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Standing Up Slowly Antagonises Initial Blood Pressure Decrease in Older Adults with Orthostatic Hypotension

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Key Words
Orthostatic hypotension · Stance · Standing up slowly · Blood pressure · Continuously measured blood pressure · Older adults

Abstract
Background: Orthostatic hypotension (OH) is common in older adults and associated with increased morbidity and mortality, loss of independence and high health-care costs. Standing up slowly is a recommended non-pharmacological intervention. However, the effectiveness of this advice has not been well studied. ***Objectives:*** The aim of this study was to investigate whether standing up slowly antagonises posture-related blood pressure (BP) decrease in a clinically relevant population of geriatric outpatients. ***Methods:*** In this cross-sectional study, 24 community-dwelling older adults referred to a geriatric outpatient clinic and diagnosed with OH were included. BP was measured continuously during 3 consecutive transitions from supine to standing position during normal, slow and fast transition. ***Results:*** The relative BP decrease at 0–15 s after slow transition was significantly lower than after normal transition (p = 0.003 for both systolic BP and diastolic BP) and fast transition (p = 0.045 for systolic BP; diastolic BP: non-significant). The relative diastolic BP decrease at 60–180 s after normal transition was significantly lower than after fast transition (p = 0.029). ***Conclusion:*** Standing up slowly antagonises BP decrease predominantly during the first 15 s of standing up in a clinically relevant population of geriatric outpatients diagnosed with OH. Results support the non-pharmacological intervention in clinical practice to counteract OH.

Introduction

Orthostatic hypotension (OH) is classically defined as a drop in blood pressure (BP) of at least 20 mm Hg of systolic BP (SBP) and/or 10 mm Hg of diastolic BP (DBP)

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after standing up [1]. OH prevails in older adults, especially in those with one or more chronic diseases [2, 3]. Older adults with OH are at risk of falling while standing up [4], which is associated with increased morbidity, high health-care costs and loss of independence [5]. Especially initial OH (iOH), defined as a BP decrease within 15 s after standing up of 40 mm Hg SBP and/or 20 mm Hg DBP, is associated with falls [6]. Interventions counteracting OH are likely to reduce the risk of falling [7].

The first steps in the management of OH in clinical practice are educational and non-pharmacological interventions [8]. OH may be counteracted by increasing the venous return in the standing position by pre-tensing the lower limbs and abdominal muscles [9]. These observations have led to the introduction of physical countermeasures, e.g., by advising patients to bend forward, cross legs, or sit down once experiencing symptoms of OH [9]. Another non-pharmacological advice given in clinical practice is to stand up slowly. However, the effectiveness of this recommendation has not been well studied [7, 10].

This study aimed to investigate whether there is evidence that standing up slowly antagonises OH in a clinically relevant population of geriatric outpatients diagnosed with OH.

Materials and Methods

Study Design

This cross-sectional study included 24 community-dwelling older adults referred to the geriatric outpatient clinic of the VU University Medical Center, Amsterdam, The Netherlands, due to problems with mobility, cognition and/or general somatic health between December 2014 and April 2015. All patients in the study population were diagnosed with classical OH, i.e., a drop of at least 20 mm Hg SBP and/or 10 mm Hg DBP after 15 s and within 3 min of standing up [1]. In addition, 13 of these patients also fulfilled the criteria for iOH, i.e., a drop of at least 40 mm Hg SBP and/or 20 mm Hg DBP within the first 15 s after standing up. OH was assessed by both intermittent and continuous BP measurements. The aetiology of OH in our population was of the non-neurogenic type. Patients were excluded if they were unable to perform multiple transitions from a supine to a standing position.

Protocol

Measurements were performed during the initial visit to the geriatric outpatient clinic and included 3 separate standing up conditions, each consisting of 5 min in a resting state in supine position, a transition period from supine to standing position and 3 min in standing position. The standing up conditions were performed in a fixed order with a transition at subsequently normal, low and high speed, called normal, slow and fast transition, respectively. Transition time was recorded with a stopwatch. For normal transitions, patients were instructed to stand up at the patient's usual pace. For slow transitions, patients were instructed to reach a sitting position within at least 5 s, to remain seated during at least 5 s and to attain a standing position at low speed. The examiner coached the patients by counting seconds during the transition. For fast transitions, patients were instructed to stand up as fast as possible. During standing, the patient was instructed to stand unsupported upright during 3 min with the left arm positioned on the chest in order to hold the BP monitor device positioned as stable as possible. Patients were questioned about OH-related symptoms after each of the transitions. The symptoms described included dizziness, light-headedness, instability and blurred vision. Conversations were reduced to a minimum during the whole protocol.

