer. Two additional exercise will be developed with kettlebell (KB): squat with 6 kg or increase loading until 10 kg; and hip trust, increase loading with support of a foot alone or with additional loading (KB of 5 or 10 kg). Finally, the subjects will keep a plank position during 15-20 seconds

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Normoxia whole-body vibration

The subjects will perform dynamic and static vibration exercise provide by a commercially available device (Galileo 2000, Novotec GmbH, Pforzheim, Alemania). The duration of the WBV session will be about 30 minutes, which will include 10 minutes warm-up consisting of slight movements, and 5 minutes of static stretching for the muscles at the end of the session.

Repetitions of 30 seconds with a frequency of 18.5 Hz will be performed. The rest interval will be 60 seconds between 4 repetitions during weeks 1–12 and 45 seconds between 5 repetitions during weeks 12–24. The vertical amplitude of WBV was set at 2.5 mm. Four stance will be performance, with the soles of both feet remained in contact with the platform:

1) Stand with feet side-by-side on the board, which produced lateral oscillations of the whole body. During the vibration training sessions, the subjects will be barefoot to eliminate any damping of the vibration caused by footwear. The angle of flexion of the knees during the vibration exercise will be set at 60°.

2) Begin with the feet placed perpendicular to the midline axis of the platform, with a foot positioned slightly ahead of the other foot. Lift the toes of the one foot and the heel of the other foot 4 mm above the surface of the platform. Bend the knees and maintain a 45°knee angle. Keep the back and head straight. Alternate legs.

3) Front foot 4 mm above the surface of the platform and back foot on ground, front knee angle 90°. Alternate legs

4) Lay down on the ground, with the knees bent and feet flat on the platform. Keep the arms at your side with your palms down. Lift the hips off the ground until the knees, hips and shoulders form a straight line. Hold your bridged position.

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Outcome Measures

Socio-Demographic Data and Lifestyle Questionnaires

A general questionnaire was administered to collect medical and demographic data to check the inclusion/exclusion criteria. As control variables, prior and after the intervention, calcium intake was estimated using a food frequency questionnaire. The bone-specific physical activity questionnaire (B-PAQ) was used to assess the physical activity level of the participants in the last 12 months.

Life Quality and Risk of Fall Questionnaires

SF-36 questionnaire will be used to know the life quality. Risk of fall will be evaluated through Fall Efficacy Scale-International (FES-I).

Cardiovascular Evaluation

Clinical tests of cardiovascular evaluation, such as recording of blood pressure with sphygmomanometer, arm-ankle index and pulse wave velocity using ultrasound Doppler technique will be used.

Cardiovascular Risk
Cardiovascular risk will be determined based on the following factors: age, sex, smoking, total cholesterol, HDL cholesterol, systolic blood pressure and diabetes, as described in the FRESCO study.

Anthropometric Measurements
Weight, height, body mass index and waist-hip ratio will measure following standart procedures.

Body composition
Body composition variables such as percentage fat, lean and bone mass will be obtain using dual-energy X-ray absorptiometry (DXA,Norland Excell Plus; Norland Inc., Fort Atkinson, United States) of whole body and corporal segment.

Bone Mineral Density
Bone mineral content (g) and density (g/cm-2) and T-score of whole body and proximal femur region will be calculated from obtained data of dual-energy X-ray absorptiometry (DXA,Norland Excell Plus; Norland Inc., Fort Atkinson, United States)

Blood Biomarkers
Standard biochemical analysis (HDL, LDL and Total Cholesterol, Triglycerides and Glucose) will be obtained of blood samples, through a clinical chemistry analyzer (Spotchem, Arkray Factory, Germany). Bone remodelling (VEGF and SDF-1), inflammatory (C-reactive protein, IL-2, IL-4, IL-6 and TNF alfa) and endothelial (ICAM-1 and VCAM-1) markers will be analyzed by ELISA technique.

Functional Capacity
Senior Fitness Test battery will be used to know of physical condition of elderly: lower limb strength (Chair stand), upper limb strength (Arm curl), lower limb flexibility (Chair sit and reach), upper limb flexibility (Back scratch), endurance (6 min. walk) and agility (8ft Up and Go) will be tested through this battery. Furthermore, core muscle strength (plank test), grip strength (hand grip) and balance (single leg stance test) will be measured

Statistical Analysis Plan (SAP)

Statistical analyses will be performed using the statistical analysis package SPSS v.20 (IBM, New York, United States). Data will be expressed as median and standard deviation. Kolmogorov–Smirnov tests will be conducted to show the distribution of the studied variables and Levene's test for homogeneity of variance. Repeated measure ANOVA will be used to compare the response of each variable, considering the sex and age as covariate. The $p < 0.05$ criterion was used for establishing statistical significance. Effect size (Cohen, 1992) will be also calculated for all variables, considering the magnitude of change as small (0.2), moderate (0.5) or large (0.8).

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