The Role of Benzodiazepines in Treating Social Anxiety Disorder

To the Editor: The article by Pollack et al. (1) in the January issue of the *Journal* is a welcome demonstration of the benefits of using benzodiazepines in the treatment of social anxiety disorder. However, the lack of a clonazepam monotherapy arm in the study demonstrates how entrenched, in the absence of evidence, the assumption has become that benzodiazepines should not be used as first-line therapy for anxiety disorders (2). Despite evidence that benzodiazepines alone may be effective for social anxiety disorder (and other anxiety disorders) (3), misunderstanding about their potential for abuse and dependency is now a common barrier to appropriate prescription of these highly effective medications. While they are not for everyone, the systematic literature is virtually unanimous in finding that benzodiazepines have a low potential for abuse in patients who are not currently abusing other substances (4), even if the patients have a past history of substance abuse (5). In addition to potentially greater efficacy for treating anxiety disorders, benzodiazepines have the advantages of immediate onset of action, fewer side effects compared with antidepressants, and a high therapeutic index. Long-term controlled trials of benzodiazepine monotherapy, including monitoring of efficacy, tolerability, and abuse in the treatment of social and other anxiety disorders, may be difficult to fund, but would be a great service to patients who suffer from these often undertreated conditions.

References

1. Pollack MH, Van Ameringen M, Simon NM, Worthington JW, Hoge EA, Keshaviah A, Stein MB: A double-blind randomized controlled trial of augmentation and switch strategies for refractory social anxiety disorder. Am J Psychiatry 2014; 171:44–53
2. Berney P, Halperin D, Tango R, Daeniker-Dayer I, Schulz P: A major change of prescribing pattern in absence of adequate evidence: benzodiazepines versus newer antidepressants in anxiety disorders. Psychopharmacol Bull 2008; 41:39–47
3. Davidson JR, Potts N, Richichi E, Krishnan R, Ford SM, Smith R, Wilson WH: Treatment of social phobia with clonazepam and placebo. J Clin Psychopharmacol 1993; 13:423–428
4. Woods JH, Winger G: Current benzodiazepine issues. Psychopharmacology (Berl) 1995; 118:107–115, discussion 118, 120–121
5. Posternak MA, Mueller TI: Assessing the risks and benefits of benzodiazepines for anxiety disorders in patients with a history of substance abuse or dependence. Am J Addict 2001; 10: 48–68

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Response to Silberman

To the Editor: We appreciate Dr. Silberman's characterization of our article as a welcome demonstration of the benefits of using benzodiazepines for the treatment of social anxiety disorder, but would like to address a number of issues raised by his letter. The study was designed to examine potential "next-step" pharmacological strategies for patients remaining symptomatic despite treatment with a selective serotonin reuptake inhibitor (SSRI)—it was thus intended as a study of treatment-resistant patients and not as one examining the question of the comparative benefits of potential first-line interventions such as SSRIs and benzodiazepines for social anxiety or other anxiety disorders.

We do, however, agree that serious reconsideration of the role of benzodiazepines for the treatment of anxiety disorders is warranted, particularly in light of evidence that they can be effective and well tolerated, and continue to be widely prescribed (1). A recent meta-analysis of studies examining the relative efficacy and tolerability of benzodiazepines and antidepressants for the treatment of anxiety disorders (2) did not demonstrate a significant efficacy advantage for either class of agents, although benzodiazepines tended to be better tolerated. However, the vast majority of studies examined in this analysis included the use of the older tricyclic agents rather than the now more commonly used SSRIs. But important questions about the use of benzodiazepines in practice remain to be conclusively addressed. Although anxious patients with remote histories of substance abuse or mild depressive symptoms can apparently be given benzodiazepines safely, it is also clear that these agents can be ineffective for or worsen depression (if used as monotherapy), or can be abused by patients with a substance abuse diathesis. Furthermore, some patients experience significant difficulties discontinuing these agents, and there is some evidence, although inconclusive, that they may hamper the efficacy of cognitive-behavioral therapy in some patients.

Taking into consideration the potential benefits of benzodiazepines and antidepressants, but recognizing the important factors that may influence their application in clinical practice, we too believe that further study in clinically relevant populations, including the development of practice guidelines for responsible prescription of benzodiazepines (3), would be of service to our patients and to the field.

