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RESEARCH ARTICLE

Initial validation of symptom scores derived from the orthostatic discriminant and severity scale

Jacquie Baker[1,3] · Justin R. Paturel[1] · David M. Sletten[4] · Phillip A. Low[4] · Kurt Kimpinski[1,2,3]

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Abstract

Objective To develop a scale to quantify and discriminate orthostatic from non-orthostatic symptoms. In the current study, we present validation and reliability of orthostatic and non-orthostatic symptom scores taken from the orthostatic discriminate and severity scale (ODSS).

Methods Validity and reliability were assessed in participants with and without orthostatic intolerance. Convergent validity was assessed by correlating symptoms scores with previously validated tools [autonomic symptom profile (ASP) and the orthostatic hypotension questionnaire (OHQ)]. Clinical validity was assessed by correlating scores against standardized autonomic testing. Test–retest reliability was calculated using an intra-class correlation coefficient.

Results Convergent validity: orthostatic (OS) and non-orthostatic (NS) symptom scores from 77 controls and 67 patients with orthostatic intolerance were highly correlated with both the orthostatic intolerance index of the ASP (OS: $r = 0.903$; NS: $r = 0.651$; $p < 0.001$) and the composite score of the OHQ: (OS: $r = 0.800$; NS: $r = 0.574$; $p < 0.001$). Clinical validity: symptom scores were significantly correlated with the total composite autonomic severity score (OS: $r = 0.458$; NS: $r = 0.315$; $p < 0.001$), and the systolic blood pressure change during head-up tilt (OS: $r = -0.445$; NS: $r = -0.354$; $p < 0.001$). In addition, patients with orthostatic intolerance had significantly higher symptom scores compared to controls (OS: 66.5 ± 18.1 vs. 17.4 ± 12.9; NS: 19.9 ± 11.3 vs. 10.2 ± 6.8; $p < 0.001$, respectively). Test–retest reliability: Both orthostatic and non-orthostatic symptom scores were highly reliable (OS: $r = 0.956$ and NS: $r = 0.574$, respectively; $p < 0.001$) with an internal consistency of 0.978 and 0.729, respectively.

Interpretation Our initial results demonstrate that the ODSS is capable of producing valid and reliable orthostatic and non-orthostatic symptom scores. Further studies are ongoing to test sensitivity, specificity and symptom severity.

Keywords Orthostatic intolerance · Autonomic dysfunction · Autonomic reflex screen · Questionnaires

Introduction

Orthostatic symptoms occur when one changes position from lying/sitting to standing. Orthostatic intolerance (OI) is associated with numerous forms of autonomic dysfunction, ranging from severe autonomic disorders (i.e., pure autonomic failure, multiple system atrophy, neurogenic orthostatic hypotension) to milder syndromes (i.e., postural tachycardia syndrome, syncope, orthostatic intolerance) [1–4]. Symptoms associated with OI such as lightheadedness, dizziness, faintness, heart palpitation, and syncope [5] are the primary cause of morbidity in patients with dysautonomia. Additionally, these symptoms are often worsened by specific stressors including, but not limited to, exertion, high ambient temperatures, hot showers and baths, consumption of large meals and prolonged standing, making orthostatic symptoms

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✉ Kurt Kimpinski
kkimpin@uwo.ca

[1] Department of Clinical Neurological Sciences, London Health Sciences Centre, Rm. C7-131, University Hospital, 339 Windermere Road, London, ON N6A 5A5, Canada

[2] Schulich School of Medicine and Dentistry, Western University, London, ON, Canada

[3] School of Kinesiology, Western University, London, ON, Canada

[4] Department of Neurology, Mayo Clinic, Rochester, MN, USA

particularly disabling and burdensome to activities of daily living [3]. However, due to the non-specific nature of orthostatic symptoms, such as lightheadedness and dizziness, other more common etiologies are often considered prior to OI and autonomic dysfunction. To add to this problem, OI can also have numerous accompanying constitutional symptoms such as: fatigue, generalized weakness, shoulder and neck pain, etc. [6]. In such cases, clinicians may focus on these symptoms, without associating them with OI. Therefore, accurate identification and distinction between orthostatic versus non-orthostatic symptomatology is important for accurate diagnoses and treatment management.

