Physical Training as Non-Pharmacological Treatment of Neurocardiogenic Syncope

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Abstract

Background: Characterized as a sudden and temporary loss of consciousness and postural tone, with quick and spontaneous recovery, syncope is caused by an acute reduction of systemic arterial pressure and, therefore, of cerebral blood flow. Unsatisfactory results with the use of drugs allowed the nonpharmacological treatment of neurocardiogenic syncope was contemplated as the first therapeutic option.

Objectives: To compare, in patients with neurocardiogenic syncope, the impact of a moderate intensity aerobic physical training (AFT) and a control intervention on the positivity of head-up tilting test (HUT) and orthostatic tolerance time.

Methods: Were studied 21 patients with a history of recurrent neurocardiogenic syncope and HUT. The patients were randomized into: trained group (TG), n = 11, and control group (CG), n = 10. The TG was submitted to 12 weeks of AFT supervised, in cycle ergometer, and the CG to a control procedure that consisted in 15 minutes of stretching and 15 minutes of light walk.

Results: The TG had a positive effect to physical training, with a significant increase in peak oxygen consumption. The CG did not show any statistically significant change before and after the intervention. After the intervention period, 72.7% of the TG sample had negative results to the HUT, not having syncope in the revaluation.

Conclusion: The program of supervised aerobic physical training for 12 weeks was able to reduce the number of positive HUT, as it was able to increase tolerance time in orthostatic position during the HUT after the intervention period. (Arq Bras Cardiol. 2014; 102(3):288-294)

Keywords: Aerobic physical training; Neurocardiogenic syncope; Head-up tilting test.

Introduction

Syncope is defined as a sudden and temporary loss of consciousness and postural tone characterized by a quick and spontaneous recovery. It is caused by an acute decrease in systemic arterial blood pressure and cerebral blood flow. Neurocardiogenic syncope (NCS) is the most frequent type of syncope, and, although benign, recurrent symptoms decrease the quality of life of patients in the same manner as chronic diseases. The passive head-up tilt test (HUT) is an effective and safe method to identify patients with suspected NCS. Its reproducibility, when positive, is approximately 82%

The physiopathology of NCS remains unclear; however, an impairment of the compensatory reflex mechanisms responsible for maintaining pressure levels in the short term is observed. In NCS, unknown trigger mechanisms activate a specific autonomic efferent response, with a decrease in the sympathetic arteriolar stimulation and/or increase in the parasympathetic tonus at the sinus node, thereby resulting in vasodilatation and/or bradycardia that decreases the systemic arterial pressure. Syncope is usually preceded by prodromes such as pallor, nausea, sweating, dizziness, visual disturbances, and palpitations. It may be triggered by orthostatic stress, particularly in hot environments, pain or emotional stress, low hydration, and prolonged fasting.

The various forms of treatment proposed for NCS have not been completely investigated. Well-conducted randomized studies have shown that preventive pharmacological therapy is ineffective, which has led to the possibility of considering nonpharmacological treatments as first-line therapeutic options. Aerobic physical training (AFT) has been extensively studied as part of the treatment for NCS. In previous studies, increased orthostasis tolerance time and blood volume as well as decreased levels of circulating vasopressin were observed in patients with NCS. Aerobic training decreases cardiac sympathetic tonus, which may cause a decrease in the
chronotropic and inotropic responses that are responsible for triggering the Bezold–Jarisch reflex when venous return is decreased because of orthostasis; in addition, it improves baroreflex sensitivity. This study aimed to clarify the effectiveness of AFT in the treatment of NCS.

Objective

This study aimed to compare the effects of moderate-intensity AFT on HUT positivity and orthostasis tolerance time with those of a control intervention in patients with NCS.

