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Standing up slowly antagonizes initial blood pressure decrease in older adults with orthostatic hypotension

Running title: Standing up slowly in older adults.

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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: To investigate whether standing up slowly antagonizes 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 three consecutive transitions from supine to standing position during normal, slow and fast transition.

RESULTS: Relative BP decrease at 0-15 seconds after slow transition was significantly lower compared to normal transition (*P* =.003 for both systolic BP and diastolic BP and fast transition (*P* =.045 for systolic BP, diastolic BP non-significant). The relative diastolic BP decrease at 60-180 seconds after normal transition was significantly lower compared with fast transition (*P* =.029).

CONCLUSION: Standing up slowly antagonizes BP decrease predominantly during the first 15 seconds 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 mmHg of systolic blood pressure (SBP) and/or 10 mmHg of diastolic blood pressure (DBP) 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 for 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 seconds after standing up of 40 mmHg SBP and/or 20 mmHg DBP, is associated with falls.[6] Interventions counteracting OH are likely to reduce the risk for 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 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 antagonizes OH in a clinically relevant population of geriatric outpatients diagnosed with OH.

Materials & 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 mmHg SBP and/or 10 mmHg DBP after 15 seconds and within 3 minutes of standing up.[1] In addition, 13 of these patients also fulfilled the criteria for iOH, i.e. a drop of at least 40 mmHg in SBP and/or 20 mmHg in DBP within the first 15 seconds 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 when they were unable to perform multiple transitions from supine to standing position. This study was approved by the Medical Ethics Committee of the VU university medical center (Amsterdam, the Netherlands). All patients gave written informed consent.

Protocol

Measurements were performed during the initial visit to the geriatric outpatient clinic and included three separate standing up conditions, each consisting of 5 minutes in a resting state in supine position, a transition period from supine to standing position, and 3 minutes in standing position. The standing up conditions were performed in a fixed order with a transition at subsequently normal, low and high speed, respectively called normal, slow and fast transition. 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 seconds; to remain seated during at least

5 seconds 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 minutes with the left arm positioned on the chest in order to hold the BP monitor device positioned as stable as possible. Patients were asked for OH related symptoms after each of the transitions. The symptoms asked consisted of: 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 was analysed using Nexfin@PC software (Nexfin@PC version 2, BM Eye, Amsterdam, the Netherlands). 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 (Matlab, version R2012b, the Mathworks, Natick, MA) and beat-to-beat BP data was averaged over 5 seconds intervals.[14]

To determine the BP profile, the following parameters were calculated for each standing up condition: (i) supine BP, defined as the mean BP in supine position during 60 seconds prior to each transition; (ii) lowest value of the averaged BP of three time periods, i.e.

0-15 seconds, 15-60 seconds and 60-180 seconds during the standing period and (iii) biggest BP decrease of the three 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. $OH_{15\text{-}180}$ was defined according to the classical OH definition between 15-180 seconds of standing up, compared with supine BP. In addition, heart rate (HR) profile was determined by using the same parameters as for the BP profile (parameters i-iii). HR difference was calculated by subtracting supine HR of 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. Multimorbidity 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, antihypertensive, anti-depressive (non SSRI) or antipsychotic drug. All medication a patient used, including OH provoking medication, was continued during the study. Complaints of orthostatic intolerance were defined as the presence of one or more symptoms comprising lightheadedness, visual disturbances, dizziness or instability during standing. To describe the patient’s physical and cognitive condition the body mass index

(BMI), 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, a β of 0.2, using a mean value of the drop of SBP after transition of 25 mmHg, an expected mean value in the intervention group 'slow transition' of 15 mmHg SBP and a standard deviation of 15 mmHg as reported in Pasma et al., resulting in N=20 patients. [15] Continuous variables with a normal distribution were presented as mean and standard deviation (SD). Values with a skewed distribution (non-Gaussian) were presented as median and interquartile range (IQR). Paired-samples t tests were used to test for significant differences in supine BP before transition, duration of transition and mean BP 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, IL). P-values below 0.05 were considered statistically significant.

Results

Patient characteristics

Table 1 shows the patient characteristics and appearance of symptoms after normal, fast and slow transition. The mean age was 79.3 years (SD 7.7). All patients had OH and thirteen 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 orthostatic intolerance after normal transition during standing.

Standing up conditions

Table 2 shows transition times, absolute blood pressure and heart rate 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 DBPs. The transition times differed significantly, with slow transition being on average 12.1 seconds longer (P <.001) than normal transition and on average 16.6 seconds longer than fast transition (P <.001).

Supine SBP and DBP were significantly higher preceding slow transition (P <.001 and P =.001) and fast transition (P <.001 and P =.007) compared with 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 and the HR response. A maximum of data of 5 patients were missing per time period.

