Non-pharmacological management of orthostatic hypotension after spinal cord injury: A critical review of the literature

D. Jason Gillis (EMMAPA) [1, 2], *Matthijs Wouda (MSc)* [2], *Nils Hjeltnes (MD)*[2]

[1] *Erasmus Mundus Master in Adapted Physical Activity (EMMAPA)*, *Katholieke Universiteit, Leuven, Belgium & The Norwegian School of Sport Science, Oslo, Norway.*

[2] *Department of Research, Sunnaas Rehabilitation Hospital, Oslo, Norway.*

[3] *The Spinal Cord Unit, Sunnaas Rehabilitation Hospital, Oslo, Norway.*

Address of correspondence:

D. Jason Gillis

Study design: Review.

Objectives: Identify and describe the body of literature pertaining to non-pharmacological management of orthostatic hypotension (OH) during the early rehabilitation of persons with a spinal cord injury (SCI).

Setting: Sunnaas Rehabilitation Hospital, Oslo, Norway.

Methods: Search strategy: A comprehensive search of electronic databases and cited references was undertaken. Selection criteria: Case studies, parallel group trials and crossover designs using random or quasi-random assignments were considered. Participants with any level or degree of completeness of SCI and any time elapsed since injury were included. Interventions must have measured at least systolic blood pressure (BP), have induce orthostatic stress in a controlled manner and have attempted to control OH during an orthostatic challenge. Data collection and analysis**:** Studies were selected, assessed and described qualitatively. Meta analysis was deemed inappropriate.

Results: Four distinct non-pharmacological interventions for OH were identified: application of compression and pressure to the abdominal region and/or legs, upper body exercise, functional electrical stimulation (FES) applied to the legs, and biofeedback. Methodological quality varied dramatically between studies. Compression/pressure, upper body exercise and biofeedback therapies have proven inconclusive in their ability to control OH. During orthostatic challenge, FES consistently attenuates the fall in BP; however its clinical application is less well established.

Conclusions: The clinical usefulness of compression/pressure, upper body exercise and biofeedback for treating OH has not been proven. Functional electrical stimulation of the legs holds the most promise.

Key words: Review; spinal cord injury; orthostatic hypotension; rehabilitation

Introduction

Rehabilitation from spinal cord injury (SCI) is often complicated by orthostatic hypotension (OH). More than half of all patients will develop OH within the first month following a SCI. [1] Symptoms may present in as many as 73.6% of all physiotherapy treatments during early rehabilitation from SCI. [2]

The most commonly cited definition of OH was put forth by The American Autonomic Society in 1996. [3] The definition requires a clinician to observe at least a 20/10mmHg reduction in systolic/diastolic blood pressure (BP) within 3 minutes of standing, or after being raised greater than 60° on a tilt table, regardless of symptom presentation.

The most common symptoms of OH observed by the reviewing authors and/or cited in the literature include; fatigue, [3] weakness, [3] light headedness, [3, 4] dizziness, [3, 4] blurred vision, [3] and neck pain. [3, 5] Overcoming the multifactorial orthostatic reaction [4] may allow stabilized SCI patients in early rehabilitation to achieve earlier mobility and progress more quickly through rehabilitation. [6] Accordingly, various management strategies have been developed, including functional electrical stimulation of the lower limbs, [11, 13-15, 19, 20] application of compression/pressure devices to abdominal and leg regions, [16, 18, 21] various types of exercise, [6, 10] and biofeedback. [12, 17]

Despite the growing body of literature, a critical review of each intervention's effectiveness has yet to be reported. The primary objective of this review is to identify and critique the body of literature pertaining to non-pharmacological management strategies of OH during SCI rehabilitation. The reviewing authors suggest that the interventions considered herein are most applicable to those patients in early rehabilitation who no longer experience acute spinal shock.

Methods

Data search

A comprehensive literature search of electronic databases and cited references was undertaken. The electronic search included MEDLINE/PubMed (1966 to April 2007), OVID-EMBASE (1980 to April 2007) and CENTRAL (issue 1, 2007). All references were retrieved and scanned for relevant citations to expand the data set. All titles and abstracts retrieved were then assessed against inclusion criteria. A log was maintained of all articles with reasons provided for any exclusion.

Study selection based on topic-related criteria

This review considered case studies, parallel group trials and crossover designs using random or quasi-random assignments. All studies must have been published in the English language. Study participants of any age or gender, with any level or completeness of SCI were included. No restrictions were placed on time elapsed since injury. Studies must have measured at least systolic blood pressure under controlled and experimental conditions. Interventions were required to be applicable during rehabilitation from SCI, to induce orthostatic stress in a controlled manner, to attempt to control OH during an orthostatic challenge and to be non-pharmacological in nature. Modifications in diet (i.e. salt and water intake) were considered to be beyond the scope of this review.

Description of selected studies

Whenever possible, data describing the effect of an OH intervention on systolic and diastolic blood pressure, patient perception and heart rate (HR) were extracted with the intent of drawing comparisons with a controlled condition. Additionally, the Downs and Black checklist [7] was used to describe the methodological quality of included references. The Downs and

Black checklist is suitable for assessing both randomized and non-randomized studies of health care interventions.

Data analysis

Due to the clinically diverse nature of OH interventions identified in this review, coupled with an under reporting of central tendency measures, statistical comparison (meta-analysis) was deemed inappropriate. Instead, descriptive comparisons are drawn below. The effectiveness of each intervention is outlined in Tables 2-6.

Results

Results of search strategy

The search strategy identified 115 potentially relevant references. Of these, 100 were identified using the electronic search strategy. The remaining 15 were identified using a cited reference search of primary articles. Screening of the titles and abstracts eliminated the vast majority of these, leaving 34 potentially relevant references. Of these 34, 19 did not meet the initial inclusion criteria. Further review of the remaining 15 references identified the possibility that two references [8, 9] may have reported findings that had been derived from previously published experiments. [10, 11] Suspicions of one study [8] were subsequently confirmed by an American Physiological Society investigation. To avoid the possibility of double counting participants and unfairly weighting results from these authors, the two studies in question [8, 9] were excluded from this review. A total of 13 references were included for review. [6, 10-21]

Participants

Detailed participant information is displayed in Table 1. A total of 138 participants with SCI were enrolled, 7 of whom were female. Mean ages ranged from 29 to 41 years. The mean time since injury was reported in 9 studies, of which 4 recruited acute patients 3 to 9 weeks post injury, [6, 15, 16, 20] and 5 studies recruited chronic patients 77 months to 12 years post injury. [10-13, 18, 20] Sixty-four percent (89/138) of participants had cervical lesions, and 36% (49/138) had thoracic lesions.

