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Editorial

Not Again: Benzodiazepines Once More Under Attack

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It seems that we are again in the midst of a new storm of concern about an epidemic of benzodiazepine (BZ) overuse, misuse, and abuse. The first concern, in the 1980s, posited BZs as an epidemic of excessive prescribing and was frequently mentioned in books, movies, and numerous lay magazine articles. There was also concern that BZs were abused or misused, caused addiction with difficult withdrawal symptoms, or taken without medical supervision by large numbers of people.

Available data from that period, while acknowledging potential problems with BZs, did not support this exaggerated view of serious hazards and widespread overuse. Although it was well known that BZs, such as other sedative hypnotics, could produce physiological dependence (usually mild) and a discontinuation syndrome (usually brief), the pharmacology and safety of these anxiolytics was well known. Categorized by elimination half-life and receptor potency, BZs were widely and successfully used to treat a variety of anxiety syndromes including acute states of anxiety, panic and trauma, medically associated anxiety and stress, as well as assisting with sleep onset at night.[1] Of greatest medical concern, however, was the abuse of BZs that was primarily seen in those who were already abusers of alcohol or other drugs. Benzodiazepine abuse was a genuine public health problem, but fortunately a relatively small issue when compared with the widespread appropriate medical use of BZs.[2] Careful door-to-door surveys of BZ use indicated that approximately 6% of those surveyed indicated that they took BZs on a regular basis during the previous year,[1,2] and this rate of long-term use was lower than in several European countries.[3] Much of BZ use in the United States was short term (3 weeks or less) and was prescribed by family practitioners

and primary care physicians.[3]

Out of concern over abuse, misuse, and adverse effects of BZs, an American Psychiatric Association task force was convened 2 decades ago to examine these worries.[4] The results of their report (cited by Olfson et al[5]) seem relevant to today's concerns. In summary, the task force found that BZs were therapeutically very effective and pharmacologically safe medications that were a great improvement over all earlier drugs used to treat anxiety in terms of efficacy, adverse effects, dependence/withdrawal, and misuse. The report emphasized that when used appropriately under medical supervision, BZs were remarkably safe drugs with relatively minor adverse effects. These were dose dependent and frequently the result from interaction with other drugs, especially those with sedative-hypnotic properties such as alcohol. Withdrawal reactions (more properly termed as *discontinuation syndromes*) were relatively mild except when BZs had been taken over a long period and at high doses.

Although meant to demonstrate an increasing use of BZs, recent survey data published by Olfson et al[5] actually suggest that BZs are still not widely overused or overprescribed; approximately 5.2% of the population (data derived from a 2008 survey of prescribing) were receiving benzodiazepines. This rate of BZ prescription is essentially the same as the approximately 5.5% usage reported in 1984.[2] Furthermore, the 2008 data review did not provide information as to the type of benzodiazepines prescribed or for what clinical conditions. It is not known how much of the use that was reported was not for psychiatric treatment but rather for short-term medical use (eg, nausea treatment and prophylaxis) or for longer-term use as in some seizure disorders. More recently, Bruce et al[6] reported that despite the rise in antidepressant treatment of anxiety disorders, BZ use for anxious patients declined only slightly as antidepressant use increased. In other words, there has not been an increase in BZ use over the past 20 years, even though BZs are more rapid and more effective anxiolytics. Nevertheless, current clinical experience indicates that prescribers and patients alike are trying to avoid using BZs, even for medically approved indications. This suggests that there may be inappropriate underprescribing for some patients.

The latest attack on BZ use comes from an editorial based on European survey data of BZ use.[7] It seems that nearly 20% of adult respondents living in Western European countries take BZs; the authors call for controlling the prescription of BZs and are more or less demanding that physicians stop prescribing them except in immediate necessary circumstances; they specifically recommend that BZs "...should especially be used only for very short periods..."

