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REVIEW ARTICLE (META-ANALYSES)

Nonpharmacologic Management of Orthostatic Hypotension: A Systematic Review

Patricia Branco Mills, MD, MHSc, FRCPC,[a,b,c,d] Carlen K. Fung, RN,[a,b] Angelique Travlos,[e] Andrei Krassioukov, MD, PhD, FRCPC[a,b,c,d]

From the [a]Division of Physical Medicine and Rehabilitation, University of British Columbia, Vancouver, British Columbia; [b]Department of Medicine, International Collaboration on Repair Discoveries, University of British Columbia, Vancouver, British Columbia; [c]GF Strong Rehabilitation Center, Vancouver, British Columbia; [d]Rehabilitation Research Program, Vancouver Coastal Health Research Institute, Vancouver Coastal Health, Vancouver, British Columbia; and [e]Faculty of Arts and Science, Queens University, Vancouver, British Columbia, Canada.

Abstract

Objective: To systematically review the literature on nonpharmacologic treatment of orthostatic hypotension.

Data Sources: MEDLINE, Cumulative Index to Nursing and Allied Health Literature, Embase, Cochrane Central Register of Controlled Trials, and SPORTDiscus were searched for human studies written in the English language between January 1980 and April 2013. Reference lists of relevant articles were reviewed for citations to expand the data set.

Study Selection: Prospective experimental studies assessing nonpharmacologic interventions for management of orthostatic drop in blood pressure in various patient populations were included. All studies identified through the literature search were reviewed independently in duplicate. Of the 642 studies, 23 met the selection criteria.

Data Extraction: Two reviewers independently extracted data for analysis, including systolic and diastolic blood pressure and orthostatic symptoms in response to postural challenge before and after the intervention. All 23 studies were assessed in duplicate for risk of bias using the Physiotherapy Evidence Database scale for randomized controlled trials and the Downs and Black tool for nonrandomized trials.

Data Synthesis: There were 8 identified nonpharmacologic interventions for management of orthostatic hypotension under 2 general categories: physical modalities (exercise, functional electrical stimulation, compression, physical countermaneuvers, compression with physical countermaneuvers, sleeping with head up) and dietary measures (water intake, meals). Owing to the clinically diverse nature of the studies, statistical comparison (meta-analysis) was deemed inappropriate. Instead, descriptive comparisons were drawn. Levels of evidence were assigned.

Conclusions: Strong levels of evidence were found for 4 of the 8 interventions: functional electrical stimulation in spinal cord injury, compression of the legs and/or abdomen, physical countermaneuvers in various patient populations, and eating smaller and more frequent meals in chronic autonomic failure. However, this conclusion is based on a limited number of studies with small sample sizes. Further research into all interventions is warranted.

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Orthostatic hypotension (OH) is characterized by an excessive drop in blood pressure with postural challenge.[1] When the orthostatic decrease in blood pressure exceeds the autoregulatory capacity of the brain or other vascular beds, debilitating symptoms in the affected individual can occur, including dizziness, nausea, fatigue, visual disturbances, cognitive slowing, and even loss of consciousness (syncope).[2,3]

OH is a common problem in various physiological states and disease conditions that disrupts the ability to maintain blood because of multifactorial issues. Underlying mechanisms leading to OH include hypovolemia, decreased skeletal muscle pump affecting venous blood flow, cardiovascular deconditioning, impaired neurovascular compensation, and neurohumoral effects.[4] The presence of OH has been associated with significant adverse

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events, including cognitive decline[5] and falls in older adults,[6] impaired quality of life in adolescents and adults,[7] and increased coronary events and mortality in middle-aged adults.[8] There is well-established evidence that OH is associated with decreased participation in rehabilitation in individuals with recent spinal cord injury[9] and increased cost of care in parkinsonian syndromes.[10]

In 1996, the definition of classic OH was described in a consensus statement by the American Academy of Neurology and the American Autonomic Society as a drop in systolic blood pressure (SBP) ≥20mmHg or diastolic blood pressure (DBP) ≥10mmHg on postural challenge, with or without symptoms, after 3 minutes of standing or head-up tilt (HUT) to at least 60° on a tilt table.[11] In the 2011 update, the consensus statement included definitions for other variants of OH, including initial and delayed OH. Initial OH is defined as a transient blood pressure decrease (≥40mmHg SBP and/or ≥20mmHg DBP) within 15 seconds of standing, whereas delayed OH was defined as OH that occurs beyond 3 minutes of postural challenge.[1]

Reviews[4,12] and guidelines[13] for management of OH recommend starting with nonpharmacologic strategies before progressing to pharmacologic strategies if the former prove insufficient. However, these articles are often lacking evidence-based citations for nonpharmacologic recommendations. Given that pharmacologic therapies for OH can cause significant cardiovascular side effects, including supine hypertension and ventricular hypertrophy,[13] it is imperative to establish which nonpharmacologic strategies can be recommended to patients for safe and effective management of OH.

Our objective was to conduct a systematic review of prospective experimental trials to provide health care professionals with evidence that supports the efficacy of nonpharmacologic interventions for the management of OH-related postural drop in blood pressure and symptoms in various patient populations. In addition, identifying gaps in the evidence can help direct research efforts to areas of priority.

Methods

Inclusion criteria

The inclusion criteria for this systematic review were prospective experimental studies on humans published in the English language. Participants had to have OH, which for the purpose of this review was defined as a drop in SBP by ≥20mmHg or a fall in SBP to <90mmHg, with postural challenge to capture data on individuals with initial, classic, and delayed OH.[1] The intervention had to be nonpharmacologic with the purpose of managing OH. Comparisons had to be made for the same subject or between subjects. Study outcomes had to report at least blood pressure in response to postural challenge. Also, a study was included if a subset of the total patients included in the study met inclusion criteria and if the outcomes of the subset were assessed and reported separately.

List of abbreviations:

DBP diastolic blood pressure
FES functional electrical stimulation
HUT head-up tilt
MSA multiple system atrophy
OH orthostatic hypotension
PEDro Physiotherapy Evidence Database
RCT randomized controlled trial
SBP systolic blood pressure

Table 1 Electronic database search strategy: Ovid MEDLINE (1980—April 11, 2013)

No.	Searches	Results
1	exp Hypotension, Orthostatic/dh, th, rh, pc [Diet Therapy, Therapy, Rehabilitation, Prevention & Control]	594
2	nonpharmacologic therapy.mp.	178
3	1 and 2	0
4	nonpharmacologic.mp.	2710
5	1 and 4	13
6	limit 1 to (evidence based medicine reviews and humans)	3
7	limit 1 to "therapy (maximizes sensitivity)"	261
8	limit 1 to (clinical trial, all or meta-analysis or randomized controlled trial)	71
9	6 or 7 or 8	261
10	limit 1 to (humans and systematic reviews)	13
11	9 or 10	271
12	limit 11 to humans	265
13	(clinical trial or meta-analysis or randomized controlled trial or systematic review).mp. [mp=title, abstract, original title, name of substance word, subject heading word, keyword heading word, protocol supplementary concept, rare disease supplementary concept, unique identifier]	755,024
14	1 and 13	74
15	12 or 14	265
16	5 or 15	275
17	limit 16 to (English language and humans)	220
18	limit 17 to yr="1980 -Current"	202

Systematic review

A systematic search was conducted to identify relevant studies published between January 1980 and April 2013 using the following electronic databases: MEDLINE, Cumulative Index to Nursing and Allied Health Literature, Embase, Cochrane Central Register of Controlled Trials, and SPORTDiscus. Librarians at the Royal College of Physicians and Surgeons of British Columbia developed search strategies. The complete search strategy for MEDLINE is described in table 1. All titles and abstracts were assessed against inclusion criteria. In cases where the abstracts did not give full information for application of criteria, the full-text versions of the studies were reviewed. Reference lists of reviewed articles and relevant studies were retrieved and scanned for citations to expand the data set.