Interventions

Systematic review of the literature identified 4 distinct non-pharmacological interventions for OH: application of compression and pressure to the abdominal region and/or legs, [16, 18, 21] upper body exercise [6, 10] functional electrical stimulation (FES) applied to the legs [11, 13-15, 19, 20], and biofeedback. [12, 17]

The effectiveness of each compression/pressure intervention is detailed in Table 2. The use of an abdominal corset [16] and leg splints [16] attenuated the fall in BP through 45° of head-up-tilting (HUT) versus control conditions; however, HR increased similarly across all conditions. The application of a gait harness during sitting significantly ($p<0.05$) increased diastolic BP, but caused no change in systolic BP or HR. [18] The addition of an anti-g-suit through 60° of HUT significantly ($p<0.005$) attenuated the fall in BP and the rise in HR versus control conditions. [21]

The effects of FES during an orthostatic challenge are presented in Table 3. When OH was induced using a controlled HUT [13, 15, 20] FES consistently attenuated the fall in BP. However, one study [14] reported an increase in systolic BP during both the controlled and experimental HUT. When the easy stand system was used to induce OH, the fall in BP was also attenuated after FES application versus control conditions.[11] When lower body negative pressure (LBNP) was used to induce OH, BP rose during the control condition and rose again during FES application. [19] The effect of FES application on HR during orthostatic challenge was not clear. Four studies observed no change, or a decrease in HR versus controls, [11, 13, 14, 19] and two observed an increase. [15, 20]

The effects of exercise on OH are presented in Table 4. Maximal arm cranking exercise performed 24h prior to a 70° HUT test significantly (p=0.017) attenuated the fall in systolic BP versus a control condition, while HR rose similarly under both conditions. Alternatively, reciprocal bilateral elbow flexion during HUT over 10 sessions facilitated the fall in BP versus a control condition. [6]

The effects of biofeedback training on systolic BP are presented in Table 5. Two case studies using similar biofeedback protocols were able to greatly attenuate the fall in systolic BP during orthostatic challenge. [12, 17]

A comparison of each intervention is presented in Table 6. Biofeedback interventions caused the greatest attenuation in the fall of BP, followed by compression/pressure, maximal exercise 24hrs prior to HUT, and FES. The results from two studies were not included in this comparison because the percentage change in BP due to an intervention could not be determined. [6, 14]

Discussion

The aim of this review was to objectively identify and critique the body of literature pertaining to non-pharmacological management of OH during rehabilitation from SCI. Key findings are critically discussed below by intervention.

Compression/pressure interventions for OH

Four distinct compression interventions were identified in this review, including leg splints, anti-g-suit, abdominal corset, and gait harness.

Pneumatic leg splints pressurized to 65mmHg significantly ($p<0.01$) attenuate the fall in BP during orthostatic challenge in acute patients with cervical lesions C5-7. [16] Although this finding added credibility to the earlier insights of Ragnarsson [23] who suggested in 1975 that a pneumatic orthosis may well reduce the tendency for OH in patients with SCI, few studies have since provided validation. In fact, findings by Hopman [23] provided an alternate view point. After assessing the effectiveness of anti-embolism stockings on blood redistribution in persons with chronic quadriplegia (n=5) and paraplegia (n=4) during seated exercise, Hopman concluded the stockings had an insignificant effect on BP. [23] It is, however, likely that the disparity can be attributed to the lower pressure used in Hopmans' stockings (10-30mmHg) [23] versus Huang's leg splints (65mmHg). [16] In any case, Hopman's research raises interesting questions that have not been addressed concerning the dose-response relationship between the pressure applied to the lower body and the gain in orthostatic tolerance.

In 1963, Vallbona [21] published findings from a sample of 12 participants (all male) with quadriplegia and 5 participants (2 women) with paraplegia who wore an anti-g suit through 60° of HUT. During the orthostatic challenge, systolic and diastolic BP significantly increased ($p<0.005$) compared to BP observed during 60° HUT with no anti-g suit. [21] The anti-g suits' effectiveness became more apparent when it was deflated at 60° HUT. The authors observed an abrupt fall in both systolic and diastolic BP by 19 and 11mmHg respectively, followed by a compensatory rise in HR. Adding support to these findings, Pitetti [24] assessed the effectiveness of an anti-g suit (pressurized to 50-75mmHg) during seated exercise in 8 persons with chronic quadriplegia and 2 with paraplegia. Although OH was not induced and systolic/diastolic BP not reported, a significantly higher ($p=0.042$) cardiac output was observed when the anti-g suit was worn. The authors concluded that the anti-g suit augmented exercise capacity by preventing the redistribution of blood to the lower extremities. This finding was subsequently supported by Hopman [23] who found a significant increase ($p<0.01$) in systolic/diastolic BP when an anti-g suit was worn during seated exercise, although an orthostatic challenge was not imposed.

Descriptions of abdominal binders began to rise in the years following Vallbona's investigation of the anti-g suit in 1963.[21] In 1968, McCleur described the characteristics of a cloth abdominal binder that was purported to serve as a temporary method of controlling OH in patients with quadriplegia. [25] One year later Jones (1969) improved upon McCleur's design by describing a more durable, inflatable plastic splint. [26] However, as with McCleur's design; Jones' new model was recommended out of clinical experience rather than systematic experimentation. Nearly 13 years later Huang provided evidence that an abdominal corset could significantly ($p<0.01$) attenuate the fall in BP during orthostatic challenge in acute patients with cervical lesions at C5-7. [16] However, Huang described 6 patients who were unable to complete the study due to symptoms of OH, even with the support of abdominal compression. Similarly, in 1986 Goldman evaluated the effect of abdominal binders on breathing in persons with chronic quadriplegia and found that 3 out of 7 participants could not tolerate HUT greater than 50°, despite wearing an abdominal belt. [27] Furthermore, in 1995, Kerks' evaluation of an abdominal binder during exercise in highly trained athletes with paraplegia (T3-6) failed to find a significant effect on cardiovascular variables during sub-maximal and maximal exercise. [28] Disconcertingly, symptoms of OH seem to persist despite abdominal compression, as evidenced by Huang, Goldman, and Kerk. Until further research is conducted to validate the findings of Huang, a definitive answer regarding the abdominal binders' effectiveness in both reducing the fall in BP and perceived symptoms of OH during orthostatic challenge remain elusive.

