Review: Bupropion and nortriptyline each increase smoking cessation rates

Hughes JR, Stead LF, Lancaster T. **Antidepressants for smoking cessation.** Cochrane Database Syst Rev. 2004;(4):CD000031.

QUESTION

Do antidepressants increase long-term abstinence from smoking?

METHODS

Data sources: Drug names found in the Cochrane Tobacco Addiction Group's specialized register, reference lists, recent reviews, and meeting abstracts were searched in PubMed and EMBASE/Excerpta Medica (March 2004). Investigators were contacted as needed.

Study selection and assessment: Randomized controlled trials (RCTs) that compared any antidepressant with placebo or another treatment and assessed smoking abstinence at ≥ 6 months. Studies were pooled using fixed effects.

Outcomes: Smoking abstinence at ≥ 6 months.

MAIN RESULTS

36 RCTs met the selection criteria. *Tricyclic antidepressants*: Nortriptyline increased smoking cessation, but when added to nicotine replacement therapy (NRT) it did not increase abstinence rates more than NRT alone (Table). *Monoamine-oxidase inhibitors:* Moclobemide did not show a statistically significant difference in abstinence at 12 months (Table). *Atypical antidepressants*: Bupropion increased smoking cessation more than placebo (Table). In smokers who had quit, bupropion did not prevent relapse more than placebo (Table). Bupropion plus NRT increased smoking cessation more than NRT alone in 1 RCT but not in another unpublished RCT (Table). 1 RCT showed that bupropion increased smoking cessation more than NRT (Table). No statistically significant difference existed between bupropion and nortriptyline. Venlafaxine did not increase abstinence rates relative to placebo (Table). *Selective serotonin-reuptake inhibitors (SSRIs)*: 5 RCTs (3 of fluoxetine, 1 of paroxetine, and 1 of sertraline) showed that SSRIs did not increase abstinence at ≥ 6 months (Table).

CONCLUSIONS

In smokers, bupropion and nortriptyline increase smoking cessation at ≥ 6 months. Selective serotonin-reuptake inhibitors do not increase abstinence.

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Antidepressants for increasing smoking cessation rates at ≥ 6 months*

Comparisons	Number of comparisons	Event rates	RBI (95% CI)	NNT (CI)
Nortriptyline vs placebo	4	17% vs 7.0%†	146% (58 to 281)	10 (7 to 17)
Nortriptyline + NRT vs nortriptyline + placebo	3	26% vs 19%†	38% (–8 to 105)	Not significant
Moclobemide vs placebo	1	25% vs 16%	57% (–33 to 268)	Not significant
Bupropion vs placebo	19	19% vs 10%†	83% (61 to 108)	12 (9 to 15)
Bupropion vs placebo for relapse prevention	2	24% vs 22%†	11% (–17 to 48)	Not significant
Bupropion + NRT vs placebo + NRT	1	22% vs 9.8%	128% (46 to 256)	8 (6 to 17)
Bupropion vs NRT	1	18% vs 9.8%	88% (18 to 198)	12 (7 to 50)
Bupropion vs nortriptyline	1	16% vs 9.6%	71% (–28 to 311)	Not significant
Venlafaxine vs placebo	1	25% vs 20%	25% (–34 to 135)	Not significant
			RBR (CI)	NNH
Bupropion + NRT vs placebo + NRT	1	19% vs 24%	20% (–30 to 51)	Not significant
SSRIs vs placebo	5	15% vs 16%†	9% (–27 to 15)	Not significant

*NRT = nicotine replacement therapy; RBR = relative benefit reduction; SSRIs = selective serotonin-reuptake inhibitors. Other abbreviations defined in Glossary; weighted event rates, NNT, NNH, and CI calculated from data in article using a fixed-effects model.
†Event rates are weighted.

COMMENTARY

Antidepressants for smoking cessation are of interest because of the higher rate of depression among smokers than nonsmokers, the occurrence of depression in some smokers after they quit, and the interaction of nicotine and antidepressants with similar brain chemical systems. The detailed review by Hughes and colleagues showed that only bupropion and, to a lesser extent, nortriptyline have strong evidence for effectiveness. SSRIs are not effective. All of these agents are useful for treatment of depression, which suggests that different neurochemical actions contribute to success in smoking cessation and that this success is not simply the result of treating subclinical depression. Both bupropion and nortriptyline interact with the dopamine and norepinephrine systems in the brain, whereas SSRIs do not. This may account for the difference in efficacy.

An important question relates to the cost-effectiveness of antidepressants. Any intervention that increases smoking cessation rates has favorable cost-effectiveness because of the many years of life saved by quitting smoking. So one would anticipate that bupropion would be cost-effective. Bupropion and nicotine patches had the most favorable profile in a recent analysis (cost per year of life saved of $2214 and $3901 for a man 50 and 54 y of age, respectively) (1). An analysis based on a U.S. RCT found an even lower cost per year of life saved for men 50 to 59 years of age ($879) (2). Nortriptyline has not been analyzed in detail, but it is available generically. This potential advantage may be counteracted by the need for closer medical monitoring and more frequent dispensing of smaller quantities to limit the risk for overdose. Overall, use of antidepressants for smoking cessation is a significant advance in helping patients because it gives more options for therapy, both initially and for retreatment. Bupropion is approved by the Food and Drug Administration for smoking cessation and has the most effectiveness data, so it remains first-line therapy along with the various forms of NRT. Nortriptyline should be a second-line agent because it has been studied less and has the potential for serious side effects. Success in smoking cessation often requires several attempts, and clinicians now have a relatively wide range of agents to choose from to maximize patients' ability to quit.

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References

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