One of the major findings of the new Olfson et al[5] survey data indicated that BZs were prescribed to elderly individuals at a higher rate than for young and middle aged patients. Benzodiazepines are now thought to be hazardous to older patients despite the common clinical importance of their use during serious illness, treatment of cancer, cardiovascular, rheumatoid and sleep disorders, as well for long-standing states of anxiety. Impairment of cognition is correctly attributed to BZs given to elderly patients. Benzodiazepines, such as other sedative hypnotics, may be associated with a dose-dependent decrease in recent recall (anterograde amnesia) or registration of recent memories (eg, the movie that was watched the night before).[8] A meta-analysis of studies examining the effect of BZs on cognition in the elderly found lasting diminution of a variety of neurocognitive functions in those elderly who took BZs chronically, but diminished memory was a relatively minor effect; most of the deficits were on concentration and psychomotor speed.[9] A similar very small negative effect was found associated with chronic benzodiazepine use in more than 2000 older persons.[10] A small pilot study of BZ discontinuation in a nursing home population found that any recent memory impairment was reversible when the BZs were discontinued (although the research subjects preferred the calming effect of the BZs to the improved memory).[11]

Benzodiazepines prescribed to elderly individuals have also been implicated in increased falls and risk of fractures. This association has been well known and is true for both long as well as short half-life medications. Like most sedative hypnotics, they can cause unsteadiness and impaired balance, usually in a dose-dependent fashion. The elderly are more susceptible to these effects and should be prescribed lower doses to prevent them. More recent data have reported that although BZs may increase the risk of falls among elderly BZ recipients, antipsychotic and antidepressant drugs are associated with a higher risk of falls in this population than are BZs.[12]

Continuing and perhaps increasing BZ abuse/misuse by substance abusers, those with personality disorders, and individuals whose life is beset by complex stress does not admit an easy fix. Simply limiting BZ availability may not actually address this problem. When triplicate prescriptions were introduced in the state of New York, BZ use declined, but alcohol and other sedative/hypnotic use increased.[16,17]

In addition to overuse, we may now be facing a concomitant opposite condition—underprescription of a useful and safe class of medications. We suggest that concern regarding overuse and potential toxicity of BZs is warranted. We agree that among some individuals, especially those with substance abuse or chronic stress problems, BZs may be overprescribed. However, we also suggest that the medical community has overreacted to concerns regarding these drugs, leading in some clinical situations to underprescription. The known pharmacology of these drugs, their efficacy, safety, and adverse effect profile should serve

What are we to make of the recent suggestion that BZs may increase the risk of developing Alzheimer disease? A survey of Canadian insurance records found an association between BZ use in the elderly (older than 65 years) and more frequent development of Alzheimer disease.[13] Although carefully controlled, the data suffer from a number of significant problems that limit the study's conclusions. It has been suggested, in fact, that BZs may decrease the risk of development of Alzheimer disease by decreasing the toxic effect of chronic stress on the central nervous system.[14]

Are BZs dangerous drugs whose prescription and use must be carefully regulated? The answer is probably yes and no. When appropriately prescribed and dosed, these drugs are effective, safe, and patients usually appreciate their rapid and reliable anxiolytic effects. There likely is and was an irrational overuse of BZs and overprescription by some prescribers.[15] Certainly BZ prescription to elderly individuals should be carefully undertaken. They should be frequently monitored and limited to low doses of short half-life medications. Benzodiazepines are probably not useful in moderate to severely afflicted demented persons, although there are no data to guide their use in this population. Clinical experience suggests that those with impaired central nervous systems may experience more intense adverse effects and possible behavioral disinhibition.

In conclusion, psychiatrists, primary care physicians, and emergency room clinicians commonly see large numbers of angry, frustrated, anxious, and/or depressed individuals who demand a BZ prescription. Those who treat or interact with substance abusing individuals (alcohol, cocaine, opioids) commonly see BZs being taken along with the abused drug. However, it is our experience, as well as in that of numerous colleagues, that clinicians are criticized and even vilified when suggesting a BZ for a patient. Patients themselves, reading about the potential for “addiction” to BZs or severe memory impairment, refuse to take what might be an effective and safe class of drugs for them.

All drugs with sedative-hypnotic properties including BZs may produce unwanted abuse, misuse, and serious adverse effects. For the elderly, these drugs may also produce serious unwanted effects. All prescribers must carefully weigh the risk versus benefit of prescribing BZs, especially insuring that the patient's diagnostic characteristics warrant BZ use. In our view, it is a poor medical practice that deprives a patient of a useful and safe therapeutic class of drugs.

as the primary reinforcers of appropriate clinical use. Prescribers should be aware of the potential for abuse and misuse; treatment should continue to be short term except in psychiatric conditions of chronic anxiety. Elderly individuals and those with functional or structural central nervous system damage should be prescribed BZs only with the greatest caution and only when clinically necessary and for the shortest period using low therapeutic doses.

AUTHOR DISCLOSURE INFORMATION

The authors declare no conflicts of interest.

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