Application of a gait harness during sitting significantly improved ($p<0.05$) diastolic, but not systolic BP in persons with chronic cervical and thoracic SCI. [18] However participants were not moved from supine to sitting or from sitting to standing, so the effectiveness of the gait harness in controlling OH with position change could not be determined.

Functional electrical stimulation interventions for OH

When OH was induced under control conditions BP (systolic/diastolic) fell on average from 114/72mmHg2 to 89/58mmHg; however, when FES was applied systolic BP only fell to an average of 97/62mmHg (Table 3). [11, 13, 15, 19, 20]

Interpretation of these results requires a discussion of variations between each FES study. Between and within studies, participant groups varied substantially in lesion level (range: C3-T12) and completeness of injury. Only a minority of references classified participants using the ASIA impairment scale. [13, 20] Several references combined participants with high and low levels of spinal cord lesions. [15, 20] Time since injury varied dramatically from 3 weeks to 12 years.

A further source of variation was found in the electrical stimulation protocol. Many references frequently adjusted FES intensity to achieve a visible contraction. It is interesting to note that a dose-response relationship between FES intensity and BP response has been established by Sampson in 2000. [20] Additional variation was found in the number of electrodes used, which ranged between 2 and 4 per participant and the electrode placement; however, it has been suggested the latter may be less relevant an issue. [20]

The equipment used to induce OH adds an additional source of variation. Use of a lower body negative pressure (LBNP) chamber has poor external validity, but more importantly, its ability to induce OH is questionable. When Raymond used LBNP to induce OH, participant systolic, diastolic and mean arterial blood pressures slightly increased from resting values. [19] Alternatively, the use of an easy-stand system by Faghri seems to possess a higher external validity than Raymond’s pressure chamber; however, when participants assume an upright position the easy-stand system features an abdominal pad that may apply pressure to the splanchnic area. This added pressure may confound comparisons of BP response between subject of different heights, but also in comparison with other methods that induce OH. A tilt table was used to induce OH in the majority of references; however, the tilting protocol varied between references in terms of the time spent at each angle of head up tilt, the absolute angle achieved, and the increments between each tilt angle.

Despite variations in experimental protocols, FES has consistently proven to attenuate the fall in BP by approximately 8/4mmHg during an orthostatic challenge under experimental conditions. However its clinical application in early SCI rehabilitation is less evident due to heavy reliance upon chronic [11, 13, 19, 20] versus acutely [15, 20] injured study participants.

Exercise interventions for OH

Two distinct exercise interventions were identified in this review, including low intensity upper body exercise [6] and maximal upper body exercise. [10] When participants (T1-L2) undertook low intensity upper body exercise during HUT they were unable to cope as well as when they were tilted without exercise. The authors intuitively attributed the lower BP in the experimental group to vasodilation and a normal response to continuous exercise. However, both groups significantly increased their orthostatic tolerance from the first to the 10th training session. The increases in orthostatic tolerance appeared to be hindered by upper body exercise, and facilitated by repeated tilting. In fact, the beneficial effects of tilting therapies in persons with SCI have been documented as early as 1969. [29]

The study by Lopes et al. [6] more effectively validates repeated tilting and, not continuous exercise, as an intervention for OH in persons with SCI.

A single bout of maximal upper body exercise eliminated OH without affecting HR response during a HUT test 24h after maximal exercise was undertaken. [10] Despite the combined analysis of persons with both upper and lower thoracic SCI, an appreciable difference was observed in the experimental group. Unfortunately, only a range of individual patient lesion levels were provided (T1-12). These findings may be more applicable in persons with low level paraplegia, where more of the sympathetic outflow that regulates BP remains intact and a larger motor functionality is present. The applicability of maximal arm cranking ergometry as an intervention for OH during early rehabilitation of SCI declines as the lesion level increases, due in large part to a loss in motor functionality with higher lesions.

Despite these findings, certain types of exercise may yet prove useful as an intervention for combating OH. For example, Petrovsky investigated BP and HR responses to isometric hand grip exercise in persons with high and low thoracic SCI and found a linear increase in systolic and diastolic BP among all participants. [30] Future research may focus on the effect of isometric exercise during orthostatic challenge in persons with SCI.

Biofeedback interventions for OH

Three patients from two case studies were taught to raise and lower their BP with the use of visual and auditory feedback.[12, 17] In both case studies the procedure consisted of learning sessions of several weeks where patients were instructed to effect change in their BP without skeletal or respiratory involvement. Blood pressure was continuously monitored and reported to the patient with positive verbal reinforcement. Orthostatic hypotension was induced using a sit to stand movement at the end of every session, [12] or by reducing knee extension from 180° to 90°. [17]

Biofeedback interventions produced an average increase of 39% in systolic BP versus control conditions. The evidence provided by Brucker's case study demonstrated one patients' ability (lesion level at T3) to increase his blood pressure willingly when seated; however, its effect during orthostatic challenge remains questionable. [12] Out of 11 sessions where the patient moved from a sitting to a standing posture, with and without attempts to increase BP, only data from the 9th training session were presented. It might be considered, however, that the passage of time itself, during the training period, might have modified the response to orthostasis However, evidence provided by Ince lends support to the findings of Brucker in that patients with high level SCI (above T6) may be able to produce marked increases in blood pressure with biofeedback training. [17]

Commenting on the definition of OH

The current definition of OH as provided by The American Autonomic Society requires at least a 20/10mmHg reduction in systolic/diastolic BP within 3 minutes of standing, or after being raised greater than 60° on a tilt table, regardless of symptom presentation. [3] However the presence or absence of symptoms can influence patient participation in daily rehabilitation.

