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Inspiratory muscle training reduces blood pressure and sympathetic activity in hypertensive patients: A randomized controlled trial

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ABSTRACT

Background: Autonomic imbalance, characterized by sympathetic hyperactivity and diminished vagal tone, is a known mechanism for essential hypertension. Inspiratory muscle training (IMT) demonstrates beneficial outcomes in a number of cardiovascular populations, which may potentially extend to patients with hypertension. The aim of this study was to further elucidate the effects of IMT on blood pressure and autonomic cardiovascular control in patients with essential hypertension.
Methods: Thirteen patients with hypertension were randomly assigned to an eight-week IMT program (6 patients) or to a placebo-IMT (P-IMT, 7 patients) protocol. We recorded RR interval for posterior analysis of heart rate variability and blood pressure, by ambulatory blood pressure monitoring (ABPM), before and after the program.
Results: There was a significant increase in inspiratory muscle strength in the IMT group (82.7 ± 28.8 vs 121.5 ± 21.8 cmH_2O, $P<0.001$), which was not demonstrated by P-IMT (93.3 ± 25.3 vs 106.1 ± 25.3 cmH_2O, $P>0.05$). There was also a reduction in 24-hour measurement of systolic (133.2 ± 9.9 vs 125.2 ± 13.0 mm Hg, $P=0.02$) and diastolic (80.7 ± 12.3 vs 75.2 ± 1.0 mm Hg, $P=0.02$) blood pressure, as well as in daytime systolic (136.8 ± 12.2 vs 127.6 ± 14.2 mm Hg, $P=0.008$) and diastolic (83.3 ± 13.1 vs. 77.2 ± 12.2 mm Hg, $P=0.01$) blood pressure in the IMT group. In relation to autonomic cardiovascular control, we found increased parasympathetic modulation (HF: 75.5 ± 14.6 vs. 84.74 ± 7.55 n.u, $P=0.028$) and reduced sympathetic modulation (LF: 34.67 ± 20.38 vs. 12.81 ± 6.68 n.u; $P=0.005$). Moreover, there was reduction of cardiac sympathetic discharge (fLF) in IMT group ($P=0.01$).
Conclusions: IMT demonstrates beneficial effects on systolic and diastolic blood pressure as well as autonomic cardiovascular control in hypertensive patients.

1. Introduction

Hypertension is known to be a major risk factor for cardiovascular morbidity and mortality [1–4]. Moreover, its severity is positively related to organ damage and the development of heart, kidney and liver failure [5]. One of the multifactorial causes of essential hypertension is autonomic imbalance, which is primarily treated by pharmacologic management [6].

Recently, several investigations have reported on the effects of non pharmacologic interventions on blood pressure management in this population [7–10]. Along these lines, previous studies have reported autonomic cardiovascular control alterations with different breathing patterns [7, 10–15], implicating a ventilatory influence on hemodynamics. Based on these results, one may posit that breathing exercises and respiration control are a viable treatment option for hypertension with a more favorable side effect profile compared to pharmacology.

Findings from previous breathing exercise programs in patients with hypertension, without an imposed external resistance or any documented improvement in inspiratory muscle strength and/or endurance, suggest that the resultant reduction in respiratory rate lowers blood pressure (BP) by favorable modulation of cardiovascular reflexes [7, 11].

Inspiratory muscle training (IMT), which does impose an external resistance to the respiratory musculature, has demonstrated beneficial training effects in patients with cardiovascular disease, specifically in patients with chronic heart failure [16]. However, to our knowledge, the effect of IMT in patients with essential hypertension has not been investigated. Moreover, there appear to be no reports about its effects on blood pressure and cardiovascular autonomic control in any cohort.

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Therefore, the purpose of this randomized trial is to test the hypothesis that an eight-week program of IMT would result in both a reduction in arterial blood pressure and improvement of autonomic cardiovascular control in patients with essential hypertension.

