11-2009

Smoking Cessation Agents and Suicide

Jill E. Lavigne
St. John Fisher College, jlavigne@sjfc.edu

Publication Information

Lavigne, Jill E. (2009). "Smoking Cessation Agents and Suicide." *British Medical Journal* 339.

Smoking Cessation Agents and Suicide

Abstract
The risk is uncertain, so patients should make an informed decision.

Disciplines
Pharmacy and Pharmaceutical Sciences

BMJ
Issue: Volume 339, 7 November 2009, p b4360

Publication Type: [Editorials]
DOI: 10.1136/bmj.b4360
ISSN: 0959-8138
Accession: 00002591-200911070-00058

[Editorials]

Smoking cessation agents and suicide

Lavigne, Jill E[1,2,a]

Author Information

[1]Wegmans School of Pharmacy, St John Fisher College, Rochester, New York, NY 14618, USA

[2]Department of Veterans Affairs, Canandaigua VA Medical Center, Veterans Integrated Service Network 2, Center of Excellence, Canandaigua, New York, USA

[a]associate professor

jlavigne@sjfc.edu

Competing interests: None declared. This work reflects the views of the author and does not represent the position of the US Department of Veterans Affairs or St John Fisher College.

Provenance and peer review: Commissioned; not externally peer reviewed.

Cite this as: *BMJ* 2009;339:b4360

Research, doi:10.1136/bmj.b3805

ABSTRACT

The risk is uncertain, so patients should make an informed decision

Success in giving up smoking can be improved through social support, problem solving or skills training, and various drugs. A combination of drugs and other treatments is most effective.1 Drugs include nicotine replacement products, varenicline (Champix), and bupropion (Zyban and generics). Varenicline and bupropion inhibit the craving to smoke through unknown mechanisms. Both drugs influence the dopamine system, which regulates cognition, mood, and behaviour.2 Both varenicline and bupropion have been associated with “changes in behaviour, agitation, depressed mood, suicidal ideation, and attempted and completed suicide” in patients who had no psychiatric history and were not taking psychotropics.3 4 Nicotine replacement products have no such known associations.3 In the linked study (doi:10.1136/bmj.b3805), Gunnell and colleagues report the first retrospective cohort study to examine suicidal thoughts and behaviours after exposure to smoking cessation products.5

In the United States, changes to labelling of varenicline have been based on biological plausibility and voluntary spontaneous reports, which represent only a small fraction of all adverse drug reactions.6 Between May 2006 and November 2007, 37 suicides and 127 cases of suicidal ideation were reported in people taking varenicline.3 The Food and Drug Administration (FDA) plans to pay “more specific attention” to psychiatric side effects in clinical trials of smoking cessation agents in the future.2

Gunnell and colleagues assessed 80 660 men and women aged 18-95 who were prescribed a new course of a smoking cessation product between 2006 and 2008. They found no association between varenicline or bupropion and fatal or non-fatal self harm.5 Failure to find such evidence or failure to attain statistical significance is not the same, however, as finding evidence that supports the null hypothesis over competing hypotheses.7 The authors note multiple sources of potential confounding. In addition, FDA analyses of varenicline noted adverse effects within the first two weeks of exposure.3 Patients experiencing severe adverse events may have discontinued the prescription before it was finished, yet the authors' analyses assume an exposure equal to the full prescription and attributed the following three months of outcomes to that exposure.

Given the limitations of these data, clinicians should remain cautious when prescribing varenicline and bupropion for smoking cessation. The box summarises current understanding on this topic.

