

Too much of a good thing: a case report of traumatic drop attacks and syncope due to orthostatic hypertension

Martin B. von Bartheld ^{1*}, Mariëlle G.J. Duffels ², and M. Louis Handoko¹

¹Department of Cardiology, Amsterdam UMC, Vrije Universiteit Amsterdam, Post Office Box 7057, 1007 MB Amsterdam, the Netherlands; and ²Department of Cardiology, Noord West Ziekenhuis Groep, Post Office Box 501, 1800 AM Alkmaar, the Netherlands

Received 23 June 2020; first decision 4 August 2020; accepted 2 November 2020

Background

Orthostatic hypertension (OHT) is the clinical opposite to orthostatic hypotension and is an under-recognized and poorly understood clinical phenomenon. Patients may experience disabling symptoms such as dizziness, chest pain, and shortness of breath. In addition, OHT is associated with important clinical outcomes such as silent cerebral infarcts and cognitive decline.

Case summary

We present the case of a 67-year-old female who experienced frequent drop attacks with and without transient loss of consciousness causing various injuries. A range of standard diagnostic procedures did not yield an explanation for her symptoms but head-up tilt (HUT) testing showed OHT and induced most of her symptoms. Upon initiation of doxazosin, an alpha-blocking drug, she was free of symptoms and blood pressure response was normal on the repeat HUT test.

Discussion

To our knowledge, this is the first report of syncope due to OHT. Orthostatic hypertension is a heterogeneous condition and may occur in young, otherwise healthy individuals but also in older patients with cardiovascular comorbidities. It is thought that symptoms occur because of excessive venous pooling (causing a drop in cardiac output) or adrenergic hypersensitivity (resulting in cerebral vasoconstriction or acute rise in cardiac afterload). Since our patient had a marked response to an alpha-blocking agent, we think baroreflex hypersensitivity is the most likely cause of her complaints. Though syncope is probably rare, OHT should be regarded as a possible explanation of orthostatic symptoms.

Keywords

Case report • Orthostatic hypertension • Syncope • Tilt testing • Drop attacks • Doxazosin • Cerebral vasoconstriction

Learning points

- In patients with orthostatic symptoms both *hypotensive* and *hypertensive* responses may occur. The latter is called orthostatic hypertension (OHT) and the underlying mechanism can cause disabling symptoms and in extreme cases syncope.
- Alpha (or beta) blocking agents may significantly improve disabling symptoms in OHT patients, depending on the mechanism involved

* Corresponding author. Tel +31 20 4444444, Email: m.vonbartheld@amsterdamumc.nl

Handling Editor: Kyriakos Dimitriadis

Peer-reviewers: Syed Zawahir and Ali Nazmi Calik

Compliance Editor: Matteo Parollo

Supplementary Material Editor: Nida Ahmed

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Introduction

Orthostatic hypertension (OHT) is the less prevalent antonym of orthostatic hypotension (OH). It is a clinically important pathological condition but it is infrequently diagnosed. It is estimated that 4% of patients with orthostatic intolerance have OHT. Patients may experience disabling symptoms of dizziness, chest pain, and shortness of breath after standing up.¹⁻⁴

We report an extreme case of OHT leading to frequent occasions of traumatic syncope.

Timeline

Last 8 years before presentation	Recurrent symptoms of traumatic drop attacks as well as dyspnoea, headaches, and chest pain after standing up.
Initial presentation	Regular diagnostic procedures for analysis of syncope—including neurological screening and loop recorder implantation—did not provide a diagnosis. Because of regular supraventricular tachycardias up to 180 b.p.m., metoprolol XR 100 mg q.d. was started and symptoms partially improved.
Two months later	Metoprolol is halved because of new symptoms of exercise induced shortness of breath but unfortunately symptoms increase again.
Several weeks later	Tilt testing shows orthostatic hypertension with blood pressure (BP) rising from 135/85 to 200/105 mmHg while provoking her familiar symptoms. Doxazosin 4 mg q.d. was prescribed.
Two months later	Absence of symptoms. Normal BP response at repeat tilt testing.
Two years later	Patient is still free of symptoms.

Case presentation

A 67-year-old Caucasian female, former smoker with hypercholesterolaemia, depression, fibromyalgia, and migraine (using propranolol 10 mg t.i.d.), was referred to the outpatient clinic for evaluation of periodic drop attacks since 8 years. The attacks, which presented with and without transient loss of consciousness (TLOC), typically occurred once a month and usually in the first minutes of walking. In general, the duration of TLOC was only seconds and episodes were accompanied by symptoms of headaches, light-headedness, dyspnoea, and chest pain. Aside from the syncopal episodes, she had these symptoms on a regular basis, sometimes every day.