2. Materials and methods

2.1. Study design/selection criteria

A prospective, randomized, controlled, double blinded trial was conducted in patients with a diagnosis of essential hypertension (of all stages) who were recruited from the Ambulatory of Hypertension *of Instituto de Cardiologia do Rio Grande do Sul*. The primary endpoint of this study was to evaluate the effects of IMT on blood pressure and the secondary endpoint was to assess the impact of the intervention on autonomic cardiovascular control variables, inspiratory muscle strength and functional capacity. Inclusion criteria for the study were: previous Hypertension diagnosis, i.e. systolic blood pressure (SBP) >140 mm Hg and/or diastolic blood pressure (DBP)>90 mm Hg [5] in any stage and clinical stability with no change in medications for at least 2 months preceding the study. Exclusion criteria were: the presence of any comorbidity (diabetes, chronic heart failure, etc), unstable angina, myocardial infarction, chronic metabolic, orthopedic, or infectious disease; treatment with steroids, hormones, or cancer chemotherapy. Individuals with a previous diagnosis of pulmonary disease (forced vital capacity<80% of predicted and/or forced expiratory volume in 1 s<70% of predicted) [17], a history of exercise-induced asthma, and/or tobacco use were not recruited.

The protocol was approved, according to the ethical guidelines of the 1975 Declaration of Helsinki, by the Committee for Ethics in Research of the Federal University of Health Sciences of Porto Alegre (Protocol 08–447) and all subjects signed an informed consent form.

Eligible subjects were randomly assigned in blocks, by electronic randomization (www.randomization.com) to IMT or placebo-IMT (P-IMT) for 8 weeks. Before and after the intervention, electrocardiogram (ECG), inspiratory muscle function, blood pressure and functional capacity were assessed. Subjects and main investigators were unaware of group allocation for any subject. No changes were made to the methodological design throughout the study.

Methodological design was based on the determinations of CONSORT Statement, 2010 [18].

2.2. Inspiratory muscle training

The enrolled patients performed IMT or P-IMT for 30 min, 7 days per week, for 8 weeks using the Threshold Inspiratory Muscle Training device (Threshold Inspiratory Muscle Trainer, Healthscan Products Inc., Cedar Grove, New Jersey). During training, subjects were instructed to maintain diaphragmatic breathing at a rate at 15 to 20 breaths/min. For the IMT group, inspiratory load was set at 30% of maximal static inspiratory pressure (PImax), and the training loads were adjusted weekly to maintain 30% of PImax during all protocol period. The P-IMT group followed the same schedule, but with no inspiratory load.

2.3. Maximal static inspiratory pressure

Inspiratory muscle function testing was performed using a pressure transducer (MVD-300, Globalmed, Porto Alegre, Brazil), connected to a system with two unidirectional valves (DHD Inspiratory Muscle Trainer, Chicago, Illinois). PImax was determined in deep inspiration from residual volume against an occluded airway with a minor air leak (2 mm). The highest pressure of six measurements (with less than 5% difference) was used to define PImax. The measurements were performed before and after the protocol by a blinded investigator, and weekly during treatment.

2.4. Ambulatory blood pressure monitoring (ABPM)

To assess changes in arterial blood pressure following the intervention, ABPM was measured by a DynaMAPA® monitor (Cardios, São Paulo, Brazil), validated according to international standards of the British Hypertension Society [19] and American Association for the Advancement of Medical Instrumentation (AAMI) [20]. The monitor was programmed to take BP every 15 min during the day and every 30 min at night for 24 h, with a properly sized cuff positioned in the non-dominant arm. Each participant received verbal and written instructions on the monitoring procedure and a diary to record sleep periods, posture, activity status, medication use, and symptoms. A contact number was provided for subjects to ask for advice and instructions or report any technical difficulty during the monitoring period. The exam was considered satisfactory when at least 85% of the 24 hour measurements were assessed.