For example, in some patients visual signs and perception of OH (i.e. syncope) may occur before BP falls to its predefined level of 20/10mmHg. [2] These patients may be unable to take part in rehabilitation; but, OH would not be diagnosed. Additionally, some patients may experience a large fall in BP before reaching 60° of HUT. These patients would also remain undiagnosed. Knowing this, many clinicians monitor patient perception of OH rather than BP during mobilization treatments. [2]

Through careful review of the literature we have identified specific inadequacies with the current definition of OH as set forth by the American Autonomic Society. [3] The reviewing authors are in general agreement with recent comments made on the definition; [31] however we place greater emphasis on patient perception of syncope due to *any* fall in BP.

Limitations

Some limitations were encountered during this study's development. The scope of this review was limited to the efficacy of each intervention; thus, ignoring assessment of equipment costs, training and the clinical time required in performing a given intervention. Also the Downs and Black scale is in many aspects a subjective tool for assessing methodological quality of both randomized and non-randomized studies. A source of bias may have been introduced when one assessor with minor training in the Downs and Black scale conducted the assessment of methodological quality. Furthermore, the assessor was not an expert in the field of orthostatic hypotension and SCI. Another source of bias was introduced when the search strategy was undertaken by only one assessor. The impact of this bias was however minimized through the use of objective search terms and inclusion criteria. Despite these threats to internal validity, the methodological rigor applied in this critical review is far superior to that of the traditional narrative review; therefore, the findings herein can provide a novel update to the field of SCI rehabilitation.

Conclusions

This literature review identified four classes of interventions for the non-pharmacological management of OH in persons with SCI: compression/pressure applied to the lower limbs and abdominal region, FES applied to the lower limbs, exercise, and biofeedback.

Compression and pressure therapies have proven inconclusive in their ability to control OH in persons with SCI. This is not to diminish the significant findings of individual studies, but rather to draw attention to the lack of randomized control trials and validating investigations that are required in an era of evidence based medicine. The same can be said for the use of exercise and biofeedback interventions for OH.

Despite the variations that exist between FES protocols, two reasonably well designed randomized control trials have shown that FES can consistently attenuate the fall in BP during an orthostatic challenge. To this point however, its clinical application is less well established due to an under-reporting of patient perception during orthostatic challenge and a limited amount of research conducted in acutely injured patients with SCI. The authors of this review feel that it is reasonable to conclude that the use of FES cannot be supported clinically until further research is undertaken using a representative population sample.

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References

1. Sidorov EV, Townson AF, Dvorak MF, Kwon BK, Steves J, Krassioukov A. Orthostatic hypotension in the first month following spinal cord injury . *Spinal Cord* 2007; Apr 10; [Epub ahead of print]

2. Illman I, Stiller K, Williams M. The prevalence of orthostatic hypotension during physiotherapy treatment in patients with an acute spinal cord injury. *Spinal Cord.* 2000; ***38****, 741-47.*

3. Consensus committee of the American Autonomic Society and American Academy of Neurology. Consensus statement on the definition of orthostatic hypotension, pure autonomic failure and multiplesystems atrophy. *Neurolog y* 1996; **46**, 1470.

4. Claydon, V. E., Steeves, J. D., & Krassioukov, A. Orthostatic hypotension following spinal cord injury: Understanding clinical pathophysiology. *Spinal Cord* 2006*;* ***44***(6), 341-351.

5. Cariga P, Ahmed S, Mathias CJ, Gardner BP. The prevalence and association of neck (coat-hanger) pain and orthostatic (postural) hypotension in human spinal cord injury. *Spinal Cord* 2002*;* ***40****, 77-82.*

6. Lopes, P., Figoni, S. F., & Perkash, I. Upper limb exercise effect on tilt tolerance during orthostatic training of patients with spinal cord injury. [Electronic version]. *Arch Phys Med Rehabil,* 1984; ***65***(5), 251-253.

7. Downs SH, Black N. The feasibility of creating a checklist for the assessment of the methodological quality both of randomized and non-randomized studies of health care interventions. *J Epidemiol Community Health*, 1998; ***52****, 377-84*

8. Engelke, K. A., Shea, J. D., Doerr, D. F., & Convertino, V. A. Autonomic functions and orthostatic responses 24 h after acute intense exercise in paraplegic subjects. [Electronic version]. *Am J Physiol,* 1994; *266*(4 Pt 2), R1,189-96.

9. Faghri, P. D., & Yount, J. Electrically induced and voluntary activation of physiologic muscle pump: A comparison between spinal cord-injured and able-bodied individuals. [Electronic version]. *Clin Rehabil*, 2002; ***16***(8), 878-885

10. Engelke, K. A., Shea, J. D., Doerr, D. F., & Convertino, V. A. Enhanced carotid-cardiac baroreflex response and elimination of orthostatic hypotension 24 hours after acute exercise in paraplegics. [Electronic version]. *Paraplegia,* 1992; ***30***(12), 872-879

11. Faghri, P. D., Yount, J. P., Pesce, W. J., Seetharama, S., & Votto, J. J. Circulatory hypokinesis and functional electric stimulation during standing in persons with spinal cord injury. [Electronic version]. *Arch Phys Med Rehabil,* 2001; ***82***(11), 1587-1595.

12. Brucker, B. S., & Ince, L. P. Biofeedback as an experimental treatment for postural hypotension in a patient with a spinal cord lesion. [Electronic version]. *Arch Phys Med Rehabil,* 1977; ***58***(2), 49-53.

13. Chao, C. Y., & Cheing, G. L. The effects of lower-extremity functional electric stimulation on the orthostatic responses of people with tetraplegia. [Electronic version]. *Arch Phys Med Rehabil,* 2005; ***86***(7), 1427-1433.

14. Davis GM, Climstein M, Kelleher P, Lukban F, Sutton JR. Cardiac performance during tilting and ES induced leg muscle contractions in paraplegics. *Med Sci Sports Exerc,* 1993; **25:**S104

15. Elokda, A. S., Nielsen, D. H., & Shields, R. K. Effect of functional neuromuscular stimulation on postural related orthostatic stress in individuals with acute spinal cord injury. [Electronic version]. *J Rehabil Res Dev,* 2000; **37**(5), 535-542

16. Huang CT, Kuhlemeri KV, Ratanaubol U. Cardiopulmonary response in spinal cord injury patients: effect of pneumatic compression devices. *Arch Phys Med Rehabil*, 1983; **64**: 101-06.

