Efficacy and safety of herbal medicines for idiopathic Parkinson's disease: a systematic review
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CRD summary
This review assessed the effectiveness and safety of herbal medicines, alone or as a combined therapy, compared with placebo or conventional treatment of idiopathic Parkinson's disease. The authors' cautious conclusion, that current evidence is insufficient to evaluate either effectiveness or safety correctly, reflects the limited evidence from studies of poor methodological quality which do not provide robust evidence.

Authors' objectives
To evaluate the efficacy and safety of herbal medicines (HMs), as a monotherapy or adjunct therapy, compared with placebo or conventional treatment of idiopathic Parkinson's disease (PD).

Searching
MEDLINE, CINAHL, AMED, the Cochrane CENTRAL Register, the Chinese Scientific Journal Database, Traditional Chinese Medicine Database, the CBM-disc, China Academic Journals Full-Text Database, China Proceedings of Conference Full-Text Database, China Doctor/Master Dissertations Full-Text Database, and a Current Controlled Trials were searched. The search strategy was based on one used by a Cochrane review on herbal medicine and guidelines of the Cochrane Movement Disorders group. No search terms were reported. Searches were conducted in July 2005 but no dates were reported. Studies published in any language were sought. Chinese and English journals were handsearched, reference lists were checked and authors were contacted for unpublished and ongoing trials.

Study selection
Study designs of evaluations included in the review
Randomised controlled trials (RCTs) were eligible for inclusion.

Specific interventions included in the review
Studies of HMs, used on their own or in combination with other conventional treatment, compared with placebo, conventional drugs or a non-pharmacological intervention were eligible for inclusion. Studies of HMs could include extracts or oral decoctions of multiple herbs or a single herb, or herbal proprietary medicines, or a compound of herbs. Other complementary and alternative medicine categories could not be coadministered in either study arm. The included studies evaluated: Cannador (cannabis); Mucuna pruriens (MP); Zhiyinxifeng granules; Kanli decoction; Bushen Pingchan decoction with Madopar; Lemaikeli with benserazide or Madopar plus vitamin B6; tailor-made Chinese herbal decoction with Madopar plus levodopa (LD) plus Artane; tailor-made Chinese herbal decoction plus Madopar plus amantadine; and Wuling capsule plus LD. The comparators were placebo; LD plus carbidopa; Madopar; Kanli decoction plus Madopar; benserazide or Madopar plus vitamin B6; LD plus Artane; Madopar plus amantadine; and LD alone. The duration of treatment ranged from 4 hours to 90 days.

Participants included in the review
Studies in patients with a clinical diagnosis of idiopathic PD were eligible for inclusion. Patients with secondary parkinsonism were excluded. In the included studies, the overall age of the participants ranged from 42 to 81 years, the proportion of men was 65% (n=323) and 94.5% of the participants were of Chinese ethnicity.

Outcomes assessed in the review
Studies that reported any of the following were eligible for inclusion: PD motor impairment rating scales, PD activities of daily living rating scales, tests of individual motor impairments, health-related quality of life, reduction in LD dose, adverse event frequency, number of withdrawals as a result of lack of efficacy and/or side-effects, and cost-effectiveness assessments. The included studies assessed outcomes using a variety of rating scales including the Unified Database of Abstracts of Reviews of Effects (DARE)
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Parkinson's Disease Rating Scale (UPDRS), Abnormal Involuntary Movement Scale (AIMS) and the Webster scale.

How were decisions on the relevance of primary studies made?
Two reviewers independently assessed studies for inclusion and resolved any disagreements by discussion.

Assessment of study quality
The validity assessment was performed qualitatively based on methods described in a Cochrane review by Crosby et al. (see Other Publications of Related Interest). The authors did not state how the validity assessment was performed, but it appeared to include an assessment of randomisation method, concealment of allocation, similarity at baseline, withdrawals, missing values, co-interventions, blinded assessors and data analysis. Each category was graded either A (good or adequate), B (unclear or not stated) or C (poor, weak or inadequate).

Data extraction
Two reviewers independently performed the data extraction and resolved any disagreements by discussion.