Study selection and data extraction

Two primary reviewers (P.B.M. and C.F.) independently reviewed the studies to determine eligibility for inclusion. Disagreement was resolved through consensus, and if necessary, by third party resolution (A.K.). Data were extracted from all included studies independently and in duplicate (P.B.M. and C.F.) into a Microsoft Excel[a] spreadsheet, with the template

adapted from the Cochrane Collaboration.[14] For all studies, the number of participants, population, intervention, type of postural challenge, blood pressure, and symptoms in response to postural challenge were extracted (primary outcomes). When not reported by study authors, the change in blood pressure with the postural challenge was calculated if sufficient data were available. Study authors were contacted for missing information. Secondary outcomes extracted included time to blood pressure recovery, standing time, time to onset of symptoms, compliance, perceived effectiveness of intervention, and adverse events. Other outcomes were not reported. Results were not reported for participants without OH.

Risk of bias assessment

Two authors (C.F. and A.T.) assessed study risk of bias independently; differences in scores were resolved by a third party (P.B.M). Quality assessment was performed using the Physiotherapy Evidence Database (PEDro)[15] scoring system for randomized controlled trials (RCTs) and the Downs and Black[16] tool for nonrandomized trials. The PEDro scale is composed of 11 yes or no quality items, 10 of which are used to calculate the final PEDro score (0−10). The Downs and Black scale consists of 27 one-point questions and 1 two-point question (scored from 0−2), resulting in a final score ranging from 0 to 28. For both tools, higher scores are indicative of greater methodologic quality. To simplify interpretation of results, studies scoring 9 or 10 on the PEDro scale or ≥24 on the Downs and Black scale were considered methodologically to be of excellent quality; scores from 6 to 8 on the PEDro scale or 20 to 23 on the Downs and Black scale were considered of good quality; scores from 4 to 5 on the PEDro scale or 15 to 19 on the Downs and Black scale were of fair quality; and scores <4 on the PEDro scale or ≤14 on the Downs and Black scale were considered of poor quality. Further, the level of evidence was evaluated using a 5-level scale (simplified form of Sackett[17]), where level 1 (the highest level of evidence) is an RCT with a PEDro score ≥6; level 2 is an RCT with a PEDro score ≤5, a nonrandomized prospective-controlled study, or a cohort study; level 3 is a case-control study; level 4 is a pre- and posttest or a case series; and level 5 is an observational report or case report with only a single subject.[18]

Statistical analysis

Owing to the clinically diverse nature of study methods, statistical comparison (meta-analysis) was deemed inappropriate. Instead, descriptive comparisons are subsequently drawn. The effectiveness of each intervention is outlined in supplemental tables S1 and S2 (available online only at http://www.archives-pmr.org/). Levels of evidence for recommendations are provided in table 2.

Results

Search strategy

A total of 642 studies were screened, with 593 identified through the electronic search after duplicates were removed (fig 1). The remaining 49 were identified through the cited reference search of primary articles. Based on inclusion criteria, 23 studies were included.[19-41] Reasons for exclusions were collected at each stage and are shown in figure 1.

Studies

Eligible studies ranged in size from 5 to 100 participants. Study quality was variable: Downs and Black scores ranged from 11 to 21, and PEDro scores ranged from 5 to 10. One study was an RCT, 11 studies were crossover trials, 2 studies were prospective controlled trials, and 9 studies were pre-post studies. Only 1 study[37] had sample size determined by power calculations to detect a meaningful difference. One study reported adverse events.[37]

Participants

Studies included participants with autonomic failure, participants with neurocardiogenic syncope, older adults, participants with spinal cord injury, and otherwise healthy adults with initial OH. Three studies[20,27,37] had participant inclusion criteria of classic OH. Three studies[36,38,42] had OH as an inclusion criterion but did not provide the definition of OH; these studies were included because patient baseline data demonstrated a drop in SBP ≥20mmHg with postural challenge. Five studies[19,24,39-41] had inclusion criteria of an SBP drop of ≥20mmHg with varying times at which the drop in SBP was detected after postural challenge. Twelve studies did not have OH as a specific inclusion criterion, but baseline blood pressure postural changes were consistent with an inclusion criterion of SBP drop of ≥20mmHg[21-23,26,28-32,35] or a fall in SBP to <90mmHg.[33,34]

Interventions

Eight nonpharmacologic interventions for OH were identified under 2 general categories: physical modalities (exercise, functional electrical stimulation [FES], compression, physical countermaneuvers, compression and physical countermaneuvers, sleeping with head up) (see supplemental table S1) and dietary measures (water intake, meals) (see supplemental table S2). Where applicable, results are reported as mean ± SD unless otherwise noted.

Physical modalities

Exercise

A literature search identified 2 pre-post studies[19,20] evaluating the effects of exercise on OH. One pre-post study[19] of fair quality on participants with symptomatic OH caused by chronic autonomic failure assessed the short-term effect of pedaling a cycle ergometer supine on the severity of OH. They found that immediately standing after a bout of supine exercise exacerbated OH. Exercise did not affect postural blood pressure in the healthy control group.

In the other fair-quality study,[20] older adults with OH, a history of orthostatic symptoms ranging from 2 to 10 years, and various medical comorbidities were taught to perform a home-based resistance training program. At 8 weeks (median, 25.5 training sessions), there was a statistically nonsignificant worsening of the drop in postural blood pressure. However, the study authors reported that most participants felt less dizzy, stronger, and more stable than before training, and there was a significant increase in dynamic strength of the arms and legs. In the long term (time not specified), 3 participants continued, 3 participants performed an abbreviated version, and 2 participants discontinued the program because of the time commitment.

Table 2 Levels of evidence for nonpharmacologic management of OH

Level of Evidence	Studies	Recommendations
Autonomic failure (eg, MSA, PAF, familial dysautonomia)		
Level 1	1 randomized crossover trial[41]	Eating smaller, more frequent meals as opposed to less, larger meals does not affect the changes in BP with orthostatic stress but does results in significantly higher supine, sitting, and standing BP and improves orthostatic symptoms
Level 1	1 randomized crossover trial[30]	PCMs or abdominal compression to 20mmHg improves orthostatic BP
Level 1	1 randomized controlled crossover trial[35]	Leg crossing with active muscle tensing improves orthostatic BP in individuals with hypoadrenergic OH, whereas leg muscle pumping with tiptoeing does not
Level 2	1 prospective controlled trial[38]	Sleeping with head up at 12° has a short-term effect but not a long-term effect on improving the orthostatic drop in systolic BP with active standing, but it does improve orthostatic tolerance both in the short term and long term as measured by the Orthostatic Disability Score
Level 4	1 pre-post study[39]	Drinking 300mL of water 45min prior to HUT does not improves orthostatic BP
Level 4	1 pre-post study[40]	Rapid drinking of 480mL of tap water 35min prior to standing improves orthostatic drop in BP
Level 4	1 pre-post study[39]	Ingesting a balanced liquid meal (commercially available Complan with glucose in a milk base) results in lowering of supine and postural BP in individuals with MSA and PAF, but not with DBH deficiency
Level 4	1 pre-post study[27]	Compression to 40mmHg with a pressure suit improves OH with compression of calves and thighs together, with or without abdominal compression; compression of either calves or thighs alone is not beneficial, whereas abdominal compression on its own is very effective
Level 4	1 pre-post study[19]	Acute bout of exercise exacerbates OH in the short term
Level 4	1 pre-post study[36]	Increasing abdominal compression from 20 to 40mmHg or using both abdominal compression and PCMs of the lower extremities concurrently results in improved orthostatic BP response
Older adults		
Level 1	1 randomized controlled crossover trial[25]	Active elastic compression bandage of lower extremities (40—60mmHg at ankles, 30—40mmHg at the hip) for 10min followed by additional abdominal compression (20—30mmHg) for 10min improves orthostatic drop in BP and orthostatic symptoms with HUT in community-living older adults
Level 1	1 randomized crossover trial[26]	Lower-limb compression bandage of 30mmHg pressure applied to both legs (from the ankle to the thigh) when supine prior to standing improves orthostatic symptoms in hospitalized older adults with >36h of bed rest
Level 1	1 RCT[37]	Sleeping with head up at 5° (6in) has no additional effects on orthostatic BP measured over 2min after standing or symptoms at 6wk when compared with no head elevation
Level 4	1 pre-post study[20]	8-wk home-based resistance training program does not improve orthostatic drop in BP
Level 4	1 pre-post study[24]	Graduated elastic compression tights with 20—30mmHg ankle pressure improves orthostatic drop in BP and orthostatic dizziness

