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ORIGINAL ARTICLE

Tilt training increases vasoconstrictor reserve in patients with neurocardiogenic syncope☆

Sérgio Laranjo[a,b,*], Mário Martins Oliveira[a,b], Cristiano Tavares[a,b], Vera Geraldes[a,b], Sofia Santos[c], Eunice Oliveira[c], Rui Ferreira[c], Isabel Rocha[a,b]

[a] *Instituto de Fisiologia e Unidade de Sistema Nervoso Autónomo, Faculdade de Medicina de Lisboa, Lisboa, Portugal*
[b] *Instituto de Medicina Molecular, Lisboa, Portugal*
[c] *Serviço de Cardiologia, Hospital de Santa Marta, Centro Hospitalar de Lisboa Central, EPE, Lisboa, Portugal*

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Abstract Neurocardiogenic syncope (NCS) is a common clinical entity resulting from an excessive reflex autonomic response, particularly during orthostatism. Treatment options are controversial and of limited effectiveness. Tilt training (TT) is a promising option to treat these patients. However, its mechanism of action and clinical impact remain unclear.
Objective: To characterize hemodynamic and autonomic responses during a TT program in patients with NCS refractory to conventional measures.
Methods: We studied 28 patients (50% male, mean age 41 ± 14 years) without structural heart disease, with NCS documented by tilt testing. The TT program included nine tilt sessions (three times a week, 30 min) (60° – 6 sessions, 70° – 3 sessions), under ECG and blood pressure monitoring combined with home orthostatic self-training and 10° head-up during sleep. Systolic volume, cardiac output, total peripheral resistance, baroreflex sensitivity and heart-rate variability were computed. Patients were reassessed at 1 month and every 6 months for a maximum of 36 months (24 ± 12 months).
Results: Over the course of the TT program there was a significant increase in total peripheral resistance (1485 ± 225 vs. 1591 ± 187 dyn s cm^{-5}, $p < 0.05$), with a decrease in standard deviation (206 ± 60 vs. 150 ± 42, $p < 0.05$). During follow-up, syncope recurred in five patients (19%), with a significant reduction in the number of episodes (4.0 ± 3.2/patient in the 12 months before TT vs. 1.4 ± 0.8/patient post-TT, $p < 0.05$).
Conclusion: In refractory NCS, TT may be an effective therapeutic option, with long-term benefits. These results appear to be due to an increase in vasoconstrictor reserve combined with a reduction in its variance.

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* Corresponding author.
E-mail address: sergiolaranjo@gmail.com (S. Laranjo).

PALAVRAS-CHAVE
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O treino de ortostatismo (tilt training) aumenta a reserva vasoconstritora em doentes com síncope reflexa neurocardiogénica

Resumo A síncope neurocardiogénica (SNc) é uma entidade clínica comum, resultante de uma resposta autonómica reflexa excessiva durante o *stress* ortostático. As diferentes opções terapêuticas são controversas e de eficácia limitada. O treino de ortostatismo (TTr) tem-se mostrado uma alternativa prometedora no tratamento destes doentes (D). No entanto, permanece por esclarecer o seu mecanismo de acção e o impacto clínico numa população com SNc recorrente.

Objectivo: Caracterizar a resposta hemodinâmica e autonómica durante um programa de TTr em doentes com SNc refractária às medidas convencionais.

População e métodos: Foram estudados 28D (50% do sexo masculino, 41 ± 14 anos), sem evidência de cardiopatia, com SNc documentada em teste de ortostatismo passivo. O TTr incluiu 9 sessões hospitalares (3×/semana, 30 minutos) com monitorização contínua de pressão arterial e frequência cardíaca (60° – 6 sessões – 70° – 3 sessões), complementadas com treino diário no domicílio e elevação da cabeceira a 10° durante o sono. O volume sistólico, o débito cardíaco, a resistência vascular periférica, a sensibilidade do barorreflexo e a variabilidade da frequência cardíaca foram calculados. Todos os doentes foram reavaliados no fim do 1° mês e no final de cada 6 meses num período máximo de 36 meses (*follow-up* 24 ± 12 meses).

Resultados: Ao longo das sessões de TTr verificou-se um aumento significativo e consistente da resistência total periférica (1485 ± 225 vs. 1591 ± 187 dyne*s/cm5, p < 0,05) associado a uma diminuição do seu desvio-padrão (206 ± 60 vs. 150 ± 42, p < 0,05). Durante o período de *follow-up*, houve recorrência de síncope em 5D (19%), com redução significativa do numero de síncopes (4.0 ± 3.2/D nos 12 meses pre-TTr vs. 1.4 ± 0.8/D pos-TTr, p < 0.05).

Conclusão: Em doentes com SNc refractária, o TTr mostrou ser uma opção terapêutica eficaz, com beneficio a longo-prazo. A melhor tolerância ao ortostatismo parece resultar do aumento da reserva vasoconstritora e da sua menor variabilidade.

Introduction

Syncope is defined as a transient loss of consciousness due to transient global cerebral hypoperfusion characterized by rapid onset, short duration, and spontaneous complete recovery. It is common in the general population, with an estimated incidence of 18.1–39.7 events/1000 person-years,[1] and has serious effects on quality of life, including high morbidity, risk of physical injury and work absenteeism.[2,3]

Neurocardiogenic syncope (NCS) is the most common form, with a higher incidence in young adults.[4,5] Its pathophysiology is poorly understood, but it has been demonstrated that alterations in the reactions of the autonomic nervous system to stressful stimuli such as active orthostatism are involved in triggering syncope.[6]

Various treatment options have been proposed over the years for NCS, ranging from behavior modification to cardiac pacing and various types of drug therapy, but none has been shown to be fully effective.

Tilt training (TT), a new non-pharmacological treatment for NCS, was proposed in 1998 by Ector et al.,[7] who showed that repeated and prolonged exposure of the cardiovascular system to orthostatic stimuli had therapeutic effects in patients with NCS. The effectiveness of tilt training has been evaluated in several non-randomized observational studies,[8–10] but the results have been inconsistent, varying according to the training protocol and particularly patient compliance. The mechanisms of action are largely unknown; it is thought that desensitization of cardiopulmonary receptors to orthostatism may be involved, as well as autonomic remodeling and alterations in baroreflex activity.

The aim of this study was to clarify the mechanisms of action of tilt training, specifically to characterize hemodynamic and autonomic responses during a TT program in patients with NCS refractory to conventional measures.

Part of this work was awarded the prize for best communication at CPC2010.

Methods

Population

Between 2007 and 2010 we studied 28 patients (50% male, mean age 41 ± 14 years), each with more than two syncopal episodes in the previous six months. All had NCS refractory to conventional measures (compression stockings and counterpulsation measures, midodrine, and paroxetine) and documented by tilt testing in accordance with our center's standard protocol. Briefly, after a supine resting period, the patient underwent passive tilt testing for 20 min at 70°; if no spontaneous syncope had occurred 375 μg sublingual nitrates were administered. The test was terminated either by a positive response or 20 min