17. Ince, LP. Biofeedback as a treatment for postural hypotension. *Psychosom Med*, 1985; **47** *(2), 182-88.*

18. Krassioukov, A. V., & Harkema, S. J. Effect of harness application and postural changes on cardiovascular parameters of individuals with spinal cord injury. [Electronic version]. *Spinal cord*, 2006; **44**(12), 780-786.

19. Raymond J, Davis GM, Bryant G, Clarke J Cardiovascular responses to an orthostatic challenge and electrical-stimulation-induced leg muscle contractions in individuals with paraplegia. *Eur J Appl Physiol*, 1999; Aug; **80**(3):205-12.

20. Sampson, E. E., Burnham, R. S., & Andrews, B. J. Functional electrical stimulation effect on orthostatic hypotension after spinal cord injury. [Electronic version] *Arch Phys Med Rehabil*, 2000; **81**(2), 139-143.

21. Vallbona C, Spencer WA, Cardus D, Dale JW. Control of orthostatic hypotension of quadriplegic patients with pressure suits. *Arch Phys Med Rehabil*, 1963; **44**: 7-18

22. Ragnarsson KT, Sell HG, McGarrity M, Ofir R. Pneumatic orthosis for paraplegic patients: functional evaluation and prescription considerations. *Arch Phys Med Rehabil*, 1975; **56**, 479-83.

23. Hopman MT, Monroe M, Dueck C, Phillips WT, Skinner JS. Blood redistribution and circulatory responses to submaximal arm exercise in persons with spinal cord injury. *Scan J Rehabil Med*, 1998; Sep; **30**(3):167-74.

24. Pitetti KH, Barrett PJ, Campbell KD, Malzaen DE. The effect of lower body positive pressure on the exercise capacity of individuals with spinal cord injury. *Med Sci Sports Exerc*. 1994; **26**: 463-68.

25. McCluer S. A temporary method of controlling orthostatic hypotension in quadriplegia. *Arch Phys Med Rehabil*, 1968 Oct; **49**(10):598-9.

26. Jones, R. F., & Burniston, G. G. A strapless pneumatic belt for the control of orthostatic hypotension in quadriplegia. [Electronic version]. *Med J Aust*, 1969; **1**(22), 1136-1137.

27. Goldman JM, Rose LS, Wiliams SJ, Silver JR, Denison DM. Effect of abdominal binders on breathing in tetraplegic patients. *Thorax*. 1988; **41**: 940-45

28. Kerk JK, Clifford PS, Snyder AC, Prieto TE, O'Hagan KP, Schot PK, Myklebust JB, Myklebust Effect of an abdominal binder during wheelchair exercise. *Med Sci Sports Exerc*, 1995; **27**:913-919.

29. Johnson RH, Crampton A, Smith, Spalding JMK. Blood pressure response to standing and Valsalva's manoeuvre: independence of two mechanisms in neurological diseases including cervical cord leasions" *Clin. Sci.* (1969) **36**, 77-86

30. Petrofsky, J. S. Blood pressure and HR response to isometric exercise: The effect of spinal cord injury in humans. [Electronic version]. *Eur J Appl Physiol*, 2001; **85**(6), 521-526.

31. Krassioukov AV, Karlsson AK, Wect, JM, Wuermser LA, Matthias CJ, Marino RJ. Assessment of autonomic dysfunction following spinal cord injury: Rational for additions to International Standards for Neurological Assessment. *J Rehabil Res Dev,* 2007; **44** (1), 103-12.

Table 1: Participant information by OH intervention.

	Reference	N (138)	Mean (±sd) Age	SCI classification	Mean (sd) time since injury
Compression/ pressure	Huang 1983 [16]	27	32 (13)	27 cervical	47 (22) days
	Krassioukov 2006 [18]	12	31.8 (11.3)	6 cervical, 6 thoracic	5.8 (8.3) years
	Vallbona 1963 [21]	17	16-43 (range)	12 cervical , 5 thoracic	3-48 months
Functional electrical stimulation	Chao 2005 [13]	16	37.3 (13.78)	16 cervical	118.87 (104.2) months
	Davis 1993 [14]	8	32.4 (2.7)	8 thoracic	-
	Eldoka 2000 [15]	5	29 (4.3)	2 thoracic, 3 cervical	3 (0.7) weeks
	Faghri 2001 [11]	14	35 (9)	7 thoracic, 7 cervical	77.3 (64.4) months
	Raymond 1999 [19]	8	41.3 (6.5)	8 thoracic	3-39 years
	Sampson 2000 [20]	6	30.3 (11.8)	5 cervical, 1 thoracic	Acute: 8.6 (1.1) weeks Chronic: 12 (2) years
Exercise	Engelke 1992 [10]	10	36 (4) *SE	10 thoracic	118 (21) months
	Lopes 1984 [6]	12	26-54	11 cervical, 1 thoracic	7.7 weeks
Bio-feedback	Brucker 1977 [12]	1	31	1 thoracic	3 years
	Ince 1985 [17]	2	23-32 (range)	2 cervical	15-18 months

Abbreviations: * Standard error (SE); Standard deviation (SD);

Table 2: compression and pressure interventions versus no treatment

	Outcome measure	Huang 1983 [16]		Krassioukov 2006 [18]	Vallbona 1963 [21]
Control	OH	0°- 45° HUT		Harness application during passive sitting	60° HUT
	Blood pressure in mmHg (SBP/DBP)	Fell from 113/71 to 77/52		cervical - 86/54 thoracic – 106/65	81/49
	Patient perception	-		-	-
	Heart rate (bpm)	Rose from 70 to 94		-	92
Intervention	OH Intervention	Corset 0°-45°	Leg splints 0°-45°	Sitting with harness	Anti-g-suit
	Blood pressure in mmHg (SBP/DBP)	Fell from 114/71 to 101/69	Fell from 113/72 to 94/62	cervical – 99/*65 thoracic – 111/*77	105/71
	Patient perception	-	-	-	-
	Heart rate in bpm	Rose from 74 to 90	Rose from 72 to 86	No significant change in HR	82

Abbreviations: Head up tilting (HUT); millimeters of mercury (mmHg); Orthostatic hypotension (OH); Blood pressure (BP); systolic blood pressure (SBP); diastolic blood pressure (DBP); beats per minute (bpm); heart rate (HR). * Significant difference ($P<0.05$).

