Modafinil improves symptoms of ADHD compared with placebo in young people


Q Is modafinil an effective treatment for attention deficit hyperactivity disorder (ADHD) in young people?

CONCLUSIONS
Modafinil improves symptoms of ADHD as assessed by teachers and by parents compared with placebo. Common adverse events were mild and usually resolved quickly.

NOTES
High dropout may have affected the analysis between groups. The higher dropout rate in the placebo group may be explained by the option given to all participants to switch to open label treatment after four weeks.

MAIN RESULTS
Modafinil significantly improved symptoms of ADHD after nine weeks (mean score change (ADHD-RS-IV School Version): −15.0 with modafinil v −7.3 with placebo, p<0.0001; total effect size: 0.69, 95% CI 0.37 to 0.82). This trend was seen at all follow-up points (weeks 1, 2, 3, 5, 7, and 9; results presented graphically). Common adverse events were more frequent in the modafinil group compared with placebo, including insomnia (48/164 (29%) with modafinil v 3/82 (4%) with placebo, p<0.05) and loss of appetite (26/164 (16%) with modafinil v 3/82 (4%) with placebo, p<0.05), although these were considered mild and did not lead to treatment withdrawal.

Comments
Attention deficit hyperactivity disorder (ADHD) is now the most commonly reported psychiatric disorder in childhood. Electrophysiological investigations have demonstrated a neurophysiological basis for ADHD, and central nervous system stimulant medications (particularly methylphenidate and dexmethylamphetamine (dexamphetamine)) are accepted as the most effective treatment. The current contentious issue with such medication recommendations is the potential for stimulant misuse and future substance abuse. Yet non-treatment may result in educational failure, poor job prospects, and impaired personal/marital relationships.

In this context, modafinil may offer an exciting alternative. Its pharmacological activity appears narrower than traditional stimulants and limited to activation of the cortex—it was initially approved to increase wakefulness in patients with narcolepsy. Unlike the usual stimulants, it does not appear to activate brain centres involved in euphoria and substance abuse. Biederman et al provide the first multicentre randomised, double-blind, placebo-controlled study of modafinil in children and adolescents with ADHD. The positive treatment outcomes of reduced symptom severity ratings, with few side effects, strongly support its clinical usefulness.

However, potential patients were excluded if they were doing well on their current stimulant medication, or if they had previously responded poorly to stimulants, so currently we do not know how either good or poor responders to the usual stimulants will function on modafinil. Also, 41% of patients discontinued modafinil before the end of the trial, and while all of these were attributed to lack of efficacy, that figure may well be higher. Finally, as the authors mention, we need studies of the long-term effects of modafinil in children. Despite these limits, modafinil holds promise as an alternative ADHD treatment.

Although this study demonstrates effects on the core symptoms of ADHD, the mechanism of action of modafinil is poorly understood. Electroencephalography demonstrates increased alpha activity in the prefrontal cortex. It is important to consider the impact of modafinil on features that are difficult to quantify, such as executive function and overall functioning.

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