Can nicotine receptor partial agonists, including cytisine and varenicline, help people to stop smoking?

Background

Nicotine receptor partial agonists aim to reduce the withdrawal symptoms people feel when they stop smoking and the pleasure people usually experience when they smoke. The most widely-available treatment in this drug type is varenicline, which is available world-wide as an aid for quitting smoking. Cytisine is a similar medication, but is only available in Central and Eastern European countries and through internet sales.

Study characteristics

We found 39 studies of varenicline compared to placebo, bupropion or nicotine patches. We also found 4 trials of cytisine, 1 of which compared it to nicotine replacement therapy. We include 1 trial of dianicline, which is no longer in development, and so not available to use. To be included, trials had to report quit rates at least 6 months from the start of treatment. We preferred the strictest available definition of quitting, and results which had been biochemically confirmed by testing blood or bodily fluids. We conducted full searches up to May 2015, although we have also included several key trials published after that date.

Key results

We found 27 trials with 12,625 people investigating varenicline at standard dose, which more than doubled the chances of quitting compared with placebo. Low-dose varenicline (4 trials, 1266 people) roughly doubled the chances of quitting, and reduced the number and severity of side effects. The number of people stopping smoking with varenicline was higher than with bupropion (5 trials, 5877 people) or with NRT (8 trials, 6264 people). Varenicline delivers one extra successful quitter for every 11 people treated, compared with smokers trying to quit without varenicline.

The most common side effect of varenicline is nausea, but this is mostly at mild or moderate levels and usually clears over time. People taking varenicline appear to have about a 25% increased chance of a serious adverse event, although these include many unrelated to treatment. Also, more people were lost from the control groups than from the varenicline groups by the end of the trials, which may mean that the event counts in the control groups is lower than it should be. After varenicline became available to use, there were concerns that it could be linked with an increase in depressed mood, agitation, or suicidal thinking and behaviour. However, the
latest evidence does not support a link between varenicline and these disorders, although people with past or current psychiatric illness may be at slightly higher risk. There have also been concerns that varenicline may slightly increase heart and circulatory problems in people already at increased risk of these illnesses. The evidence is currently unclear whether or not they are caused or made worse by varenicline, but we should have clearer answers to these questions when a further study is published later in 2016.

Quality of the evidence

Varenicline studies were generally of high quality, providing evidence we consider reliable and robust. We rate the quality of the evidence comparing varenicline with NRT as moderate quality (reasonably confident of the stability), since in some of them the participants knew which treatment they were receiving (i.e. non-blinded trials). Evidence from the cytisine trials is judged low quality (limited confidence), as there are only 2 trials, with few participants.

A forest plot illustrating the effect of standard dose varenicline versus placebo on quitting smoking at longest follow-up (≥ 6 months)

Citation:

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