BP Measurement

Continuously measured SBP and DBP were obtained with a digital photoplethysmograph (Nexfin®, BM Eye, Amsterdam, The Netherlands) [11] with a cuff placed on the left middle finger. Beat-to-beat BP data were analysed using Nexfin® PC software (version 2, BM Eye). BP data were manually marked starting at the moment patients attained a quiet supine position and a stable standing position, respectively. During each standing period, the Physiocal calibrator of the Nexfin®, which is automatically on, was switched off to prevent missing BP data [12]. During the following supine periods, the Physiocal calibrator was switched on again to maintain optimal calibration [13]. BP data during the transition time were excluded from analysis due to noise. Data were exported to Matlab (version R2012b, the Mathworks, Natick, Mass., USA), and beat-to-beat BP data were averaged over 5-second intervals [14].

To determine the BP profile, the following parameters were calculated for each standing up condition: (1) supine BP, defined as the mean BP in supine position during 60 s prior to each transition; (2) lowest value of the averaged BP of 3 time periods, i.e., 0–15, 15–60 and 60–180 s during the standing period, and (3) biggest BP decrease of the 3 time periods, determined by subtracting the lowest averaged BP of each aforementioned time period from the supine BP. Relative BP decrease was defined as the BP decrease after standing up in relation to the supine BP. OH_{15-180} was defined according to the classical OH definition between 15 and 180 s of standing up compared to supine BP. In addition, the heart rate (HR) profile was determined using the same parameters as for the BP profile (parameters 1–3). HR difference was calculated by subtracting the supine HR from the lowest averaged HR.

Patient Characteristics

Demographic and clinical data were obtained by questionnaires and from medical charts. A positive history of falling was defined as one or more self-reported fall incidents in the past year. Multi-morbidity was defined as 2 or more of the following chronic diseases: chronic obstructive pulmonary disease, diabetes mellitus, hypertension, malignancy, myocardial infarction, Parkinson's disease and rheumatoid/(osteo)arthritis. For the present study, we defined cardiovascular disease as presence of at least one of the following: hypertension, peripheral artery disease, myocardial infarction and transient ischemic attack or cerebral vascular accident. OH-provoking medication was defined as the intake of one or more vasodilating, anti-hypertensive, anti-depressive (non-SSRI) or anti-psychotic drugs. All medications a patient used, including OH-provoking medication, were continued during the study. Complaints of orthostatic intolerance were defined as the presence of one or more symptoms including light-headedness, blurred vision, dizziness or instability during standing. To describe the patient's physical and cognitive condition, the body mass index, Short Physical Performance Battery (SPPB), hand grip strength in a standing position and Mini-Mental State Examination (MMSE) were used [15].

Statistical Analysis

The sample size was calculated based on an α of 0.05 and a β of 0.2, using a mean value of the drop of SBP after transition of 25 mm Hg, an expected mean value in the intervention group 'slow transition' of 15 mm Hg SBP and a standard deviation (SD) of 15 mm Hg as reported by Pasma et al. [15], resulting in 20 patients. Continuous variables with a normal distribution were presented as means and SD. Values with a skewed distribution (non-Gaussian) were presented as medians and interquartile ranges (IQR). Paired-samples t tests were used to test for significant differences in supine BP before transition, duration of transition and mean BP and HR decrease per time interval of each standing up condition. Patients were excluded from the analysis if >30% of the BP values in each time interval were randomly missing due to technical errors of the BP device. Statistical analysis was performed using the Statistical Package for the Social Sciences (SPSS, version 22, Chicago, Ill., USA). p values <0.05 were considered statistically significant.

Statement of Ethics

This study was approved by the Medical Ethics Committee of the VU University Medical Center, Amsterdam, The Netherlands. All patients gave written informed consent.