(*continued on next page*)

Table 2 (*continued*)

Level of Evidence	Studies	Recommendations
Neurocardiogenic syncope		
Level 1	1 placebo-controlled randomized crossover trial[31]	Isometric handgrip with arm tensing for 2min at onset of symptoms of impending syncope improves orthostatic drop in BP and orthostatic symptoms
Level 2	1 controlled prospective trial,[33] 1 pre-post study[34]	Active tensing of the lower extremities with or without leg crossing, whole body tensing, squatting, or moving the head between the knees improves orthostatic BP and orthostatic symptoms with HUT[33] and active standing[34]
Spinal cord injury		
Level 1	2 randomized crossover trial,[21,22] 1 pre-post study[23]	FES over contractile muscles of the lower extremity improves orthostatic BP, standing time, and presyncopal symptoms in individuals with motor complete tetraplegia during HUT
Level 1	1 randomized crossover trial[29]	Elastic abdominal binder, with a target 10% reduction in seated girth measurement when seated in upright wheelchair, decreases prevalence of OH with active sitting
Level 2	1 randomized crossover trial[28]	Inflatable abdominal corset at 35mmHg or bilateral pneumatic leg splints at 65mmHg are significantly better than no device in maintaining BP during HUT
Level 4	1 pre-post study[23]	FES over bony prominences of the lower extremities improves orthostatic BP and presyncopal symptoms in individuals with motor complete tetraplegia during HUT
Initial OH		
Level 2	1 controlled crossover study[32]	Lower-body muscle tensing for 40s after standing from squatting improves orthostatic BP and orthostatic symptoms

Abbreviations: BP, blood pressure; DHB, dopamine-beta-hydroxylase deficiency; PAF, primary autonomic failure; PCM, physical countermaneuver.

Conclusions: exercise

There is level 4 evidence that an acute bout of exercise exacerbates OH in the short term in individuals with chronic autonomic failure[19] and that an 8-week home-based resistance training program does not improve orthostatic blood pressure in older adults with OH.[20]

Functional electrical stimulation

Three studies[21-23] were identified that examined FES for the management of OH. All studies consisted of participants with spinal cord injury.

All 3 studies found that FES of the lower-extremity musculature improved OH with progressive HUT, with better responses at increasing intensities of stimulation.[23] The good-quality RCT[21] also demonstrated that FES improved orthostatic symptoms and significantly increased time in the vertical HUT position by an average of 14 minutes. The fair-quality pre-post study[23] saw an effect on blood pressure regardless of the site of stimulation (muscles vs noncontractile sites). The authors hypothesized that a positive effect on blood pressure with electrical stimulation, but no muscular activation, could be explained by activation of pain receptors triggering the sympathetic nervous system, resulting in increased blood pressure.

Conclusions: FES

There is level 1 evidence that FES over muscles of the lower extremity improves orthostatic blood pressure,[21-23] standing time,[21] and orthostatic symptoms[21,23] in individuals with spinal cord injury during HUT. There is level 4 evidence that FES over bony prominences of the lower extremities also improves orthostatic blood pressure and symptoms during HUT in this population.[23]

Compression of the abdomen and/or lower limbs

Seven studies[24-30] were identified looking at abdominal and/or lower-extremity compression for management of OH.

Three of these studies looked at compression for management of OH in older adults. A single-blinded randomized placebo-controlled crossover trial[25] of excellent quality demonstrated that when used during HUT, active elastic compression bandage of lower extremities (40−60mmHg at ankles, 30−40mmHg at the hip) followed by additional abdominal compression (20−30mmHg), compared with sham intervention, resulted in improved orthostatic drop in blood pressure and orthostatic symptoms. A good-quality nonblinded randomized controlled crossover trial[26] was conducted on older hospitalized adults for various medical conditions with >36 hours of bed rest. Lower-limb compression bandage of 30mmHg applied to both legs when supine prior to standing significantly decreased orthostatic symptoms, but it did not affect prevalence of OH compared with the unbandaged state. In 1 poor-quality pre-post study,[24] graduated elastic compression tights with 20 to 30mmHg of ankle pressure resulted in statistically significant improvement in the drop in blood pressure caused by HUT in 10 older adults with OH and a history of falls. Orthostatic dizziness was abolished in 7 of the 10 participants.

Two studies examined the effect of compression in participants with chronic autonomic failure and OH. One was a good-quality randomized crossover trial[30] that examined the effect of abdominal compression of 20mmHg using an inflatable belt on participants with familial dysautonomia. This study found that abdominal compression significantly increased postural SBP but

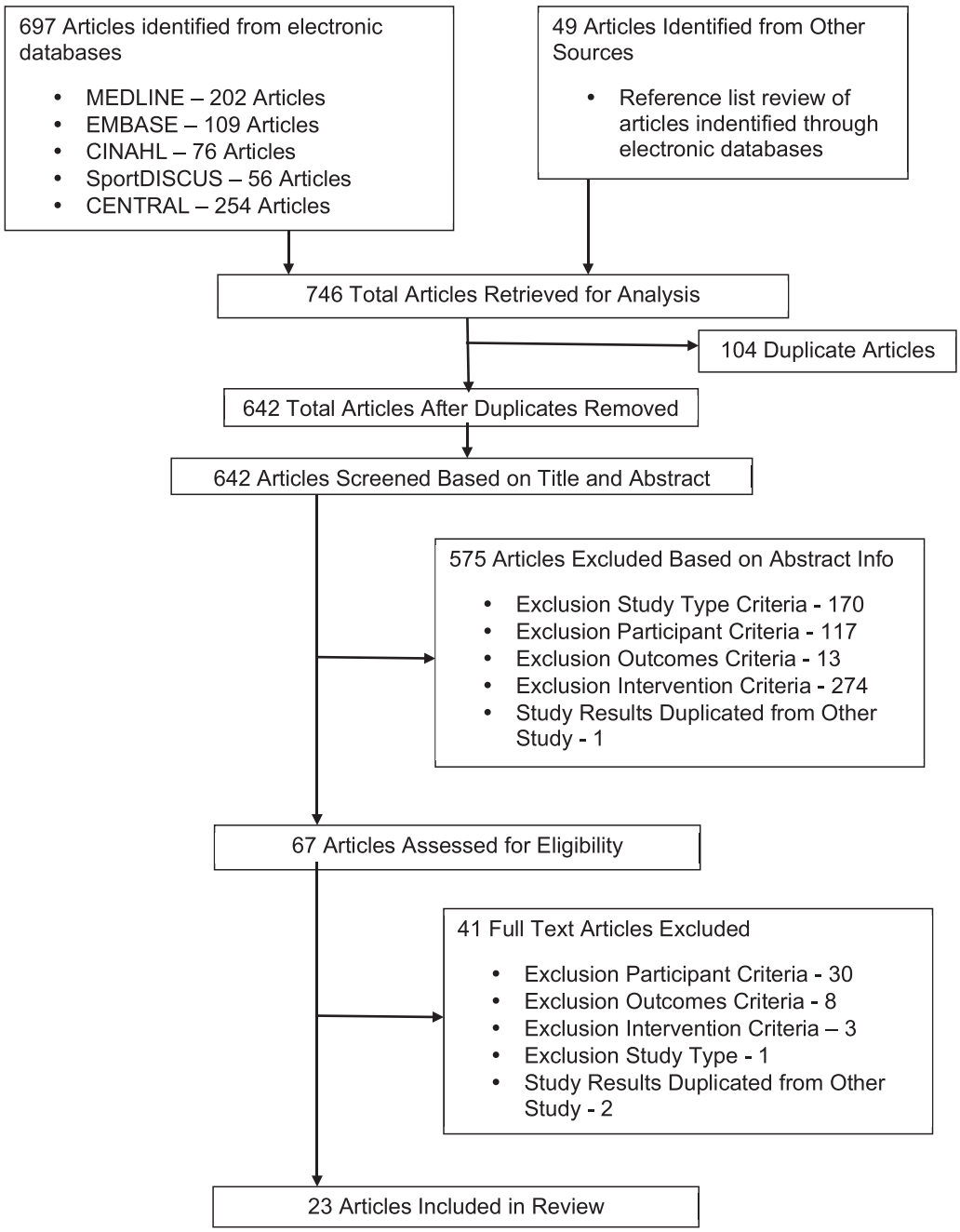

Fig 1 Studies selection flowchart. Abbreviation: CINAHL, Cumulative Index to Nursing and Allied Health Literature.