Methods

This prospective study included 21 sedentary patients with positive HUT results and a history of recurrent NCS (>2 episodes, with the last episode having occurred during the 6 months before the start of this study). These patients underwent the diagnostic test after being referred to the General Cardiology, Arrhythmia, and Neurology Outpatient Clinics of the Hospital das Clínicas of the School of Medicine of Ribeirão Preto–USP. Following inclusion in the study, the patients were reassessed by a cardiologist to rule out cardiac and neurological causes of syncope. They also underwent complementary tests, including resting electrocardiogram (12 leads), Doppler-echocardiogram, and 24-h electrocardiogram (Holter). The selected individuals were studied in the absence of drugs that could interfere with the response of the analyzed variables. Patients with suspected chronic diseases such as diabetes and coronary artery disease were excluded from the study, along with those who had some orthopedic or functional limitation that prevented them from performing aerobic exercise.

The study was approved by the Research Ethics Committee of our institution. All patients provided written informed consent.

The passive HUT

During the test, the patients were maintained in the supine position with a saddle support for 20 min on a tilt table. The following parameters were assessed at baseline and tilt: surface electrocardiogram, instantaneous heart rate (cardio tachometer), and arterial blood pressure by auscultatory method and beat-by-beat using the plethysmographic method (Finapres – Ohmeda – 2300).

After the resting period in the horizontal supine position, the table was tilted to a vertical position at an angle of 70º (head-up tilt) in less than 10 s and the test was continued for 45 min. The test was immediately interrupted if the patient reached the preset positivity criteria. In this case, the table was quickly returned to the horizontal position or the Trendelenburg position, when necessary, for a period of 5 min or until complete recovery of the patient. Both the initial and re-evaluation tests were performed using the same methodology.

The ergospirometric test (ET)

All patients underwent the maximal cardiopulmonary exercise test. The protocol involved dynamic physical effort to be applied while sitting on a cycle ergometer with an electromagnetic brake (Corival 400, Quinton). The power applied to the cycle ergometer was of the ramp-type, and the intensity was determined individually according to the formula developed by Wasserman et al., which was based on anthropometric characteristics, age, and gender. The patients were encouraged to apply effort until the point of exhaustion. During the test, the initial ramp was preceded by a period of 4 min at minimum load (3–4 Watts) and a constant speed of 60 rotations per min, with the aim of warming up the physiological systems involved in oxygen delivery and allowing them to reach the steady-state. In this protocol, the ventilatory variables were obtained using an ergosiometry device (CPX/D MedGraphics) that allowed the acquisition, processing, and recording of these variables on a breath-to-breath basis. The peak values of oxygen consumption (VO), and heart rate (HR) were expressed as the mean of the last 30 s of recording during the effort period.

Intervention protocol

Following confirmation of diagnosis based on the HUT, all patients received general guidance on how to avoid situations and places that could trigger syncope, such as excessive heat, closed crowded environments, dehydration, prolonged fasting, remaining in a vertical position for a long time, and emotional stress. They received instructions to increase the intake of water, perform isometric contraction maneuvers, and/or lie down on experiencing the first presyncopal symptoms. In addition, they were asked to note, in a diary, the dates of any syncope episodes and/or presyncopal symptoms experienced during the intervention period.

To incorporate a training protocol, the individuals were randomized into 2 groups: a trained group (TG, n = 11) and a control group (CG, n = 10). The TG was subjected to a 12-week program of supervised AFT using a cycle ergometer. The intensity of training was prescribed such that the HR was maintained between the value corresponding to the ventilatory anaerobic threshold (VAT) and that corresponding to 10% below the respiratory compensation point (RCP). A heart rate monitor (Polar®) was used throughout the session. Training took place twice a week and lasted for 35 min, and the patient was instructed to perform 2 more unsupervised sessions. If the patient was unable to attend the scheduled session, another session was rescheduled for the same week to ensure that all supervised sessions were conducted. To ensure adherence to external training, the unsupervised sessions were subjected to weekly control using a spreadsheet given to the patient that was checked at every session.

The CG was subjected to a control procedure that included 15 min of stretching, 15 min of light walking below the prescribed target HR, and 10 min of relaxation. The HR was monitored throughout the procedure using an HR monitor (Polar®) to ensure that it was maintained below the calculated target HR. Two weekly sessions were performed over a period of 12 weeks.