Currently, there is no simple instrument, easily accessible for clinicians to help make this distinction and to discriminate symptoms as being orthostatic or non-orthostatic. Current validated questionnaires focused on orthostatic symptoms include, but are not limited to the: (1) Autonomic Symptom Profile (ASP), and (2) Orthostatic Hypotension Question (OHQ). The ASP is a comprehensive questionnaire (169 questions) with a focus on all aspects of autonomic dysfunction, with OI being a small portion of this assessment [7]. In contrast, the OHQ is short and the calculated results are easily obtainable and restricted to the assessment of the severity of orthostatic symptoms and the effects on daily living. However, the OHQ focuses on symptoms related to low blood pressure problems as opposed to generalized OI [8]. While these instruments provide important information on orthostatic symptoms, they do not address how orthostatic symptoms are differentiated from non-orthostatic symptoms.

Therefore, we developed the orthostatic discriminant and severity scale (ODSS) to help discriminate symptoms as being either orthostatic or non-orthostatic in nature. The ODSS is a short, 33-question, self-report questionnaire that provides an orthostatic score and non-orthostatic score. The ODSS implements clinical questions routinely used in practice by neurologists and clinicians to identify symptoms as being either orthostatic or non-orthostatic. The objectives of the current study were to analyze the orthostatic scores and non- orthostatic symptom scores derived from the ODSS with respect to: (1) Convergent validity, (2) Clinical validity and (3) Test–retest reliability.

Methods

Study participants

This was a prospective study evaluating validity and reliability of the ODSS in persons with orthostatic intolerance against asymptomatic healthy controls. Patients were recruited from the autonomic disorder laboratory within the Department of Clinical Neurology, University Hospital, London, Canada. All patients were seen by a neurologist to confirm the presence of orthostatic intolerance. In addition, all healthy participants were examined to confirm the absence of any neurological condition including any autonomic dysfunction and symptoms related to OI. In addition, healthy participants were excluded if they fell under any one of the following categories: (1) pregnant or lactating females, (2) clinically significant coronary artery disease, (3) concomitant therapy with anticholinergic, alpha- and beta-adrenergic antagonists or other medications which could interfere with autonomic functioning, and (4) failure of other organ systems or systemic illness that could affect autonomic function or participants' ability to cooperate. All study participants completed the autonomic reflex screen (ARS) and three self-report questionnaires (autonomic symptom profile, orthostatic hypotension questionnaire, orthostatic discriminant and severity scale). Study participants were asked to repeat the ODSS 2 weeks later in order to calculate test–retest reliability. Ethical approval for this study was obtained from the Health Sciences Research Ethics Board at Western University and written informed consent was obtained from each participant prior to study commencement.

Clinical evaluation

Autonomic reflex Screen

Standardized autonomic testing was performed as previously described [9, 10]. In brief, the quantitative sudomotor axon reflex test (QSART) was used to evaluate post-ganglionic sympathetic axon integrity using a QSWEAT device (WR Medical Electronics Co., Stillwater, MN, USA) and multi-compartmental sweat capsules. Adrenergic function was assessed using beat-to-beat blood pressure and heart rate responses to the Valsalva maneuver (VM) and Head-up Tilt (HUT). Cardiovagal function was assessed using heart rate response to deep breathing (HR_{DB}) and Valsalva ratio (VR) calculated from the VM. Heart rate and blood pressure were continuously recorded using an electrocardiography (ECG) device (Model 3000 Cardiac Trigger Monitor, IVY Biomedical Systems, Inc., Branford, CT, USA) and Nexfin hemodynamic monitoring system (BMEYE Cardiovascular, Amsterdam, Netherlands), respectively. All data were recorded and analyzed using WR Testworks™ software.

Composite autonomic scoring scale (CASS)

The composite autonomic scoring scale (CASS) was derived from the ARS as previously described [11]. The CASS provides a quantitative measure of the severity and distribution of autonomic dysfunction. The 10-point CASS is divided into the following three indices: Cardiovagal Index (0–3), Adrenergic Index (0–4) and Sudomotor Index (0–3).