not DBP. The other was a poor-quality pre-post study[27] on participants with multiple system atrophy (MSA), primary autonomic failure, and diabetic autonomic neuropathy. The studies examined the effect of a lower-body positive pressure suit with 5 separate compartments inflated to 40mmHg, with either all of the sites compressed or separate compression of bilateral calves, bilateral thighs, bilateral calves and thighs, or lower abdomen compared with no compression. Compression of all compartments or the abdominal compartment alone significantly decreased the orthostatic drop in SBP with HUT, whereas compression of the other compartments did not. Ten participants selected compression of all compartments as being most effective at improving orthostatic symptoms, followed by abdominal compression (n=2) and bilateral calves compression (n=1).

Two randomized crossover trials examined the effect of compression on participants with cervical spinal cord injury. One was a fair-quality study[28] using an inflatable abdominal corset at 35mmHg or bilateral pneumatic leg splints at 65mmHg. Application of either compressive device was significantly better than no device in maintaining blood pressure with HUT. At higher angles, the abdominal corset proved significantly better at maintaining blood pressure than the pneumatic leg splints. The other was a good-quality study[29] that demonstrated that elastic abdominal compression bandage, tightened to achieve approximately 10% reduction in seated girth measurement, eliminated postural drop in blood pressure consistent with OH in 3 of 7 participants with previously documented OH on active sitting.

Conclusions: compression

In community-living older adults with OH, there is level 1 evidence that 40 to 60mmHg of pressure at the ankle with 30 to 40mmHg pressure at the hip[25] and level 4 evidence that 20 to 30mmHg ankle pressure provided by active elastic compression bandage of lower extremities[24] improve orthostatic blood pressure drop and orthostatic symptoms. There is level 1 evidence that use of lower-limb compression bandage of 30mmHg pressure applied to both legs (from the ankle to the thigh) when supine prior to standing improves orthostatic symptoms in hospitalized older adults with >36 hours of bed rest.[26]

In individuals with chronic autonomic failure, there is level 1 evidence that abdominal compression to 20mmHg with an inflatable belt increases blood pressure with standing.[30] There is level 4 evidence in this population that compression to 40mmHg with a pressure suit improves OH with compression of calves and thighs together with or without abdominal compression; compression of either calves of thighs alone is not beneficial, whereas abdominal compression on its own is very effective.[27]

In individuals with spinal cord injury, there is level 1 evidence that an elastic abdominal binder, with a target 10% reduction in seated girth measurement when seated in an upright wheelchair, decreases prevalence of OH with active sitting.[29] There is level 2 evidence in this population that application of either inflatable abdominal corset at 35mmHg or bilateral pneumatic leg splints at 65mmHg is significantly better than no application of a device for maintaining blood pressure during HUT.[28]

Physical countermaneuvers

Physical countermaneuvers are specific actions or exercises that involve tensing of muscle groups in the upper or lower extremities, performed with the goal of immediately increasing blood pressure. Literature search identified 6 studies[30-35] looking at the use of physical countermaneuvers for management of OH.

Three of these studies had participants with vasovagal syncope. One study of good quality was a placebo-controlled randomized crossover trial[31] comparing isometric handgrip with active arm tensing for 2 minutes at the onset of symptoms of impending syncope with HUT with sham control. Active arm tensing was found to improve postural blood pressure, improve orthostatic symptoms, and prevent syncope. One fair-quality prospective controlled trial[34] compared the effect of active tensing of the lower extremities with or without leg crossing, whole body tensing, squatting, and putting the head between the knees on blood pressure with active standing. Participants were provided with training. Maneuvers were started at the moment of rapid fall in blood pressure in association with symptoms of impending syncope with standing and were sustained for 40 to 60 seconds. All maneuvers resulted in a short-term increase in blood pressure; lower-body tensing with leg crossing was the most effective of all maneuvers. Vasovagal symptoms returned once maneuvers were discontinued. A good-quality pre-post study[33] demonstrated that active tensing of the lower extremities with leg crossing for a duration of >30 seconds can abort or delay impending faints, with associated improvements in blood pressure. After termination of the maneuver, symptoms did not return in 5 participants. Long-term follow-up demonstrated that approximately 50% of participants had ongoing benefits with use of this maneuver in daily life. In 3 of the participants, hand grip with arm tensing was also examined. There was a stabilizing effect on blood pressure with arm tensing during HUT, but not to the same extent as with leg crossing and tensing. Furthermore, symptoms were not improved with arm tensing.

One fair-quality controlled crossover trial[32] examined the effect of lower-body muscle tensing for 40 seconds on participants with initial OH. There was a significant improvement in the drop in blood pressure on active standing with use of the physical countermaneuvers. On follow-up there was symptomatic improvement in 90% of participants who continued to use the physical countermaneuvers.

One good-quality randomized controlled crossover trial[35] examined the effect of 1 minute of tiptoeing or leg crossing on participants with hypoadrenergic OH from various neurogenic causes. After active standing, leg crossing significantly increased blood pressure, whereas tiptoeing did not.

One good-quality randomized crossover trial[30] of participants with familial dysautonomia compared blood pressure responses with active standing during use of several physical countermaneuvers or abdominal compression at 20mmHg with an inflatable belt. Squatting was the most effective intervention to raise blood pressure, followed by abdominal compression of 20mmHg, bending forward, and leg crossing with active muscle tensing. Many participants required assistance to perform the physical countermaneuvers.

Conclusions: physical countermaneuvers

In individuals with neurocardiogenic syncope, there is level 1 evidence that isometric handgrip with arm tensing for 2 minutes at the onset of symptoms of impending syncope improves orthostatic drop in blood pressure and orthostatic symptoms.[31] There is level 2 evidence that active tensing of the lower extremities with or without leg crossing, whole body tensing, squatting, or putting the head between the knees improves orthostatic blood pressure and orthostatic symptoms with HUT[33] and active standing[34] in this population.

There is level 2 evidence that in individuals with initial OH, lower-body muscle tensing for 40 seconds after standing from squatting improves orthostatic blood pressure and orthostatic symptoms.[32]

There is level 1 evidence that leg crossing with active muscle tensing,[30,35] bending forward with arms crossed over the abdomen, or squatting[30] improves orthostatic blood pressure in individuals with autonomic failure, whereas leg muscle pumping with tiptoeing does not.[35]

Compression and physical countermaneuvers

One fair-quality pre-post study[36] using both compression and physical countermaneuvers to manage OH was identified. Researchers examined the effect during HUT of a modified anti-gravity suit at either 20 or 40mmHg of abdominal compression, crossed legs with active muscle tensing, or a combination of the 2 interventions on participants with autonomic failure from various neurogenic conditions. A higher level of abdominal compression was associated with higher blood pressure on orthostatic challenge. Addition of leg crossing to abdominal compression improved orthostatic blood pressure responses. Leg crossing alone was not as effective as abdominal compression of 40mmHg.

Conclusions: compression and physical countermaneuvers

There is level 4 evidence that physical countermaneuvers and abdominal compression improves orthostatic blood pressure in

individuals with autonomic failure from neurogenic conditions.[36] Increasing abdominal compression from 20 to 40mmHg or using both abdominal compression and physical countermaneuvers of the lower extremities concurrently results in improved orthostatic blood pressure response.