Table 3: Functional electrical stimulation (FES) of the legs interventions versus no treatment

	Outcome measure	Chao 2005 [13]	Davis 1993 [14]	Elokda 2000 [15]	Faghri 2001 [11]	Raymond 1999[19]	Sampson 2000 [20]
Control	OH	0-90° HUT	0- 70° HUT	0-60° HUT	Sit to stand	Lower body negative pressure	0-90° HUT
	Blood pressure in mmHg (SBP/DBP)	Fell from 105/66 to 85/57	Rose 9-15	Fell from 118/70 to 90/ 60	Fell from 108/75 to 99/68	Rose from 123/72 to 129/ 76	Fell from 115/65 to 92/56
	Patient perception	75% report symptoms at 90°	-	-	-	-	-
	HR mean (bpm)	Rose from 65 to 86	Rose from 73 to 96	Rose from 74 to 105	Rose 20% ✝	Rose 5-6bpm	Rose from 70 to 96
Intervention	OH Intervention	FES + 0-90°HUT	FES+ HUT	FES + HUT	FES + sit to stand	LBNP + FES	HUT + FES
	Blood pressure in mmHg (SBP/DBP)	Fell to 93/59	SBP rose >9-15	Fell to 98/61	109/78	132/78	100/65
	Patient perception	46% report symptoms at 90°	-	-	-	-	-
	HR mean (bpm)	82	Fell 4-12	112	Rose 10% ✝	No change	115

Abbreviations: Head up tilting (HUT); millimeters of mercury (mmHg); Orthostatic hypotension (OH); Blood pressure (BP); systolic blood pressure (SBP); diastolic blood pressure (DBP); beats per minute (bpm); heart rate (HR). ✝ Absolute values were not published by the original authors.

Table 4: Exercise interventions versus no treatment

	Outcome measure	Engelke 1992 [10]	Lopes 1984 [6]
Control	OH	70° HUT	10 sessions of 70° HUT
	Blood pressure in mmHg (SBP/DBP)	SBP fell from 118 to 106, or 10% (p=0.025). DBP not altered.	Only the mean BP at termination angle for 10 sessions of 70° HUT could be determined (122/70)
	Patient perception	-	-
	HR mean (bpm)	Rose by 29bpm (p<0.001)	Mean HR at termination angle for 10 sessions of 70° HUT was 63
Intervention	OH Intervention	maximal exercise 24h before 70° HUT	Upper arm exercise + 70° HUT (10 sessions)
	Blood pressure in mmHg (SBP/DBP)	SBP fell from 116 to 113, or 2.5%. DBP not altered	Only the mean BP at termination angle for 10 session of 70° HUT could be determined (117/76)
	Patient perception	-	-
	HR mean (bpm)	Rose by 30bpm (p<0.001)	Mean HR at termination angle for 10 sessions of 70° HUT was 67

Abbreviations: Head up tilting (HUT); millimeters of mercury (mmHg); Orthostatic hypotension (OH); Blood pressure (BP); systolic blood pressure (SBP); diastolic blood pressure (DBP); beats per minute (bpm); heart rate (HR).

Table 5: Biofeedback interventions versus no treatment

	Outcome measure	Brucker 1977 [12]	Ince 1985 [17]
Control	OH	Sit to stand	Lowering legs
	Blood pressure in mmHg (SBP/DBP)	SBP fell to 50mmHg after two minutes of standing	C2/3 - fell from 110/70 to 75/40 C5 – fell from 101/62 to 85/60
	Patient perception	-	-
	HR mean (bpm)	-	.
Intervention	OH Intervention	Biofeedback	Biofeedback training
	Blood pressure in mmHg (SBP/DBP)	SBP fell to 88mmHg after 5 minutes of standing	C2/3 – was able to raise and maintain SBP 120 C5 – raised and maintained SBP between 110-120
	Patient perception	-	-
	HR mean (bpm)		

Abbreviations: Head up tilting (HUT); millimeters of mercury (mmHg); Orthostatic hypotension (OH); Blood pressure (BP); systolic blood pressure (SBP); diastolic blood pressure (DBP); beats per minute (bpm); heart rate (HR).

Table 6: Comparison of % BP changes between all interventions

Intervention (reference)	**Percentage and actual (mmHg) attenuation of systolic BP fall with orthostasis**	**Percentage and actual (mmHg) attenuation of diastolic BP fall with orthostasis**
Leg splints (Huang 1983) [16]	12%** (16mmHg) at 20° 23%** (17mmHg) at 45°	11%** (5mmHg) at 20° 24%**(10mmHg) at 45°
Abdominal corset (Huang1983) [16]	11%** (16mmHg) 20° 18%* (23mmHg) 45°	0 at 20° 16%* (17mmHg) at 45°
Gait harness (Krassioukov 2006) [18]	0% (thoracic) 15% (cervical)	20%* (thoracic) 20%* (cervical)
Anti-g-suit (Vallbona 1963) [21]	Rose 22%** (24mmHg)	30%** (30mmHg)
FES (Chao 2005) [13]	8.6% (8mmHg)	3% (1mmHg)
FES (Davis 1993) [14]	Rose >9-15mmHg	Rose >9-15mmHg
FES (Eldoka 2000) [15]	7%* (8mmHg)	1% (2mmHg)
FES (Faghri 2001) [11]	9% (11mmHg)	0
FES (Raymond 1999) [19]	2% (3mmHg)	2% (2mmHg)
FES (Sampson 2000) [20]	8% (8mmHg)	13% (11mmHg)
Maximal exercise (Engelke 1992) [10]	7.5% (9mmHg)	-
Upper body exercise (Lopes 1984) [6]	Unable to determine	Unable to determine
Biofeedback (Brucker 1977) [12]	43% (38mmHg)	-
Biofeedback (Ince 1985) [17]	Approximately 34% (range = 30-45mmHg)	-

Abbreviations: **significant at p<0.01; *significant at p<0.05; Head up tilting (HUT); millimeters of mercury (mmHg); Orthostatic hypotension (OH), Blood pressure (BP); systolic blood pressure (SBP); diastolic blood pressure (DBP); beats per minute (bpm); heart rate (HR)

APPENDIX A – DETAILED SEARCH STRATEGY

(Please note that the appendix are provided so that reviewers can better assess the methods used by the authors and are not intended for publication)

Search Methods for identification of studies

Studies were identified using an electronic database search and a cited reference search of all the reference lists of collected studies.

