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Antidepressants for smoking cessation

Objectives

There are at least three reasons to believe antidepressants might help in smoking cessation. Firstly, nicotine withdrawal may produce depressive symptoms or precipitate a major depressive episode and antidepressants may relieve these. Secondly, nicotine may have antidepressant effects that maintain smoking, and antidepressants may substitute for this effect. Finally, some antidepressants may have a specific effect on neural pathways, *eg* inhibiting monoamine oxidase, or receptors, *eg* blockade of nicotinic-cholinergic receptors, underlying nicotine addiction.

This review assessed the effect and safety of antidepressant medications to aid long-term smoking cessation. The medications include bupropion (Zyban), fluoxetine, moclobemide, nortriptyline, paroxetine, selegiline, sertraline, St John's wort, varenicline (Champix) and venlafaxine.

Search and selection strategy

The authors searched the Cochrane Tobacco Addiction Group Specialised Register which includes reports of trials indexed in the Cochrane Central Register of Controlled Trials (CENTRAL), MEDLINE, EMBASE, PsycINFO and other reviews and meeting abstracts in July 2013.

They considered randomised trials comparing antidepressant medications to placebo or an alternative pharmacotherapy for smoking cessation. They also included trials comparing different doses, using pharmacotherapy to prevent relapse or re-initiate smoking cessation or to help smokers reduce cigarette consumption. They excluded trials with less than six months follow-up.

The main outcome measure was abstinence from smoking after at least six months follow-up in patients smoking at baseline, expressed as a risk ratio (RR). They used the most rigorous definition of abstinence available in each trial, and biochemically validated rates if available.

Main results

Twenty-four new trials were identified since the 2009 update, bringing the total number of included trials to 90.

There was high-quality evidence that, when used as the sole pharmacotherapy, bupropion significantly increased long-term cessation (44 trials, n=13 728, RR 1.62, 95% CI 1.49–1.76).

There was moderate-quality evidence, limited by a relatively small number of trials and participants, that nortriptyline also significantly increased long-term cessation when used as the sole pharmacotherapy (six trials, n=975, RR 2.03, 95% CI 1.48–2.78).

There is insufficient evidence that adding bupropion (12 trials, n=3487, RR 1.9, 95% CI 0.94–1.51) or nortriptyline (four trials, n=1644, RR 1.21, 95% CI 0.94–1.55) to nicotine replacement therapy (NRT) provides an additional long-term benefit.

Based on a limited amount of data from direct comparisons, bupropion and nortriptyline appear to be equally effective and of similar efficacy to NRT (bupropion *vs* nortriptyline three trials, n=417, RR 1.30, 95% CI 0.93–1.82; bupropion *vs* NRT eight trials, n=4096, RR 0.96, 95% CI 0.85–1.09; no direct comparisons between nortriptyline and NRT).

Pooled results from four trials comparing bupropion to varenicline showed significantly lower quitting with bupropion (n=1810, RR 0.68, 95% CI 0.56–0.83).

Meta-analyses did not detect a significant increase in the rate of serious adverse events among participants taking bupropion, though the confidence interval only narrowly missed statistical significance (33 trials, n=9631, RR 1.30, 95% CI 1.00–1.69). There is a risk of about 1 in 1000 of seizures associated with bupropion use. Bupropion has been associated with suicide risk, but whether this is causal is unclear. Nortriptyline has the potential for serious side-effects but none have been seen in the few small trials for smoking cessation.

There was no evidence of a significant effect for SSRIs on their own (RR 0.93, 95% CI 0.71–1.22, n=1594; two trials fluoxetine, one paroxetine, one sertraline) or as an adjunct to NRT (three trials of fluoxetine, n=466, RR 0.70, 95% CI 0.64–1.82). Significant effects were also not detected for MAOIs (RR 1.29, 95% CI 0.93–1.79, n=827; one trial moclobemide, five selegiline), venlafaxine (one trial, n=147, RR 1.22, 95% CI 0.64–2.32), or St John's wort (two trials, n=261, RR 0.81, 95% CI 0.26–2.53).

Authors' conclusions

The antidepressants bupropion and nortriptyline aid long-term smoking cessation. Adverse events with either medication appear rarely to be serious or lead to stopping medication. Evidence suggests that the mode of action of bupropion and nortriptyline is independent of their antidepressant effect and that they are of similar efficacy to NRT. Evidence also suggests that bupropion is less effective than varenicline, but further research is needed to confirm this finding. Evidence suggests that neither SSRIs nor MAOIs aid cessation.

Citation

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