Sleeping with head up

Two studies were identified as meeting inclusion criteria for sleeping with head up as an intervention for OH. One was a good-quality nonblinded RCT[37] on community-living older adults with chronic symptomatic OH, the only study in this review that was statistically powered and reported adverse events. The use of sleeping with 5° (6in) of head elevation compared with no head elevation for 6 weeks did not result in significant changes in blood pressure on active sit to stand. However, blood pressure measurements were taken for only 2 minutes after standing. Both the participants sleeping with head up and the controls reported overall symptomatic improvement. Sleeping with head up was associated with increased incidence of ankle edema at 6 weeks.

The other study was a poor-quality prospective controlled trial[38] on participants with hypoadrenergic OH from mixed causes (history of acute poliomyelitis, Hodgkin disease causing dysautonomia, unknown etiologies). They studied the effects of sleeping with 12° of head elevation without fludrocortisone compared with fludrocortisone. Effects of fludrocortisone are not reported in this article. All participants were given a diet containing 150 to 200mmol sodium and a minimal water intake of 2L per day. After 1 week, sleeping with head elevation significantly improved the drop of SBP with active standing; blood pressure results were not significant at a mean of 14 months (range, 8–70mo) of follow-up. However, orthostatic tolerance as measured by the Orthostatic Disability Score improved significantly both after 1 week and at follow-up.

Conclusions: sleeping with head up

There is level 1 evidence that in older adults, sleeping with 5° of head elevation has no additional effects on orthostatic blood pressure or symptoms at 6 weeks when compared with no head elevation in older adults with OH. However, blood pressure measurements were taken for only 2 minutes after standing; therefore, any effect on OH occurring beyond this timeframe was not captured.[37] There is level 2 evidence that in individuals with hypoadrenergic OH, sleeping with 12° of head elevation had a short-term effect but not a long-term effect on improving the orthostatic drop in SBP with active standing, but it does improve orthostatic tolerance in both the short and long terms as measured by the Orthostatic Disability Score.[38] Adverse events with sleeping with head up included ankle edema, sliding to the end of the bed, and pain in the soles of feet because of pressure from the footboard.

Dietary measures

Water intake

Two studies[39,40] that examined the effect of drinking water on OH were identified. Both were poor-quality pre-post studies on participants with MSA or primary autonomic failure. One study[40] examined the effect of drinking 480mL of tap water at room temperature over a period of 5 minutes, 35 minutes before standing. It found a significant improvement in the orthostatic drop in blood pressure 1 minute after active standing with water drinking. The other study[39] looked primarily at the effect of meals on OH (results are subsequently reported in the Meals section). This study also examined the effect of drinking 300mL of water on 6 of the participants and found that 45 minutes after water drinking, there was a nonsignificant worsening in orthostatic blood pressure with HUT.

Conclusions: water intake

In individuals with autonomic failure there is level 4 evidence that rapid ingestion of 480mL of tap water 35 minutes prior to standing improves orthostatic drop in blood pressure[40] and that drinking 300mL of water 45 minutes prior to HUT nonsignificantly worsens orthostatic blood pressure response.[39] These conflicting results are from 2 small poor-quality studies that used different volumes of water with different postural challenges.

Meals

Two studies[39,41] looked at the effect of meals on OH in individuals with chronic autonomic failure. One study was a good-quality nonblinded randomized crossover trial[41] on participants with MSA or primary autonomic failure. They compared the effect of eating 6 small meals in 1 day, with the extra 3 meals given as midmorning, midafternoon, and supper snacks, versus 3 large meals in 1 day. Both phases had a total caloric intake of 2.5MJ, and participants were not allowed to drink coffee. Eating 3 larger meals resulted in lower SBP in lying, sitting, and standing conditions compared with eating 6 smaller meals. Blood pressure dropped to lower levels between the larger meals compared with the smaller meals. There was no significant improvement in the postural change in SBP with sitting or standing blood pressure between the smaller versus larger meals. However, orthostatic symptoms and standing tolerance were improved with smaller meals. The other study was a poor-quality pre-post study[39] on the effects of a balanced liquid meal containing commercially available Complan with glucose in a milk base in participants with chronic autonomic failure. In those with MSA and primary autonomic failure, the liquid meal significantly lowered supine blood pressure, and postural blood pressure with HUT dropped to significantly lower levels after meal ingestion. In the 2 participants with dopamine-beta-hydroxylase deficiency, the liquid meal had variable but minimal effects on blood pressure and symptoms while supine and during HUT.

Conclusions: meals

There is level 1 evidence that in individuals with chronic autonomic failure from MSA and primary autonomic failure, eating smaller, more frequent meals as opposed to larger, less frequent meals does not affect the changes in blood pressure with orthostatic stress but does result in significantly higher supine, sitting, and standing blood pressure and improved orthostatic symptoms.[41] There is level 4 evidence that ingesting a balanced liquid meal containing commercially available Complan with glucose in a milk base results in lowering of supine and postural blood pressure in individuals with MSA and primary autonomic failure, but not with dopamine-beta-hydroxylase deficiency.[39]

Discussion

Strong levels of evidence were found for improvement of OH with 4 of the 8 interventions: FES in spinal cord injury, compression of the legs and/or abdomen, physical countermaneuvers in various patient populations, and eating smaller and more frequent meals in chronic

autonomic failure (see table 2). There is level 1 evidence that sleeping with 5° of head elevation for 6 weeks does not improve OH measured over 2 minutes after standing in older adults. However, there is a need for further research into all strategies for nonpharmacologic management of OH because conclusions that were drawn for each intervention were based on a few studies with small numbers of participants and varying levels of quality. Importantly, there was only 1 study that reported on adverse events.

Because there are significant cardiovascular side effects associated with the use of pharmacologic measures to manage OH, particularly in vulnerable populations (eg, older adults), it is crucial to establish the effectiveness and safety of nonpharmacologic interventions. There are also issues with feasibility, practicality, and compliance that need to be addressed in any potential intervention. Studies in this review rarely considered how treatment affected functional ability, and no trials examined the effects on quality of life.

Recommendations for future studies

When conducting research in this field, it is crucial to first determine whether the individual has OH as per blood pressure measurements because posturally related symptoms may be caused by conditions other than OH (eg, postural tachycardia syndrome).[43] The treatment approach for these conditions can be very different from that for OH. This review's inclusion criteria of participants having a demonstrated postural drop in blood pressure resulted in the exclusion of studies that had participants with a history of posturally related symptoms but no documented drop in blood pressure with postural challenge. This included several studies on salt supplementation and gentle cardiovascular reconditioning that were identified through the literature search. As a result, we were unable to find evidence in the present literature that demonstrated whether salt supplementation or gentle cardiovascular reconditioning improves OH.

Although guidelines recommend treating OH symptoms without targeting a specific blood pressure,[13,44] it is also important that studies report blood pressure responses to postural challenge after an intervention, especially if the study is not controlled; otherwise, it is difficult to determine whether improvement in symptoms is the result of cardiovascular changes or a placebo effect. Furthermore, it is useful to report the absolute blood pressure levels in addition to the change in blood pressure with postural challenge. An intervention that raises lying and/or upright blood pressure back into the cerebrovascular autoregulatory range can lead to an improvement in orthostatic tolerance, even though the absolute drop in blood pressure might be unchanged or still within what is considered a hypotensive range.[45] This may explain why several studies demonstrated improvement in orthostatic symptoms despite minimal changes in orthostatic blood pressure drop.[20,26,38,40,41] Therefore, it is equally important to capture both orthostatic blood pressure and symptoms when investigating effects of interventions for the management of OH. Because changes in postural blood pressure may or may not be associated with changes in symptoms, outcome measures that capture improvement in functional abilities and/or quality of life should also be used.

Study limitations

The strength of our findings is limited by small study sizes, variable quality of study design, and inability to perform a meta-analysis on the results because of the heterogeneity of study methods. Articles reviewed were limited to English and although the search strategy to identify studies for this review was comprehensive, given the broad nature of the topic reviewed, it is possible that some studies may have been missed. However, it is unlikely that this would be a large enough number of studies to change the conclusions of this review. In addition, because the quality of the included studies was generally poor, results must be interpreted with some caution. This article has tried to take these factors into account by assessing risk of bias and assignation of levels of evidence.

