Attitudes Toward Benzodiazepines Over the Years

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Benzodiazepines have been used extensively for the treatment of anxiety and related disorders since the 1960s. Although they have been proven to be effective as first-line treatment for anxiety disorders, during the 1980s public perception and concern for abuse liability and physical dependence with long-term use gave rise to a great deal of controversy. Negative perceptions toward the use of benzodiazepines for treating anxiety not only caused severely ill patients to go untreated or undertreated but also called into question whether the illness itself was worthy of treatment. Although new pharmacologic and psychological treatments for anxiety are available, psychopharmacologists continue to endorse benzodiazepines as primary or adjunct treatment for anxiety disorders. The intent of this article is to provide a historic overview of these issues and to offer some general clinical principles to help minimize the risk of abuse and dependence with benzodiazepine use.

Overview

Benzodiazepines became widely available in the 1960s and have been prescribed to hundreds of millions of people over the past 4 decades. Benzodiazepines are effective antianxiety and hypnotic medications and have favorable side effect profiles compared with other psychotropic medications. The rapid onset with low toxicity and the desirable therapeutic actions of benzodiazepines as anxiolytics, sedatives, anticonvulsants, and muscle relaxants have led to their continued use in treating anxiety disorders today. Side effects include sedation and ataxia, but these are usually not sustained, and there are no known irreversible effects from long-term administration. Tolerance to anxiolytic effects appears rare, and the biological mechanisms of action of benzodiazepines are among the best understood of any intervention. Benzodiazepines offer symptomatic relief for some of humankind’s most prevalent and distressing conditions.

Despite the favorable aspects of benzodiazepine use, 3 issues have caused confusion and concern over the years: (1) a trivialization of anxiety disorders, which was implicit in the anti–benzodiazepine sentiment during the 1980s, (2) a concern that these agents were being overprescribed and abused, and (3) a concern for potential physical dependence and withdrawal reactions when discontinued.

Treatment Attitudes

During the 1980s, depression and psychosis were viewed as biological illnesses, while persistent anxiety was not. Not treating someone who would benefit from medication is underprescribing, and not using adequate doses (as with antidepressants) is undertreatment. A review of data from a 1979 survey of patients meeting DSM-III criteria for generalized anxiety disorder (GAD) revealed that only 27% had received a benzodiazepine in the prior year. Patients either received a benzodiazepine for anxiety or no treatment at all; of patients who met clinical criteria for treatment of anxiety and were candidates for therapy, 73% went without medication. A decade later, the situation had not improved. A 1990 review of Epidemiologic Catchment Area data indicated that the
majority of anxious patients with high levels of psychic distress had not received drug treatment.

The treatment concerns of the 1980s carried into the 1990s, although fewer patients went untreated because of newer antidepressants being used for anxiety. Nearly one third of patients in a 1989–1991 sample of adults with anxiety disorders did not receive any medication for treatment of their anxiety disorder; in a 1996 follow-up, almost one third still were not receiving medication. There was a decrease in benzodiazepine treatment and an increase in antidepressant treatment in 1996 for GAD patients who did not have comorbid depression or another anxiety disorder. These findings represented a shift in the type of medications prescribed for GAD, from exclusive benzodiazepine treatment to the combination of benzodiazepine and antidepressant treatment.

The underprescription of benzodiazepines in the 1980s was fueled by the perception that patients who sought treatment for their anxiety (particularly with benzodiazepines) were seeking a “high” or a “buzz,” which distorted the truth about the anxiolytic effects of these agents as well as the need for treatment. Implicit in the anti-benzodiazepine sentiment was a trivialization of anxiety disorders and anxious distress. The idea was that anxiety is always transient, a reflection of the human condition, and stands for or is a symptom of something else. Systematic scrutiny of anxious patients in the 1990s helped reverse some of this prejudice by confirming that patients who receive treatment are ill, have high levels of psychic distress, and generally meet criteria for anxiety or panic disorders. Since severe anxiety has been associated with a high risk of suicide,7–10 the price paid for undertreatment is quite high. The change in attitude toward anxiety disorders and the introduction of antidepressants that are effective against anxiety led to less undertreatment of these disorders, although concern about abuse liability and physical dependence remained associated with benzodiazepines.