After 12 weeks, both groups were re-evaluated using HUT and ET.
Statistical analysis

Data are expressed as means ± standard deviations and medians. For intergroup analysis of anthropometric data, analysis of variance (ANOVA) was used. Fisher’s exact test was used to compare the response to the HUT and the intervention. To compare the number of syncope episodes between groups, the Poisson model with random effects was used. Spearman's correlation coefficient was used to assess the association between the 2 quantitative variables. The level of statistical significance was 5%.

Results

The anthropometric characteristics and basal hemodynamic parameters are shown in Table 1. There was no statistically significant difference between groups.

The results obtained in the ergospirometric stress tests are presented in Table 2. There was no significant difference between groups during the preintervention period. After 12 weeks of aerobic training, the TG exhibited a tendency for higher peak HR, with VO₂ peak and VO₂ at AT being significantly higher in the TG than in the CG. The CG did not exhibit any statistically significant changes in ergospirometry variables before and after the training period. After the intervention, the TG exhibited a higher VO₂ at AT compared with the CG.

Figure 1 shows an analysis of the number of syncope episodes experienced by the patients during 3 distinct periods: from 1 year to 6 months before the intervention (P1), during the 6 months before the intervention (P2), and 3 months after the start of the intervention (P3). The TG exhibited a statistically significant difference between periods P1 and P3 and between P2 and P3, whereas the CG did not exhibit any statistically significant difference between P1 and P3. On comparing both groups, a significant difference was observed for P3.

In the initial evaluation of both groups, all individuals exhibited a positive HUT result (Table 3). There was no statistically significant difference between groups in orthostasis tolerance time before the intervention (Table 4).

After the intervention period, 72.7% patients in the TG exhibited a negative HUT, with no episodes of syncope reported during re-evaluation. In the CG, only 30% patients exhibited a negative HUT; this difference was significant (Table 3). Individuals with a positive HUT result after the intervention, those in the TG exhibited an increased orthostasis tolerance time compared with those in the CG. This difference was statistically significant (Table 4).

There was no correlation between the increase in physical capacity (delta of peak VO₂) and increase in orthostasis tolerance time (delta of orthostasis tolerance time) in both groups.

Discussion

NCS is a transient functional impairment of the autonomic nervous system that primarily affects healthy young women who do not exhibit signs of structural heart disease or neurological disease. Patients who experience recurrent episodes experience limitations in their daily and professional activities, which greatly affects their quality of life.

The pharmacological treatment of syncope, which is based on medications such as beta blockers, fludrocortisone, and serotonin reuptake inhibitors, is part of the available therapeutic arsenal; however, in the vast majority of patients, pharmacological therapy for the treatment of this dysautonomia does not offer effective results.

Therefore, a variety of nonpharmacological approaches have been proposed. These include prevention by avoiding the triggering factors, e.g., increasing water intake throughout the day, avoiding the vertical position at rest, avoiding prolonged fasting, and undergoing passive postural training (tilt training), and the use of maneuvers to avoid syncope when the patient exhibits the so-called prodromes. In these situations, the patients can be instructed to perform maneuvers or adopt postures that prevent the progression of the presyncope to syncope, such as crossing of the legs in the vertical position, isometric effort with the upper limbs, and change to the horizontal position. Among these measures, physical training has been gaining importance.

Table 1 – Antropometric characteristics and basal hemodynamic parameters in the trained group (TG) and control group (CG)

| Gender | Mean (SD) |
|--------|-----------|
| TG     |           |
| Male   | 2         |
| Female | 9         |
| Age (years) | 32 (10) | 26 (8) |
| Height (cm)    | 164 (9.4) | 163.5 (5.5) |
| Body mass (kg) | 67 (11.2) | 63 (10.0) |
| Heart rate (bpm) | 64 (8)    | 65 (7) |
| Systolic arterial pressure (mmHg) | 110.9 (17.1) | 109.0 (17.1) |
| Diastolic arterial pressure (mmHg) | 71.8 (12.7) | 69.0 (11.0) |

