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ORIGINAL ARTICLE

Autonomic activity and biomarker behavior in supine position and after passive postural stress in different orthostatic intolerance syndromes

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KEYWORDS
Autonomic nervous system;
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Tilt test

Abstract
Introduction and objectives: Orthostatic intolerance (OI) syndromes are a confusing topic and determining a specific diagnosis to achieve optimal treatment can be troublesome. We sought to assess biomarker, hemodynamic and autonomic variables in OI patients (autonomic dysfunction [AD], postural orthostatic tachycardia syndrome [POTS] and neurally mediated syncope [NMS]) and healthy controls during supine and head-up tilt position in order to achieve a better diagnosis.
Results: In response to head-up tilt, patients with AD presented a marked decrease in systolic blood pressure (SBP) (p=0.002), and a blunted increase in heart rate (HR) (p=0.04). Baroreceptor gain was almost absent in supine position and did not change in response to tilt. Patients with POTS had lower values of atrial natriuretic peptide (p=0.03) but similar neurohormonal biomarkers and hemodynamic and baroreceptor function in supine position compared to healthy subjects. However, in response to head-up tilting greater reductions in stroke volume (p=0.008) and baroreceptor gain (p=0.002) and greater rises in HR (p=0.001), total peripheral resistance (p=0.008), low frequency component of SBP variability (LF-SBP) (p=0.003) and plasma noradrenaline (p=0.03) were observed. Patients with NCS had similar biomarkers and autonomic indices to healthy subjects in supine position, but a larger decrease in baroreceptor gain (p=0.007) and a greater rise in LF-SBP (p=0.004) and plasma adrenaline (p=0.003) response to head-up tilting.

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Conclusion: Although different OI syndromes share similar symptoms, including blurred vision, syncope and dizziness particularly during orthostatism, they differ markedly regarding biochemical, autonomic and hemodynamic parameters. Assessment of these differences may be helpful for better diagnosis and management.

PALAVRAS-CHAVE
Sistema nervoso autónomo;
Biomarcadores;
Intolerância ortostática;
Teste de tilt

Atividade autonómica e neurohormonal em doentes com intolerância ortostática durante o supino e após ortostatismo passivo

Resumo
Introdução e objetivos: As síndromes de intolerância ortostática (IO) continuam a ter uma avaliação difícil e um diagnóstico específico para se obter o melhor tratamento é frequentemente problemático. Para melhor esclarecimento destas patologias avaliamos os biomarcadores, parâmetros hemodinâmicos e atividade autonómica em doentes com diversos tipos de OI (disfunção autonómica (DA), síndrome de taquicardia postural ortostática (POTS) e com síncope neuromediada (SNM)) e comparamos com controles saudáveis durante a posição supina e após ortostatismo passivo (teste de tilt – TT).
Resultados: Em resposta ao TT doentes com DA, tiveram uma grande diminuição na pressão arterial sistólica (PAS, p = 0,002) e um aumento muito atenuado da frequência cardíaca (FC, p = 0,04). O ganho dos barorrecetores era quase residual na posição supina e não mudou em resposta ao TT. Doentes com POTS comparados com normais apresentaram menores valores de ANP (p = 0,03), mas valores de catecolaminas, parâmetros hemodinâmicos e função dos barorrecetores semelhantes na posição supina. No entanto, em resposta ao TT observou-se maior redução no volume de ejeção (SV, p = 0,008), e do ganho dos barorreceptores (p = 0,002), e um maior aumento da frequência cardíaca (FC, p = 0,001), da resistência periférica total (TPR, p = 0,008), do componente de baixa frequência de PAS (LF_SBP, p = 0,003) e da noradrenalina plasmática (p = 0,03). Doentes com SNM tinham biomarcadores e índices autonómicos similares aos controlos em supino, mas uma redução maior no ganho dos barorreceptores (p = 0,007), um maior aumento da LF_SBP (p = 0,004) e da adrenalina plasmática (p = 0,003) em resposta ao TT.
Conclusão: Apesar das diferentes síndromes de IO apresentarem sintomas semelhantes, como visão turva, tonturas e síncope especialmente durante o ortostatismo, eles marcadamente diferem quanto ao comportamento dos parâmetros bioquímicos, autonómicos e hemodinâmico ao ortostatismo passivo. A avaliação destas diferenças pode ser útil para um melhor diagnóstico e abordagem terapêutica.

Introduction

Orthostatic intolerance (OI) is a confusing topic due to the different clinical conditions it describes and also the lack of an uniform nomenclature.[1]

The term orthostasis literally means standing upright. OI may be defined as ''the development of symptoms while standing that are relieved by recumbency''.[2] However, special equipment is usually required to detect these abnormalities.

Standing involves an interplay of blood volume, physical, neurologic, humoral, and vascular factors which compensate for the effects of gravity on venous pooling.[1,2]

OI is not always due to dysfunction of autonomic or other compensatory mechanisms, but can also be due to inadequate responses of compensatory mechanisms to environmental stressors. For example, someone who is dehydrated may be unable to stand up without dire consequences, but autonomic dysfunction is not present; instead, the autonomic nervous system and other compensatory systems cannot adequately compensate for the loss of extracellular volume.[3] On the other hand, pure autonomic failure induces OI because compensatory factors governed by the autonomic nervous system are inadequate. Patients with this condition not only cannot easily stand but clearly have detectable autonomic abnormalities in all positions. Therefore, OI encompasses any condition with inadequate regulation of blood flow, heart rate (HR), and blood pressure that is most easily demonstrable during orthostatic stress but may be present in all postures.

In order to help clarify OI syndromes we compared neurohormonal, hemodynamic and autonomic nervous system features in patients with different OI syndromes to