ABUSE LIABILITY

Concern over the chronic use and potential abuse of benzodiazepines motivated a comprehensive probability-based national household survey of the medical use of psychotherapeutic medication conducted in 1979 and published in 1984.2 Findings from this study showed that long-term use (i.e., daily for ≥ 1 year) of anxiolytics was relatively rare, occurring among only 15% of all anxiolytic users, which is a rate of 1.6% of all adults between the ages of 18 and 79 years in the general population. In regard to benzodiazepines specifically, 11% of the U.S. population had used a benzodiazepine in the past year. Occasional use, defined as using the medication for 1 to 2 days at a time, was reported by 45% of the population, and two thirds reported using these agents regularly for periods less than 2 weeks. Eighty percent of those who had used benzodiazepines in the past year reported that the longest period of daily use was less than 4 months.

The authors concluded that many chronic benzodiazepine users are older, meet diagnostic criteria for anxiety disorders, and have multiple health problems.5,10 These patients are usually monitored by their physicians at regular intervals. The study did not support the stereotype of benzodiazepine users. Studies in the 1990s found that, except in patients with preexisting chemical dependency, abuse of benzodiazepines is rare.15 While experts agree that benzodiazepines pose a higher risk of dependence and abuse than most potential substitutes, they pose a lower risk than older sedatives and recognized drugs of abuse.10 However, in the 1980s, in response to the perceived addictiveness of benzodiazepines, some states (New York, for example) and some countries enacted legislation (a triplicate prescription program) intended to regulate indiscriminate prescribing of benzodiazepines and quell concerns of the potential for addiction and abuse with long-term use. The New York State triplicate prescription program took effect on January 1, 1989. The initial response was large decreases in benzodiazepine prescriptions but large increases in prescriptions for older, less safe therapeutic agents such as meprobamate and methyprylon (Table 1).15 A retrospective analysis of sedative-hypnotic overdose in New York City for the years 1988 and 1989 showed that while there were fewer total benzodiazepine overdoses in 1989 compared with 1988, there was a statistically significant increase in nonbenzodiazepine sedative-hypnotic overdoses. In 1990, the American Psychiatric Association Task Force on Benzodiazepines concluded that benzodiazepines are not drugs of abuse, although benzodiazepine abuse is common among people who are actively abusing alcohol, opiates, cocaine, or sedative hypnotics.15

In fact, anxiety may be a causal risk factor for alcoholism. Anxiety disorders that can be comorbid with alcoholism include panic disorder, social phobia, obsessive-compulsive disorder, GAD, and posttraumatic stress disorder.18 Although treatment of an anxiety disorder can rarely, if ever, be expected to cure alcoholism, the identification of and treatment for the anxiety would be expected to improve the prognosis for the alcoholism or help to prevent its progression if caught early. Ciraulo et al.19 reviewed the literature on benzodiazepine use among alcoholics exposed to these drugs during detoxification who were continued on them for the treatment of anxiety and insomnia and found that prevalence of use was greater than in the general population but comparable to other groups of psychiatric patients. Because alcoholics appear susceptible to benzodiazepine abuse, physicians must endeavor to rule out chemical dependency in their patients prior to initiating treatment with benzodiazepines.

By 1999, an international group of experts recommended the use of benzodiazepines for anxiety disorders, even for long periods.11 Most experts today would de-
discontinuation.21–24 agitation, insomnia, and sensory disturbances and is wors-
tinuation syndrome is characterized by rebound anxiety, 

6 J Clin Psychiatry 2005;66 (suppl 2) serotonin reuptake inhibitors (SSRIs), which were her-

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mended to gradually taper benzodiazepines when attempt-

make intermittent, structured attempts to taper.