References

1. Vasile RG, Bruce SE, Goisman RM, Pagano M, Keller MB: Results of a naturalistic longitudinal study of benzodiazepine and SSRI use in the treatment of generalized anxiety disorder and social phobia. Depress Anxiety 2005; 22:59–67
2. Offidani E, Guidi J, Tomba E, Fava GA: Efficacy and tolerability of benzodiazepines versus antidepressants in anxiety disorders: a systematic review and meta-analysis. Psychother Psychosom 2013; 82:355–362
3. el-Guebaly N, Sareen J, Stein MB: Are there guidelines for the responsible prescription of benzodiazepines? Can J Psychiatry 2010; 55:709–714

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Electroconvulsive Therapy is a Standard Treatment; Ketamine is Not (Yet)

To The Editor: Alan Schatzberg's commentary in the March issue, "A Word to the Wise About Ketamine" (1), urges caution in the clinical use of ketamine pending further research and data collection. We agree with this position and would like to share our clinical experience with seriously depressed patients who have received ketamine infusions prior to electroconvulsive therapy (ECT) referral. In the last year, we have seen at least half a dozen patients who, when they presented for ECT consultation, gave histories of having had either single or repeated ketamine infusions at a private anesthesiologist's office in New York City. These patients had either no, or very transient, antidepressant benefit from the ketamine or unpleasant adverse effects (mainly dissociative); they were subsequently referred by their psychiatrists for consideration of ECT. Most of these patients were profoundly depressed, and some were suicidal. If a ketamine challenge is to become a standard step in the treatment algorithm for treatment-resistant depression, the risks of not just the ketamine itself, but the delay in definitive treatment, must be taken into account.

Seriously depressed patients who have failed to respond to one or more antidepressant medication trials should be referred for ECT consultation, sooner rather than later, to ensure optimal outcomes. Suicide risk in this population is elevated, as is the potential for ongoing medical morbidity, not to mention the continued suffering from the depressive episode itself. A recent study (2) comparing three ketamine infusions with three ECT treatments in 1 week touted ketamine as a superior treatment and received considerable media attention (3). A reasonable interpretation of that research is that it replicated the finding of a signal of early antidepressant response with ketamine. However, ketamine remains completely unproven as a definitive treatment for a major depressive episode. Seriously ill psychiatric patients are often desperate for dramatic cures; their health care providers, acknowledging that our current treatments are often lacking, are also eager for the newest breakthroughs. Such desperation and enthusiasm should not cloud our clinical judgment; proven, evidence-based treatments, including ECT for seriously depressed patients, should be offered before unproven, experimental approaches, no matter how "in vogue" those approaches may be.

References

1. Schatzberg AF: A word to the wise about ketamine. Am J Psychiatry 2014; 171:262–264
2. Ghasemi M, Kazemi MH, Yoosefi A, Ghasemi A, Paragomi P, Amini H, Afzali MH: Rapid antidepressant effects of repeated doses of ketamine compared with electroconvulsive therapy in hospitalized patients with major depressive disorder. Psychiatry Res 2014; 215:355–361
3. Arehart-Treichel J: Ketamine outperforms ECT in depression study. Psychiatr News, Jan 2014, p 17

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Community Treatment for Violence in Released Inmates With Schizophrenia

To the Editor: The recent article by Keers et al. (1) on prisoners released to the community in England and Wales provides important research on the relationships between prisoners with serious mental illnesses, persecutory delusions, and violent incidents in the postrelease period. However, one of the conclusions reached by the authors does not seem supported by their data.

In their abstract, the authors conclude that "maintaining psychiatric treatment after release can substantially reduce violent recidivism among prisoners with schizophrenia." But the rates given in Table 2 of the article for violent incidents, during the period of study, are nearly identical for inmates with schizophrenia who received treatment during incarceration and then either stopped or continued treatment after release (27.3% and 24.5%, respectively). Both rates are significantly lower than for prisoners who received no treatment (50%).

A conclusion, based on this data, is that community follow-up in the postrelease period, which typically includes continuation of pharmacotherapy, counseling, and case management, has little effect in reducing violence for inmates with schizophrenia—provided they received treatment in prison. This is contrary to commonly held beliefs (2, 3) and merited some discussion.

A message to be taken from this study, which the authors did not comment upon, is that correctional mental health professionals have reason to be hopeful that the treatment they provide to their patients with schizophrenia during incarceration can reduce violent incidents after prison, even when treatment does not continue.

References

1. Keers R, Ullrich S, Destavola BL, Coid JW: Association of violence with emergence of persecutory delusions in untreated schizophrenia. Am J Psychiatry 2014; 171:332–339
2. Lamberti JS: Understanding and preventing criminal recidivism among adults with psychotic disorders. Psychiatr Serv 2007; 58: 773–781
3. Baillargeon J, Binswanger IA, Penn JV, Williams BA, Murray OJ: Psychiatric disorders and repeat incarcerations: the revolving prison door. Am J Psychiatry 2009; 166:103–109