Conclusions

The current review provides recommendations for the effectiveness of nonpharmacologic interventions for management of OH in various groups of individuals. The number of published good-quality prospective experimental trials on nonpharmacologic management of OH is low. Therefore, it remains difficult to draw firm conclusions about the evidence regarding the effectiveness and safety of treatment. Further research into all interventions is warranted. Clinicians and researchers investigating an intervention for the management of OH should include participants with documented drop in SBP and DBP according to established criteria for OH with postural challenge. Future studies should document and report on lying and upright blood pressure, postural drop in blood pressure and symptoms, adverse events, and importantly, should consider the effect of treatment on functional abilities and quality of life.

Supplier

a. Microsoft Corp, 1 Microsoft Way, Redmond, WA 98052.

Keywords

Diet therapy; Hypotension, orthostatic; Orthostatic intolerance; Physical therapy modalities; Rehabilitation

Corresponding author

Patricia Branco Mills, MD, MHSc, FRCPC, GF Strong Rehabilitation Centre, 4255 Laurel St, Vancouver, BC V5Z 2G9, Canada.
E-mail address: patricia.mills@vch.ca.

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Supplemental Table S1 Physical modalities for management of OH

Author (year) Country Risk of Bias Score Study Design Sample Size	Methods	Outcome
Exercise		
Smith and Mathias (1995)[19] UK D&B=15 Pre-post N=47	P: chronic autonomic failure; MSA (n=15), PAF (n=15), dopamine-beta-hydroxylase deficiency (n=2); healthy controls (n=15; results not reported) I: pedaling a cycle ergometer supine at workloads of 25, 50, and 75Ww each for 3min (total 9min of exercise) PC: active standing from supine OM: BP, symptoms	(1) Postural drop in SBP/DBP was less before vs immediately after exercise in MSA: −62±23/−35±16 vs −68±23/−39±19mmHg ($P>.05$); PAF: −64±19/−37±11 vs −68±23/−42±16mmHg ($P>.05$); dopamine-beta-hydroxylase deficiency: patient 1: −45/−26 vs −66/−44mmHg; patient 2: −29/−19 vs −51/−28mmHg (2) Lowest standing SBP/DBP was higher before vs after exercise: MSA: 94±19/59±16 vs 79±16/53±19mmHg ($P<.005$, $P>.05$); PAF: 86±19/53±16 vs 72±12/45±12mmHg ($P<.001$, $P<.05$); dopamine-beta-hydroxylase deficiency: patient 1: 83/46 vs 63/35; patient 2: 82/40 vs 68/32mmHg (3) 26/32 patients had more postural symptoms after than before exercise
Zion et al (2003)[20] USA D&B=18 Pre-post N=8	P: older adults, age ≥60y I: home-based resistance training program for 8wk: squats, heel raises, hip extension/flexion, knee extension/flexion, ankle plantar-/dorsiflexion, biceps curls, chest presses. Timing: 1h. Frequency: every other day. Target: 3 sets, 12 repetitions with resistance progression. Intensity: tailored to each participant. PC: active standing from supine; HUT to 60° OM: BP, symptoms	(1) Postural drop in SBP/DBP was less before vs after the program with active standing at 2min: −37±38/−1±17 vs −44±38/−16±29mmHg ($P>.05$) (2) Standing SBP/DBP after 2 min was higher before vs after the program: 104±30/64±14 vs 101±29/55±28mmHg ($P>.05$) (3) BP results with HUT were similar to active standing ($P>.05$) (4) After the program, most said they felt stronger, more stable, and less dizzy than before training (exact numbers not provided)
FES		
Cheing and Chao (2006)[21] Hong Kong PEDro=7 NB randomized crossover trial N=16	P: motor complete tetraplegia I: FES over knee extensors/flexors, foot plantar-/dorsiflexors PC: graded HUT (0°, 15°, 30°, 45°, 60°, 75°, 90) OM: BP, standing time (orthostatic tolerance), symptoms	(1) Adding FES attenuated the drop in SBP/DBP by 4±4/2±3mmHg ($P<.05$) for every 15° incremental increase in the angle of HUT (2) FES increased the overall mean standing time by 14±4min ($P=.003$) (3) At 90° HUT, 75% without vs 47% with FES had presyncopal symptoms
Elokda et al (2000)[22] USA PEDro=5 NB randomized crossover trial N=5	P: complete tetraplegia (n=2) and paraplegia (n=3), 2−4wk post-SCI I: FES over knee extensors, foot plantar flexors PC: graded HUT (0°, 15°, 30°, 45°, 60°) OM: BP	(1) Postural drop in SBP/DBP was less with vs without FES at all angles: 15° (−2±3/−3±2 vs −8±3/−5±2mmHg), 30° (−7±3/−6±2 vs −20±3/−11±2mmHg), 45° (−13±3/−6±2 vs −21±3/−12±2mmHg), 60° (−20±3/−8±2 vs −28±3/−10±2mmHg); all $P<.05$, except ΔDBP at 15° and 60°, $P>.05$ (2) SBP/DBP was lower without vs with FES at all angles: 15° (111±2 vs 116±2mmHg), 30° (99±2 vs 111±2mmHg), 45° (98±2 vs 105±2mmHg), and 60° (91±2 vs 98±2mmHg); all $P<.05$
Sampson et al (2000)[23] Canada D&B=16 Pre-post N=6	P: motor complete SCI, lesions >T6; recent injury (n=3), chronic injury (n=3)I: FES over quadriceps and pretibial muscles with varying intensities (0, 48, 96, and 160mA) during HUT by 10° increments every 3min C: FES over noncontractile sites (patellae and malleoli) PC: HUT from 0° to 90° OM: BP, perceived presyncope score	(1) SBP ($P=.001$) and DBP ($P=.002$) increased with increasing stimulation intensities and decreased with increasing angle of tilt ($P<.001$) regardless of the site of stimulation (results presented in a graph) (2) The higher the FES intensity, regardless of the stimulation site, the greater the tilt incline tolerated ($P=.049$)

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Supplemental Table S1 (*continued*)

Author (year) Country Risk of Bias Score Study Design Sample Size	Methods	Outcome
Compression of the abdomen and/or lower limbs		
Henry et al (1999)[24] UK D&B=14 Pre-post N=10	P: older adults, age >60y, symptomatic OH with history of falls I: graduated elastic compression tights, 20–30mmHg ankle pressure PC: HUT to 90° OM: BP, symptoms	(1) Postural drop in SBP over 3min was less with compression than without: −0.4±25 vs −20±12mmHg (P=.005) (2) Orthostatic dizziness was abolished in 7/10 patients with compression
Podoleanu et al (2006)[25] Italy PEDro=9 SB randomized, placebo-controlled, crossover trial N=21	P: older adults, age >60y, history of orthostatic intolerance I: elastic compression bandage of lower extremities (40–60mmHg at ankles, 30–40mmHg at the hip) for 10min followed by additional abdominal compression (20–30mmHg) for 10min C: sham: elastic bandages applied at 5mmHg pressure ankles/hips. PC: HUT to 60° OM: BP, symptoms, Specific Symptom Scale Questionnaire for orthostatic intolerance	(1) Postural drop in SBP was less with vs without compression of the lower limbs for 10min (−2±30 vs −13±28mmHg; P=.003) and the abdomen for an additional 10min (−2±33 vs −19±31mmHg; P=.002) (2) HUT SBP with active vs sham compression was 127±17 vs 112±25mmHg (P=.003) after 10min of leg compression and 127±21 vs 106±25mmHg (P=.002) after 10min of abdominal compression (3) In the compression vs sham group, 90% vs 53% of patients remained asymptomatic (P=.02); abdominal compression was more effective at reducing symptoms; mean Specific Symptom Scale score decreased from 35±12 during the month before compression to 23±11 after 1mo of compression (P=.01)
Gorelik et al (2004)[26] Israel PEDro=7 NB randomized crossover trial N=61	P: older adults, age >65y, hospitalized for various conditions, >36h of bedrest I: lower-limb compression bandage of 30mmHg from ankles to thighs PC: passive sitting OM: presence of OH (defined as a fall of ≥20mmHg and/or ≥10mmHg in SBP/DBP, respectively), symptoms	(1) After 3min sitting, 34/61 (55.7%) patients without vs 34/61 patients with compression bandages developed OH (P>.05) (2) Dizziness (35 vs 16; P<.01) and palpitations (23 vs 6; P<.001) over 3min was more prevalent in the unbandaged vs bandaged state; this trend continued at 5 min
Denq et al (1997)[27] USA D&B=14 Pre-post N=14	P: chronic autonomic failure: PAF (n=9); MSA (n=3); diabetic autonomic neuropathy (n=2) I: lower-body positive pressure suit, 5 separate compartments inflated to 40mmHg: bilateral calves; bilateral thighs; bilateral calves and thighs (legs); lower abdomen; all sites compressed PC: HUT to 80° OM: BP, symptoms	(1) Postural drop in SBP at 5min was only significantly less with all compartments compressed (−41±37mmHg, P<.005) and abdomen compressed (−54±35mmHg, P<.01) vs without compression (−66±36mmHg) (2) HUT SBP significantly increased with all compressed (116±28mmHg, P<.05) and abdomen compressed (102±25mmHg, P<.05) vs without compression (90±7mmHg) (3) Efficacy in reducing orthostatic symptoms: all>abdomen>legs=calves>thighs (4) 10/14 patients chose all compartments compression as the most efficacious maneuver in reducing symptoms
Huang et al (1983)[28] USA PEDro=5 Randomized crossover study N=27	P: motor complete tetraplegia I: (1) inflatable abdominal corset at 35mmHg; (2) bilateral pneumatic leg splints at 65mmHg PC: HUT to 20° and 45° OM: BP	(1) Postural drop in SBP/DBP was less with abdominal or leg compression vs without compression at 20° HUT (−5±16/0±4 or −5±16/−4±12 vs −17±19/−8±14mmHg; P<.05) and 45° HUT (−13±19/−2±12 or −19±18/−10±13 vs −36±19/−19±15mmHg; P<.05) (2) At 45° HUT, abdominal compression was more effective than leg compression for minimizing the drop in BP (P<.01)