Studies21,25,26 in the early 1980s indicated that regular, 
long-term administration of benzodiazepines at therapeu-
tic dosage levels can produce physical dependence, lead-
ing to symptoms of withdrawal upon abrupt termination (rather than gradual taper). In addition, a 1990 compari-
son27 of the effects of abrupt discontinuation of therapeutic 
doses of short half-life versus long half-life benzodiaze-
pines revealed that discontinuation syndrome occurred 
earlier and was more severe with short half-life than with 
long half-life benzodiazepines. Hence, it is always recom-
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CONCLUSION

Twenty years ago, my predictions for the foreseeable 
future were that benzodiazepines would remain a pharmacologic maintay of the clinical management of anxiety and that new developments in understanding of the pharmacologic modification of benzodiazepine receptor effi-
cacy would yield therapeutic strategies to diminish the chief clinical concern of physical dependence and the atten-
dant possibility for some patients of discontinuation syndrome. To some extent, the initial success of bussi-

scribe anxiety disorders as recurrent or chronic disorders 
requiring treatment beyond the short term. These disorders 
are not usually cured, but rather controlled. Regular moni-
toring is important in patients who are prescribed benzo-
diazepines over the long term, especially because physical 
dependence can develop over time.

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administering the medication.20 Benzodiazepine discon-
tinuation syndrome is characterized by rebound anxiety, 
agitation, insomnia, and sensory disturbances and is wors-

tened by longer administration, higher dose, and abrupt discontinuation.21–24

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Although discontinuation syndrome is an almost inevi-
table consequence of abruptly stopping even modest thera-
petic doses of a benzodiazepine, and ongoing benzo-
diazepine use even without dose escalation can lead to 
discontinuation syndrome,27 withdrawal distress is asso-
ciated with almost all psychotropic therapies, including β-blockers and tricyclic antidepressants, yet these patients 
are not labeled as physically dependent. Even the selective 
serotonin reuptake inhibitors (SSRIs), which were her-

alded as safe and effective treatments for depression and 

anxiety in the late 1980s and the 1990s, came to demon-
strate a discontinuation syndrome.29 People misunderstand 
the difference between physical dependence and abuse. 
Dependence only means care must be taken when stop-
ping the drug; dependence does not imply abuse, drug-
seeking, or lack of benefit.

Patients who have tolerated and responded to benzo-
diazepine treatment without excessive side effects 
are frequently reluctant to discontinue and often relapse 
upon discontinuation. Clinicians must distinguish rebound 
symptoms from relapse. Some studies28,30 have shown that 
subgroups of patients who are unable to discontinue with 
slow taper alone successfully discontinued by using com-
bined drug taper and behavioral techniques.

While long-term treatment could be necessary, some 
general clinical principles may help to minimize the ne-
cessity of chronic benzodiazepine treatment for acute 
problems, and thereby minimize physical dependence. 
First, distinguish acute symptomatic distress driven by re-
cent psychosocial events from an Axis I disorder. Second, 
at the outset of treatment, provide patient information 
about the goals and limitations of benzodiazepine pharma-
cotherapy, including the meaning of physiologic adapta-
tion and its implications. Third, adopt a dynamic stance to 
treatment designed to determine the lowest effective dose, 
reevaluate in the short term and over the long term, and 
made intermittent, structured attempts to taper.

CONCLUSION

Table 1. Effect of New York State Benzodiazepine Restrictions on Alternative Psychotherapeutic Medications Prescribed in 1988 
and 1989 (in thousands of prescriptions) 

<table>
<thead>
<tr>
<th>Medication</th>
<th>New York State 1988 (95% CI)</th>
<th>New York State 1989 (95% CI)</th>
<th>% Change</th>
<th>US Total Minus New York State 1988 (95% CI)</th>
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<th>% Change</th>
</tr>
</thead>
<tbody>
<tr>
<td>Methyprylon</td>
<td>22 (21–24)</td>
<td>41 (39–43)</td>
<td>84</td>
<td>123 (119–127)</td>
<td>104 (100–108)</td>
<td>–15</td>
</tr>
<tr>
<td>Ethchlorvynol</td>
<td>17 (15–18)</td>
<td>22 (21–23)</td>
<td>29</td>
<td>218 (212–224)</td>
<td>178 (172–184)</td>
<td>–18</td>
</tr>
<tr>
<td>Butabarbital</td>
<td>46 (44–48)</td>
<td>60 (57–63)</td>
<td>31</td>
<td>715 (703–727)</td>
<td>608 (596–620)</td>
<td>–15</td>
</tr>
<tr>
<td>Hydroxyzine</td>
<td>530 (520–540)</td>
<td>608 (597–619)</td>
<td>15</td>
<td>6829 (6783–6875)</td>
<td>6756 (6710–6802)</td>
<td>–1.1</td>
</tr>
<tr>
<td>Chloral hydrate</td>
<td>43 (41–45)</td>
<td>102 (98–106)</td>
<td>136</td>
<td>529 (519–539)</td>
<td>527 (517–536)</td>
<td>–0.4</td>
</tr>
<tr>
<td>Buspironeb</td>
<td>154 (149–159)</td>
<td>333 (325–341)</td>
<td>116</td>
<td>1782 (1761–1803)</td>
<td>2194 (2173–2215)</td>
<td>+23.1</td>
</tr>
<tr>
<td>Fluoxetineb</td>
<td>147 (142–152)</td>
<td>356 (341–371)</td>
<td>142</td>
<td>2754 (2727–2780)</td>
<td>5778 (5751–5805)</td>
<td>+109.8</td>
</tr>
</tbody>
</table>