Qualitative assessment of the adrenergic phases associated with the Valsalva maneuver (late phase II and phase IV) were used when providing an adrenergic score. A score of 1–3 is indicative of mild autonomic dysfunction, 4–6 as moderate, and 7–10 as severe autonomic dysfunction. An additional score of 0 was used to indicate no autonomic dysfunction. Therefore, in the context of the current study with the use of healthy control participants, an 11-point CASS was used (0–10).

Questionnaires

Orthostatic discriminant and severity scale (ODSS)

The ODSS was developed by clinicians experienced in autonomic dysfunction and specific orthostatic disorders, an epidemiologist with experience in questionnaire development and administration, by reviewing other validated questionnaires, and by extensive interactions with patients with orthostatic intolerance to identify symptom commonalities. The ODSS is a self-report questionnaire comprised of 33 questions. The questions implemented are used routinely in practice to identify orthostatic intolerance. The questions included symptom frequency, severity, duration and recovery in addition to specific orthostatic stressors, such as, prolonged standing, meal consumption and heat stress. Non-orthostatic symptoms were comprised of questions related to constitutional symptoms including, generalized weakness, fatigue and pain. In addition, symptoms of lightheadedness and dizziness unrelated to upright posture and unrelated to a change in position were included. The questions are preceded by instructions to rate each item by selecting the response that best described the symptoms one experiences on an average basis. The recall period was over the past year. This timeframe was chosen to ensure: (1) Symptoms were persistent and consistent, (2) Patients had sufficient time to experience a variety of circumstances in which their symptoms could have been affected (i.e., hot weather), (3) The timeframe was not too long so that symptoms that long since passed and no longer present were not being recorded. The primary items were scored on a dichotomous scale as either "yes" or "no" questions followed by conditional questions pertaining to frequency, severity, duration, and symptom recovery. Conditional questions were used to save time for patients with few or no symptoms. Access to the questionnaire can be found at: https://www.surveymonkey.com/r/guestODSS.

Scoring: The ODSS provides an orthostatic symptoms score and a non-orthostatic symptoms score. The Orthostatic symptoms score is calculated as the sum of 22 questions related to orthostatic intolerance, while the non-orthostatic symptoms score is calculated as the sum of 11 questions pertaining to more generalized symptoms. There were ten conditional questions requiring a 'yes' or 'no' response. Conditional questions were given a weighted value of either 1 or 2. Questions indicative of orthostatic intolerance were given a value of 2, whereas generalized symptoms and symptoms unrelated to the upright position were given a value of 1. The following is a sample question indicative of orthostatic intolerance: "In the past year, have you experienced symptoms of faintness, dizziness, and/or lightheadedness soon after standing up from a sitting or lying position?" A positive response would be given a value of 2, whereas a negative response would receive a value of 1. In the event of a positive response, follow-up questions would ensue. Follow-up questions were assessed using a 7-point Likert scale. A 7-point Likert scale was chosen in order to offer more points of discrimination. Answers indicative of orthostatic intolerance were weighted more heavily. The following is an example of a follow-up question in the event the previous question had a positive response: "Please rate the amount of relief of your symptoms of faintness, dizziness and/or lightheadedness upon lying/sitting back down". A response of 'No relief at all' would receive a weighted score of 1, whereas 'Complete relief' would receive a weighted score of 7. Similarly, if the answer for a conditional question for non-orthostatic symptoms is "No", this would warrant a score of 2, as higher scores are indicative of orthostatic intolerance. The lowest attainable orthostatic and non-orthostatic scores are both a score of 7 because the lowest value for each question has a value of 1. The highest attainable orthostatic symptoms score is 109 and 72 for a non-orthostatic symptoms score.

Autonomic symptom profile (ASP)

The autonomic symptom profile (ASP) is a self-report questionnaire comprised of 169 questions pertaining to symptoms related to overall autonomic dysfunction. The results of the ASP yield ten subscale scores (11 for men) to assess severity of symptoms within the following domains: orthostatic intolerance, bladder dysfunction, diarrhea, gastroparesis, secretomotor dysfunction, syncope, sleep disorder, constipation, vasomotor symptoms, and pupillomotor symptoms and sexual dysfunction for men [7].

