Effectiveness and safety of treatments for degenerative ataxias: a systematic review

CRD summary
This review found that quality studies to evaluate the safety and efficacy of treatments for degenerative ataxia were scarce. No valid information on the actual value of physical rehabilitation and psychological support as treatments for degenerative ataxia was available and further investigation with improved study designs was necessary. These conclusions appear appropriate considering the limitations of available data.

Authors' objectives
To evaluate the effectiveness and safety of treatments for degenerative ataxia.

Searching
MEDLINE, EMBASE, Cochrane Central Register of Controlled Trials (CENTRAL) and Centre for Reviews and Dissemination website (databases not specified) were searched to March 2007 without language restrictions. Reference lists were examined for additional studies.

Study selection
Studies that assessed the effectiveness and safety of pharmacological, rehabilitative or psychological treatments for degenerative ataxia were eligible for inclusion. Any study design with at least three participants and at least six-months follow-up was included. Most included studies assessed pharmacological treatments (a variety of agents and doses were described); one study assessed rehabilitation therapy. In most studies participants had Friedreich's ataxia, but a variety of other types of ataxia were included. Where reported, mean age ranged from 14.7 to 56.8 and the proportion of females ranged from 20.7% to 68.7%. Most studies assessed changes in neurological impairments in response to treatment and cardiomyopathy. Changes in functional capacity were reported in some studies.

Studies were selected independently by two reviewers. Disagreements were resolved by consensus or consultation with a third reviewer if consensus was not possible.

Assessment of study quality
The methodological quality of clinical trials was assessed using the Jadad scale (in terms of randomisation, blinding and follow-up) and a quality score out of 5 was derived. The number of reviewers that performed quality assessment was not reported.

Data extraction
The number of reviewers that performed data extraction was not reported.

Methods of synthesis
The studies were combined in a narrative synthesis.

Results of the review
Twenty-five studies were included (n=540, range three to 87): 10 randomised controlled trials (RCTs) (n=220); one non randomised controlled trial (n=56); and 14 case series (n= 264). Jadad scores were 1 for one RCT, 3 for three RCTs, 4 for six RCTs and 5 for one RCT. Loss to follow-up ranged from 0 to 26.9%. No RCTs conducted intention-to-treat analysis.

Follow-up ranged from 3.5 to 48 months; it was 12 months in most studies.

There was some evidence that 5-hydroxytryptophan was more effective than placebo in the improvement of neurological symptoms in patients with Friedreich's ataxia, olivopontocerebellar atrophy or cerebellar atrophy. Positive effects were reported in two of three RCTs and two case series reported positive effects.
Idebenone was found to be more effective than placebo for reducing mean thickness of some but not all cardiac dimensions in patients with the hypertrophic cardiomyopathy associated with Friedreich's ataxia, but patient response was highly variable (one RCT). Three case series reported reductions in some but not all cardiac dimensions. One of two case series reported a reduction in cardiac hypertrophy. Findings for changes in neurological impairment were mixed (one RCT and two case series). Three case series reported improvements in some measures of functional capacity from baseline.

There was limited evidence for other therapies.

Authors' conclusions
Availability of quality studies to evaluate safety and efficacy of treatments for degenerative ataxia was scarce. No valid information on the actual value of physical rehabilitation and psychological support as treatments for degenerative ataxia was available. Further investigation with improved study designs was necessary.

CRD commentary
The review question was supported by broad inclusion criteria for participants, intervention, outcomes and study design. Studies in all languages were sought, which reduced the risk of language bias. The authors did not report any attempts to identify unpublished studies and so publication bias could not be ruled out. Study selection was performed in duplicate, which reduced the risk of errors and bias; it was unclear whether such precautions were taken for other review processes. The quality of clinical studies was assessed using an appropriate tool and the authors acknowledged the limitations of including poor-quality study designs (case series). The authors' conclusions appear appropriate considering the limitations of available data.

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

Research: The authors stated that further trials in different patient groups (using international collaborations for necessary statistical power) were needed. An appropriate and validated neurological assessment instrument for each type of ataxia was required to allow comparison between studies. More research was needed on the effects of physical rehabilitation on patients with degenerative ataxia (effectiveness and cost-effectiveness). Patients' perspectives needed to be considered to ensure relevant outcome measures were used and health-related quality of life measurement should always be included. Molecular and structural neuroimaging characteristics could be used as indicators of clinical effectiveness in future trials.

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