a Data from Weintraub et al. 15

b Prescriptions for new anxiolytics (buspirone) and antidepressants (fluoxetine) as alternatives to benzodiazepines increased both nationally and in 

New York State.
rone, which became available in the late 1980s, reflected the promise of a nonbenzodiazepine agent with efficacy for anxiety. With a slow onset of action (as long as 4 weeks to full therapeutic effect), buspirone lacked the reliable early efficacy of the benzodiazepines but may have been more suitable than benzodiazepines for the treatment of some chronically anxious patients.31

In the 1990s, many clinicians favored benzodiazepines with relatively short half-lives over longer-acting agents because of their lower risk of cumulative sedation, psychomotor impairment, and amnestic effects.32,33 At the same time, many other clinicians favored drugs with long half-lives because they are less likely to produce an intense discontinuation syndrome.32,34 Today, newer antidepresant medications, particularly SSRIs, have become increasingly recognized as the pharmacologic treatment of choice for several anxiety disorders,35,36 despite their lack of a broad-spectrum acute anxiolytic effect. Recent analyses of service utilization data between 1987 and 1997 from 2 nationally representative surveys indicated a trend toward declining use of benzodiazepines, although they continued to be used by nearly one third of outpatients treated for anxiety disorders in 1999. Some expert psychopharmacologists continue to endorse benzodiazepines as a primary or adjunct treatment for several anxiety disorders.13

Given the heterogeneity of patients and disorders for which benzodiazepines are prescribed alone or adjunctively, no set of guidelines serves all, but increased circumspection with respect to prescribing is in order for those with previous chemical dependency18 and for the elderly.11,38–41 Prescribing is not carefree but requires monitoring to obtain an optimal benefit-risk ratio. The lowest effective dose and duration should be used. Intermittent reviews for possible taper and discontinuation are clearly necessary. The use of supplemental medication or behavioral therapy to enhance taper is a promising strategy. With increased understanding of the mechanisms of physical dependence may come efficient and effective strategies for minimizing discontinuation symptoms.

Regular, long-term use of benzodiazepines was controversial in the 1980s despite the fact that benzodiazepines are less toxic in overdose than alternatives, are safe, and have little liability for abuse among patients without a history of abuse. The essential clinical questions of the 1980s were: Do people who get benzodiazepine treatment merit it? and Do people who merit treatment for anxiety get it?

Today’s answer to the first question is a positive one. Over the last several years, substantial progress has been made both in the recognition of anxiety as a disorder and in the pharmacologic and psychological treatment of anxiety disorders. Benzodiazepine-treated patients are not automatically viewed as drug-seekers like the old stereotype. But the answer to the second question reveals little progress. Many people with anxiety disorders do not receive any treatment for their symptoms. Benzodiazepines or other treatments can be used safely to provide these patients with relief.

**Drug names:** buspirone (BuSpar and others), butabarbital (Butisol Sodium and others), fluoxetine (Prozac and others), hydroxyzine (Vistaril, Atarax, and others), meprobamate (Miltown, Tranmep, and others).

**Disclosure of off-label usage:** The author has determined that, to the best of his knowledge, no investigational information about pharmaceutical agents has been presented in this article that is outside U.S. Food and Drug Administration—approved labeling.

**REFERENCES**