Table 1. Patient characteristics (n = 24)

Sociodemographics	
Mean age (SD), years	79.3 (7.7)
Female	14
Living at home	21
Health status	
Use of walking aid	8
History of falling	16
Multi-morbidity	17
Cardiovascular disease	18
Median number of medications [IQR]	7 [5–11]
Mean BMI (SD)	25.9 (4.1)
Median MMSE [IQR]	27 [24–29]
Physical performance	
Mean handgrip strength (SD), kg	26.5 (9.6)
Median SPPB [IQR]	9 [7–11]
Orthostatic hypotension	
iOH[a]	13
OH_{15-180}[b]	24
OH-provoking medication	18
Complaints of OH after normal transition	13
Complaints of OH after slow transition	10
Complaints of OH after fast transition	18

All variables are presented as numbers unless indicated otherwise. BMI = Body mass index. [a] iOH was defined as a decrease of at least 40 mm Hg SBP and/or 20 mm Hg DBP during the first 15 s after standing up compared to supine BP after transition at normal speed. [b] OH_{15-180} was defined as a decrease of at least 20 mm Hg SBP and 10 mm Hg DBP during 15–180 s after standing up compared to supine BP after transition at normal speed.

Results

Patient Characteristics

Table 1 shows the patient characteristics and complaints of OH after normal, fast and slow transition. The mean age was 79.3 years (SD 7.7). All patients had OH, and 13 out of 24 patients also had iOH. Sixteen out of 24 patients had a history of falling, 18 patients used OH-provoking medication, and 13 patients had complaints of OH after normal transition during standing.

Standing Up Conditions

Table 2 shows transition times, absolute BP and HR per standing up condition.

Comparison of Transition Time and the Supine BP

Table 3 depicts the mean differences of transition times and supine SBP and DBP. The transition times differed significantly, with slow transition being on average 12.1 s longer (p < 0.001) than normal transition and on average 16.6 s longer than fast transition (p < 0.001).

Supine SBP and DBP were significantly higher preceding slow transition (p < 0.001 and p = 0.001) and fast transition (p < 0.001 and p = 0.007) compared to the supine SBP and DBP preceding normal transition.

Comparison of the Relative BP and HR Response

Table 4 depicts the mean differences of the relative BP change for all patients and the ones with iOH as well as the HR response. A maximum of data of 5 patients were missing per time period.

The relative BP decrease at 0–15 s was significantly lower after slow transition than after normal transition (OH: p = 0.003 for both SBP and DBP; iOH: p = 0.020 and p = 0.047 for SBP and DBP, respectively) and fast transition (p = 0.045 for SBP; non-significant for DBP). In the group of patients with iOH, the relative DBP decrease at 0–15 s was significantly higher after normal transition than after fast transition (p = 0.014).

BP decrease at 15–60 s was not dependent on transition. At 60–180 s, the relative DBP decrease was signifi-

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Table 2. Transition time, absolute BP and HR of different standing up conditions

	Normal	Slow	Fast
Transition time, s	11.5 (6.12)	23.7 (5.72)	7.05 (3.69)
Supine BP before transition, mm Hg			
SBP	144.5 (27.5)	154.2 (30.9)	156.2 (30.0)
DBP	71.5 (13.2)	74.9 (14.3)	75.0 (14.5)
BP 0–15 s, mm Hg			
SBP	102.3 (25.8)	116.6 (24.9)	116.0 (33.3)
DBP	52.8 (14.6)	57.6 (13.4)	60.0 (22.7)
BP 15–60 s, mm Hg			
SBP	99.3 (26.9)	102.1 (25.2)	104.5 (27.1)
DBP	58.4 (15.7)	58.0 (12.3)	58.7 (12.1)
BP 60–180 s, mm Hg			
SBP	108.4 (24.9)	115.3 (28.1)	113.8 (27.7)
DBP	61.8 (11.6)	63.9 (11.2)	62.5 (12.1)
Supine HR before transition, bpm	70.1 (9.92)	69.7 (9.82)	69.8 (9.40)
HR 0–15 s, bpm	69.8 (24.1)	76.4 (12.9)	80.4 (22.1)
HR 15–60 s, bpm	73.5 (18.5)	76.6 (12.8)	72.8 (20.7)
HR 60–180 s, bpm	71.9 (19.1)	75.3 (12.8)	73.5 (14.5)

All data are presented as means (SD). bpm = Beats per minute.

