Efficacy of treatments for orthostatic hypotension: a systematic review
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CRD summary
This review of 36 trials concluded that the 21 commonly recommended interventions for orthostatic hypotension had a limited evidence base supporting their use, so further large, high quality, randomised controlled trials were needed to underpin clinical practice for this condition. These conclusions reflect the evidence and are likely to be reliable.

Authors' objectives
To assess the effectiveness of all non-pharmacological and pharmacological interventions for orthostatic hypotension.

Searching
MEDLINE, EMBASE, CINAHL, The Cochrane Library, PsycINFO, the British Nursing Index, and Current Controlled Trials website were searched (inception to February 2012) with no language restriction using specified search terms. Additional searches were undertaken using Google. The reference lists of eligible articles were handsearched, in addition to those in narrative reviews.

Study selection
Included studies had to be randomised controlled trials (RCTs) that compared an intervention with placebo and measured postural drop as an outcome (defined as a sustained reduction of systolic blood pressure of at least 20mmHg or diastolic blood pressure of 10mmHg within three min of standing or head-up tilt to at least 60° on a tilt table). The primary outcome measures of interest were changes in orthostatic symptoms, change in office blood pressure (lying and standing/tilted systolic and diastolic blood pressure, and postural drop).

Trials that involved astronauts, healthy volunteers or measured post-prandial hypotension or neurally mediated hypotension (vasovagal syncope) as opposed to orthostatic hypotension were excluded.

The interventions were fluid, hydration, water; salt, sodium chloride oxilofrine, potassium chloride; bed tilt, elevating bed; counter manoeuvres/manoeuvres; compression stocking/hose/bandage/garment, abdominal compression; antihypertensives; fludrocortisone; erythropoietin; sympathomimetics (midodrine, dihydroxyphenylserine, yohimbine, ephedrine, pseudoephedrine, dihydroergotamine); acetyl cholinesterase inhibition, pyridostigmine; selective serotonin reuptake inhibitors; serotonin-norepinephrine reuptake inhibitors; vasopressin analogues; methylphenidate; dextroamphetamine; caffeine; dopamine receptor antagonist (metoclopramide, domperidone); and indomethacin.

In a third of included trials, patients had a mean or median age of older than 65 years; in a few trials, patients had a mean or median age older than 75 years. Eleven different populations were identified throughout the included studies, with a few studies inadequately characterising the underlying cause of orthostatic hypotension. Over a third of the trials included a varied mix of patients, rather than concentrating on one specific disease process.

The number of reviewers assessing study eligibility was not stated.

Assessment of study quality
Trials were assessed for quality, with consideration of baseline comparability of each arm, method of randomisation and allocation concealment, effectiveness of patient and staff blinding, and use of intention to treat.

The number of reviewers assessing study quality was unclear.

Data extraction
Details of the populations, interventions, trial quality and outcomes were tabulated.

Over half of the trials were extracted in by two reviewers, with the rest assessed by a single reviewer.

Methods of synthesis
Meta-analysis was not undertaken because of heterogeneity in patients, study designs, study interventions, and reported outcome measures. Results were grouped by intervention in a narrative synthesis.

Results of the review
Thirty-six trials (1,268 participants) were included in the review examining 21 interventions. Trial quality was unclear in most cases as method of randomisation was described in only 8%, whilst only 33% of trials described patient blinding and 14% of trials described outcome assessor blinding.

Sleeping head-up and using clonidine produced minor improvements in postural drop in blood pressure (although the postural drop with clonidine remained very large). The following interventions consistently produced an improvement in postural drop blood pressure of higher than 10mmHg: compression bandages; indomethacin; oxilofrine; potassium chloride; and yohimbine.

Both midodrine and pyridostigmine displayed an inconsistent trend towards worsening of the postural drop in blood pressure. The following therapies consistently resulted in worsening of the postural drop in blood pressure: amezinium; glypressin; octreotide; and xamoterol. Those interventions that worsened the postural drop raised the lying blood pressure considerably more than the standing blood pressure, with the overall effect of widening the gap between the two.

Only compression bandages and potassium chloride resulted in significant improvements in orthostatic hypotension symptoms.

Authors’ conclusions
Many commonly recommended interventions for orthostatic hypotension had a limited evidence base supporting their use. High quality, randomised controlled trials were needed to underpin clinical practice for this condition.

CRD commentary
This review addressed a clear (if broad) question, accompanied by appropriate inclusion criteria prespecified in a protocol. A range of appropriate databases were searched, with some effort devoted to searching the grey literature. However, given the wide range of interventions included, the search sensitivity may have been suboptimal and direct head-to-head comparisons of the interventions may have provided useful additional information. Methods for ensuring the unbiased selection and appraisal of studies were not reported, but are unlikely to result in bias, especially in the absence of quantitative synthesis.

Lack of quantitative synthesis was appropriately justified, with the authors’ conclusion referring to the need for high quality randomised trials and standardisation of outcome measures. The authors explicitly acknowledged uncertainty accruing from small trial size and lack long-term follow-up data, stating that the evidence-base precluded the ability to draw strong positive conclusions about any of the interventions examined in the review.

The authors’ conclusions reflect the evidence and are likely to be reliable.

Implications of the review for practice and research
Practice: The authors did not state any implications for practice.

Research: The authors stated that further research was needed to establish which measure best correlated with symptoms and quality of life in orthostatic hypotension. Large, well-designed, randomised, placebo-controlled trials that focus on changes in lying and standing blood pressure, postural drop, symptoms, quality of life and functional ability were required.

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