Long-Term Use of Benzodiazepines

Implications and guidelines

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SUMMARY

Problems associated with physical dependence and abuse of benzodiazepines by a small percentage of patients have reduced their popularity from the most commonly prescribed psychoactive drug in the 1970s to being prescribed for mainly short periods. Patients who benefit from long-term benzodiazepine use are nearly ignored by the medical community as a whole. This article details what patient population can improve from long-term benzodiazepine therapy, the risks and benefits of treatment, and how to select appropriate candidates.

RÉSUMÉ

Les problèmes reliés à la dépendance physique et à l'abus des benzodiazépines par un faible pourcentage de patients ont contribué à la baisse de popularité qu'elles ont connue dans les années 1970 alors qu'elles occupaient le premier rang des médicaments psycho-actifs prescrits; actuellement, on les prescrit surtout à court terme. Globalement, la communauté médicale ignore pratiquement les patients qui bénéficieraient des benzodiazépines à long terme. Cet article décrit quelle population de patients aurait avantage à recevoir un traitement de benzodiazépines à long terme, les risques et les avantages de ce traitement, et propose une méthode appropriée pour identifier leux qui sont à risque d'abuser d'une telle médication.

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BENZODIAZEPINES WERE INTRODUCED in the early 1960s and were enthusiastically received as the new miracle drugs to treat anxiety disorders. Compared with other available drugs, ie, barbiturates, they were safer, offering little chance for a lethal overdose, were less addictive or prone to abuse, and were more effective anxiolytics. This led to a rapid shift by the medical community to prescribing benzodiazepines, which peaked in 1973, when benzodiazepines totalled 53% of all prescribed psychoactive drugs and about 6% of all prescriptions.[1]

Concerns, however, soon arose about addiction and abuse, especially problems with withdrawal. By 1982 prescription rates had fallen by 30%. Since then, even with the introduction of newer, more effective benzodiazepines, like alprazolam (Xanax), only limited recovery of the prescriptions has occurred.[2]

The aim of this article is twofold: 1) to address some of the concerns of the medical community over the long-term use of benzodiazepines and 2) to help identify patients who will profit from their use and point out those at risk of abusing the drugs. It is important for physicians to be aware of these points so they are more comfortable prescribing the drugs to reduce patients' symptoms. Family physicians are the largest group of physicians treating anxiety disorders and the largest prescribers of benzodiazepines, whereas psychiatrists prescribe less than 20% of all anxiolytics in this country.[3]

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Anxiety disorders

A recent survey by the National Institutes of Mental Health showed that the 6-month prevalence rate of anxiety disorders among the adult population in the United States was 8.3%. Only 23% of these individuals had received any form of treatment.[4] This survey makes it evident that anxiety disorders, the most common psychiatric problem in the community, usually go untreated. The anxiety disorders that appear to benefit from long-term benzodiazepine treatment are panic disorder, with or without agoraphobia, agoraphobia, generalized anxiety disorder, and social phobia.

Panic disorder is associated with severe episodes of anxiety, which occur spontaneously and without provocation. Common symptoms of these attacks include shortness of breath, dizziness, palpitations, sweating, tingling or numbness, and chest pains or tightness. These attacks can also be associated with a fear of doing something "crazy" or a fear of dying. If persons with panic disorder begin to avoid places

or situations that they believe cause their panic attacks, they have developed panic attacks with agoraphobia.

Agoraphobia, however, can occur without panic attacks preceding it. In this instance patients fear being in places or situations from which escape might be difficult or embarrassing. They can also fear having something embarrassing or incapacitating occur to them in front of others, ie, vomiting, fainting, or loss of bladder or bowel control. Examples of common phobias are being outside of the home alone; being in a crowd or standing in a line; and being in a bus, train, or car or driving through a tunnel or over a bridge.

Generalized anxiety disorder is characterized by excessive or unrealistic worry about two or more of life's main concerns (eg, child, family, finances) that is persistent and distressing. These fears are associated with symptoms of motor tension, autonomic hyperactivity, and hypervigilance.

Social phobia, the last of this group of disorders, is characterized by fears of embarrassing or humiliating oneself in front of others by saying or doing the wrong thing. The most frequently avoided situations include speaking in public, meeting strangers, eating or drinking in public, urinating in a public lavatory, and situations in which the individual could face possible criticism or humiliation. All of these disorders are associated with overwhelming episodes of anxiety and involve the development of phobic and avoidance patterns.

Over the years, psychiatry has placed greater emphasis on properly defining illness and has spent more time observing the natural history of illnesses. Consequently it is now clear that anxiety disorders follow a chronic course and place the patient at increased risk of social isolation, depression, and alcohol abuse, and in some cases they end in suicide.[5] Furthermore, the symptoms can be eradicated by appropriate therapy but can return rapidly upon cessation of treatment.[6,7] Before the onset of the disorder, however, the patients are usually normal, with good social, occupational, and interpersonal skills. Unfortunately, as the disorder progresses the individual gradually becomes less able to perform socially and at work, and phobias and avoidance patterns develop that eventually lead to these consequences. Therefore proper diagnosis and early intervention is crucial if the individual is to continue functioning at an acceptable level.