The relative BP decrease at 0-15 seconds was significantly lower after slow transition compared to normal transition (OH: *P* =.003 for both SBP and DBP; iOH: *P* =.020 and *P* =.047 for systolic and diastolic BP respectively) and fast transition (*P* =.045 for SBP, non-significantly for DBP). In the group of patients with iOH, the relative DBP decrease at 0-15 seconds was significantly higher after normal transition compared to fast transition (*P* =.014).

BP decrease at 15-60 seconds was not dependent on transition. At 60-180 seconds, the relative diastolic BP decrease was significantly lower after normal transition compared to fast transition (*P* =.029), 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 standing up conditions. Eight out of 24 patients used beta blockers. Although these patients were less able to increase the HR in response to standing up in comparison with patients not using beta blockers, four of these patients showed a less severe BP decrease after slow transition compared to normal transition.

Discussion

This study showed that standing up slowly antagonizes 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 seconds after standing up, when compared with standing up at normal speed. It could be hypothesized that during and directly after slow transition, the use of the skeletal muscle pump is more effective due to the longer time period of transition compared with 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 seconds 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 is constituted by a direct neural response with increase in heart rate as a direct effector. It could be hypothesized that during slow transition, the heart rate increases in concordance with or as a reaction of the more effective use of the muscle pump. After this first orthostatic response, the effects caused by the volume shift become more important.

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

Although the response rate of standing up slowly is only 4 out of 24 patients who no longer meet the criteria for iOH, it should be put into perspective by the fact that it 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 three different transition speeds after which a period of standing up followed. Supine BP increased after three periods of standing up without being compensated by the 5 minutes in supine rest, whereas communication and interaction with the patient was reduced to a minimum. We hypothesize that the supine BP rises after each standing up condition due to physical strain on the body and that 5 minutes rest in supine position is, although reported in literature[15], not sufficient in this group of patients. To the best of our knowledge, this effect has not been previously reported in 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 a period of rest before measuring OH should be longer than 5 minutes.

Continuously vs. intermittently measured BP

These results underline the importance of the use of continuous measuring BP devices, which are the only means to assess iOH and are of great importance to a clinician to analyse the continuous BP response to orthostatic stress.[6, 14, 15, 19] Patients with iOH are likely to have complaints of orthostatic intolerance 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 therewith loss of cerebral blood flow (CBF), when the SBP is not able to recover to at least 80% of baseline BP within 30 seconds after this BP decrease.[6, 20] Hypothetically, the BP response in the first 15 seconds and the ability to recover from this BP decrease is an important hallmark of BP regulation and occurrence of orthostatic intolerance during the rest of the standing period, which cannot be detected using sphygmomanometer measurements.[20] Future studies are necessary to identify phenotypes of BP regulation and recovery.

Strengths & Limitations

This is the first study performed to provide evidence for the validity of advice to stand up slowly presented to older adults with OH. Strengths of the study are the use of continuously measured BP and the use of a well-characterized 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 fixed order in transitions because of the resulting increase in supine BP per transition period.

Conclusion

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

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Conflict of Interest

The authors have declared no conflicts of interests.

Author Contributions

ESB, EMR, MCT, OJV, CGM and ABM designed the study. ESB 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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Table 1. Patient characteristics.

Characteristic	All (n=24)
Socio-demographics	
Age in years, mean (SD)	79.3 (7.7)
Female	14
Living at home	21
Health status	
Use of walking aid	8
History of falling	16
Multimorbidity	17
Cardiovascular disease	18
Number of medication, median [IQR]	7 [5-11]
BMI in kg/m^2, mean (SD)	25.9 (4.1)
MMSE, median [IQR]	27 [24-29]
Physical performance	
Handgrip strength in kg, mean (SD)	26.5 (9.6)
SPPB, median [IQR]	9 [7-11]
Orthostatic hypotension	
iOH [a]	13
$OH_{15\text{-}180}$ [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 n, unless indicated otherwise. MMSE= Mini Mental State Examination, SPPB= Short Physical Performance Battery, BP= blood pressure, SBP= systolic BP, DBP= diastolic BP, OH= orthostatic hypotension, iOH= initial orthostatic hypotension.

[a] iOH was defined as a decrease of at least 40 mmHg SBP and/or 20 mmHg DBP during the first 15 seconds after standing up compared to supine BP.

[b] OH_{15-180} was defined as a decrease of at least 20 mmHg SBP and 10 mmHg DBP during 15 to 180 seconds after standing up compared to supine BP, after transition at normal speed.

Table 2. Transition times, absolute blood pressure and heart rate of different standing up conditions.