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Supplemental Table S1 (*continued*)

Author (year) Country Risk of Bias Score Study Design Sample Size	Methods	Outcome
Wadsworth et al (2012)[29] Australia PEDro=8 NB randomized crossover trial N=14	P: SCI, lesions >T2, 1y post-SCI I: elastic abdominal binder when seated in upright wheelchair, target 10% reduction in seated girth measurement PC: active sitting OM: presence of OH (definition not provided)	(1) 7/14 patients had OH with active sitting: 4/7 patients had OH regardless of compression and 3/7 patients only had OH without compression
Tutaj et al (2006)[30] USA PEDro=7 NB randomized crossover trial N=17	P: familial dysautonomia I: abdominal compression with inflatable belt at 20mmHg (PCM intervention results reported in relevant section) PC: active standing from supine OM: BP	(1) Without abdominal compression, postural drop in SBP/DBP was mean (range): −53 (−85 to −46)/−39mmHg (−53 to −33mmHg); abdominal compression increased standing SBP by 27mmHg (9−41mmHg) (P=.001) and DBP by 2mmHg (0−4mmHg) (P>.05)
PCM		
Brignole et al (2002)[31] Italy PEDro=7 SB placebo- controlled randomized crossover study N=19	P: vasovagal syncope, history of ≥1 (pre-) syncopal episodes, positive HUT; healthy controls (n=32; results not reported) I: isometric handgrip with arm tensing for 2min at onset of presyncope C: sham: hand grip without arm tensing for 2min at onset of symptoms PC: HUT to 60° OM: BP, symptoms	(1) Postural drop in SBP/DBP was less with vs without arm tensing: −29±43/4±28 vs −59±29/22±15mmHg (P<.05) (2) HUT SBP/DBP increased with vs without arm tensing: 105±38/71±24 vs 73±21/51±20mmHg (P<.05) (3) In the active vs sham group, 63% vs 11% became asymptomatic and 5% vs 47% developed syncope on HUT (P=.02) (4) During 9±3mo of follow-up, arm tensing protocol was performed in 95/97 (98%) of episodes of impending syncope and was successful in preventing syncope in 94/95 (99%) episodes
Krediet et al (2007)[32] The Netherlands D&B=16 NB controlled crossover study N=20	P: initial OH (abnormally large transient BP decrease 5−15s after postural challenge; n=13); healthy control (n=7; results not reported) I: LBMT: tensing all skeletal muscles in the abdomen, buttocks, and legs at maximal voluntary capacity for 40s after standing PC: active squat to stand OM: BP, questionnaire on perceived effectiveness of LBMT	(1) Postural drop in SBP/DBP with standing was less with than without LBMT: −34/−19 vs −55/−30mmHg (P<.05) (2) Standing SBP/DBP increased with vs without LBMT in mean (range): 111 (67−163)/69 (43−87) vs 90 (70−123)/88mmHg (69−105mmHg) (P<.05) (3) During follow-up at 2mo (1−26mo), 8/10 patients using LBMT reported fewer symptoms, and 9/10 patients perceived some or much benefit from the maneuver in daily life
Krediet et al (2002)[33] The Netherlands D&B=21 Pre-post N=21	P: vasovagal syncope, history of ≥1 (pre-) syncopal episodes, positive HUT I: (1) LCMT for >30s at the onset of HUT-provoked symptoms; (2) maximal voluntary isometric handgrip exercise at the moment of impending faint (n=3) PC: HUT to 60° OM: BP, heart rate, symptoms	(1) Lowest SBP/DBP with HUT rose from 65±13/43±9 to 106±16/65±10mmHg (P<.05) (2) During LCMT, prodromal symptoms disappeared in all patients, and none lost consciousness; after termination of LCMT, symptoms did not return in 5 patients (3) At median (range) of 10mo (7−14mo) follow-up, 13/20 patients reported LCMT in daily life with benefit; 3 patients had no syncopal complaints since the test; 2 patients still suffered faints and did not use LCMT (4) Isometric handgrip exercise: some stabilizing effect on BP but far less pronounced than with LCMT; hand gripping could not abort the faint and all 3 patients had to be tilted back to horizontal within 1min

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Supplemental Table S1 (*continued*)