Because of the drop attacks, she fractured her radial head, wrist, and humerus (twice) on separate occasions. Physical examination was unremarkable upon presentation as was blood examination (including normal thyroid/adrenal function). Neurological analysis (including electroencephalogram, computed tomography, and cerebral magnetic resonance imaging) was normal, as were electrocardiogram, echocardiography, and 72 h ambulatory rhythm monitoring.

Exercise testing (max 80 W) provoked symptoms of dyspnoea, chest pain, and light-headedness with a slightly hypertensive blood pressure (BP) course (max 197/67 mmHg) but no signs of ischaemia. An implanted loop recorder registered only normal sinus rhythm during eight consecutive syncope episodes. Unrelated to the drop attacks, regular supraventricular tachycardias of 180 b.p.m. were observed for which propranolol was switched to metoprolol 100 mg q.d., reducing both her tachycardias and some of her symptoms. However, because of progressive dyspnoea, the beta-blocker was halved, unfortunately causing her original complaints to return. Echocardiography, ambulatory rhythm monitoring, and exercise testing were negative again for significant abnormalities. Subsequent coronary computed tomography angiography did not show significant coronary artery disease. Hereafter, supine and upright measurements of BP and a passive head-up tilt test (Figure 1) were performed. Both of which interestingly provoked her symptoms. Within 30 s after standing her BP rose from 130/85 to 180/90 mmHg while she developed her familiar complaints of dyspnoea, chest pain, headaches, and light-headedness. After lying down, SBP quickly returned to stable values of 135 mmHg and symptoms declined. The same occurred with 70° tilt testing. After 90 s, her BP had risen to 200/105 mmHg, it remained high for more than 15 min and her symptoms returned. Nitroglycerine also provoked a hypertensive response. Her heart rate remained stable following standing and tilting and she did not faint.

As we suspected autonomic dysfunction with excessive catecholamine release, we started the alpha-blocker doxazosin 4 mg q.d. Two months later, she reported that she was free of symptoms besides minor dizziness after standing up and we repeated the tilt test (Figure 2). Following standing and 70° tilt testing, SBP decreased from 140 to 120 mmHg and remained stable throughout the next 30 min without any complaints. After nitroglycerine, a typical hypotensive response occurred.

Two years later, she is still free of symptoms.

Discussion

We report a case of frequent traumatic drop attacks in a patient with OHT.

To date, orthostatic intolerance symptoms such as dyspnoea, dizziness, chest pain, and headache have been reported in OHT patients¹⁻⁴ but to our knowledge, this is the first report of syncope. Upon initiation of an alpha-blocker, our patient was free of symptoms.

Orthostatic hypertension, usually defined as a postural increase of at least 20 mmHg Systolic blood pressure (SBP),⁵ is the haemodynamic and paradoxical opposite of OH. Although it is an ill recognized entity, it is estimated that up to 4% of patients with orthostatic intolerance have OHT.² Patients can present at a relatively young age

