A systematic review of the management of orthostatic hypotension after spinal cord injury


CRD summary
This review concluded that among pharmacologic interventions, there was supportive evidence for use of midodrine in management of orthostatic hypotension after spinal cord injury. Functional electrical stimulation was one of the only nonpharmacologic interventions with some evidence to support its utility. Small sample sizes and poor-quality included studies mean these conclusions may be not reliable.

Authors' objectives
To assess the effectiveness of pharmacologic and nonpharmacologic interventions for the management of orthostatic hypotension after spinal cord injury.

Searching
MEDLINE, CINAHL, EMBASE and PsycINFO. Search terms were reported. Reference lists of retrieved publications were screened for additional studies.

Study selection
Randomised controlled trials (RCTs), prospective cohort studies, case-control studies, pre-post studies and case reports that evaluated pharmacologic and nonpharmacologic interventions for the management of orthostatic hypotension in patients with spinal cord injury were eligible for inclusion. Studies were excluded if they did not report relevant outcomes that evaluated orthostatic hypotension. The outcomes reported in the review included change in blood pressure and symptoms of orthostatic hypotension.

Included studies evaluated the following pharmacologic interventions: midodrine, fludrocortisone, dihydroergotamine, ephedrine and L-threeo-3,4-dihydroxyphenylserine (L-DOPS). The nonpharmacologic interventions used in included studies were fluid and salt intake, pressure intervention, functional electrical stimulation and exercise. Where reported, the age of included patients ranged from 16 to 72 years.

The authors did not state how many reviewers assessed studies for inclusion.

Assessment of study quality
The quality of RCTs was assessed using the 11-item PEDro scale (maximum score 10). The quality of other types of studies was assessed using a modified Downs and Black scale (maximum score of 28). In both instances a higher score indicated higher methodological quality.

Two reviewers independently performed the validity assessment.

Data extraction
The authors did not state how data were extracted.

Methods of synthesis
Studies were combined in a narrative synthesis supported by accompanying data tables.

Results of the review
Twenty-six studies were included in the review (n=496): eight evaluated pharmacologic interventions and twenty-one evaluated non-pharmacologic interventions. Sample size ranged from one to 231. The studies were generally of poor quality. The quality score of RCTs ranged from 2 to 5; the quality core of other studies ranged from 7 to 22.

Pharmacologic management:
One RCT reported that midodrine improved exercise performance in some patients with spinal cord injury. One case series showed no effect of fludrocortisone on orthostatic hypotension in patients with spinal cord injury. One case report showed that daily ergotamine in combination with fludrocortisone prevented symptomatic orthostatic hypotension in a patient with spinal cord injury.

One observational study reported that ephedrine reduced the likelihood of patients who experienced hypotension. One case report showed that L-DOPS in combination with salt supplementation led to a marked reduction of syncopal attacks, a decrease of hypotension symptoms and an increase of daily activity.

**Nonpharmacologic management:**

Two observational studies reported that salt and fluid regulation in combination with other pharmacologic interventions reduced symptoms of orthostatic hypotension. One RCT showed that pressure from elastic stockings and abdominal binders increased cardiovascular physiologic responses during sub-maximal, but not maximal, upper-extremity exercises; other studies showed contradictory findings.

Three RCTs reported that functional electrical stimulation as a treatment adjunct minimised cardiovascular changes during postural orthostatic stress in patients with spinal cord injury. One RCT showed that simultaneous upper-extremity exercise increased orthostatic tolerance during a progressive tilt exercise in patient with paraplegia; one RCT showed no effect of this intervention in patients with tetraplegia. One pre-post study reported that body weight support treadmill training did not improve orthostatic tolerance during a tilt test.

**Authors’ conclusions**

Of the pharmacologic interventions, there was supportive evidence from a low-quality RCT for use of midodrine in the management of orthostatic hypotension after spinal cord injury. Functional electrical stimulation was the only nonpharmacologic interventions with some evidence to support its utility.

**CRD commentary**

The review addressed a clear question. The inclusion criteria were broad for study designs and not specified for outcomes. Relevant databases were searched. Efforts were made to find published studies, but not unpublished studies, thereby potential for publication bias was introduced. The authors did not state whether language restriction were applied to the search, which made it difficult to assess the risk of language bias. Steps were taken to minimise biases and errors in the review process by having more than one reviewer undertake validity assessment; it was unclear whether study selection and data extraction were performed in duplicate. Relevant criteria were used to examine study quality. A narrative synthesis was appropriate given the diversity of included studies. In light of the small sample sizes and poor quality of included studies, the authors' conclusions may be not reliable.

**Implications of the review for practice and research**

**Practice:** The authors stated that if nonpharmacologic interventions failed, midodrine may be considered for the management of orthostatic hypotension after spinal cord injury.

**Research:** The authors stated that despite a wide range of physical and pharmacologic measures recommended for the management of orthostatic hypotension in the general population, very few had been evaluated for use in patients with spinal cord injury. Future studies were required to quantify the effectiveness of treatments for orthostatic hypotension in patients with spinal cord injury. More research was also required to determine the feasibility of functional electrical stimulation to manage orthostatic hypotension.

**Funding**

Rick Hansen Man in Motion Foundation and Ontario Neurotrauma Fund.

**Bibliographic details**

This is a critical abstract of a systematic review that meets the criteria for inclusion on DARE. Each critical abstract contains a brief summary of the review methods, results and conclusions followed by a detailed critical assessment on the reliability of the review and the conclusions drawn.