Author (year) Country Risk of Bias Score Study Design Sample Size	Methods	Outcome
Krediet et al (2005)[34] The Netherlands D&B=15 NB controlled prospective trial N=44	P: vasovagal syncope, history of ≥1 (pre-) syncopal episodes, positive HUT I: group A (n=12): LCMT vs no LCMT; group B (n=9): whole body tensing vs LCMT; group C (n=14): squatting vs baseline; group D (n=9): head bent between knees vs baseline; training provided, maneuvers started at the moment of rapid fall in BP in association with orthostatic symptoms, sustained for 40–60s PC: HUT to 60° OM: BP	(1) HUT SBP/DBP increased with vs without PCMs: LCMT (104±18/69±12 vs 77±8/54±8mmHg; $P<.05$), no LCMT (120±13/53±11 vs 75±14/53±11mmHg; $P<.05$), whole body tensing (115±23/73±16 vs 73±6/51±8mmHg; $P<.05$), squatting (122±15/74±10 vs 76±13/50±10mmHg, $P<.05$), head between knees (115±16/70±16 vs 69±8/48±7mmHg, $P<.05$) (2) LCMT was more effective than no LCMT and whole body tensing in increasing BP ($P<.05$)
Tutaj et al (2006)[30] USA PEDro=7 NB randomized crossover trial N=17	P: familial dysautonomia I: (1) bending forward with arms crossed over abdomen; (2) squatting; (3) leg crossing by pressing calves and thighs of both legs against each other (abdominal compression results reported in relevant section) PC: active standing from supine OM: BP	(1) Postural drop in SBP/DBP was −53/−39mmHg ($P=.003$) without PCMs (2) SBP/DBP increased during squatting by 49/38mmHg ($P<.05$), bending forward by 23/12mmHg ($P<.005$), and leg crossing by 8/12mmHg ($P<.05$)
Ten Harkel et al (1994)[35] The Netherlands PEDro=6 NB randomized controlled crossover trial N=14	P: hypoadrenergic OH; PAF (n=4), Hodgkin disease (n=1), multiple sympathectomies (n=1), damage of vasomotor center in medulla oblongata (n=1); healthy patients (n=6; results not reported) I: leg muscle pumping (tiptoeing) or tensing (leg crossing) for 1min, started after 2min of active standing PC: active standing OM: BP	(1) Without PCMs, postural drop in SBP/DBP after 2min standing was −51±21/−22±12mmHg (2) Tiptoeing increased SBP by 4±13mmHg ($P>.05$) but not DBP (−1±7mmHg; $P>.05$) (3) Leg crossing increased standing SBP/DBP by 18±18/10±11mmHg ($P<.05$) (4) After termination of PCM, BP gradually returned to previous standing levels
Compression and PCM		
Smit et al (2004)[36] USA D&B=17 Pre-post N=23	P: chronic autonomic failure: PAF (n=4), MSA (n=7), progressive autonomic neuropathy (n=8), diabetic neuropathy (n=3), (sub)acute panautonomic neuropathy (n=3), extensive sympathectomies (n=1) I: abdominal compression with modified antigravity suits, conditions: (1) no compression; (2) 20mmHg compression; (3) 40mmHg compression; (4) crossed legs; (5) crossed legs plus 20mmHg compression; (6) crossed legs plus 40mmHg compression; (7) abdominal elastic binder of 15–20mmHg PC: active standing, HUT to 40°–60° OM: BP	(1) 40mmHg of abdominal compression increased SBP/DBP with HUT by mean (range) of 30 (7–69)/14mmHg (2–36mmHg)($P<.05$) (2) 40mmHg of compression caused higher increase in SBP/DBP than 20mmHg: 21 (1–48)/10mmHg (−5 to 27mmHg) vs 17 (0–56)/8mmHg (−3 to 22mmHg) ($P<.05$) (3)HUT SBP/DBP increase was higher during crossed legs with abdominal compression of 20mmHg: 26 (−4 to 72)/10mmHg (−9 to 3mmHg) and 40mmHg: 30 (10–66)/13mmHg (4–32mmHg), than without compression: 15 (−6 to 43)/6mmHg (−6 to 20mmHg) ($P<.05$) (4) Abdominal elastic binder increased active standing SBP/DBP in 9 patients by 11 (−3 to 36)/6mmHg (−3 to 14mmHg) ($P<.05$)

(*continued on next page*)

Supplemental Table S1 (*continued*)

Author (year) Country Risk of Bias Score Study Design Sample Size	Methods	Outcome
SHU		
Fan et al (2011)[37] Ireland PEDro=7 NB RCT N=100	P: community-living older adults (>60y), chronic symptomatic OH I: SHU at 5° (6in) head elevation for 6wk (n=66) C: no head elevation during sleep (n=34) PC: active standing from supine OM: BP, frequency of dizziness	(1) SHU vs control attenuated the postural drop in SBP/DBP on standing for 2min by 3±17/0±6 vs 2±10/0±6mmHg ($P>.05$) (2) Increase in standing SBP/DBP was less with SHU vs control: 2±16/3±5 vs 2±7/2±4mmHg ($P>.05$) (3) Both SHU ($P=.004$) and controls ($P=.001$) had significantly fewer episodes of dizziness per week after intervention; difference between the 2 groups was nonsignificant (4) Compliance with SHU was 77% (5) AE: increased incidence of ankle edema
Ten Harkel et al (1992)[38] The Netherlands D&B=14 NB prospective controlled trial N=9	P: Hypoadrenergic OH, mixed causes (acute poliomyelitis, Hodgkin disease, unknown etiologies) I: sleeping with 12° head up tilt without fludrocortisone (n=4) C: SHU with fludrocortisone (results not reported; n=5); all patients: diet with 150−200mmol sodium and a minimal water intake of 2L/d PC: active standing from supine OM: BP, Orthostatic Disability Score	(1) SHU alone reduced the decrease in SBP/DBP on standing for 1min after 1wk for all patients (−53±23/−31±20 vs −64±29/−25±17mmHg; $P<.01$ for SBP) but not after 14mo (range, 8−70mo) of n=6 follow-up (−71±28/−28±15 vs −45±33/−19±20mmHg; $P>.05$) (2) Orthostatic Disability Score improved in all patients after 1wk and appeared consistent during follow-up ($P<.001$)

Abbreviations: AE, adverse events; BP, blood pressure; C, control; D&B, Downs and Black scale; I, intervention; LBMT, lower-body muscle tensing; LCMT, leg crossing and lower-body muscle tensing; NB, not blinded; OM, outcome measures; P, population; PAF, primary autonomic failure; PC, postural challenge; PCM, physical countermaneuver; SB, single blinded; SCI, spinal cord injury; SHU, sleeping with head up.

Supplemental Table S2 Dietary measures for management of OH

Author (year) Country Score Research Design Sample Size	Methods	Outcome
Water intake		
Mathias et al (1991)[39] UK D&B=12 Pre-post N=6	P: chronic autonomic failure; MSA (n=2), PAF (n=4) I: drinking 300mL of water (meal intervention reported in relevant section) PC: HUT to 45° OM: BP	(1) HUT SBP/DBP at 45min before vs after drinking decreased from 81±17/50±15 to 79±20/48±12mmHg ($P>.05$)
Shannon et al (2002)[40] USA D&B=14 Pre-post N=18	P: chronic autonomic failure; MSA (n=9), PAF (n=9); symptoms of orthostatic intolerance but no OH, otherwise healthy (n=9; results not reported) I: drinking 480mL of water in <5min, 35min before standing PC: active standing from sitting OM: BP, maximal tolerated standing time	(1) Standing SBP/DBP after 1min increased from 83±20/53±11 at baseline to 114±30/66±18mmHg after drinking ($P<.01$)
Meals		
Mathias et al (1991)[39] UK D&B=12 Pre-post N=17	P: chronic autonomic failure: MSA (n=10, 5 males, 5 females), PAF (n=5, 2 males, 3 females), dopamine-beta-hydroxylase deficiency (n=2, 1 male, 1 female) I: balanced liquid meal containing commercially available Complan with glucose in a milk base PC: HUT to 45° OM: BP	(1) Postural drop in SBP/DBP increased when measured 45min after HUT with vs without meal ingestion in MSA: −61±34/−34±25 vs −38±27/−17±22mmHg ($P<.05$) and PAF: −87±32/−47±27 vs −79±35/−34±27mmHg ($P<.05$) (2) In dopamine-beta-hydroxylase deficiency, BP response was variable: 1 patient had a rise/drop in SBP/DBP of 3/−17mmHg with HUT after meal ingestion; in the other patient, drop in SBP/DBP with HUT decreased with vs without meal ingestion (27/25 vs 38/27mmHg)
Puvi-Rajasingham and Mathias (1996)[41] UK PEDro=6 NB randomized crossover trial N=7	P: chronic autonomic failure: MSA (n=4), PAF (n=3) I: 6 small meals in 1d; extra 3 meals given as midmorning, midafternoon, and supper snacks C: 3 large meals in 1d Both conditions: total caloric intake 2.5MJ, no coffee PC: active supine to sit then stand OM: BP, symptoms	(1) Postural drop in SBP decreased when measured after 30min of ingesting small vs large meals with sitting (−22±9 vs −27±14mmHg, $P>.05$) and standing (−28±14 vs −30±10mmHg, $P>.05$) (2) SBP/DBP decreased more with larger meals vs smaller meals in sitting (109±15/66±10 vs 151±10/78±10mmHg, $P<.05$) and standing (89±14/50±9 vs 103±17/66±14mmHg; SBP: $P<.05$, DBP: $P>.05$) (3) 5 patients had more symptoms of postural dizziness after large meals; 2 patients who were unable to stand for 5min after large meals were able to stand for a longer period of time with small meals

Abbreviations: BP, blood pressure; C, control; D&B, Downs and Black scale; I, intervention; NB, not blinded; OM, outcome measures; P, population; PAF, primary autonomic failure; PC, postural challenge.