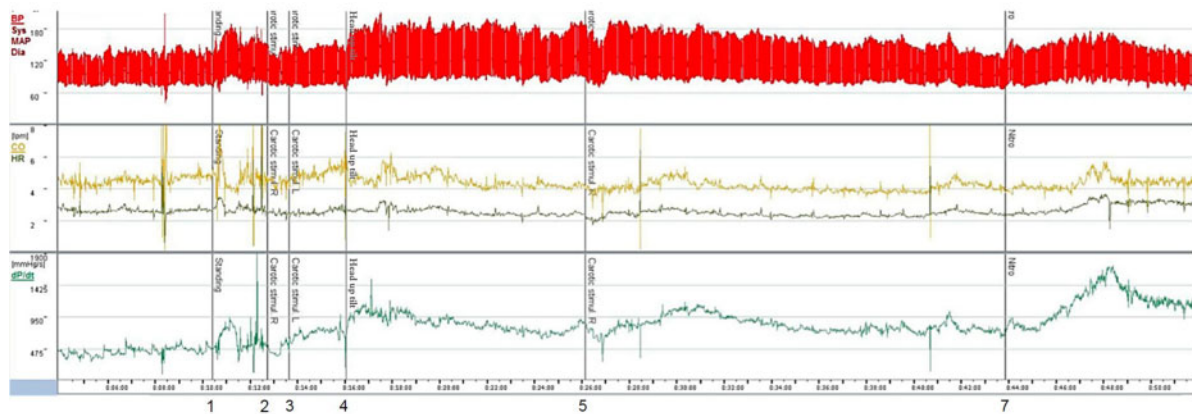


Figure 1 Tilt test registration before doxazosin. Blood pressure rises directly after standing up, head-up tilt, and nitroglycerine administration. The numbers refer to the different phases in the tilt test. (1) standing, (2) right carotid stimulus, (3) left carotid stimulus, (4) head-up tilt, (5) right carotid stimulus, (6) left carotid stimulus, and (7) nitroglycerine administration. BP, blood pressure; CO, cardiac output; HR, heart rate.

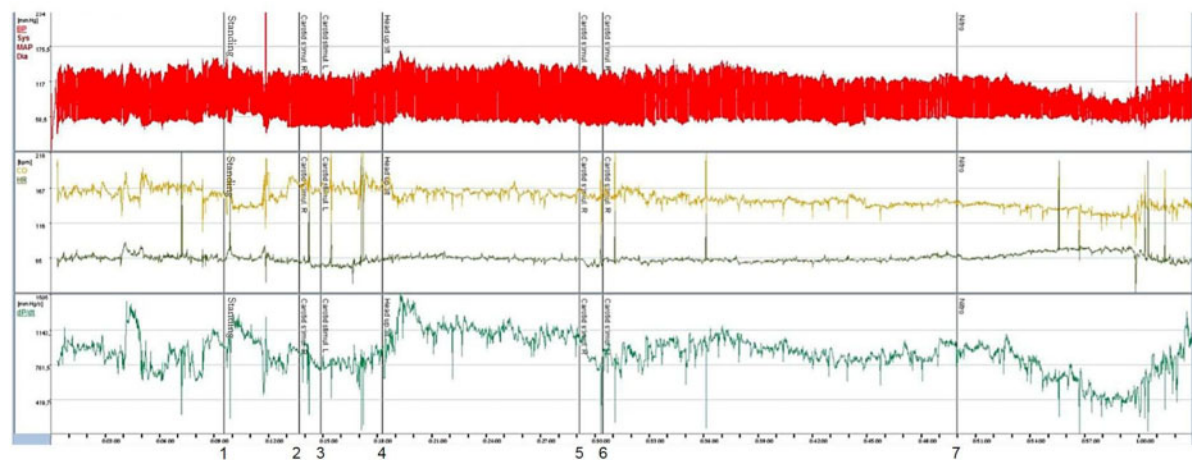


Figure 2 Second tilt test, after doxazosin. Now, following standing and head-up tilt, blood pressure remained stable. After nitroglycerine, a significant drop in blood pressure occurred.

(15–45 years) and there is a five or six-to-one predominance of women.⁶ It is regularly seen in conjunction with essential hypertension, type II diabetes mellitus and dysautonomias and it has been associated with clinical outcomes such as silent cerebral infarcts and cognitive decline.^{5,7,8}

The pathophysiology underlying OHT is poorly understood. Mechanistic studies on OHT are scarce and of small sample size. Several studies found increased levels of plasma norepinephrine and vasopressin in OHT patients standing upright compared with healthy controls,^{7–9} suggesting it involves overstimulation of the sympathetic system.

In the first reports of OHT in the 1980s, it was postulated that excessive venous pooling could trigger a hyperadrenergic response. In a study

of 12 young OHT patients, the orthostatic fall in cardiac output (measured by CO₂ rebreathing) was double that of normotensive subjects.⁹ After reducing venous pooling with a pressure suit, both the fall in cardiac output as well as the excessive rise in standing BP were significantly reduced. In a recent study using non-invasive finger cuff measurements, Petersen *et al.*¹⁰ also observed a significant decrease in cardiac output in 44 female subjects in response to tilt. The authors did not assess venous pooling but assumed the fall in cardiac output was caused by decreased venous return. Theoretically, however, we think that cardiac output could also be attenuated by an acute rise in cardiac afterload due to very high levels of peripheral arterial resistance.

