Modafinil for fatigue in multiple sclerosis

E Willoughby

Single daily dose of modafinil is of benefit

Fatigue is a perplexing and at times incapacitating symptom in multiple sclerosis. It has both physical and cognitive components and its severity is not closely related to the extent of neurological disability, nor to clinical or laboratory measures of inflammatory activity, nor to depression. Treatment is unsatisfactory, with few controlled studies and with interpretation of results hindered by somewhat blunt clinical scales to measure effects. Evidence is accumulating that fatigue in multiple sclerosis is due to dysfunction of the CNS, but lack of understanding of the underlying pathophysiology makes a rational approach to treatment difficult. The paper by Rammo- han et al (this issue, pp 179–183) is a useful addition to the limited literature on the subject. It demonstrates improvement in fatigue in patients with multiple sclerosis taking 200 mg modafinil a day.

Modafinil stimulates wakefulness and, compared with amphetamines, has a more selective action in the brain and fewer side effects. It is an α-1 adrenergic agonist with complex actions also on other neurotransmitter systems. A relatively long half life makes single, daily dosing practicable. Interest in its effect on fatigue was stimulated by a study showing effectiveness in reducing daytime sleepiness in narcolepsy—at the same time measures of fatigue were improved. There is clearly overlap between fatigue and sleepiness, but in many patients the symptoms can be distinguished reasonably well.

Limitations of the present report in patients with multiple sclerosis are the single blind design, a standard dose titration sequence for modafinil and placebo and, especially, the short time on active treatment. Although 200 mg modafinil a day was of benefit, a higher dose of 400 mg was not. Increased side effects on the higher dose is a more likely explanation than loss of responsiveness to the treatment after 2 weeks. It was noted that some patients did better on the higher dose, and it would be expected that there may be considerable variation among patients in the doses producing both side effects and improvement in symptoms.

Further studies on modafinil for fatigue in multiple sclerosis are warranted, with the need for a double blind study assessing treatment for longer periods, with titration of the dose for individual patients. Potential for habituation with modafinil seems relatively low but needs careful assessment.

J Neurol Neurosurg Psychiatry 2002;72:150

Editorial Commentary

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Powell et al acknowledge that they could only evaluate the overall framework for delivering rehabilitation rather than its specific components. They have offered important new evidence to support the wider development of community-based multidisciplinary rehabilitation teams. Wilson has reminded us that it is wasteful spending hours delivering unevaluated therapy that may be of little or no benefit to a patient. The challenge now is to find evidence-based ways of determining more precisely what these teams should actually do, when, and for how long.

Competing interests: none declared

REFERENCE


CT after head injury

Which CT features help predict outcome after head injury?

D J Wyper

Presence of subarachnoid blood and overall appearance are helpful

In the paper by Wardlaw et al (this issue, pp 188–192) it is shown that the presence of subarachnoid blood and “overall appearance” of a CT scan could be added to the already established variables of age, Glasgow coma score, and pupil reaction to improve prediction of 1 year survival after head injury. This has been a thorough investigation and should be of practical benefit in improving the predictive model. A deficiency, which is recognised by the authors, is that the interrater variability in classifying the overall appearance of scans has still to be established. It remains to be seen whether or not this classification proves to be sufficiently robust for day to day application within increasingly busy neuroradiology departments.

Although this paper has focused on CT, MRI may be a better imaging modality for prognostic estimation, especially on account of its ability to detect brain stem lesions. If the current constraints around access for patients with acute head injury at the time of admission can be tackled then there could be a gradual shift towards MRI.

It is also clear that more subtle outcome measures are difficult to predict. Neuropsychiatric status after mild head injury has been investigated1 and variables including CT failed to predict outcome.

J Neurol Neurosurg Psychiatry 2002;72:151

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