Electronic search:

An electronic search was performed in MEDLINE/PubMed, OVID-EMBASE, and the Cochrane central register of controlled trials (CENTRAL).

MEDLINE/PubMed

MEDLINE/PubMed was searched from 1966 to March 2007 using a mixture of free text terms and MeSH headings restricted to humans, but no language restrictions. MEDLINE/PubMed search strategy consisted of two phases:

Phase I: The initial search strategy

The following terms were entered into MEDLINE/PubMed search field :"(parapleg* OR tetrapleg* OR quadraplegia OR spinal cord injury) AND (orthostatic hypotension OR syncope) AND (therapeutics OR rehabilitation) NOT (drug OR pharmacological) NOT (review)"

Phase II: Expanding the dataset

All relevant studies that met inclusion criteria were saved to the MEDLINE clipboard. The option to search "related articles" was then used to expand the initial dataset.

OVID-EMBASE

OVID-EMBASE was searched from 1980 to March 2007 using a mixture of free text terms and MeSH headings restricted to humans, but with no language restrictions. The search strategy consists of two phases:

Phase I: The initial search strategy

The following terms were sequentially entered into the OVID-EMBASE search field:

1. spinal cord injury OR parapleg$ OR quadrapleg$ OR tetrapleg$
2. explode "orthostatic hypotension" / all subheadings
3. explode "blood pressure" / all subheadings

4. explode “hypotension” / all subheadings
5. explode “syncope” / all subheadings
6. explode “therapy” / all subheadings
7. #1 AND #2
8. # 3 OR #4 OR #5
9. #6 AND #7
10. #8 AND #9
11. #10 limit to human

Phase II: Expanding the dataset

All relevant studies that met inclusion criteria were displayed together in EMBASE and the option to search “similar articles” was used to expand the initial dataset.

<u>CENTRAL</u>

Cochrane CENTRAL (issue 1, 2007) was searched using a mixture of free text terms and MeSH headings restricted to humans, but with no language restrictions. The search strategy consists of two phases:

Phase I: The Initial search strategy

The following terms were sequentially entered into the CENTRAL search field:

1. quadriplegia OR paraplegia
2. spinal AND cord AND injury
3. #1 OR #2
4. orthostatic OR hypotension
5. blood AND pressure
6. #4 OR #5
7. rehabilitation OR therapeutics
8. physical AND medicine
9. #7 OR #8
10. #3 AND #6 AND #9

Phase II: Expanding the dataset

All relevant studies that meet inclusion criteria were displayed together, and when available, the option to search "similar articles" through electronic hyperlinks imbedded within The Cochrane Library were used to expand the initial dataset.

Cited reference search

A cited reference search of each study was undertaken to expand the dataset. All relevant references contained within the body of an included study were assessed according to the inclusion criteria.

APPENDIX B – APPLICATION OF INCLUISON CRITERIA AND REASONS FOR EXCLUSION

Application of inclusion criteria, and reasons for exclusions

Study reference	INCLUSION CRITERIA				EXCLUSIONS
	Type of study	Types of participants	Types of interventions	Outcome measures	Cite any reasons for exclusion
Brucker 1977	Yes	Yes	Yes	Yes	
Chao 2005	Yes	Yes	Yes	Yes	
Cole 1967	Yes	Yes	No	Yes	The response to positional change was monitored, however, there was no intervention provided to reduce the OH
Davis 1993	Yes	Yes	Yes	Yes	
Davis 1988					This article (proceedings) could not be obtained, despite contacting the author and contacting RESNA.
Elokda 2000	Yes	Yes	Yes	Yes	
Engelke 1992	Yes	Yes	Yes	Yes	
Engelke 1994	Yes	Yes	Yes	Yes	Some results published in this article seem to be collected from the same subjects and experiment as Engelke 1992
Faghri 2002	Yes	Yes	Yes	Yes	Some results published in this article seem to be collected from the same subjects and experiment as Faghri 2001
Faghri 2001	Yes	Yes	Yes	Yes	
Figoni 1991	Yes	Yes	No	Yes	Selection of subjects was not randomized. OH was not induced in any way; the intervention (FES knee extension) was not suited to combat OH.

Continued…

Goldman 1988	Yes	Yes	No	No	Despite an orthostatic stress being induced; BP was not measured, so the effect of the abdominal binder on OH cannot be determined.
Hopman 1992	Yes	Yes	No	Yes	Although the anti-g suite may act as an intervention to combat OH, the study design did not involve inducing an orthostatic stress, and therefore the anti-g suits' effectiveness in reducing OH is unknown.
Hopman 1993	Yes	Yes	No	Yes	Although the anti-g suite may act as an intervention to combat OH, the study design did not involve inducing an orthostatic stress, and therefore the anti-g suits' effectiveness in reducing OH is unknown.
Hopman (1998). Scand J Rehabil Med	Yes	Yes	No	No	This paper uses the same subjects and nearly the same protocol as the below (Hopman '98- limits to max ex). The only difference is that subjects aren't taken to maximal effort. The study must be excluded because it does not attempt to induce any orthostatic stress. However, it is quite useful because it investigates the effect of anti-g suit, pressure/compression and FES on blood pressure response.
Huang 1983	Yes	Yes	Yes	Yes	
Hopman (1998). Int J Sports Med	Yes	Yes	No	Yes	This study must be excluded because it does not attempt to induce any orthostatic stress. However, it is quite useful because it investigates the effect of anti g suit, pressure/compression and FES on blood pressure response.
Hooker 1993	Yes	Yes	No	Yes	This study design does not induce OH. Any effect of the intervention (arm cranking exercise) on OH cannot be determined.
Ince 1985	Yes	Yes	Yes	Yes	
Johnson 1969	Yes	Yes	No	Yes	This is a case study of 2 patients exposed to tilting, and their subsequent response. There was no OH intervention.
Jones 1969	No	No	No	No	This paper describes the design of an abdominal compression device that could be used to combat OH, however, no intervention was applied, no OH was induced, and no measures of BP were taken.

