Bupropion for attention deficit hyperactivity disorder (ADHD) in adults.

Verbeeck W, Bekkering GE, Van den Noortgate W, Kramers C.

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Abstract

BACKGROUND:
Attention deficit hyperactivity disorder (ADHD) is a prevalent neurobiological condition, characterized by behavioral and cognitive symptoms such as inattention, impulsivity and/or excessive activity. The syndrome is commonly accompanied by psychiatric comorbidities and is associated with educational and occupational underachievement. Although psychostimulant medications are the mainstay of treatment for ADHD, not all adults respond optimally to, or can tolerate, these medicines. Thus, alternative non-stimulant treatment approaches for ADHD have been explored. One of these alternatives is bupropion, an aminoketone antidepressant and non-competitive antagonism of nicotinic acetylcholine receptors. Bupropion is registered for the treatment of depression and smoking cessation, but is also used off-label to treat ADHD.

OBJECTIVES:
To assess the effects and safety of bupropion for the treatment of adults with ADHD.

SEARCH METHODS:
We searched the Cochrane Central Register of Controlled Trials (CENTRAL), MEDLINE, Embase, and seven other databases in February 2017. We also searched three trials registers and three online theses portals. In addition, we checked references of included studies and contacted study authors to identify potentially relevant studies that were missed by our search.

SELECTION CRITERIA:
We included all randomized controlled trials (RCTs) that evaluated the effects (including adverse effects) of bupropion compared to placebo in adults with ADHD.
DATA COLLECTION AND ANALYSIS:
Two review authors (WV, GB) independently screened records and extracted data using a data extraction sheet that we tested in a pilot study. We extracted all relevant data on study characteristics and results. We assessed risks of bias using the Cochrane 'Risk of bias' tool, and assessed the overall quality of evidence using the GRADE approach. We used a fixed-effect model to pool the results across studies.

MAIN RESULTS:
We included six studies with a total of 438 participants. Five studies were conducted in the USA, and one in Iran. All studies evaluated a long-acting version of bupropion, with the dosage ranging from 150 mg up to 450 mg daily. Study intervention length varied from six to 10 weeks. Four studies explicitly excluded participants with psychiatric comorbidity and one study included only participants with opioid dependency. Four studies were funded by industry, but the impact of this on study results is unknown. Two studies were publicly funded and in one of these studies, the lead author was a consultant for several pharmaceutical companies and also received investigator-driven funding from two companies, however none of these companies manufacture bupropion. We judged none of the studies to be free of bias because for most risk of bias domains the study reports failed to provide sufficient details. Using the GRADE approach, we rated the overall quality of evidence as low. We downgraded the quality of the evidence because of serious risk of bias and serious imprecision due to small sample sizes. We found low-quality evidence that bupropion decreased the severity of ADHD symptoms (standardized mean difference -0.50, 95% confidence interval (CI) -0.86 to -0.15, 3 studies, 129 participants), and increased the proportion of participants achieving clinical improvement (risk ratio (RR) 1.50, 95% CI 1.13 to 1.99, 4 studies, 315 participants), and reporting an improvement on the Clinical Global Impression - Improvement scale (RR 1.78, 95% CI 1.27 to 2.50, 5 studies, 337 participants). There was low-quality evidence that the proportion of participants who withdrew due to any adverse effect was similar in the bupropion and placebo groups (RR 1.20, 95% CI 0.35 to 4.10, 3 studies, 253 participants). The results were very similar when using a random-effects model and when we analyzed only studies that excluded participants with a psychiatric comorbidity.

AUTHORS' CONCLUSIONS:
The findings of this review, which compared bupropion to placebo for adult ADHD, indicate a possible benefit of bupropion. We found low-quality evidence that bupropion decreased the severity of ADHD symptoms and moderately increased the proportion of participants achieving a significant clinical improvement in ADHD symptoms. Furthermore, we found low-quality evidence that the tolerability of bupropion is similar to that of placebo. In the pharmacological treatment of adults with ADHD, extended- or sustained-release bupropion may be an alternative to stimulants. The low-quality evidence indicates uncertainty with respect to the pooled effect estimates. Further research is very likely to change these estimates. More research is needed to reach more definite conclusions as well as clarifying the optimal target population for this medicine. Treatment response remains to be reported in a DSM5-diagnosed population. There is also a lack of knowledge on long-term outcomes.