ORIGINAL ARTICLE

Evaluation of Orthostatic Hypotension: Relationship of a New Self-report Instrument to Laboratory-Based Measures

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OBJECTIVE: **To compare measured autonomic deficits (composite autonomic severity score [CASS]) with a brief self-report scale we developed to measure severity of symptoms of orthostatic hypotension.**

PATIENTS AND METHODS: **Patients were recruited in 2 phases: from August to October 2002 and in April 2004. All patients underwent full evaluation in the autonomic laboratory, from which a CASS of autonomic deficits was derived. Patients also completed the 5-item self-report Orthostatic Grading Scale, which inquires about symptoms of orthostatic intolerance due to orthostatic hypotension (eg, severity, frequency, and interference with daily activities).**

RESULTS: **Of 145 patients, 97 (67%) had orthostatic hypotension. The 5-item scale demonstrated strong internal consistency (coefficient α=.91). Patients with orthostatic hypotension had significantly higher scores on each questionnaire item and CASS subscores than those without orthostatic hypotension. The scale items correlated significantly with each of the CASS subscores, maximally with the CASS adrenergic subscore.**

CONCLUSIONS: **Orthostatic hypotension is not the only cause of reduced orthostatic tolerance, and some patients may have orthostatic hypotension but be asymptomatic. Results of this study indicate that this 5-item questionnaire is a reliable and valid measure of the severity of symptoms of orthostatic hypotension and that it can supplement laboratory-based measures to provide a rapid, more complete clinical assessment. This questionnaire would also be useful as a brief screening device for orthostatic intolerance to aid physicians in identifying patients who may have orthostatic hypotension.**

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ARS = Autonomic Reflex Screen; BP = blood pressure; CASS = composite autonomic severity score; OGS = Orthostatic Grading Scale

Orthostatic intolerance is a relatively common condition for which patients are referred for evaluation in the autonomic laboratory. Although orthostatic intolerance is often thought to be synonymous with orthostatic hypotension,[1] the 2 conditions are not always concurrent. Some patients have orthostatic intolerance without orthostatic hypotension, such as those with postural tachycardia syndrome[2,3]; conversely, some patients with orthostatic hypotension may not have symptoms of orthostatic intolerance because of expanded cerebral autoregulation that maintains adequate cerebral perfusion despite a decrease in blood pressure (BP).[4]

A standardized laboratory-based scale[5] developed by one of the authors (P.A.L.) to measure the severity of autonomic deficits by using autonomic function tests and a comprehensive self-report questionnaire[6] assessing autonomic symptoms in general have been validated. However, no study has specifically evaluated the relationship between the severity of orthostatic intolerance due to orthostatic hypotension as perceived by patients (symptoms) and our laboratory-based scoring system (deficits). We posit that the frequency and severity of symptoms of orthostatic intolerance are overall highly correlated with the degree of adrenergic dysfunction. To test such a hypothesis, we compared the laboratory-measured autonomic deficits (composite autonomic severity score [CASS]) with a brief self-report scale we developed to rate the severity of orthostatic intolerance.

PATIENTS AND METHODS

Data were collected in 2 stages. In the first stage, we collected data from a consecutive series of patients with neurogenic orthostatic hypotension who were seen in the Mayo Clinic Autonomic Reflex Laboratory in Rochester, Minn, from August to October 2002. Orthostatic hypotension was defined as a sustained reduction in systolic BP of 20 mm Hg or greater within 3 minutes of head-up tilt.[7] The second stage consisted of a consecutive series of patients referred to the Mayo Autonomic Reflex Laboratory in April 2004, except for those referred for complex regional pain syndrome (who undergo a different set of tests). These patients may or may not have had orthostatic hypotension. Reasons for referral included spells, peripheral neuropathies, gastrointestinal dysmotility problems, dizziness, fatigue, and autonomic disorders in general (proved or suspected). Demographics and medication information were

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extracted from the medical records. Additionally, the laboratory staff routinely reviewed medication status at the time of testing.

All patients completed a standardized Autonomic Reflex Screen (ARS) that includes continuous noninvasive monitoring of heart rate and BP during 5 minutes of supine rest, followed by 5 minutes of head-up tilt (70°). The ARS consists of a battery of noninvasive laboratory tests of known sensitivity, specificity, reproducibility, and clinical relevance used to evaluate cardiovagal, adrenergic, and postganglionic sudomotor function.[5] The severity of autonomic deficit, quantified for each participant using ARS, was converted to CASS, which corrects for the confounding effects of age and sex. Participants also completed a 5-item questionnaire (Self-report Orthostatic Grading Scale [OGS]) that we developed to provide a subjective grading scale of the severity of orthostatic intolerance in patients with orthostatic hypotension. Our autonomic laboratory technicians were available to answer any question that the patients may have had while completing the questionnaire.

