Review: nortriptyline and bupropion each increase smoking cessation rates


Clinical impact rating: GP/FP/Primary care: IM Respiratory

Do antidepressants increase long term abstinence from smoking?

**METHODS**

Data sources: drug names found in the Tobacco Addiction Group’s specialised register, reference lists, and meeting abstracts were searched in PubMed and EMBASE/Excerpta Medica in 2002. Investigators were contacted.

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

Outcome: abstinence.

**MAIN RESULTS**

30 RCTs were included. Tricyclic antidepressants. Nortriptyline increased smoking cessation (5 RCTs) (table). Monoamine oxidase inhibitors. 1 RCT of moclobemide did not show a statistically significant difference in abstinence at 12 months (table). Atypical antidepressants. 16 RCTs showed that bupropion was better than placebo for increasing abstinence (table). 2 RCTs compared bupropion with nicotine replacement therapy; 1 showed a benefit for bupropion, whereas the other unpublished RCT did not (table). 1 RCT compared bupropion with nortriptyline and showed no statistical difference (table). 1 study comparing venlafaxine with placebo did not show a statistically significant difference (table). Selective serotonin reuptake inhibitors (SSRIs). 4 RCTs (2 fluoxetine, 1 paroxetine, 1 sertraline) showed that SSRIs did not increase abstinence at ≥6 months (table).

**CONCLUSIONS**

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

Hughes et al live up to the Cochrane Collaboration’s reputation in this review, which shows benefit for 2 antidepressants (bupropion and nortriptyline) for long term abstinence in smoking cessation. This supports the US Public Health Service Guideline “Treating Tobacco Use and Dependence,” which gives a clear recommendation that all patients attempting to quit should be encouraged to use effective pharmacotherapies.

While it is encouraging to learn of effective interventions, one aspect of this type of research may go unnoticed, which is the level of behavioural support that occurs. Typically, both experimental and control subjects receive counselling, but how much are they talking about? For example, in one high quality study included in the meta-analysis, all patients received individual counselling weekly for the first 7 weeks and at weeks 6, 9 and 12, with telephone counselling at the fourth and fifth months. This could mean as much as 2 hours of individual counselling! Compare this with the level of behavioural support given in a busy clinical practice, which could be, “Here is your prescription, see you in 6 months, good luck.” If one wants to replicate the results of research in clinical practice, then one should try to replicate the methods under which the original research was conducted. Many factors may account for relapse, but when patients claim that “these medications don’t work,” physicians should inquire whether they were given with the appropriate amount of behavioural support.

Clearly, all smokers should be offered effective pharmacological assistance with quitting. This currently means 2 antidepressants (bupropion and nortriptyline) along with nicotine replacement therapy, for which there is overwhelming evidence of effectiveness. However, physicians also need to remember to include the appropriate amount of psychosocial and behavioural support, which gives our patients the best chance to achieve long term abstinence.

**Antidepressants for increasing smoking cessation rates at ≥6 months**

<table>
<thead>
<tr>
<th>Comparisons</th>
<th>Number of RCTs</th>
<th>Weighted event rates</th>
<th>RBI (95% CI)</th>
<th>NNT (CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Nortriptyline v placebo</td>
<td>5†</td>
<td>19% v 7.6%</td>
<td>144% (66 to 257)</td>
<td>10 (7 to 15)</td>
</tr>
<tr>
<td>Moclobemide v placebo</td>
<td>1</td>
<td>25% v 16%</td>
<td>57% (31 to 263)</td>
<td>Not significant</td>
</tr>
<tr>
<td>Bupropion v placebo</td>
<td>16</td>
<td>18% v 10%</td>
<td>73% (52 to 102)</td>
<td>13 (10 to 17)</td>
</tr>
<tr>
<td>Bupropion v NRT</td>
<td>1</td>
<td>18% v 9.8%</td>
<td>88% (19 to 197)</td>
<td>12 (7 to 41)</td>
</tr>
<tr>
<td>Venlafaxine v placebo</td>
<td>1</td>
<td>25% v 20%</td>
<td>25% (33 to 134)</td>
<td>Not significant</td>
</tr>
<tr>
<td>Bupropion v nortriptyline</td>
<td>1</td>
<td>16% v 9.6%</td>
<td>71% (26 to 303)</td>
<td>Not significant</td>
</tr>
</tbody>
</table>

**RBR (CI) | NNH**

| Bupropion v NRT | 1 | 19% v 24% | 20% (–29 to 51) | Not significant |
| SSRIs v placebo | 4 | 15% v 15% | 3% (–26 to 25) | Not significant |

*NRT = nicotine replacement therapy; RBR = relative benefit reduction; RCTs = randomised controlled trials; SSRIs = selective serotonin reuptake inhibitors.*

Other abbreviations defined in glossary; weighted event rates, RBI, NNT, RBR, NNH, and CI calculated from data in article.

†In 1 RCT, both groups also received nicotine replacement therapy.

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For example, Charles J Bentz MD, FACP
St Vincent Hospital and Medical Center
Portland, Oregon, USA

1 Fiore MC. Treating tobacco use and dependence: an introduction to the US Public Health Service Guideline '' which gives a clear recommendation that all patients attempting to quit should be encouraged to use effective pharmacotherapies.