In contrast to the venous pooling theory, Lee and Kim² did not find a decrease in cardiac output and stroke volume in OHT patients

compared with controls (also using finger cuff devices). Rather than reduced cardiac output, they suggested that the increase in peripheral resistance was probably caused by alpha-adrenergic baroreceptor hypersensitivity. Conditions facilitating autonomic neuropathy are ageing, essential hypertension, and diabetes mellitus. It has been shown that patients with DM have a five-fold prevalence of OHT compared with non-diabetic controls¹¹ and baroreflex hypersensitivity could perhaps trigger an overshoot of catecholamines.

Patients with OHT frequently report dizziness which is conceptually easy to link to decreasing cardiac output when standing up. However, dyspnoea, chest pain, and headaches are not. We think that shortness of breath and chest pain may be afterload-related and that the headaches and (pre)syncope events in OHT patients could result from cerebral vasoconstriction. Novak illustratively showed a case of orthostatic cerebral hypoperfusion syndrome where during tilt, cerebral blood flow progressively declined while systolic BP exceeded the upper range of the device (205 mmHg) and symptoms of extreme dizziness emerged.¹² Cerebral vasoconstriction could also be the reason why silent cerebral infarcts are frequently seen in OHT patients.

Orthostatic hypertension most likely is a heterogeneous condition with different mechanisms of action depending on age and comorbidities. In the cohorts of Streeten and Petersen, patients were young (mean <40 years) and excessive venous pooling was a more likely cause of symptoms than autonomic neuropathy. In the study by Lee on the other hand, patients were much older (mean 70 years) and had comorbidities such as hypertension (70%) and diabetes (21%). It is possible that these patients primarily suffered from excessive catecholamine release and therefore could also benefit from alpha-blocking agents. In a trial, doxazosin was administered to older OHT patients with multiple comorbidities and it was shown that the alpha-blocker effectively reduced orthostatic rise in BP.¹³

Rare causes of orthostatic hypertensive intolerance include norepinephrine transporter deficiency, pheochromocytoma, and disordered mast-cell activation.⁵ These are not likely causes in our patient due to absence of inflammatory symptoms, a relatively benign course of the disease and adequate response to alpha-blockade.

Besides a hypertensive response, another clinical entity may coexist with OHT which is postural tachycardia syndrome, where patients have an increase of at least 30 b.p.m. upon standing.⁸ It shares a similar pathophysiological mechanism as OHT and symptoms may be quite identical to those our patient experienced. Although we saw no increase in heart rate upon standing, higher doses of metoprolol seemed to reduce some of her complaints in the past. The mechanism behind that effect, however, remains elusive as second-generation beta-blockers have no beneficial effect on vascular constriction but in fact induce peripheral vasoconstriction.¹⁴

Several limitations apply. First, we did not observe actual syncope during tilt testing and theoretically her syncope may not have been caused by the same mechanism as the one we observed during the test. However, nearly all symptoms were provoked during tilting including light-headedness. Also, common differential diagnoses causing syncope such as structural cardiac disease (e.g. valvular stenosis, hypertrophic cardiomyopathy, cardiac masses, etc.) and arrhythmias (including carotid sinus syndrome)

have sufficiently been excluded, as were neurological disorders (epileptic seizures and cerebrovascular pathologies). Due to the traumatic nature of the attacks, psychogenic pseudosyncope is very unlikely. Finally, we excluded hypertension secondary to endocrine disorders such as Cushing's syndrome or hyperthyroidism. Upon initiation of an alpha-blocker, our patient was free of symptoms and BP response normalized at repeat tilt testing, further strengthening the hypothesis of OHT-mediated syncope.

In summary, we report a case with pronounced OHT, presenting with traumatic syncope. Although such an extreme case is probably rare, OHT may be a more common cause of orthostatic symptoms than generally thought. Depending on the pathophysiological mechanism (alpha-sensitivity, beta-sensitivity, or both) symptoms may be reduced by medications modulating the affected pathway such as alpha-blockers (e.g. doxazosin or prazosin) or beta-blockers which may also include carvedilol, a beta-blocker with alpha1-adrenoceptor blocking activity.



Lead author biography

Dr Bob von Bartheld works as a cardiologist at Amsterdam University Medical Center in the Netherlands. He obtained a PhD in 2016 and currently he is working as a fellow in Cardiovascular MRI.

Supplementary material

Supplementary material is available at *European Heart Journal - Case Reports* online.

Slide sets: A fully edited slide set detailing this case and suitable for local presentation is available online as [Supplementary data](#).

Consent: The authors confirm that written consent for submission and publication of this case report including images and associated text has been obtained from the patient in line with COPE guidance.

Conflict of interest: none declared.

Funding: none declared.

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