Continued…

Kerk 1995	Yes	Yes	No	No	Although the study used an abdominal binder, the study design does not induce OH. Any effect of the intervention (abdominal binder) on OH cannot be determined. No measures of BP were taken.
Krassioukov 2006	Yes	Yes	Yes	Yes	
Lopes 1984	Yes	Yes	Yes	Yes	
McCluer 1968	No	No	No	No	This paper describes the design of an abdominal compression device that could be used to combat OH, however, no intervention was applied, no OH was induced, and no measures of BP were taken.
Maloney 1979	Yes	Yes	Yes	No	The effect of the corset on blood pressure while changing body position was not assessed.
McLean 1995	Yes	Yes	No	No	This article must be excluded because it does not induce orthostatic stress and does not directly measure BP.
Pitetti 1994	Yes	Yes	No	No	Despite the lower body positive pressure increasing blood redistribution, its effect on OH cannot be determined because no orthostatic stress induced.
Petrofsky 2001	Yes	Yes	No	Yes	Although the intervention (static contractions of the upper/lower body) may prove useful in combating OH, this study cannot prove this because OH was not induced.
Raymond 1999	Yes	Yes	Yes	Yes	
Raymond 2001	Yes	Yes	Yes	No	Blood pressure was not measured
Raymond 2002	Yes	Yes	No	Yes	Orthostatic stress was not induced.
Sampson 2000	Yes	Yes	Yes	Yes	
Vallbona 1963	Yes	Yes	Yes	Yes	

APPENDIX C: REFERENCES OF EXCLUDED STUDIES

Cole, T. M., Kottke, F. J., Olson, M., Stradal, L., & Niederloh, J. (1967). Alterations of cardiovascular control in high spinal myelomalacia. [Electronic version]. *Archives of Physical Medicine and Rehabilitation, 48*(7), 359-368.

Davis GM, Figoni SF, Glaser RM, Seiber OL, Servedio FJ, Suryaprasad AG. Cardiovascular effects of ES induced isometric leg exercise during tilting in paraplegics. *Medicine and science in sports and exercise*. 1988; 20 2:23

Engelke, K. A., Shea, J. D., Doerr, D. F., & Convertino, V. A. (1994). Autonomic functions and orthostatic responses 24 h after acute intense exercise in paraplegic subjects. [Electronic version]. *The American Journal of Physiology, 266*(4 Pt 2), R1189-96.

Faghri, P. D., & Yount, J. (2002). Electrically induced and voluntary activation of physiologic muscle pump: A comparison between spinal cord-injured and able-bodied individuals. [Electronic version]. *Clinical rehabilitation, 16*(8), 878-885

Figoni, S. F., Glaser, R. M., Rodgers, M. M., Hooker, S. P., Ezenwa, B. N., & Collins, S. R., et al. (1991). Acute hemodynamic responses of spinal cord injured individuals to functional neuromuscular stimulation-induced knee extension exercise. [Electronic version]. *Journal of rehabilitation research and development, 28*(4), 9-18.

Goldman JM, Rose LS, Wiliams SJ, Silver JR, Denison DM. (1988). Effect of abdominal binders on breathing in tetraplegic patients. *Thorax.* 41: 940-45

Hopman MTE, Oeseburg B, Binkhorst RA. (1992). The effect of an anti –G suit on cardiovascular response to exercise in persons with paraplegia. *Medicine and science in sports and exercise.* 24: 984-90

Hopman MTE, Kamerbeek ICE, Pistorius M, Binkhorst RA. (1993). The effect of an anti G suit on the maximal performance of individuals with paraplegia. *International journal of sports medicine*. 14: 357-61

Hopman MT, Monroe M, Dueck C, Phillips WT, Skinner JS. (1998). A. Blood redistribution and circulatory responses to submaximal arm exercise in persons with spinal cord injury. *Scandinavian journal of rehabilitation medicine*. Sep;30(3):167-74.

Hopman MT, Dueck C, Monroe M, Philips WT, Skinner JS (1998). B. Limits to maximal performance in individuals with spinal cord injury. *International journal of sports medicine.* Feb;19(2):98-103.

Hooker SP, Greenwood JD, Boyd LA, Hodges MR, McCune LD, McKenna GE. (1993). Influence of posture on arm exercise tolerance and physiologic response in persons with spinal cord injured paraplegia. *European journal of applied physiology.*. 67: 563-6.

Johnson, R. H., Smith, A. C., & Spalding, J. M. (1969). Blood pressure response to standing and to valsalva's manoeuvre: Independence of the two mechanisms in neurological diseases including cervical cord lesions. [Electronic version]. *Clinical science, 36*(1), 77-86.

Jones, R. F., & Burniston, G. G. (1969). A strapless pneumatic belt for the control of orthostatic hypotension in quadriplegia. [Electronic version]. *The Medical journal of Australia, 1*(22), 1136-1137.

Kerk JK, Clifford PS, Snyder AC, Prieto TE, O'Hagan KP, Schot PK, Myklebust JB, Myklebust (1995). Effect of an abdominal binder during wheelchair exercise. *Medicine and science in sports and exercise.* 27:913-919.

McCluer S. A temporary method of controlling orthostatic hypotension in quadriplegia. *Archives of physical medicine and rehabilitation.* 1968 Oct;49(10):598-9. No abstract available.

Maloney F. (1979). Pulmonary function in quadriplegia: effects of a corset. *Archives of physical medicine and rehabilitation.* 60: 261-65

McLean KP, Jones PP, Skinner JS. (1995). Exercise prescription for sitting and supine exercise in individuals with tetraplegia. *Medicine and science in sport and exercise.* 27: 15-21.

Pitetti KH, Barrett PJ, Campbell KD, Malzaen DE. (1994). The effect of lower body positive pressure on the exercise capacity of individuals with spinal cord injury. *Medicine and science in sport and exercise.* 26: 463-68.

Petrofsky, J. S. (2001). Blood pressure and heart rate response to isometric exercise: The effect of spinal cord injury in humans. [Electronic version]. *European journal of applied physiology, 85*(6), 521-526.

Raymond, J., Davis, G. M., Clarke, J., & Bryant, G. (2001). Cardiovascular responses during arm exercise and orthostatic challenge in individuals with paraplegia. [Electronic version]. *European journal of applied physiology, 85*(1-2), 89-95.

Raymond J, Davis GM, Van der Plas M. (2002) Cardiovascular response during submaximal electrical stimulation-induced leg cycling in individuals with paraplegia. *Clinical physiology and functional imaging.* 22:92-98