SD: Standard deviation.
Table 2 – Description of the variables measured in the ergospirometric test before and after intervention in the trained group (TG) and control group (CG)

| Group   | Period | Variable | n | Mean | SD | CV | Minimum | Median | Maximum |
|---------|--------|----------|---|------|----|----|---------|--------|---------|
| Control | Before | HR rest  | 10 | 65   | 7  | 11 | 11      | 63     | 77      |
|         |        | HR peak  | 10 | 168  | 14 | 9  | 143     | 173    | 183     |
|         |        | VO<sub>p</sub>peak | 10 | 24.3 | 7.55 | 31.06 | 16 | 22.95 | 40 |
|         |        | VO<sub>AT</sub> | 10 | 12.4 | 3.27 | 26.39 | 8 | 12 | 20 |
|         | After  | HR rest  | 10 | 66   | 6  | 9  | 59      | 65     | 82      |
|         |        | HR peak  | 10 | 169  | 17 | 10 | 123     | 172    | 181     |
|         |        | VO<sub>p</sub>peak | 10 | 22.84 | 7.25 | 31.72 | 14.3 | 22 | 38 |
|         |        | VO<sub>AT</sub> | 10 | 11.8<sup>‡</sup> | 3.12 | 26.44 | 9 | 11 | 19 |
| Trained | Before | HR rest  | 11 | 64   | 8  | 12 | 51      | 66     | 78      |
|         |        | HR peak  | 11 | 162  | 16 | 10 | 133     | 166    | 180     |
|         |        | VO<sub>p</sub>peak | 11 | 21.1<sup>‡</sup> | 4.02 | 19.03 | 14 | 21.15 | 26.8 |
|         |        | VO<sub>AT</sub> | 11 | 12<sup>‡</sup> | 1.48 | 12.36 | 9 | 12 | 14 |
|         | After  | HR rest  | 11 | 66   | 10 | 15 | 52      | 64     | 83      |
|         |        | HR peak  | 11 | 169  | 10 | 6  | 150     | 171    | 181     |
|         |        | VO<sub>p</sub>peak | 11 | 25.35<sup>‡</sup> | 3.93 | 15.51 | 21.6 | 25 | 34.8 |
|         |        | VO<sub>AT</sub> | 11 | 14.27<sup>‡</sup> | 2.28 | 16 | 10 | 14 | 19 |

SD: standard deviation; CV: coefficient of variation; HR: heart rate; AT: anaerobic threshold; p ≤ 0.05; VO<sub>p</sub> peak in the trained group before and after the intervention.

because of the positive results observed in terms of a decrease in and/or elimination of NCS episodes<sup>1,20,24,33,34</sup>. In our study, AFT resulted in a significant increase in VO<sub>p</sub> at stress peak and at VAT in the TG<sup>26</sup>. Moreover, the CG did not exhibit significant changes in oxygen delivery parameters during stress, either at submaximal levels or at maximal levels. These findings suggest that in the TG, the physiological adaptations induced by aerobic training are responsible for the decrease in the number of individuals with a positive HUT result and increased orthostasis tolerance time after 12 weeks of the intervention.

In 2007, Gardenghi et al<sup>24</sup> conducted a 4-month study about the impact of different therapeutic methods (moderate AFT, passive postural training, pharmacological treatment, and control) on the improvement of the baroreceptor reflex in patients with NCS and observed that only AFT was effective in increasing arterial baroreflex sensitivity, which decreased in the studied group. Brum et al<sup>25</sup> reported that physical training increased baroreflex sensitivity in normotensive and hypertensive rats. In 1998, Gava et al<sup>33</sup> described the decrease in sympathetic cardiac tonus in rats with spontaneous hypertension after physical training, which decreased cardiac chronotropic and inotropic responses that are responsible for triggering the Bezold–Jarisch reflex when venous return is decreased because of gravitational stress.