Orthostatic hypotension questionnaire (OHQ)

The orthostatic hypotension questionnaire (OHQ) is a ten question self-report questionnaire to assess symptoms related to low blood pressure problems. The OHQ yields the following two sub-scores: Part I: the orthostatic hypotension symptoms assessment (OHSA), consisting of six questions to measure the presence and severity of orthostatic symptoms, and Part II: the orthostatic hypotension daily activity scale (OHDAS), consisting of four

questions to assess the impact of orthostatic symptoms on daily activities [8]. Each item is scored on an 11-point scale from 0 to 10, with 0 indicating no symptoms/no interference and 10 indicating the worst symptoms/complete interference. Included in the questionnaire is an additional option of "cannot do for other reasons". Average OHSA and OHDAS scores are obtained by averaging the response scores in the respective sections [8].

Statistical analysis

Descriptive statistics are presented as mean ± standard deviation. All measures between persons with and without orthostatic intolerance were compared using an independent *t* test. Statistical correlations were performed using Spearman's correlation coefficient. An alpha level of 0.05 was used to denote significance. All statistical analyses were performed using SPSS® statistical software version 21 for Windows (SPSS, Inc., Chicago, IL, USA).

Validity

Convergent validity was assessed by correlating the results of the ODSS with previously validated tools. The ODSS was correlated with the Orthostatic Index of the ASP and the average OHDAS and OHSA scores calculated from the OHQ. Clinical validity was evaluated by assessing the relationship between the ODSS and a clinically validated orthostatic challenge (Head-up Tilt test), and the total CASS derived from all components of the ARS.

Reliability

Test–retest reliability was calculated using a Model 3 (two-way mixed, consistency) single measure intra-class correlation coefficient between week 1 and week 2 ODSS scores. Cronbach's alpha was determined as a measure of internal consistency for both the orthostatic and non-orthostatic symptoms scores. All items were included in the calculation of internal consistency.

Results

A total of 77 persons without orthostatic intolerance (age: 54 ± 20 years) and 67 participants with confirmed orthostatic intolerance (47 neurogenic orthostatic hypotension (NOH); 12 postural tachycardia syndrome (POTS); eight syncope) (age: 57 ± 19 years) ($p = 0.45$) completed the study. All diagnoses were confirmed by a neurologist (KK) prior to testing. NOH was clinically defined as a sustained reduction in systolic blood pressure ≥ 30 mmHg within 3 min of head-up tilt (HUT) without an appropriate compensatory tachycardia [5]. The NOH population consisted of idiopathic NOH ($n = 21$), Parkinson's Disease +NOH ($n = 12$), Diabetic autonomic neuropathy ($n = 7$), multiple system atrophy ($n = 4$), pure autonomic failure ($n = 1$) and autoimmune autonomic ganglionopathy ($n = 2$). POTS was clinically defined by a heart rate increment ≥ 30beats/min within 5 min of HUT in the absence of orthostatic hypotension, along with orthostatic symptoms [5, 12, 13]. Syncope was defined as a transient loss of consciousness preceded by prodromal symptoms including, but not limited to, pallor, diaphoresis, nausea, lightheadedness, dizziness, weakness, visual disturbances, etc. [14]. Table 1 shows the

Table 1 Autonomic reflex screen in persons with and without orthostatic intolerance

QSART (μL ± SD)	Orthostatic intolerance average ± SD	Non-orthostatic intolerance average ± SD	*p* value
Forearm	0.90 ± 0.90	1.09 ± 1.10	0.30
Proximal leg	0.69 ± 0.91	1.18 ± 1.20*	0.01
Distal leg	0.51 ± 0.55	1.17 ± 1.31*	< 0.001
Foot	0.54 ± 0.48	0.99 ± 0.88*	= 0.02
Deep breathing (bpm)	10.3 ± 11.7	17. ± 9.4*	< 0.001
Valsalva ratio	1.5 ± 0.5	1.9 ± 0.4*	< 0.001
Head-up tilt			
Resting HR (bpm)	72.7 ± 11.9	63.9 ± 11.8*	< 0.001
ΔHR (bpm)	18.5 ± 15.7	23.0 ± 11.7	0.06
Resting SBP (mmHg)	146.2 ± 29.3	126.7 ± 19.9*	< 0.001
ΔSBP (mmHg)	− 61.9 ± 36.5	− 20.1 ± 10.5*	< 0.001

