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EVIDENCE-BASED REVIEW

Non-nicotine pharmacotherapies for smoking cessation ☆

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Summary International chronic obstructive pulmonary disease guidelines recommend that smokers be strongly advised to quit, and should be offered help in doing so. The most effective smoking-cessation interventions combine behavioural support with pharmacotherapies. For smokers who do not wish to use nicotine replacement treatments, bupropion is a safe and effective non-nicotine alternative first-line treatment. Nortriptyline and clonidine have demonstrated efficacy in aiding smoking cessation, but are regarded as second-line therapies. A number of other non-nicotine treatments show promise, but more data are required before these can be recommended in assisting smokers to stop.

Introduction

Interventions to aid smoking cessation are among the most important treatments that can be offered to smokers to improve their current and future health and reduce the risk of premature death. In the year 2000, an estimated 4.83 million premature deaths worldwide were a direct consequence of smoking.[1] Chronic obstructive pulmonary disease (COPD) accounted for one-fifth of these deaths.

Smokers who are susceptible to developing COPD suffer a progressive decline in lung function, resulting in significant disability. For these people, smoking cessation is the only intervention that has

☆The following Cochrane reviews have been cited in this evidence-based review: Silagy C, et al. Nicotine replacement therapy for smoking cessation, Issue 3, 2004; Hughes JR, et al. Antidepressants for smoking cessation, Issue 4, 2004; Hughes JR, et al. Anxiolytics and antidepressants for smoking cessationm Issue 4, 2004; Lancaster T, et al. Silver acetate for smoking cessation, Issue 3, 1997; Gourlay SG, et al. Clonidine for smoking cessation, Issue 3, 2000; Stead LF, et al. Lobeline for smoking cessation, Issue 3, 1997; Lancaster T, et al. Mecamylamine (a nicotine antagonist) for smoking cessation, Issue 2, 1998; David S, et al. Opioid antagonists for smoking cessation, Issue 3, 2001. Copyright Cochrane Library, reproduced with permission.

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been proven to modify the course of airways obstruction, and can result in improving pulmonary function, decreasing respiratory symptoms, and decreasing acute respiratory tract infections.[2] International COPD guidelines recommend that smokers be strongly advised to quit, and should be offered help in doing so.[3]

Most smokers say they want to stop, and about two-thirds will make an attempt each year. However, many will choose to make an unaided quit attempt; a method that has only a small chance of long-term success.[4] The primary reason why many smokers find it difficult to quit is because of their dependence on nicotine. Tobacco smoke provides rapid delivery of nicotine to the central nervous system, where it facilitates the release of a number of neurotransmitters, such as dopamine and noradrenaline.[5] In dependent smokers, nicotine deprivation precipitates a withdrawal syndrome, consisting of symptoms such as irritability, low mood, poor concentration, and urges to smoke that can undermine a smokers' attempt to quit.[6]

Two smoking-cessation medications are in common use: nicotine replacement therapy (NRT), of which there are six different products, and bupropion (Zyban). NRT acts by replacing some of the nicotine smokers would have received from their cigarettes, and in doing so reduces the severity of withdrawal symptoms. NRT approximately doubles the chance of long-term abstinence (odds ratio [OR] = 1.74; 95% CI: 1.64–1.86),[7] although the absolute success rate depends upon the intensity of the additional support provided and the type of smoker being treated.[8] Although effective, this medication is no magic cure, and at least 70% of smokers who try to quit using NRT relapse within a year.[9] A large number of studies examining the efficacy of various non-nicotine pharmacotherapies for smoking cessation have been published. This paper attempts to summarise the findings of systematic reviews of these treatments.

Method

We searched the Cochrane Library, PubMed, and PsychLit databases for systematic reviews of non-nicotine pharmacotherapies for smoking cessation. We have relied mainly on systematic reviews contained in the Cochrane Library, as these have clear and strict criteria for entry into the reviews (Table 1). Seven reviews of non-nicotine treatments for smoking cessation have been published in the Cochrane Library: antidepressants, anxiolytics, clonidine, lobeline, mecamylamine, opioid antagonists, and silver acetate.[10–16] On the basis of conclusions from these reviews, and smoking-cessation guidelines,[17,18] we allocated treatments to one of three categories: (1) first-line medications for smoking cessation; (2) second-line medications for smoking cessation; and (3) medications not currently recommended for smoking cessation.

First-line medications for smoking cessation

Bupropion, an atypical antidepressant, is the first, and, so far, the only non-nicotine treatment licensed for smoking cessation.

Table 1 Summary of criteria for entry into Cochrane reviews of non-nicotine pharmacotherapies for smoking cessation.

Study types	Randomised trials with adequate control group.
Participants	Current smokers and recent quitters.
Intervention	Use of a non-nicotine pharmacotherapy to aid smoking cessation or to prevent relapse. Most interventions combined pharmacotherapy with behavioural support and compared the treatment with placebo or an alternative smoking-cessation aid.
Outcome measures	Abstinence from smoking measured for at least 6 months after starting treatment.* Wherever possible the strictest criteria for abstinence outcome were used. Preference was given to continuous, or sustained, abstinence rates and biochemical verification of self-reported abstinence. Some reviews required studies to report biochemically validated abstinence to be included.[12,15,16] Where biochemical verification of abstinence was undertaken, only those participants whose self-reports were validated were included as abstainers. One review included studies that measured cigarette reduction by 50% or less of baseline.[10] Intention-to-treat analysis was used wherever possible. Participants lost to follow-up were counted as smokers.

*Clonidine review required at least 12 weeks of follow-up.[13]*Opioid antagonists review included short-term follow-ups that looked at withdrawal symptoms.[16]