

Does bupropion exacerbate anxiety?

Courtney Nemeth Wiseman, MD, MPH, and Jessica L. Gören, PharmD, BCPP

For many clinicians, bupropion is the “go-to” medication for treating depressed patients who smoke, have concerns about sexual dysfunction side effects, and/or worry about weight gain. Bupropion is FDA-approved for preventing seasonal major depressive episodes in patients with seasonal affective disorder and is indicated as a smoking cessation aid.

“Anxious depression”—defined as depression with high levels of anxiety—is associated with poorer outcomes than “non-anxious” depression.¹ Prescribing medications for these patients can be challenging. Some clinicians believe that bupropion exacerbates anxiety and should not be used to treat patients who experience both anxiety and depression.

Reports from our patients and our cumulative clinical experience are key factors in developing expertise in selecting appropriate medications. When informing our patients about what to expect from medications, however, it can be useful to combine anecdotal evidence with knowledge of the facts or lack thereof. Are there data to support or contradict the idea that bupropion can cause anxiety while treating depression?

What the research shows

The drug manufacturer reports a “substantial proportion of patients treated with Wellbutrin experience some degree of increased restlessness, agitation, anxiety, and insomnia, especially shortly after initiation of treatment.”²

In 2001, Rush et al³ published the results of a 16-week study (n = 248) assessing pretreatment anxiety levels and response to sertraline or bupropion. The authors con-

cluded that anxious and depressed patients who received sertraline didn’t experience a superior anxiolytic or antidepressant response compared with bupropion.³ The same authors came to similar conclusions in a retrospective analysis of a pair of 8-week randomized, controlled, double-blind trials of selective serotonin reuptake inhibitors (SSRIs) and bupropion.⁴

In 2001, Nieuwstraten et al⁵ compared bupropion with SSRIs for treating depression by reviewing several randomized, double-blind, controlled trials. The relative risk of developing “anxiety/agitation” was 1.32 (95% confidence interval, 0.85 to 2.04), which was not statistically significant.

In a 2008 meta-analysis, Papakostas et al⁶ pooled individual patient data from 10 randomized, double-blind, placebo-controlled trials. Their aim was to compare the efficacy of bupropion to SSRIs in treating “anxious depression.” They found no difference in timing or degree of improvement in anxiety symptoms between groups based on Hamilton Anxiety Scale or Hamilton Depression Rating Scale—Anxiety-Somatization (HDRS-AS) scores. The authors recommended that antidepressant choice should not be based on concerns about worsening anxiety symptoms in depressed patients.⁶

Another meta-analysis by Papakostas et al⁷ of the same 10 randomized, double-blind, placebo-controlled trials suggested SSRIs may confer an advantage over bupropion in treating a subset of patients with “anxious depression,” which they defined as a HDRS-AS score ≥ 7 . The authors noted the advantage was statistically significant, although “modest.”

Dr. Wiseman is Instructor, Clinical, Contributing Services Faculty, Department of Psychiatry and Behavioral Sciences, Feinberg School of Medicine, Northwestern University, Chicago, IL. Dr. Gören is Associate Professor, Department of Pharmacy Practice, University of Rhode Island, Kingston, RI; Senior Clinical Pharmacist Specialist, Department of Pharmacy, Cambridge Health Alliance; and Instructor in Psychiatry, Harvard Medical School, Boston, MA.

Disclosure

The authors report no financial relationship with any company whose products are mentioned in this article or with manufacturers of competing products.

Some smaller studies have suggested that bupropion does not increase anxiety

Related Resource

- American Psychiatric Association. Mixed anxiety-depressive disorder. Diagnostic and statistical manual of mental disorders, 4th ed, text rev. Washington, DC: American Psychiatric Association; 2000:780-781.

Drug Brand Names

Bupropion • Wellbutrin, Zyban	Escitalopram • Lexapro Sertraline • Zoloft
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Other smaller studies suggest that bupropion does not increase anxiety.^{8,9} A pilot study (N = 24, no placebo control) concluded that bupropion XL was comparable to escitalopram in treating anxiety in outpatients with generalized anxiety disorder.⁸

Because designing and executing drug trials can be expensive, it is not surprising that most of the evidence cited above derives from pharmaceutical company-sponsored or industry-affiliated work. As such, we should evaluate available evidence within the context of what we hear from and observe in our patients.

Our opinion

When assessing patients with depression and anxiety, we must carefully evaluate symptoms to distinguish between depression with associated anxiety symptoms and depression with a comorbid anxiety disorder.

If a patient suffers from depression with associated anxiety symptoms (“anxious depression”), keep in mind that although some data demonstrate a superior response to SSRIs, other studies show no difference in effect. Some research—albeit smaller, less compelling studies—suggests that bupropion may decrease anxiety.

If your patient suffers from comorbid depression and an anxiety disorder, bupropion would not be a first-line choice because it is not FDA-approved to treat anxiety disorders. Although it is possible that anxiety/agitation could result from bupropion use, there is not sufficient data to support its reputation as “anxiogenic.”

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