Table 3. Comparison of transition times and supine SBP and DBP of different standing up conditions (n = 24)

	Slow versus normal		Normal versus fast		Slow versus fast	
	MD (SD)	p value	MD (SD)	p value	MD (SD)	p value
Transition time, s	12.1 (4.1)	*<0.001*	4.5 (4.4)	*<0.001*	16.6 (3.7)	*<0.001*
Supine SBP, mm Hg	9.6 (8.3)	*<0.001*	−11.6 (11.5)	*<0.001*	−2.0 (7.7)	0.219
Supine DBP, mm Hg	3.4 (4.6)	*<0.001*	−3.5 (5.8)	*<0.007*	−0.1 (3.0)	0.892

p values <0.05 were considered statistically significant and are presented in italics. Interpretation: The mean supine SBP before slow transition was 9.6 mm Hg higher than the mean supine SBP before normal transition. MD = Mean difference.

cantly lower after normal transition than after fast transition ($p = 0.029$); the other transition conditions did not reach significance.

Four out of 24 patients did no longer meet the criteria of OH while standing up after slow transition compared to normal transition.

HR response did not significantly differ between the standing up conditions. Eight out of 24 patients used β-blockers. Although these patients were less able to increase the HR in response to standing up than patients not using β-blockers, 4 of these patients showed a less severe BP decrease after slow transition than after normal transition.

Discussion

This study showed that standing up slowly antagonises posture-related BP decrease. Furthermore, the effect of standing up slowly is more strongly seen in patients with iOH, and a proportion of 4 patients with iOH did no longer meet the criteria for iOH after standing up slowly.

Speed of Standing Up

Standing up slowly was beneficial in counteracting the relative BP during the first 15 s after standing up when compared with standing up at normal speed. It could be hypothesised that during and directly after slow transi-

Table 4. Comparison of the relative BP change and HR of different standing up conditions

	Slow versus normal			Normal versus fast			Slow versus fast		
	n	MD (SD)	p	n	MD (SD)	p	n	MD (SD)	p
Relative BP decrease									
All patients									
SBP 0–15 s (in mm Hg), %	20	–5.9 (7.7)	*0.003*	19	1.0 (8.7)	0.615	22	–4.7 (10.4)	*0.045*
DBP 0–15 s (in mm Hg), %	20	–7.1 (9.3)	*0.003*	19	6.1 (13.4)	0.061	22	–1.1 (12.1)	0.664
SBP 15–60 s (in mm Hg), %	20	–0.3 (9.2)	0.889	20	–0.9 (8.7)	0.667	22	–0.7 (6.2)	0.582
DBP 15–60 s (in mm Hg), %	20	1.5 (8.5)	0.438	20	–2.2 (6.3)	0.143	22	–0.4 (6.8)	0.787
SBP 60–180 s (in mm Hg), %	22	0.0 (5.5)	0.973	21	–1.8 (6.3)	0.199	22	–2.0 (4.9)	0.072
DBP 60–180 s (in mm Hg), %	22	1.0 (5.2)	0.400	21	–2.8 (5.4)	*0.029*	22	–1.7 (4.8)	0.113
Patients with iOH									
SBP 0–15 s (in mm Hg), %	10	–7.4 (8.3)	*0.020*	10	4.5 (7.5)	0.092	12	–1.8 (12.3)	0.615
DBP 0–15 s (in mm Hg), %	10	–6.6 (9.1)	*0.047*	10	10.8 (11.2)	*0.014*	12	3.6 (10.7)	0.267
HR decrease									
All patients									
HR 0–15 s, bpm	22	1.0 (5.4)	0.391	22	–5.4 (18.7)	0.194	24	–3.9 (16.6)	0.258
HR 15–60 s, bpm	24	3.5 (14.9)	0.261	23	–3.5 (13.3)	0.228	23	0.2 (8.1)	0.929
HR 60–180 s, bpm	24	3.8 (12.3)	0.146	24	–1.9 (13.1)	0.477	24	1.7 (5.2)	0.095