Measures

Orthostatic Grading Scale. Our 5-item self-report questionnaire was designed on the basis of questions routinely asked by clinicians and researchers specializing in autonomic disorders during initial consultation with patients who have orthostatic hypotension. The 5 questions address frequency and severity of orthostatic symptoms, relationship of symptoms to orthostatic stressors, and the impact of symptoms on activities of daily living and standing time (Table 1). Respondents rate each item on a scale of 0 to 4. Adding the scores for the individual items creates a total score.

Composite Autonomic Severity Score. We quantified severity of autonomic deficit with the objective 10-point CASS (Appendix 1), which is based on ARS. Primary components include the quantitative sudomotor axon reflex test, orthostatic BP and heart rate responses to tilt, heart rate response to deep breathing, the Valsalva ratio, and beat-to-beat BP response to the Valsalva maneuver, tilt, and deep breathing. The range for CASS is 0 (no deficit) to 10 (maximal deficit). Patients with a subscore of 3 or less on CASS have mild autonomic failure, those with subscores of 7 to 10 have severe autonomic failure, and those with scores between these 2 ranges have moderate autonomic failure.

TABLE 1. **Self-report Orthostatic Grading Scale**

1. Frequency of orthostatic symptoms	
0	I *never or rarely* experience orthostatic symptoms when I stand up
1	I *sometimes* experience orthostatic symptoms when I stand up
2	I *often* experience orthostatic symptoms when I stand up
3	I *usually* experience orthostatic symptoms when I stand up
4	I *always* experience orthostatic symptoms when I stand up
2. Severity of orthostatic symptoms	
0	I *do not* experience orthostatic symptoms when I stand up
1	I experience *mild* orthostatic symptoms when I stand up
2	I experience *moderate* orthostatic symptoms when I stand up and *sometimes* have to sit back down for relief
3	I experience *severe* orthostatic symptoms when I stand up and *frequently* have to sit back down for relief
4	I experience *severe* orthostatic symptoms when I stand up and *regularly faint* if I do not sit back down
3. Conditions under which orthostatic symptoms occur	
0	I *never or rarely* experience orthostatic symptoms under any circumstances
1	I *sometimes* experience orthostatic symptoms under certain conditions, such as prolonged standing, a meal, exertion (eg, walking), or when exposed to heat (eg, hot day, hot bath, hot shower)
2	I *often* experience orthostatic symptoms under certain conditions, such as prolonged standing, a meal, exertion (eg, walking), or when exposed to heat (eg, hot day, hot bath, hot shower)
3	I *usually* experience orthostatic symptoms under certain conditions, such as prolonged standing, a meal, exertion (eg, walking), or when exposed to heat (eg, hot day, hot bath, hot shower)
4	I *always* experience orthostatic symptoms when I stand up; the specific conditions do not matter
4. Activities of daily living	
0	My orthostatic symptoms *do not interfere* with activities of daily living (eg, work, chores, dressing, bathing)
1	My orthostatic symptoms *mildly interfere* with activities of daily living (eg, work, chores, dressing, bathing)
2	My orthostatic symptoms *moderately interfere* with activities of daily living (eg, work, chores, dressing, bathing)
3	My orthostatic symptoms *severely interfere* with activities of daily living (eg, work, chores, dressing, bathing)
4	My orthostatic symptoms *severely interfere* with activities of daily living (eg, work, chores, dressing, bathing). *I am bed or wheelchair bound because of my symptoms*
5. Standing time	
0	On most occasions, I can stand as long as necessary without experiencing orthostatic symptoms
1	On most occasions, I can stand *more than 15 minutes* before experiencing orthostatic symptoms
2	On most occasions, I can stand *5-14 minutes* before experiencing orthostatic symptoms
3	On most occasions, I can stand *1-4 minutes* before experiencing orthostatic symptoms
4	On most occasions, I can stand *less than 1 minute* before experiencing orthostatic symptoms

Statistical Analyses

We evaluated the internal consistency of the OGS with coefficient α and used factor analysis to examine the factor structure of the scale. Descriptive statistics include mean (SD) for the OGS and median (interquartile range) for CASS. The *t* test was used to examine group differences on the OGS, and the Wilcoxon rank sum test was used to examine group differences on CASS. Spearman correlations were used to examine the relationship among the OGS items, CASS subscores, and systolic BP response to head-up tilt. $P<.05$ was considered statistically significant.