Methods of synthesis
How were the studies combined?
The studies were presented in a narrative synthesis, grouped into categories: HM as a monotherapy, HM as an adjunct therapy, adverse events and withdrawals. Each study was described in the text and additional descriptive information was tabulated.

How were differences between studies investigated?
Differences could be observed from inspection of the tables. Additional differences were discussed in the text.

Results of the review
A total of 28 RCTs met the inclusion criteria but only 9 (n=551) were included in the review. Sample sizes ranged from 9 to 103 patients.

There was considerable heterogeneity between the included studies in terms of interventions and outcome measures. Only 2 studies reported methods of randomisation and concealment of allocation to both assessors and participants. Simplicity at baseline was only graded as good in 3 studies; the remaining 6 were graded as poor. Withdrawals were not reported or were unclear in 7 studies, with 2 studies reporting that more than 10% of the participants withdrew from the study. Most studies did not account for missing values. Data analysis was classified as poor in 7 studies.

HM as a monotherapy.

MP seed powder and LD co-administered with carbidopa resulted in a similar degree of dyskinesia when measured by the AIMS and the Goetz scale. MP exhibited a more rapid onset of action and a longer ‘on’ time when compared with LD plus carbidopa (1 study).

In a study comparing cannabis with placebo, cannabis had no therapeutic effect on L-dopa-induced dyskinesia, overall UPDRS or PDQ-39 (1 study).

Madopar compared with Zhiyinxifeng granules showed a similar efficacy in one study, while another study found a relatively higher efficacy of Kanli decoction compared with Madopar. Both studies measured outcomes by improvement in overall Webster scale scores.

HM as an adjunct therapy.

All 5 studies in this category reported that combined use of herbal and conventional treatment produced a lower post-treatment score (i.e. a better outcome) using various scales when compared with HM monotherapy or conventional drugs.
Adverse events and withdrawals.

Adverse events of HM monotherapy were only reported in 3 studies. One study comparing MP with LD and carbidopa reported one drop-out due to short-lasting vomiting after the 'ingestion of 30 g of MP'. Other side-effects were mild. A second study comparing Cannador with placebo described no occurrence of serious adverse events requiring hospital admission. Mild adverse events were more frequent in the Cannador group (37 events) compared with the placebo group (15 events). A study of Zhiyinxifeng granules reported 2 cases of dry mouth, 3 cases of sleep disturbance and 1 case of constipation, compared with no obvious side-effects observed in the Madopar group.

Adverse events of HM adjunct therapy were only reported in 2 studies. One study reported the treatment group using Lemaikeli, vitamin B6 and benserazide or Madopar as having an adverse event rate of 9%, with reports of nausea, anorexia, abdominal distension, hypotension, insomnia and ‘on-off’ syndromes, but these were not clearly defined. The second study reported that 8% of patients in the combined group using Wuling capsule and LD complained of minor abdominal discomfort.

Authors’ conclusions

The current evidence is insufficient to evaluate the efficacy and safety of various HMs.

CRD commentary

The review addressed a clear question that was defined in terms of the participants, intervention, outcomes and study design. Several relevant sources were searched and attempts were made to locate unpublished studies. No language restrictions were applied, thus limiting the possibility of publication bias. The authors attempted to minimise bias and error during the review process by carrying out the study selection and data extraction processes in duplicate. The authors did not report how the validity assessment was performed, so it is not possible to assess the likelihood of reviewer bias. A total of 28 studies met the inclusion criteria but only 9 were included in the review. The authors did not state why the remaining studies were excluded, therefore it is not possible for the reader to evaluate likely bias or the loss of potentially relevant data. Given the methodological and clinical diversity of the studies, a narrative synthesis was appropriate. The authors’ cautious conclusions correctly reflect the limited evidence from studies of poor methodological quality, which are unable to provide robust evidence.

Implications of the review for practice and research

Practice: The authors stated that the evidence reported in the review is insufficient to warrant any clinical recommendations. Research: The authors stated that further RCTs of HMs, with improved reporting and rigorous trial design, should be conducted. Follow-up should be longer term and include an assessment of adverse effects and an economic evaluation.

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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.