QSART quantitative sudomotor axon reflex test, *HR* heart rate, *SBP* systolic blood pressure, Δ change from rest

*Significantly different values

results obtained from the autonomic reflex screen. Persons with orthostatic intolerance had reduced sweat volumes at the proximal leg, distal leg and foot relative to the persons without orthostatic intolerance. Cardiovagal tests (HRDB and VR) were also significantly lower in persons with orthostatic intolerance ($p < 0.001$). Resting HR and SBP were significantly higher in our orthostatic population ($p < 0.001$). Meanwhile, the absolute drop in SBP on head-up tilt was significantly larger ($p < 0.001$), with a non-significant peak compensatory tachycardia ($p < 0.06$). In response to Valsalva, all NOH patients had absent adrenergic phases, which contributed to a higher adrenergic index associated with the composite autonomic scoring scale (CASS). Lastly, the total CASS was significantly higher in the orthostatic population (4.4 ± 3.5) versus the non-orthostatic population (0.37 ± 0.83; $p < 0.001$).

Questionnaires

Non-orthostatic participants had significantly lower OHDAS (0.07 ± 0.26; $p < 0.001$) and OHSA (0.20 ± 0.54; $p < 0.001$) scores calculated from the OHQ, resulting in a significantly lower composite OHQ score (0.14 ± 0.31) and significantly lower Orthostatic Indices derived from the ASP (4.0 ± 5.8) compared to participants with orthostatic intolerance (OHDAS: 4.87 ± 3.05; OHSA: 4.63 ± 2.77; Composite OHQ: 4.75 ± 2.70; ASP:28.25 ± 8.8; $p < 0.001$).

Validity

Convergent Validity: Orthostatic (OS) and Non-orthostatic (NS) scores were significantly correlated with the Orthostatic Index derived from the ASP (OS: $r = 0.903$; NS: $r = 0.651$; $p < 0.001$) (Fig. 1a), and the Composite Score of the OHQ: (OS: $r = 0.800$; NS: $r = 0.574$; $p < 0.001$) (Fig. 1b). Clinical Validity: Persons with orthostatic intolerance obtained significantly higher orthostatic scores compared to study participants without orthostatic intolerance (66.5 ± 18.1 vs. 17.4 ± 12.9, respectively; $p < 0.001$) (Fig. 2a). Additionally, persons with orthostatic intolerance scored higher on the non-orthostatic symptom score compared to non-orthostatic participants (19.9 ± 11.3 vs. 10.2 ± 6.8, respectively; $p < 0.001$) (Fig. 2a). Orthostatic and non-orthostatic scores were significantly correlated with the total CASS score derived from the autonomic reflex screen (OS: $r = 0.458$; NS: $r = 0.315$; $p < 0.001$), and both had a significant negative correlation with the drop in systolic blood pressure on head-up tilt (OS: $r = -0.445$; NS: $r = -0.354$; $p < 0.001$) (Fig. 2b).

Test–retest reliability

Test–retest reliability for orthostatic scores was strong ($r = 0.96$; $p < 0.001$), with an internal consistency of 0.98. The test–retest reliability for non-orthostatic scores was moderate ($r = 0.57$; $p < 0.001$) with an internal consistency of 0.73. On average, the non-orthostatic study population completed the second ODSS 18 ± 6 days later, and our orthostatic population 19 ± 6 days later ($p = 0.65$).