TABLE 2. **Values on the Orthostatic Grading Scale and Composite Autonomic Severity Score for Patients With and Without Orthostatic Hypotension***

	Orthostatic hypotension		
	With (n=97)	Without (n=48)	*P* value
Orthostatic Grading Scale,† mean (SD)			
1	1.96 (1.32)	0.85 (1.03)	<.001
2	1.80 (1.03)	1.00 (1.05)	<.001
3	1.98 (1.35)	0.83 (1.31)	<.001
4	1.75 (1.32)	0.52 (0.90)	<.001
5	1.91 (1.44)	1.23 (1.68)	.01
Total	9.32 (5.46)	4.44 (5.10)	<.001
Composite Autonomic Severity Score,‡ median (interquartile range)			
Sudomotor	2.00 (2.00)	0.00 (1.00)	<.001
Cardiovagal	2.00 (2.00)	0.00 (1.00)	<.001
Adrenergic	3.00 (1.00)	0.00 (1.00)	<.001
Total	6.00 (4.00)	1.00 (3.00)	<.001

*1 = frequency of symptoms; 2 = severity of symptoms; 3 = symptoms with orthostatic stress; 4 = interference with activities of daily living; 5 = standing time.
†Group comparisons performed with the *t* test.
‡Group comparisons performed with the Wilcoxon rank sum test.

RESULTS

Sample Characteristics

Our study consisted of 145 patients with a mean age of 60.8 years (SD, 15.5 years) and an even distribution of men and women (52% men). (Three patients were excluded because they had known orthostatic intolerance due to postural tachycardia syndrome; the focus of this study was on orthostatic intolerance due to orthostatic hypotension.) The racial breakdown was 98% white, 1% African American, and 1% Asian, which is representative of our patient population.

Of these 145 patients, 97 (67%) had orthostatic hypotension on testing; 28 (29%) were taking medication to control their orthostatic symptoms. Only 2 (4%) of those without orthostatic hypotension were taking medication to control orthostatic symptoms. Forty-four patients with orthostatic hypotension (45%) and 21 of those without orthostatic hypotension (44%) were taking medication that could cause orthostatic hypotension. Clinical diagnoses included multiple system atrophy, diabetic autonomic neuropathy, peripheral neuropathy, Parkinson disease, and idiopathic neurogenic orthostatic hypotension.

Orthostatic Grading Scale

The 5-item scale demonstrated strong internal consistency (coefficient α=.91). Factor analysis revealed a single factor solution accounting for 74% of the variance. Factor loadings for the 5 items ranged from 0.78 to 0.90. Values for the OGS items and CASS for patients with and without orthostatic hypotension are given in Table 2. As expected, the groups differed significantly on each of the questionnaire items except for standing time, providing evidence of the construct validity of the scale. The groups also differed significantly on each of the CASS subscores. Spearman correlation coefficients for the OGS items, change in systolic BP on tilt, and CASS subscores are given in Table 3. The scale items correlated significantly with each of the laboratory-based CASS subscores, providing additional evidence of the construct validity of this brief self-report questionnaire.

Using the CASS adrenergic subscore as the gold standard, we calculated sensitivity and specificity of the OGS. We set the CASS adrenergic subscore at 3 or greater, and for OGS values of 9 or greater, we calculated a sensitivity of 65.6% and a specificity of 69.2%. If an OGS value of 10 or greater was used, sensitivity was 58.2%, and specificity was 78.2%.

Additionally, we compared the score results between patients with orthostatic hypotension who were taking antihypotensive drugs (ie, midodrine, fludrocortisone) vs those who were not. There were no differences in CASS subscores (for all, $P>.05$). However, the treated group scored significantly higher on all 5 questionnaire items (Table 4). We also compared patients with orthostatic hypotension who were taking drugs known to cause orthostatic hypotension vs those who were not. The 2 groups did not differ significantly on any of the 5 questionnaire items (for all, $P>.05$). The group not taking medications that could cause orthostatic hypotension had a higher CASS adrenergic subscore (median, 3.00 vs 2.00; $P=.02$). There were no significant differences in CASS cardiovagal or CASS sudomotor subscores between the 2 groups.

