Antidepressant Tx for anxiety disorders: How long?

This systematic review/meta-analysis provides some long-awaited evidence regarding the length of time to treat to minimize the risk of relapse.

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PRACTICE CHANGER

Keep patients on antidepressant therapy for anxiety disorders for a year or longer before considering a taper.

STRENGTH OF RECOMMENDATION

A: Based on a systematic review/meta-analysis of several good quality randomized controlled trials.[1]

Batelaan NM, Bosman RC, Muntingh A, et al. Risk of relapse after antidepressant discontinuation in anxiety disorders, obsessive-compulsive disorder, and post-traumatic stress disorder: systematic review and meta-analysis of relapse prevention trials. *BMJ*. 2017;358:j3927. Erratum in: *BMJ*. 2017;358:j4461.

ILLUSTRATIVE CASE

A 42-year-old woman with generalized anxiety disorder and panic attacks has been treated with sertraline 100 mg/d for the past 8 months. She has also engaged in cognitive behavioral therapy (CBT) for 6 months. Her Generalized Anxiety Disorder-7 score has decreased from 19 prior to treatment to 5 at present. Now she would like to stop her antidepressant medication because she feels better. Would you recommend that she discontinue her medication at this point?

Anxiety disorders are common, often chronic, and can cause significant morbidity and impairment.[2,3] First-line treatments for anxiety disorders include CBT and antidepressants, particularly selective serotonin reuptake inhibitors and serotonin-norepinephrine reuptake inhibitors.[4-6]

There is limited evidence regarding duration of antidepressant therapy for anxiety disorders. Previous studies have shown a high risk of relapse after discontinuation of antidepressants.[6] A review of current practice patterns regarding pharmacologic treatment of depression and anxiety indicates an uptick in longer term antidepressant use for up to 2 years.[7] However, long-term studies to guide treatment decisions are lacking.

STUDY SUMMARY

Clear benefit of continuing treatment up to 1 year

This systematic review and meta-analysis evaluated studies that looked at relapse rates and time to relapse in patients treated for anxiety disorders.[1] The authors used PubMed, Cochrane, and Embase to identify studies involving patients treated for a variety of disorders, including generalized anxiety disorder (GAD), posttraumatic stress disorder (PTSD), panic disorder (PD), obsessive-compulsive disorder (OCD), and social phobia. Eligible studies enrolled patients with anxiety disorders who had a positive response to an antidepressant and then randomized them in a double-blind fashion to either discontinuation of antidepressants and starting placebo (stopping group) or continuation of antidepressants (continuation group) for a duration of 8 to 52 weeks. The primary outcomes were relapse rate and time to relapse.

Twenty-eight studies met the inclusion criteria for the meta-analysis, with a total of 5233 patients (2625 patients in the antidepressant group and 2608 patients in the placebo group). A breakdown of the trials by indiication included OCD (7), PD (6), GAD (6),

social phobia (5), and PTSD (4). The authors graded the overall risk of bias to be low but noted that attrition bias was present in most studies.

Results. Relapse was more likely in the stopping group (odds ratio [OR] = 3.11; 95% confidence interval [CI], 2.48-3.89; n = 28 studies). Heterogeneity for relapse rate was low (I^2 = 8.07%). Subgroup analyses by type of antidepressant, mode of discontinuation, and exclusion of patient comorbidities yielded similar results. Relapse prevalence was 16.4% in the antidepressant group and 36.4% in the stopping group. Additionally, time to relapse was shorter when antidepressants were discontinued (hazard ratio [HR] = 3.63; 95% CI, 2.58-5.10; n = 11 studies). Again, the heterogeneity for relapse rate was low (I^2 = 0%). The original publications did not consistently report medication tolerability or withdrawal symptoms, preventing analysis of these. Dropout rates were higher in the stopping group (OR = 1.31; 95% CI, 1.06-1.63; n = 27 studies).

This study provides evidence that stopping antidepressant treatment for anxiety disorders before 1 year increases the risk of relapse.

WHAT'S NEW

No more guessing about how long to treat

Previously, there was limited evidence to guide decisions about the duration of antidepressant treatment for anxiety disorders. This study provides evidence that stopping antidepressant treatment before 1 year increases the risk of relapse.

CAVEATS

Potential bias … bias … and more bias

While the authors used standard and appropriate methodologies for this type of study, some significant threats to validity remained. All but 2 studies in the analysis were industry funded. Publication bias is another potential issue, even though the authors identified and included 6 unpublished studies, 4 of which had negative results.

Additionally, the authors graded 11 of 28 trials as having a high likelihood of selective reporting bias, meaning that important portions of the original studies' results may not have been published. Most studies were at high risk for attrition bias, resulting in loss of information when patients dropped out of the study. While this happened more often in the stopping groups, it is still possible that there are unidentified harms or unexpected outcomes in the medication groups.

While PTSD and OCD are no longer considered anxiety disorders, subgroup analyses found no difference in relapse rates between these diagnoses and the others included in the studies. Finally, treatment duration longer than 52 weeks has not been studied, so the optimal treatment duration is unknown.

CHALLENGES TO IMPLEMENTATION

Patients may resist continuing treatment once symptoms abate

Some patients may want to discontinue antidepressant treatment if their anxiety symptoms improve prior to 1 year. It may be difficult to convince them that continuing treatment will prevent relapse of their condition. Providing patients with information about the increased relapse rate with stopping medication early (with an estimated number needed to treat of 5) may help patients make a more informed decision. JFP

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