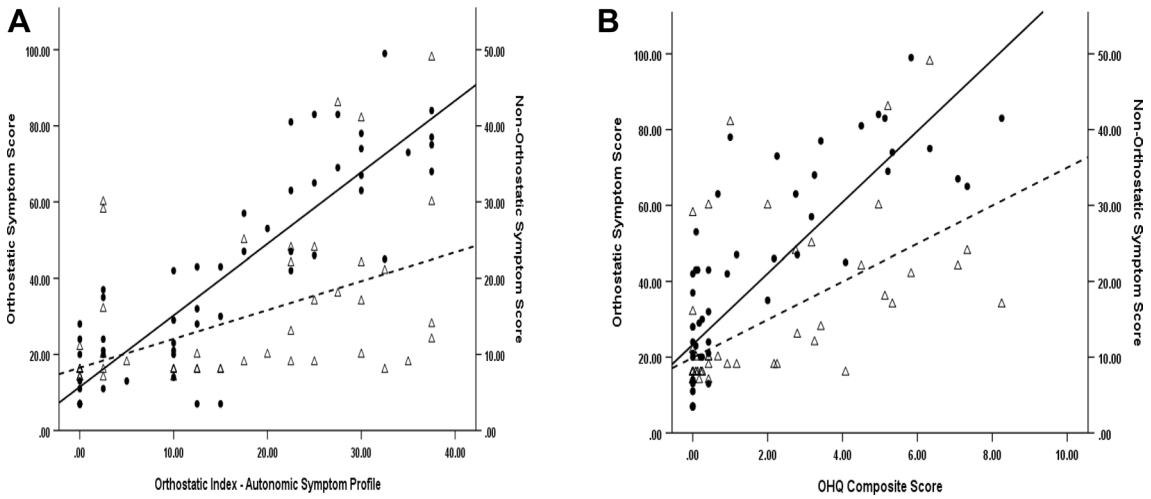

Fig. 1 Correlations between orthostatic (OS) and non-orthostatic (NS) symptom scores derived from the orthostatic discriminant and severity scale and previously validated tools demonstrate strong convergent validity. **a** Symptom scores were significantly correlated with the orthostatic Index of the autonomic symptom profile (OS: $r = 0.903$; NS: $r = 0.651$; $p < 0.001$). **b** Symptom scores were significantly correlated with the composite score of the orthostatic hypotension questionnaire (OHQ) (OS: $r = 0.800$; NS: $r = 0.574$; $p < 0.001$)

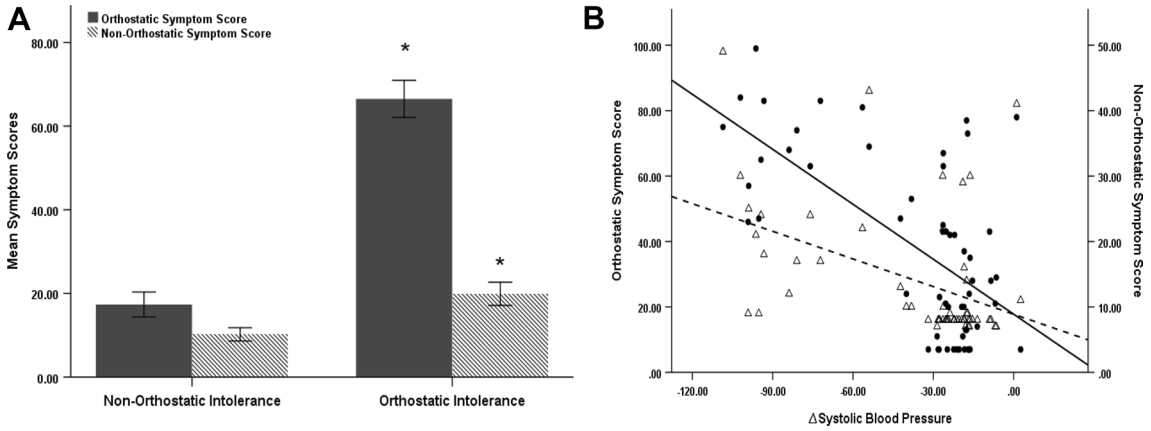

Fig. 2 Clinical validity of the orthostatic discriminant and severity scale. **a** Persons with orthostatic intolerance demonstrate significantly larger orthostatic and non-orthostatic symptom scores compared to person without orthostatic intolerance (*$p < 0.001$). **b** Orthostatic ($r = -0.445$; $p < 0.001$) and non-orthostatic ($r = -0.354$; $p < 0.001$) symptom scores demonstrate a significant negative correlation with the change in systolic blood pressure in response to Head-up Tilt of the autonomic reflex screen