DISCUSSION

To our knowledge, this is the first study to compare a self-report grading scale for orthostatic intolerance in patients with putative orthostatic hypotension to a laboratory-measured composite score of autonomic deficits. The simple 5-item questionnaire proved to be of good internal consistency and demonstrated a unitary factor structure. It also had robust correlations with autonomic deficits (CASS), resulting in good sensitivity and specificity compared to the CASS adrenergic subscore. The strongest correlation was, as expected, with the CASS adrenergic subscore, followed by the cardiovagal subscore and then the sudomotor subscore. The correlation between the questionnaire and sudomotor function may appear surprising because sudomotor function certainly does not affect orthostatic tolerance. However, adrenergic failure in most patients is

TABLE 3. **Spearman Correlations for the Orthostatic Grading Scale Items, Systolic Blood Pressure Response to Head-Up Tilt, and Composite Autonomic Scoring System Subscores (N=145)***

Orthostatic Grading Scale, question	Question						Change in systolic blood pressure† (mm Hg)	Composite Autonomic Scoring System			
	1	2	3	4	5	Total		Sudomotor	Cardiovagal	Adrenergic	Total
1		.83‡	.81‡	.72‡	.59‡	.90‡	.18	.26‡	.36‡	.41‡	.42‡
2			.76‡	.72‡	.62‡	.87‡	.27§	.21§	.36‡	.36‡	.38‡
3				.67‡	.62‡	.89‡	.18	.22§	.34‡	.42‡	.41‡
4					.64‡	.85‡	.13	.30‡	.38‡	.44‡	.48‡
5						.81‡	.00	.15	.17§	.20§	.23‡
Total							.16	.23‡	.34‡	.40‡	.41‡

*1 = frequency of symptoms; 2 = severity of symptoms; 3 = symptoms with orthostatic stress; 4 = interference with activities of daily living; 5 = standing time.
†From baseline to head-up tilt at 70°.
‡$P<.01$.
§$P<.05$.

part of generalized autonomic failure; thus, cardiovagal and sudomotor deficits occur concurrently. Among the 5 items on the questionnaire, the level of interference with activities of daily living showed the strongest correlation with the CASS subscores. This information emphasized the impact that orthostatic hypotension has on patients' activities of daily living since we specifically asked patients to rate solely how orthostatic hypotension/orthostatic intolerance affects their activities of daily living. However, some patients, such as those diagnosed as having multiple system atrophy or Parkinson disease, may have severe extrapyramidal and other neurologic deficits (such as postural instability) that may render it difficult to isolate the effect of orthostatic hypotension from symptoms due to these deficits. Therefore, we expected a less robust correlation with this specific item. Conversely, the weakest correlation occurred between standing time and CASS subscores. This could be explained by the fact that symptoms of orthostatic hypotension are due to cerebral hypoperfusion. Patients who develop orthostatic hypotension slowly may adjust to it through expansion of their cerebral autoregulation range[4] and may remain asymptomatic despite major orthostatic changes.

Of note, orthostatic hypotension is not the only cause of reduced orthostatic tolerance. Because the purpose of the questionnaire was to evaluate orthostatic symptoms due to orthostatic hypotension specifically, we excluded patients who had orthostatic intolerance due to postural tachycardia syndrome. A few patients with normal tests reported orthostatic intolerance that was thought to be due to postural instability, vertigo, or metabolic abnormalities or to a nonorganic basis. As we had presumptive but no definite diagnosis, these patients were included in the analysis (in the group without orthostatic hypotension).

Medications can ameliorate, aggravate, or occasionally cause orthostatic symptoms. For autonomic function tests, patients are instructed to discontinue any medication known to affect BP or sweating before being tested in the autonomic laboratory. Nonetheless, such medications could potentially affect the self-reported orthostatic symptoms. Of interest is the observation that patients who received treatment for their orthostatic hypotension symptoms scored significantly higher on the questionnaire than those who did not, although the 2 groups did not differ in their autonomic deficits (CASS). Such a finding is not surprising and likely reflects the fact that the decision to treat orthostatic hypotension is often based on patients'

TABLE 4. **Values on the Orthostatic Grading Scale and Composite Autonomic Severity Score for Patients With Orthostatic Hypotension Who Are or Are Not Taking Antihypotensive Medication***

	Orthostatic hypotension		
	Taking medication (n=28)	Not taking medication (n=69)	*P* value
Orthostatic Grading Scale,† mean (SD)			
1	2.71 (1.01)	1.65 (1.32)	<.001
2	2.43 (0.74)	1.55 (1.04)	<.001
3	2.79 (1.03)	1.65 (1.34)	<.001
4	2.43 (1.46)	1.46 (1.23)	.001
5	2.39 (1.03)	1.70 (1.55)	.03
Total	12.75 (3.67)	7.93 (5.48)	<.001
Composite Autonomic Severity Score,‡ median (interquartile range)			
Sudomotor	2.00 (2.00)	2.00 (2.00)	.58
Cardiovagal	2.00 (1.00)	1.00 (2.00)	.09
Adrenergic	3.00 (0.00)	3.00 (1.00)	.16
Total	6.00 (3.00)	5.00 (4.00)	.12

*1 = frequency of symptoms; 2 = severity of symptoms; 3 = symptoms with orthostatic stress; 4 = interference with activities of daily living; 5 = standing time.
†Group comparisons performed with the *t* test.
‡Group comparisons performed with the Wilcoxon rank sum test.

reported symptom severity, not on the severity of orthostatic hypotension as detected on testing.