Current knowledge on products used for smoking cessation

* Nicotine replacement products may be useful as a "first line" approach for smoking cessation

* Consistent with the varenicline label, patients should strive to quit "cold turkey" on a specified date to minimise exposure

* Before prescribing or refilling a prescription for varenicline or bupropion, a psychiatric history and suicide risk assessment using the Beck scale for suicide ideation may be useful. Current morbidity or distress may suggest use of cessation counselling and postponement of drugs other than nicotine replacement products

* Varenicline is labelled for use in conjunction with counselling, which may also provide an opportunity to screen for suicidal thoughts or behaviours

* Psychiatric morbidity that emerges during treatment should be referred to a mental health provider

* Any serious adverse effects should be reported to the Medicines and Healthcare Products Regulatory Agency in the UK or the FDA in the US

Future research should consider the effectiveness of a variety of nicotine replacement products in combination (for example, nicotine patch and nicotine gum). In the US, the Department of Veterans Affairs has tackled the paucity of safety information on the use of varenicline by developing a guidance document to help providers in the safe and appropriate use of the agent.8 The department is also conducting a retrospective cohort study of smoking cessation agents and associated mental health disorders. The diversity of outcome measures across studies will continue to challenge direct comparisons. Problems with collecting data—for example, under-reporting secondary to improper coding—are likely to persist.

Data limitations about the risk of suicide may contribute to reports of doctors disregarding these FDA warnings. In a study of black box warnings on suicide for gabapentin (used for epilepsy, chronic neuropathic pain, herpes zoster, and hot flushes), almost half of the US neurologists studied reported that the warning would not affect their practice.9 Most did not routinely assess depression, and neither did they warn patients about the potential risk of suicidal thoughts or behaviours, even when they discussed the risk of other adverse events. Yet, the drug safety literature suggests that patients would prefer therapeutic failure (to keep smoking) rather than risk therapeutic harm (suicidal ideation, self harm, or suicide).10 The potential adverse event is severe, irreversible, immediate, and involves a "dread disease," whereas other smoking cessation interventions (nicotine replacement, social support, problem solving, or skills counselling) are effective and carry no known risk of such side effects. Finally, patients cannot report suicide related adverse events or make a treatment preference if doctors do not fully inform them about the risks, uncertain though they may be.

1 US Department of Health and Human Services Public Health Service. Treating tobacco abuse and dependence: quick reference guide for clinicians. 2008 Update. www.ahrq.gov/clinic/tobacco/tobaqrg.pdf. [Context Link]

2 Kuehn BM. Studies linking smoking cessation drug with suicide risk spark concerns. *JAMA* 2009;301:1007-8. **Ovid Full Text** | **Bibliographic Links** | [Context Link]

3 US Food and Drug Administration. Postmarket reviews: the smoking cessation aids varenicline and buproprion: Suicidal ideation and behavior. *Drug Safety Newsletter* 2009;2:1-4. www.fda.gov/downloads/Drugs/DrugSafety/DrugSafetyNewsletter/ucm107318.pdf. [Context Link]

4 Hughes JR, Stead LF, Lancaster T. Antidepressants for smoking cessation. *Cochrane Database Syst Rev* 2009;(3):CD000031. **Get It @ Fisher** | [Context Link]

5 Gunnell D, Irvine D, Wise L, Davies C, Martin RM. Varenicline and suicidal behaviour: a cohort study based on data from the General Practice Research Database. *BMJ* 2009;339:b3805. **Ovid Full Text** | **Bibliographic Links** | [Context Link]

6 Institute of Medicine. The future of drug safety. National Academies Press, 2007. [Context Link]

7 Rothman KJ, Greendland S, Lash TL. Precision and statistics in modern epidemiologic studies. Modern Epidemiology. 3rd ed. Lippincott Williams, 2008:128-47. [Context Link]

8 Pharmacy Benefits Management-Medical Advisory Panel. Varenicline criteria for prescribing. Pharmacy Benefits Management Services, Veterans Health Administration, Department of Veterans Affairs, 2008. www.pbm.va.gov/default.aspx. [Context Link]

9 Shneker BF, Cios JS, Elliott JO. Suicidality, depression screening, and anti-epileptic drugs: reaction to the FDA alert. *Neurology* 2009;72:987-91. [Context Link]

10 Strom BL. When should we perform pharmacoepidemiology studies? Pharmacoepidemiology. 4th ed. John Wiley & Sons, 2005:59-66. [Context Link]