2.5. Heart rate variability (HRV)

Acquisition of the electrocardiogram signal was performed immediately before and after the interventions. Measurements were taken with the subject resting comfortably in supine position, head elevation of 30°, knees resting on a wedge and controlled breathing. The breathing control was conducted by musical sounds in which the respiration rate was about 12 breaths/min (I:E = 2:3). For the analysis of the heart rate variability, temporal series of RR intervals, obtained by the continuous ECG signal (sample rate — 1 kHz) registered by a Biopac MP150 system (Biopac, California, USA), were interpolated and later submitted to spectral analysis through an auto regressive model developed in Matlab language (Matlab 6.0, Mathworks Inc., USA). The spectral analysis of collected signals was done using software capable of this type of analysis [21], allowing for the preliminary processing of the registered signals and evaluation of all the needed parameters obtained by the self-regressive model. The temporal series spectra of the tachogram, related to each selected segment, were evaluated quantitatively considering the values of HRV and the relation between the power of the components LF and HF of HRV or sympathetic–vagal balance (LF/HF). The outcome variable consisted on the analysis of HRV, performed by an individual blinded to subject group assignment.

2.6. Cardiopulmonary exercise testing

Maximal functional capacity was evaluated with an incremental exercise test, with simultaneous measurement of ventilatory expired gas analysis, on a cycloergometer (Inbrasport, Porto Alegre, Brazil). A ramp protocol was employed with a constant speed of 60 rpm (rotations per minute), starting load of 25 W and increments each 2 min of 15 or 25 W, depending on patients physical condition, to reach volitional fatigue at approximately 10 min. Twelve-lead electrocardiographic tracings were obtained beat-to-beat (Inbramed APEX 2000, Porto Alegre, Brazil). Blood pressure was measured every 2 min with a standard cuff sphygmomanometer. Metabolic and ventilatory variables were measured during and after exercise by 20-s mean aliquots, using a computer-aided gas analyzer (VO_{2000} Inbrasport) that was calibrated prior to each test. During the test, we analyzed minute ventilation (V_E), oxygen consumption (VO_2), carbon dioxide production (VCO_2), respiratory exchange ratio, (VCO_2/ VO_2) and ventilatory equivalents for oxygen (V_E/VO_2) and carbon dioxide (V_E/VCO_2). Based on this data, the maximal oxygen consumption ($VO_{2máx}$) was determined, as well as the first (L1) and second (L2) ventilatory thresholds.

2.7. Statistical analysis

Data were analyzed by the Statistical Package for Social Sciences (version 10.0, SPSS, Chicago, Illinois) and tested with the Kolmogorov–Smirnov for normality. All the variables fulfilled normality criteria. Descriptive data are presented as mean ± SD. Baseline and blood pressure data were compared by the Student *t* test for continuous variables or by the Fisher exact test for categorical variables. Heart rate variability components and PImax were analyzed by two-way analysis of variance for repeated measures (ANOVA), and post-hoc analysis was conducted by the Neuman–Keuls test. A *P*-value<0.05 was considered statistically significant for all tests.

3. Results

3.1. Baseline characteristics

From July 2009 to September 2010, 168 patients with essential hypertension were screened for the study. Out of those, 149 patients did not meet the inclusion or met one or more of the exclusion criteria, and so, 19 patients were randomized. For the 9 patients allocated in the IMT group, 1 had a new diabetes diagnosis during the protocol, 1 had an alteration in pharmacologic management and 1 refused to continue the protocol. Thus, 3 subjects were excluded from the IMT group after initial enrollment. For the 10 patients allocated to P-IMT, 1 became pregnant at the end of the protocol and could not do the final assessment, 1 had a new heart failure diagnosis during the protocol and 1 had an alteration in pharmacologic management. Therefore, 13 patients completed the protocol, 6 patients in the IMT group and 7 patients in the P-IMT group. A flow diagram of included, excluded and the final number of participants is illustrated in Fig. 1. Clinical characteristics for both groups, baseline scores, including diastolic and systolic BP, heart rate variability and PImax, were comparable between the two groups (Table 1).

3.2. Inspiratory muscle strength

There was a significant increase in PImax in IMT group (82.7 ± 28.8 vs 121.5 ± 21.8 cmH_2O, $P<0.001$ for time effect and $P=0.003$ for interaction effect). Conversely, the P-IMT group did not show any change in respiratory muscle strength following treatment (93.3 ± 25.3 vs 106.14 ± 25.3 cmH_2O, $P>0.05$) (Fig. 2). The IMT induced improvement in PImax was apparent after the 5 week of training and reached a 47% increase after 8 weeks.