Our study has limitations. The concordance between symptoms and deficits applies to patients with orthostatic hypotension and cannot be applied to the general population. Patients with orthostatic intolerance without orthostatic hypotension (such as those with postural tachycardia syndrome) have modest deficits, and concordance may be much lower. This was not a population-based or prospective study. Before we can generalize on the value of the test applied to the general population, a prospective population-based study would be necessary.

CONCLUSIONS

Our 5-item questionnaire provides reasonable correlations with laboratory scores in patients with orthostatic hypotension. Although some correlations were not as robust as we might have expected, the results are not surprising. Orthostatic hypotension may be the dominant clinical symptom in some patients, but in others it may be a minor problem and may be hidden in a complex of other symptoms. The impact of orthostatic hypotension can vary substantially from patient to patient depending on the patient's overall functional status. Finally, orthostatic hypotension can be asymptomatic because of an expanded autoregulated range.[4]

Our study results provide confirmation that autonomic, especially adrenergic, deficits are responsible for a significant component of symptoms of orthostatic intolerance, as measured with our OGS, in patients with orthostatic hypotension. However, the agreement is imperfect and underscores the importance of combining the autonomic history with the laboratory quantitation of autonomic failure. On the basis of this study, our brief 5-item questionnaire is a reliable and valid measure of the severity of symptoms of orthostatic hypotension that can supplement laboratory-based measures to provide a rapid, more complete, clinical assessment. The instrument would also be useful as a brief screening device for orthostatic intolerance that could aid physicians in identifying patients who may have orthostatic hypotension.

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APPENDIX 1. **Composite Autonomic Scoring Scale***

Sudomotor subscore

1. Any of the following alterations
   a. Single QSART site abnormal *or*
   b. Length-dependent pattern (distal sweat volume <1/3 of forearm or proximal leg values) *or*
   c. Persistent sweat activity at foot (TST, anhidrosis present but <25%)
2. Any of the following alterations
   a. Single QSART site <50% of lower limit of normal
   b. Two or more QSART sites reduced (TST anhidrosis, 25%-50%)
3. Two or more QSART sites <50% of lower limit

Cardiovagal subscore

1. HR_{DB} mildly reduced but >50% of minimum
2. HR_{DB} reduced to <50% of minimum
3. Both HR_{DB} and Valsalva ratio reduced to <50% of minimum

Adrenergic subscore†

The adrenergic subscore is based on beat-to-beat BP alterations during the VM and tilt upright testing. A score of 1 is given for any of the following changes in VM
   a. Phase II_e reduction >20 but <40 mm Hg mean BP *or*
   b. Phase II_l does not return to baseline *or*
   c. Pulse pressure reduction to <50% of baseline

If VM is normal, a score of 1 can be assigned if the following changes occur at tilt upright testing
   a. Excessive oscillations in mean BP (>20 mm Hg occupying at least 50% of tilt upright time)
   b. Pulse pressure reduction to <50% of baseline
   c. Transient decrease in systolic BP >20 mm Hg with recovery within 1 minute
   d. Systolic BP reduction >20 mm Hg beyond 1 minute
   e. Diastolic BP reduction >10 mm Hg beyond 1 minute
   f. Overshoot at tilt back >20 mm Hg systolic BP

A score of 2 is assigned if mean BP decrement in phase II_e of VM is >40 mm Hg. If a score of 1 is determined from the VM, it can be increased to 2 if the following changes on tilt upright testing occur
   a. Transient systolic BP decrease >30 mm Hg with recovery within 2 minutes
   b. Systolic BP reduction >20 mm Hg beyond 1 minute
   c. Diastolic BP reduction >10 mm Hg beyond 1 minute

A score of 3 is assigned if the following changes occur in the VM
   a. Phase II_e mean BP reduction >40 mm Hg plus absent Phase II_l and IV

One additional point is assigned if a reduction in manual systolic BP >30 mm Hg occurs beyond 2 minutes and is sustained for at least 2 minutes during tilt upright testing

*BP = blood pressure; HR_{DB} = heart rate response to deep breathing; QSART = quantitative sudomotor axon reflex test; TST = thermoregulatory sweat test; VM = Valsalva maneuver.

†Phases refer to components of the VM: II_e and II_l are early and late portions, respectively.