Discussion

The objective of the present study was to demonstrate validity and reliability of the orthostatic and non-orthostatic symptom scores derived from the orthostatic discriminant and severity score (ODSS). The ODSS was designed to identify symptoms including dizziness, lightheadedness and faintness as being either orthostatic or non-orthostatic in nature. Our results reveal three major findings. First, the orthostatic and non-orthostatic symptom scores derived from the ODSS demonstrate strong convergent validity as evidenced by the strong positive correlations with previously validated tools (ASP and OHQ). Second, the orthostatic and non-Orthostatic Symptom Scores demonstrate strong clinical validity as evidenced by: (1) Significant correlations with the blood pressure drop in response to an orthostatic challenge (Head-up Tilt). (2) Significant correlations with the total CASS derived from tests of the ARS which are reproducible and standardized [11], and (3) patients diagnosed with orthostatic intolerance produced significantly higher orthostatic and non-orthostatic symptom scores compared to participants without orthostatic intolerance. Third, both orthostatic and non-orthostatic symptom scores were reproducible as indicated by strong test–retest reliabilities.

In the preliminary evaluation of the orthostatic and non-orthostatic symptom scores that are derived from the ODSS, it was first important to show that both symptom scores were valid and reliable. To test convergent validity, the current study demonstrated that symptom scores were highly correlated with previously standardized tools for assessing orthostatic intolerance, namely the ASP and the OHQ [7, 8]. In order to investigate the ability of the ODSS to discriminate orthostatic from non-orthostatic symptoms, follow-up studies are ongoing with clinical populations more likely to have more generalized symptomatology. Following assessment of these populations, we predict that orthostatic and non-orthostatic scores will reliably differ, making a distinction possible.

To investigate the clinical validity of the ODSS, symptom scores were correlated against the systolic blood pressure (SBP) drop on head-up tilt and the total CASS derived from the autonomic reflex screen. While the negative correlation between symptom scores and the change in SBP was significant, it is important to note that the study population was heterogeneous. For example, our orthostatic intolerance group was comprised of individuals with NOH, POTS, syncope and OI. Despite the heterogeneous nature of this group, there was still a significant and strong correlation with the drop in SBP. With ongoing recruitment, we aim to be able to separate the OI group on the basis of their clinical diagnoses and correlate the symptom score against more defining physiological parameters (i.e., HR in POTS patients, and SBP drop in NOH patients). Finally, orthostatic and non-orthostatic symptom scores were significantly correlated with the tCASS. It is not uncommon for patients with orthostatic intolerance to also have other more generalized symptoms, which would explain why non-orthostatic symptoms would also correlate with the tCASS, but to a lesser degree. Therefore, it is expected that the symptom scores between patients with and without orthostatic intolerance will not be so black and white and patients with orthostatic intolerance will not present with only orthostatic symptoms. However, we predict that these scores will differ from patients without orthostatic intolerance, and that there will be a reliable divergence between orthostatic and non-orthostatic scores, making a distinction possible based on the use of both scores.

Orthostatic intolerance (OI) can produce a wide array of symptoms including lightheadedness, dizziness, and

faintness. OI is important to detect because (1) it may be associated with increased morbidity, mortality, and more progressive forms of autonomic dysfunction, (2) it may be improved with treatment, (3) it may reduce unnecessary tests and treatments that could further complicate a patient's orthostatic symptoms, and (4) can be used to monitor symptoms changes over time particularly in response to treatment. The overall aim of the ODSS is that it will be able to address all four of these important issues related to OI.

