Published in final edited form as:

Evid Based Med. 2014 June ; 19(3): 92. doi:10.1136/eb-2013-101619.

Study suggests varenicline safe and effective among adults with stable depression

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Context

Varenicline is one of our most effective smoking cessation pharmacotherapies.[1] However, post marketing reports of neuropsychiatric adverse events led the US Food and Drug Administration to issue a warning of potential increased risk of depression, suicidality, agitation and hostility (http://www.fda.gov/NewsEvents/Newsroom/PressAnnouncements/ucm170100.htm). These reports usually lack the medical history and circumstantial details required for proper adjudication. Moreover, because patients with psychiatric disorders were excluded from pivotal varenicline trials and because changes in negative affect are expected during nicotine withdrawal it was difficult to gauge the risk in this potentially vulnerable group.

Methods

In total, 525 smokers with stably treated current or past major depression were randomized to varenicline or placebo for 12 weeks. Participants included smokers receiving antidepressants (72%) and/or those successfully treated in the last 2 years. Over one-third of the participants reported lifetime suicidal ideation/behavior. The study excluded those with current or past psychotic, bipolar or severe personality disorders or current suicidal or homicidal risk.

Findings

Continuous abstinence was higher for varenicline vs placebo (OR=3.35, 95% CI 2.16 to 5.21) and both groups experienced a significant decline in depression and anxiety. No differences were observed in psychiatric adverse events, including anxiety and mood disorders, hostility/aggression or suicidal ideation/behavior (the latter, 6% in the varenicline and 7.5% in the placebo group).

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Competing interests

PMC is a site principal investigator and MK-H a co-investigator on a clinical trial sponsored by Pfizer. They have also received grants and non-financial support from Pfizer, including medication for a National Institutes of Health (NIH)-funded trial.

Commentary

This study is the first to directly evaluate the safety and efficacy of varenicline among depressed and recently treated smokers. Although the varenicline cessation rates were somewhat lower than those observed in pivotal trials,[2] the OR is similar and still favorable. The study provides the strongest evidence to date that smokers with past and current depression treated with varenicline can successfully quit smoking; and that the overall risk of neuropsychiatric side effects is low and not increased by varenicline. A major strength of this study is the use of repeated standardized psychiatric assessments, which revealed an overall decline in anxiety and depression and no change in other psychiatric symptoms, as opposed to an exacerbation, which might have otherwise been expected. These results are consistent with others that failed to show an enhanced risk of neuropsychiatric events with varenicline in psychiatric[3] and non-psychiatric patients,[4] including large observational studies investigating suicidality[5] and psychiatric hospitaisations.[6] Taken together, these results are less ominous than those emerging from the post marketing reports, and importantly, provide the clinical community with an empirical basis on which to base treatment decisions. The study did not include patients with untreated or unstable depression or those with other psychiatric disorders and most patients had depression scores in the mild range. Hence the findings may not generalize to those with more serious psychiatric disturbances, although previous studies in schizophrenia produced similar results.[3] Suicidal ideation was low (6.0–7.5%) and did not differ across the groups. A suicide attempt is extremely rare in this and other studies making it difficult to completely evaluate drug relatedness, although large observational studies have not found a signal-relating varenicline to suicidal behaviour.[5, 6] However, there is a context for understanding suicidality in relation to smoking: nicotine dependence has the third highest population attributable fraction for suicide attempts of any psychiatric diagnosis after major depression and borderline personality,[7] and is associated with suicide risk in patients seeking treatment independent of having a psychiatric disorder.[8]

This study adds to a body of empirical evidence suggesting that varenicline is a safe and effective medication for smoking cessation in patients without and with psychiatric disorders. The risk of neuropsychiatric adverse events among these groups may be no more than expected among smokers attempting to quit; and for some, symptoms of depression and anxiety during cessation may be attenuated by varenicline.[4] In contrast, the risks of continued smoking for cardiovascular disease, cancer and other chronic diseases are well established. Continued research on smoking cessation among those with psychiatric disorders is highly important as such individuals have a disproportionately high smoking prevalence.

References

1. Cahill K, Stead LF, Lancaster T. Nicotine receptor partial agonists for smoking cessation. Cochrane Database Syst Rev 2012;(4):CD006103.
2. Jorenby DE, Hays JT, Rigotti NA, et al. Varenicline Phase 3 Study Group. Efficacy of varenicline, an alpha4beta2 nicotinic acetylcholine receptor partial agonist, vs placebo or sustained-release bupropion for smoking cessation: a randomized controlled trial. JAMA 2006;296:56–63. [PubMed: 16820547]

3. Williams JM, Anthenelli RM, Morris CD, et al. A randomized, double-blind, placebo-controlled study evaluating the safety and efficacy of varenicline for smoking cessation in patients with schizophrenia or schizoaffective disorder. J Clin Psychiatry 2012;73:654–60. [PubMed: 22697191]

4. Cinciripini PM, Robinson JD, Karam-Hage M, et al. Effects of varenicline and bupropion sustained-release use plus intensive smoking cessation counseling on prolonged abstinence from smoking and on depression, negative affect, and other symptoms of nicotine withdrawal. JAMA Psychiatry 2013;70:522–33. [PubMed: 23536105]

5. Gunnell D, Irvine D, Wise L, et al. Varenicline and suicidal behaviour: a cohort study based on data from the General Practice Research Database. BMJ 2009;339:b3805. [PubMed: 19797344]

6. Meyer TE, Taylor LG, Xie S, et al. Neuropsychiatric events in varenicline and nicotine replacement patch users in the Military Health System. Addiction 2013;108:203–10. [PubMed: 22812921]

7. Yaworski D, Robinson J, Sareen J, et al. The relation between nicotine dependence and suicide attempts in the general population. Can J Psychiatry 2011;56:161–70. [PubMed: 21443823]

8. Bohnert KM, Ilgen MA, McCarthy JF, et al. Tobacco use disorder and the risk of suicide mortality. Addiction 2014;109:155–62. [PubMed: 24134689]