Whole plant cannabis extracts in the treatment of spasticity in multiple sclerosis: a systematic review
Lakhan SE, Rowland M

CRD summary
This review concluded that there was evidence that combined extracts of cannabis (delta^9-tetrahydrocannabinol and cannabidiol) may provide therapeutic benefit for spasticity symptoms in patients with multiple sclerosis. In light of the good quality of the included trials, the authors' cautious conclusions appear to be appropriate, although the small number of trials should be borne in mind.

Authors' objectives
To assess the efficacy of whole plant cannabis extracts in the treatment of spasticity in multiple sclerosis.

Searching
MEDLINE and Cochrane Central Register of Controlled Trials (CENTRAL) were searched for published English-language studies from 1999 to April 2009. Search terms were reported. Reference lists of retrieved publications were also screened.

Study selection
Randomised controlled trials (RCTs) that compared whole plant cannabis extracts (combined extracts of delta^9-tetrahydrocannabinol and cannabidiol) with a placebo (for a treatment period of under six months) in multiple sclerosis patients were eligible for inclusion. The eligible patients had to have clinically stable spasticity established prior to the trial. Trials reporting objective measures of pre-treatment and post-treatment spasticity were included. Only trials with a quality score of at least 4 points on the Jadad scale were eligible for inclusion.

The review outcomes included reduction in spasticity, change in muscle tone (assessed by Ashworth score), change in severity of spasticity (assessed by Visual Analogue Scale), disability relating to mobility (assessed by Rivermead Mobility Index), walking time and adverse events.

In the included trials, the dose regime of combined extracts of both delta^9-tetrahydrocannabinol and cannabidiol ranged from 2.5mg to 120mg daily. The intervention duration of included trials ranged from two to 15 weeks.

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

Assessment of study quality
The quality of trials was assessed using a Jadad scale, a 5-point scale evaluating randomisation, blinding and withdrawal.

The authors did not report how many reviewers performed the validity assessment.

Data extraction
It appeared that mean changes from baseline for the outcomes were extracted.

Two reviewers independently extracted data and resolved disagreements by consensus.

Methods of synthesis
The trials were combined in a narrative synthesis, supported by accompanying data tables.

Results of the review
Six double-blind RCTs were included in the review (n=820 patients). The sample size ranged from 14 to 395 patients.
Three RCTs had a quality score of 5 points.

Five RCTs reported that cannabis extracts may decrease spasticity and improve mobility in patients with multiple sclerosis, but one RCT showed no reduction in spasticity.

One RCT showed that cannabis extracts were associated with a significant improvement in muscle tone as assessed by Ashworth scale compared with placebo (p=0.002). Five RCTs reported little to no improvement in the Ashworth scale compared with placebo.

Two RCTs reported that cannabis extracts were associated with a significant improvement in severity of spasticity as assessed by Visual Analogue Scale compared with placebo (p<0.05 and p=0.001), but one RCT reported no significant difference between the two groups.

All six RCTs reported that side effects from combined extracts of delta9-tetrahydrocannabinol and cannabidiol were generally well-tolerated.

Results of the outcomes of walking time and disability relating to mobility were also reported.

Authors’ conclusions
There was evidence that combined extracts of delta9-tetrahydrocannabinol and cannabidiol may provide therapeutic benefit for spasticity symptoms in patients with multiple sclerosis.

CRD commentary
The inclusion criteria of the review were clear. Relevant databases were searched. Efforts were made to find published studies but not unpublished studies, which have introduced the potential for publication bias. The decision to restrict the review to English-language studies may have increased the risk of language bias. Methods were used to minimise reviewer errors and bias in the extraction of data, but it was not clear whether similar steps were taken in study selection and validity assessment.

Relevant criteria were used to examine the trial quality. Given the diversity of included trials, a narrative synthesis was appropriate.

In light of the good quality of the included trials, the authors' cautious conclusions appear to be appropriate, although the small number of trials should be borne in mind.

Implications of the review for practice and research
Practice: The authors stated that the therapeutic potential of cannabinoids in patients with multiple sclerosis should be given considerable attention.

Research: The authors stated that future studies are required to compare the safety of combined cannabis extracts with traditional treatment. Future studies should focus on the distinction between perceived symptom relief and objective physiological changes in patients with multiple sclerosis. Future studies should also evaluate cannabis extracts with a range of dosage in order to balance potential side effects with maximum therapeutic benefit.

Funding
Not stated.

Bibliographic details

PubMedID
19961570
Record Status
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.