

Executive summary

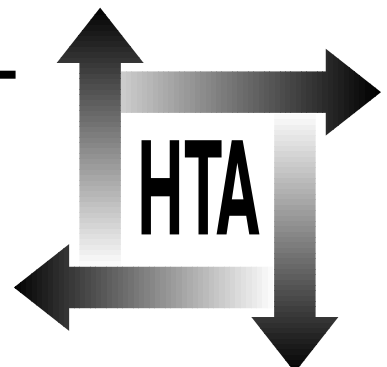
Treatments for fatigue in multiple sclerosis: a rapid and systematic review

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**Health Technology Assessment
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Executive summary

Background

Multiple sclerosis (MS) is an important problem both for people with the disease and for society. There is no cure, and alleviation of symptoms forms the cornerstone of care. Excessive fatigue that severely limits activity is experienced by at least two-thirds of the estimated 60,000 people with MS in the UK.

Objectives

- To identify current treatments for fatigue in MS and their evidence-base.
- To systematically review the evidence for those treatments that have been investigated in more than one rigorous study, in order to determine their effectiveness and cost-effectiveness.

Methods

The review was carried out in two stages: a formal scoping review (to assess the range of interventions used by people with MS), and a systematic review for treatments that had been identified as promising and that had been investigated in clinical trials (as identified in the scoping review). A systematic review of research on costs and cost-effectiveness of those interventions identified as promising was also performed.

Electronic databases, including MEDLINE and EMBASE, were searched for the period 1991–June 1999 (scoping review) and 1966–December 1999 (systematic review). Reference lists from publications were also searched, and experts were contacted for any additional information not already identified.

Results

Interventions identified for the treatment of fatigue in MS

- Behavioural advice. This is the main element of initial clinical management and no rigorous research of its effectiveness was identified.

- Drugs (amantadine, pemoline, potassium-channel blockers and antidepressants).
- Training, rehabilitation and devices (cooling vests and electromagnetic fields).
- Alternative therapies (bee venom, cannabis, acupuncture/acupressure and yoga).

Only two drugs, amantadine and pemoline, met the criteria for full systematic review.

Effectiveness of amantadine

One parallel and three crossover trials were found, involving a total of 236 people with MS. All studies were open to bias. All studies showed a pattern in favour of amantadine compared with placebo, but there is considerable uncertainty about the validity and clinical significance of this finding. This pattern of benefit was considerably undermined when different assumptions were used in the sensitivity analysis.

Effectiveness of pemoline

One parallel and one crossover trial were found involving a total of 126 people with MS. Both studies were open to bias. There was no overall tendency in favour of pemoline over placebo and an excess of reports of adverse effects with pemoline.

Health economic analysis

The drug costs of amantadine and pemoline are modest (£200 and £80 per annum, respectively). No economic evaluations were identified in the systematic review, and available data were insufficient to allow modelling of cost-effectiveness in this rapid review.

Conclusions

There is insufficient evidence to allow people with MS, clinicians or policy makers to make informed decisions on the appropriate use of the many treatments on offer.

Only amantadine appears to have some proven ability to alleviate the fatigue in MS, though only a proportion of users will obtain

benefit and then only some of these patients will benefit sufficiently to take the drug in the long term.

Recommendations for research

The frequency, severity and impact of fatigue, the poverty of available research, and the absence of any ongoing research, suggest that new research is an urgent priority. People with MS, clinicians and policy makers should work together to ensure that the evidence required is collected as quickly as possible by encouraging involvement in rigorous research.

Research should not be restricted to the two drugs reviewed in depth in this report. All interventions identified in the scoping review (see above) should be considered, as should basic scientific research into the underlying mechanism of fatigue in MS.

Publication

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NHS R&D HTA Programme

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