Characteristic	Normal	Slow	Fast
Transition times in seconds (s)	11.5 (6.12)	23.7 (5.72)	7.05 (3.69)
Supine BP before transition in mmHg			
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. in mmHg			
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. in mmHg			
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. in mmHg			
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 in bpm	70.1 (9.92)	69.7 (9.82)	69.8 (9.40)
HR 0-15 s. in bpm	69.8 (24.1)	76.4 (12.9)	80.4 (22.1)
HR 15-60 s. in bpm	73.5 (18.5)	76.6 (12.8)	72.8 (20.7)
HR 60-180 s. in bpm	71.9 (19.1)	75.3 (12.8)	73.5 (14.5)

All data are presented as mean (SD). BP= blood pressure, SBP= systolic BP, DBP= diastolic BP, HR= heart rate, bpm= beats per minute.

Table 3. Comparison of transition times and supine systolic and diastolic blood pressure of different standing up conditions.

	n	Slow vs Normal		n	Normal vs Fast		n	Slow vs Fast	
Transition time and BP		MD (SD)	p-value		MD (SD)	p-value		MD (SD)	p-value
Transition time in s.	24	12.1 (4.1)	**<.001**	24	4.5 (4.4)	**<.001**	24	16.6 (3.7)	**<.001**
Supine SBP (mmHg)	24	9.6 (8.3)	**<.001**	24	-11.6 (11.5)	**<.001**	24	-2.0 (7.7)	.219
Supine DBP (mmHg)	24	3.4 (4.6)	**.001**	24	-3.5 (5.8)	**.007**	24	-0.1 (3.0)	.892

N= number, MD= mean difference, SD= standard deviation, s.= seconds, BP= blood pressure, SBP= systolic BP, DBP= diastolic BP.

P-values (p) <.05 are considered statistically significant and are presented in bold.

Interpretation: the mean supine systolic BP before slow transition was 9.6 mmHg higher compared with the mean supine systolic BP before normal transition.

Table 4. Comparison of the relative blood pressure change and heart rate of different standing up conditions.

	n	Slow vs Normal		n	Normal vs Fast		n	Slow vs Fast	
		MD (SD)	p		MD (SD)	p		MD (SD)	p
Relative BP decrease									
All patients									
SBP 0-15 s. in mmHG, %	20	- 5.9 (7.7)	**.003**	19	1.0 (8.7)	.615	22	-4.7 (10.4)	**.045**
DBP 0-15 s. in mmHG , %	20	-7.1 (9.3)	**.003**	19	6.1 (13.4)	.061	22	-1.1 (12.1)	.664
SBP 15-60 s. in mmHG , %	20	-0.3 (9.2)	.889	20	- 0.9 (8.7)	.667	22	-0.7 (6.2)	.582
DBP 15-60 s. in mmHG , %	20	1.5 (8.5)	.438	20	-2.2 (6.3)	.143	22	-0.4 (6.8)	.787
SBP 60-180 s. in mmHG , %	22	0.0 (5.5)	.973	21	-1.8 (6.3)	.199	22	-2.0 (4.9)	.072
DBP 60-180 s. in mmHG , %	22	1.0 (5.2)	.400	21	-2.8 (5.4)	**.029**	22	-1.7 (4.8)	.113
Patients with iOH									
SBP 0-15 s. in mmHG , %	10	-7.4 (8.3)	**.020**	10	4.5 (7.5)	.092	12	-1.8 (12.3)	.615
DBP 0-15 s. in mmHG , %	10	-6.6 (9.1)	**.047**	10	10.8 (11.2)	**.014**	12	3.6 (10.7)	.267
HR decrease									
All patients									

HR 0-15 s. in bpm	22	1.0 (5.4)	.391	22	-5.4 (18.7)	.194	24	-3.9 (16.6)	.258
HR 15-60 s. in bpm	24	3.5 (14.9)	.261	23	-3.5 (13.3)	.228	23	0.2 (8.1)	.929
HR 60-180 s. in bpm	24	3.8 (12.3)	.146	24	-1.9 (13.1)	.477	24	1.7 (5.2)	.095

N= number, MD= mean difference, SD= standard deviation, BP=blood pressure, SBP= systolic, DIA= diastolic, s.= seconds, HR= heart rate.

Relative BP decrease is defined as percentage of BP drop compared to supine BP.

P-values <.05 are considered statistically significant and are presented in bold.

Interpretation relative BP: in the 0-15 second interval of standing up, patients after slow transition had 5.9% less relative SBP decrease, compared with patients after normal transition.

Interpretation HR: in the 0-15 second interval of standing up, patients after slow transition had an average heart rate of 1.01 beats per minute higher, compared with patients after normal transition.