Mitsnangi and Hainsworth<sup>35</sup> and Carrol et al<sup>21</sup> reported an increase in orthostasis tolerance time in patients with NCS who underwent AFT, a finding consistent with our findings. Increased circulating blood volume and decreased levels of circulating vasopressin were observed in these patients. Convertino et al<sup>22</sup> found a significant increase in the circulating plasma volume of individuals subjected to moderate intensity AFT.

In this context, it is worth noting the study conducted by Allen et al<sup>15</sup> in 1945, wherein 2 identical twins with positive tilt tests were studied. One of them performed physical training over 3 weeks, whereas the other remained sedentary. After the intervention period, the sedentary twin exhibited a positive HUT result, whereas the active twin exhibited a negative HUT result.

AFT, in addition to promoting beneficial changes in the autonomic modulation of the cardiovascular system in patients with NCS, can also increase blood volume, hemoglobin levels, and muscle tonus in the lower limbs (when exercise involves these muscle groups)<sup>36</sup>. Moreover, physical training is responsible for the increase in the final diastolic and systolic volumes, which may interfere with the stimulation of ventricular C fibers that trigger NCS.<sup>5,16</sup>

Although the present study was not designed to explore the physiopathological mechanisms responsible for syncope, which are many and complex, and considering that we assessed the effects of a 12-week physical training program, it is unlikely that the increase in circulating plasma volume is key to the reported findings.<sup>20,33-35,37</sup> In this study, changes in arterial baroreceptor reflex sensitivity probably played an important role in the effects observed in the trained group, considering that other studies have reported these adaptations to short- and long-duration aerobic physical exercise.<sup>24,25,38,39</sup>
Table 3 – Results of the head-up tilt test before and after the intervention in the trained group (TG) and control group (CG)

|                | TG (n = 11) |   | CG (n = 10) |   |
|----------------|------------|---|-------------|---|
|                | Before     | After | Before     | After |
| Positive       | 11 (100%)  | 3 (27.3%) | 10 (100%)  | 7 (70%) |
| Negative       | 0          | 8 (72.7%)* | 0          | 3 (30%)* |

*p ≤ 0.05; HUT result between the TG and CG after the intervention.

Table 4 – Orthostasis tolerance time before and after the intervention in the trained group (TG) and control group (CG)

| Group     | Time  | n   | Mean  | SD   | CV   | Minimum | Median | Maximum |
|-----------|-------|-----|-------|------|------|---------|--------|---------|
| Control   | Before| 10  | 31.3  | 12.9 | 41.2 | 9       | 35.5   | 44      |
|           | After | 10  | 27.6* | 13.6 | 49.3 | 4       | 25.5   | 45      |
| Trained   | Before| 11  | 28.6† | 13.8 | 48.0 | 8       | 32     | 44      |
|           | After | 11  | 39.9**| 9.9  | 25.1 | 18      | 45     | 45      |

SD: standard deviation; CV: coefficient of variation; *p ≤ 0.05; orthostasis tolerance time (min) after the intervention between the CG and TG. †p ≤ 0.05; orthostasis tolerance time in the TG before and after the intervention.
Conclusions
The 12-week supervised AFT program was effective in decreasing the number of patients with positive HUT results and increasing the orthostasis tolerance time after the intervention period in patients with NCS.

Limitations
The effects of physical training as a nonpharmacological procedure for the treatment of NCS require further investigations. Because of the short follow-up period used in the present study, syncope recurrence could not be evaluated and the clinical impact of the intervention on the natural progression of the disease could not be determined.

Author contributions
Conception and design of the research: Takahagi VCM, Gallo Júnior L; Acquisition of data: Takahagi VCM, Costa DC, Crescêncio JC; Analysis and interpretation of the data and Statistical analysis: Takahagi VCM; Writing of the manuscript: Takahagi VCM, Costa DC; Critical revision of the manuscript for intellectual content: Gallo Júnior L.

Potential Conflict of Interest
No potential conflict of interest relevant to this article was reported.

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