The presence of OI can be indicative of more serious and progressive forms of autonomic dysfunction. Included in this group are patients with neurogenic orthostatic hypotension (NOH), pure autonomic failure, multiple system atrophy, autoimmune autonomic ganglionopathy, general neuropathies, Lewy body disorders, etc. Typically, patients are referred to specialists for treatment and management of these diseases. However, it is not unusual for patients to suffer from falls and full syncopal episodes, prior to accurate identification of orthostatic symptoms. Therefore, earlier symptoms assessment could lead to earlier diagnosis, more focused tests and specialized treatments.

Orthostatic symptoms can also produce non-specific symptoms such as headache, muscle and non-specific neck pain, fatigue or generalized weakness [6, 15]. In such cases, patients' complaints may be dismissed due to the non-specific nature of the symptoms, or they can misguide clinicians in making a proper diagnosis. More common syndromes and disorders related to lightheadedness and dizziness, such as inner ear/vestibular issues, benign positional vertigo, migraines, hypoglycemia, anemia and even certain medications may be considered prior to OI and autonomic dysfunction. Therefore, early and accurate identification of OI can reduce the need for unnecessary tests and avoid the use of incorrect treatments that could further complicate symptoms. For example, NOH is a form of OI characterized by a drop in systolic blood pressure $\geq$ 30 mmHg upon standing [5]. However, approximately 50% of NOH patients have associated supine hypertension [16]. Traditional use of anti-hypertensives to treat hypertension greatly exacerbates the blood pressure drop upon standing, which in turn exacerbates the level of OI experienced by these patients, and increases the potential for falls and more acute adverse events. Therefore, proper identification of OI helps reduce unnecessary testing and helps to focus treatment approaches.

Significance

The overall aim of the ODSS is not only to identify and quantify orthostatic symptoms, but to discriminate true orthostatic intolerance from other syndromes and disorders that may present with similar symptomatology. Syndromes such as chronic fatigue, chronic pain and fibromyalgia may have symptomatology similar to that of orthostatic intolerance. However, there is also usually more widespread non-orthostatic symptoms. Similarly, patients with orthostatic intolerance, perhaps due to autonomic dysfunction, may also have many constitutional symptoms, making accurate diagnoses more complicated. In both scenarios, it is important to discriminate orthostatic from non-orthostatic symptoms in the presence of a wide array of symptoms in order to identify or rule out autonomic dysfunction. Therefore, while this symptom discrimination is important, prior to evaluating the ability of the ODSS in making this distinction, assessments of validity and reliability of the symptom score were necessary. In the current article, we have demonstrated preliminary evidence that the ODSS is capable of producing scores that are both valid and reliable.

Study limitations

The ODSS has demonstrated preliminary evidence that it provides scores of orthostatic and non-orthostatic symptoms that are both valid and reliable. Furthermore, the ODSS is capable of accurately identifying orthostatic symptoms in patients with OI. In addition, studies including other clinical populations are ongoing with the aim of demonstrating its ability to discriminate between orthostatic and non-orthostatic symptomatology. Despite the promising results, the current study contains the following limitations: (1) The current study aimed to validate the symptom scores of the ODSS in a population of patients with known orthostatic intolerance, and (2) the sensitivity and specificity were not assessed. To address these limitations, the next steps are to continue with recruitment of patients with and without orthostatic intolerance prior to any autonomic testing. This aspect of the study will be done in a single-blinded fashion with the researchers blinded to the results of the autonomic testing and final clinical diagnoses. In addition, we aim to describe the severity of orthostatic intolerance based on the calculated orthostatic and non-orthostatic scores. Following completion of the second part of the study, we plan to make the ODSS publicly available so clinicians have easy and global access to the scale.

Conclusions

The current study demonstrates the ability of the orthostatic discriminant and severity scale to produce orthostatic and non-orthostatic symptom scores that are both valid and reliable. Orthostatic and non-orthostatic symptom scores were significantly larger in persons with orthostatic intolerance versus persons without, these scores demonstrated strong correlations with existing instruments, and were significantly correlated with the results of standard clinical autonomic testing, including an orthostatic challenge.

Author contributions JB and KK each contributed to experimental design, data analysis and manuscript preparation.

Compliance with ethical standards

Conflict of interest On behalf of all authors, there are no conflicts of interest.

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