Relative BP decrease is defined as the percentage of BP drop compared to supine BP. Interpretation of relative BP decrease: in the 0- to 15-second interval of standing up, patients had a 5.9% lower relative SBP decrease after slow transition than after normal transition. Interpretation of HR decrease: in the 0- to 15-second interval of standing up, patients had an average HR of 1.01 bpm higher after slow transition than after normal transition. p values <0.05 were considered statistically significant and are presented in italics. MD = Mean difference; bpm = beats per minute.

tion, the use of the skeletal muscle pump is more effective due to the longer time period of transition compared to normal transition. The prolonged activation of the muscles during standing up at low speed, but also the vigorous activation of the muscles during standing up at high speed, could both be beneficial. The skeletal muscle pump increases the intramuscular pressure and reduces venous blood pooling associated with OH [16]. After 15 s of standing up, the positive effect of standing up slowly on relative BP decrease disappeared. This could be explained by the fact that during the prolonged period of quiet standing the continued pooling of blood in the abdominal region, the biggest reservoir during orthostatic shifts [17], overrules the initial positive effect of the skeletal muscle pump.

iOH has a different pathophysiology than classical OH. The initial orthostatic response consists of a direct neural response with increase in HR as a direct effector. It could be hypothesised that during slow transition, the HR increases in concordance with or as a reaction to the more effective use of the muscle pump. After this first orthostatic response, the effects caused by the volume shift become more important.

Seated postural hypotension [18], a prevalent condition, should also be taken into account during the short period of time that patients remained in a sitting position during slow transition.

Although the response rate to standing up slowly was only 4 out of 24 patients who no longer met the criteria for iOH, these results should be put into perspective by considering the fact that standing up slowly is a relatively safe intervention without side effects and considerably easy to perform by patients in their daily lives.

Order of Transitions

The protocol was designed as a fixed order of standing up conditions with 3 different transition speeds after which a period of standing up followed. Supine BP increased after 3 periods of standing up without being compensated by the 5 min in supine rest, whereas communication and interaction with the patient was reduced to a minimum. We hypothesise that the supine BP rises after each standing up condition due to physical strain on the body and that 5 min rest in supine position is, although reported in the literature [15], not sufficient in this group of patients. To the best of our knowledge, this effect has not been previously reported in the literature. Calculation of relative BP decreases compensated for this effect in the statistical analyses. Future studies should explore this effect and take the increase in BP during postural transitions into account. For clinical practice, this could imply that the period of rest before measuring OH should be longer than 5 min.

Continuously versus Intermittently Measured BP

These results underline the importance of the use of continuous BP-measuring devices, which are the only means to assess iOH and are of great importance to the clinician to analyse the continuous BP response to orthostatic stress [6, 14, 15, 19]. Patients with iOH are likely to have complaints of OH and a higher risk of falling [6]. The importance of iOH as a clinically relevant parameter of orthostatic intolerance can be explained by the large SBP decrease and concomitant loss of cerebral blood flow if the SBP does not recover to at least 80% of baseline BP within 30 s after this BP decrease [6, 20]. Hypothetically, the BP response in the first 15 s and the ability to recover from this BP decrease are important hallmarks of BP regulation and occurrence of orthostatic intolerance during the rest of the standing period, which cannot be detected using intermittent measurements [20]. Future studies are necessary to identify phenotypes of BP regulation and recovery.

Strengths and Limitations

This is the first study to provide evidence of the validity of advising older adults with OH to stand up slowly. Strengths of the study are the use of continuously measured BP and the use of a well-characterised cohort of older patients visiting a geriatric outpatient clinic, providing a clinically relevant study population. In retrospect, limitations of the study are the use of a fixed order of transitions because of the resulting increase in supine BP per transition period.

Conclusion

Standing up slowly antagonises BP decrease during the first 15 s of standing up in older patients with OH. The results underpin the use of non-pharmacological interventions in clinical practice.

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Authors' Contribution

E.S.B., E.M.R., M.C.T., O.J.V., C.G.M.M. and A.B.M. designed the study. E.S.B. performed the data analysis and drafted the manuscript. All authors revised the manuscript and approved the final version of the manuscript.

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Disclosure Statement

The authors have no conflicts of interest to declare.

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