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Benzodiazepines, Posttraumatic Stress Disorder, and Veterans: Good News and Why We're Not Done Yet

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The articles by Lund et al[1] and Bernardy et al[2] provide important information on posttraumatic stress disorder (PTSD), our work as psychiatrists, and the treatment choices we offer our patients.

First, data presented by Lund et al demonstrate significant change in the gender and age of combat veterans with PTSD. For gender, the percentage of female veterans with an initial PTSD diagnosis increased modestly by percentage (1.3 percentage point absolute change), but, when compared to the absolute number of veterans, the impact on veteran health care is better appreciated. Female veterans with PTSD increased from approximately 11,000 to 37,000. Since many of these female veterans served recently in Afghanistan or Iraq and thus likely are of child-bearing age, it is vital to consider the potential for benzodiazepines to cause preterm labor or low birth weight.[3,4]

The age at initial diagnosis of PTSD shifted to a younger age. This fact almost certainly occurred with the influx of veterans from the conflicts in Afghanistan and Iraq. At first glance, a decline of initial diagnosis age from 54 to 47 years is not striking, but it is important to remember that in the Veterans Affairs (VA) system, the age at diagnosis is at least 19 years to include at least some military service. The relevant age change, therefore, occurs not over the range of 0 to 54 but instead within the narrower window between ages 19 to 54. The age decline, then, was from 35 years after age 19 to only 28 years after age 19. In percentage terms, the change is 7/35, or 20%, a figure that would have corporate marketing executives scrambling to respond with updated materials, methods, and campaigns. These numbers not only reflect the present conflict but also hint at another important demographic shift within VA PTSD clinics: the existing veteran patients with PTSD will slowly begin to resemble a geropsychiatry population. Are we offering annual dementia-screening examinations for Vietnam veterans in PTSD programs, and, if the cognitive evaluation results suggest the presence of short-term memory problems, will we address the adverse cognitive effects of benzodiazepines?

Next, Lund et al demonstrate a shift away from prescribing benzodiazepines for PTSD. This shift is evident in lower doses for established patients and fewer patients with a new diagnosis of PTSD receiving benzodiazepines. We can learn about psychiatric practice within the VA from these trends. Unfortunately, Lund et al did not address whether the benzodiazepine was started by a primary care physician, other specialist (eg, neurologist), or a psychiatrist, information that would be most useful to know.

Although Lund et al did not design their study to understand the reasons for declining benzodiazepine use, this issue of the *Journal* also includes an article (Bernardy et al[2]) from the same group that analyzes VA prescribing practices for PTSD within the VA health care system. Both articles suggest that benzodiazepine use was altered in response to the 2004 VA/Department of Defense (DoD) Clinical Practice Guideline on PTSD.[5] Although the available data cannot establish a definitive link between the VA/DoD Clinical Practice Guideline and benzodiazepine prescribing patterns, it is difficult not to attribute a positive effect to the VA's in-house educational efforts focused on PTSD care in general and on mental health needs of the veterans returning from Afghanistan and Iraq. Similarly, the VA National Center for PTSD offers a variety of educational programs. Published treatment guidelines co-authored by the National Center for PTSD recommend selective serotonin reuptake inhibitor (SSRI)/serotonin-norepinephrine reuptake inhibitor (SNRI) antidepressants and generally discourage benzodiazepine prescribing.[6] One interpretation of the declining benzodiazepine use is an indication of the VA psychiatry community attempting—and succeeding—in following expert advice with respect to benzodiazepines. Support for this hypothesis can be found in Bernardy and colleagues' report of an increase in the percentage of veterans with PTSD taking an SSRI or SNRI antidepressant.

The dissuasion from benzodiazepines rightfully raises a question as to when these medications can be prescribed appropriately for the patient with PTSD. Several situations may be addressed with benzodiazepines, including short-term treatment of insomnia, adjunctive treatment of panic disorder with an SSRI or SNRI antidepressant, or for neurologic conditions such as rapid eye movement (REM) behavior disorder or periodic limb movements in sleep. When used for any of these conditions, benzodiazepine use is best kept to the minimum required dose and duration of therapy.

Sleep complaints are prominent among patients with PTSD. Combat veterans with PTSD commonly demonstrate limb movements during sleep,[7] and REM behavior disorder has been reported in a series of combat veterans.[8] However, aside from comorbidity of these conditions with PTSD, the relationship between REM sleep disturbances and PTSD seems unresolved. With regard to nightmares, however, prazosin has been established as an effective intervention for nightmares during PTSD,[9] and one study[10] suggests it

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may be underutilized. Further acceptance of prazosin for nightmares may reduce further benzodiazepine use within this population.

Data from Bernardy et al[2] suggest the alternative explanation of trading benzodiazepines for other medications. Over the period 2005–2009, the percentage of veterans with PTSD taking prazosin increased from 4.7% to 9.1%, but the percentage of veterans taking nonbenzodiazepine hypnotics increased from 4.1% to 12.8%. Further, 10.4% of veterans with PTSD were prescribed quetiapine despite evidence for the efficacy of prazosin over quetiapine in PTSD[11] and an association of atypical antipsychotic medications with an increased rate of obstructive sleep apnea.[12]

Why, given the downsides to benzodiazepines for PTSD, are these medications prescribed at all? One important concept is the presence of possible comorbid conditions. Neither of the 2 articles includes information on psychiatric conditions (eg, panic disorder) and neurologic disorders (periodic leg movements in sleep, REM behavior disorder) that may have been treated appropriately with benzodiazepines. The most commonly prescribed benzodiazepine reported by Lund et al was clonazepam, a medication commonly recognized as useful for these 3 conditions. Thus, the benzodiazepine use attributed to PTSD may be lower than reported.

These two articles raise the difficult issue of picking the harm to be avoided when treating insomnia associated with PTSD. One harm avoidance measure might be for local hospital leaders to place formulary restrictions on short-acting, high-potency benzodiazepines. The outpatient use of alprazolam is one possible candidate for such restriction. Another possible intervention is an alternative to benzodiazepines, such as mirtazapine or trazodone. However, these 2 antidepressants bring the potential to adversely affect cognition from antihistaminic side-effects. Atypical antipsychotics for insomnia bring the possibility of weight gain and possibly the metabolic syndrome. Is it better to accept suboptimal PTSD care, suffer slow cognition, or gain weight? As a follow-on study, it would be interesting to compare benzodiazepine prescribing trends to the trends in body mass index, type II diabetes, and obstructive sleep apnea among veterans diagnosed with PTSD. If the decline in benzodiazepine use reflects greater use of evidence-based psychotherapies for PTSD, then we're winning. If, on the other hand, we have substituted atypical antipsychotics for benzodiazepines and data show an increase in obesity and its complications among those veterans who were given antipsychotic medication, then perhaps the issue of undertreated PTSD has merely changed form.

Finally, prescribing a benzodiazepine for PTSD is not without harm. When we offer a benzodiazepine to the patient with PTSD, to what extent are we treating our own discomfort with a patient who clearly is suffering with anxiety? The better course of action is to start an SSRI/SNRI antidepressant and begin either a cognitive or a behavioral therapy for PTSD. There is overwhelming evidence to support these therapies as documented in the most recent (2010) version of the VA/DoD guidelines for PTSD.[10] Does giving clonazepam to the patient with PTSD break the rule of "don't just do something—sit there!" When supervising residents, I have found one of the more difficult teaching concepts is instructing the residents on how to internalize a patient's uncomfortable affect, process it, and then return the modulated affect to the patient. This skill is an invaluable one. When our patients talk about the horrors of combat, we should avoid dispensing a benzodiazepine to treat our own anxiety. Instead, the nonjudgmental and supportive physician can comfort the patient by validating the veteran's intense emotional reaction to the horrors of combat while also endorsing a genuine hope for clinical improvement through evidence-based psychopharmacology and psychotherapy. This seemingly minor interpersonal intervention provides courage for the patient to continue with an SSRI/SNRI and return for evidence-based psychotherapy.

With regard to psychotherapy, benzodiazepines interfere with prolonged exposure therapy. Given that prolonged exposure is one of the VA's recommended interventions for PTSD, it is difficult to justify starting a benzodiazepine without a clear comorbid indication. Further, the risk of substance use disorders among veterans with PTSD argues against unnecessarily starting benzodiazepines. Accidents are another reason to avoid benzodiazepines. Nonmedical use and motor vehicle accidents may result from benzodiazepine prescribing. During the period 2004–2008, the number of emergency department visits for nonmedical benzodiazepine use increased from 143,500 to 271,700, an 89% change overall, with the lowest risk of nonmedical use in persons over 50 years of age.[13] Approximately 81,000 of these visits resulted in a hospital admission, and, notably, these emergency department visits exclude fatalities, suicide attempts, or accidental overdoses. Multiple studies demonstrate that users of benzodiazepines face an increased risk of causing a motor vehicle accident,[14] and combat veterans as a group face an elevated risk of accidental death by trauma, particularly from motor vehicle accidents.[15] Together, these safety issues provide good reason to avoid benzodiazepines in PTSD, particularly among younger combat veterans.

In my clinical practice, the psychiatrist's role is recognizing medical and neurologic comorbidity, medicating the most intense anxiety symptoms with an SSRI or SNRI antidepressant, and furthering the psychiatrist-patient relationship to engage the patient in evidence-based psychotherapy for PTSD. The value of SSRI and SNRI antidepressants in managing PTSD is well established, and prazosin is a fine adjunctive therapy for nightmares, but, to provide robust long-lasting clinical improvement, the best action is steering our patients toward the highly impressive results from cognitive processing of trauma and prolonged exposure psychotherapies.

Drug names: alprazolam (Xanax, Niravam, and others), clonazepam (Klonopin and others), mirtazapine (Remeron and others), prazosin (Minipress and others), trazodone (Oleptro and others), zolpidem (Ambien, Edluar, and others).

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