Treatments

Several treatments are currently available for anxiety disorders. These include pharmacotherapy, psychotherapy, analysis, and behavioral and cognitive therapies. These treatments, however, are not always available to patients for a variety of reasons, including access to resources, financial constraints, and patient suitability for some forms of treatment.

Benzodiazepine use has a number of benefits over these other forms of treatment. Compared with other medications they are less prone to abuse and addiction,[3] as well as being relatively safe. In addition, they are readily available, inexpensive, and can begin to ameliorate the symptoms within days. An added bonus to the patient is the ability to face other issues complicating the illness, without overwhelming anxiety.

Risks of long-term use

When a patient is started on benzodiazepines, the initial goal is to find a dosage that is effective in reducing symptoms but is not associated with dose-related side effects. This treatment, though, is not without risk. It is essential for the prescribing physician to acknowledge these risks and discuss them fully with all potential candidates.

The most common side effect is sedation, which is a problem mainly during the initial phase of treatment. It has been demonstrated that all patients will develop some tolerance to sedation but not to the anxiolytic effects.[8] When using these drugs one must warn patients of the associated problems of sedation, such as impaired concentration when driving, but also be aware that the aim is to find a dose without this side effect. Another related side effect is amnesia, which can be seen with benzodiazepines, especially with lorazepam (eg, Ativan) and triazolam (Halcion).[9] Cognitive impairment is another side effect to which patients do not develop tolerance. As a general rule, the older a patient is, the lower the initial dose should be and the smaller the increments by which one increases the dose. If any evidence of cognitive impairment is seen, the dosage should

be reduced immediately and tapered off. Afterward one can offer a trial with an alternate benzodiazepine at the equivalent of a reduced dose.

Three areas of concern with long-term benzodiazepine treatment are drug abuse, drug dependence, and drug addiction. Drug abuse is defined as the intermittent use of certain substances for reasons other than intended, mainly for a euphoric effect, or in a harmful way. A number of studies have shown that benzodiazepines are not "enjoyable" and do not produce euphoric effects in patients with anxiety.[10-16] In contrast, alcoholics and patients with a history of drug abuse have been found to prefer benzodiazepines over placebo.[11-14,17] Clinical evidence from numerous studies demonstrates benzodiazepine abuse in alcoholics, users of several drugs, and opiate abusers.[11,18-26] *Table 1* lists characteristics of patients at high risk for developing benzodiazepine abuse and of patients who are abusing substances.

In contrast, drug dependence is characterized by the development of tolerance and physical dependence.[8] Drug dependence and tolerance are not issues in patients with anxiety disorders treated with benzodiazepines.[11] A few physicians in Germany have reported isolated cases of tolerance in a small number of patients using benzodiazepines exclusively.[27-30] However, most cases of tolerance have been documented in patients using the drugs in an abusive manner, ie, alcoholics or other drug abusers.

Physical dependence alone, however, does not imply drug dependence, but it is an important issue. Physical dependence is diagnosed by the presence of withdrawal symptoms upon cessation of a medication. This phenomenon has been extensively reported in the literature in relation to benzodiazepine use, even at recommended doses.[31-34] Recent evidence suggests that it is directly related to the duration of treatment and inversely related to the drug's half-life.[35,36] It is essential to explain to the patient this concept and its consequences, ie, withdrawal symptoms can appear if the medication is discontinued abruptly. Symptoms include restlessness, tremor, agitation, sweating, insomnia, and in the severest form, grand mal seizures.

Drug addiction is the severest form of drug dependence and occurs when an individual develops a psychological as well as a physical dependence on a substance. Heroin and cocaine addiction are common examples of this form of dependence, in which the individual is dependent on the medication and abusing it at the same time.

Table 1. **IDENTIFYING POSSIBLE DRUG ABUSE**

FACTORS INCREASING THE RISK OF DRUG ABUSE
• History of substance abuse
• History of alcohol abuse
• Antisocial personality disorder
• Borderline personality disorder
• Alcoholic parents
• History of poor impulse control
CLUES TO POSSIBLE DRUG ABUSE
• Patient gives vague or inconsistent history
• Patient becomes demanding or aggressive during interview
• Patient refuses physical examination
• Patient demands certain drugs by name
• Patient refuses other treatments
• Patient refuses to allow others to be interviewed
• Patient continually loses prescriptions
• Patient does not attend regularly

Conclusion

Long-term benzodiazepine therapy is of benefit in certain anxiety disorders, ie, panic disorder with or without agoraphobia, agoraphobia, generalized anxiety disorder, and social phobia. Although other drugs are available, ie, tricyclics for panic disorder and buspirone (Buspar) for generalized anxiety disorder, many patients have no other options or do not respond and require long-term benzodiazepine treatment. Advantages of this approach include low cost, availability, rapid relief of symptoms, and effective therapy for most patients. This therapy is associated with certain risks, but if the drug is properly prescribed and monitored, these risks can be minimized. Safety measures include titrating doses,

especially in the elderly, close observation and follow up, and proper screening and education of patients.

For effective treatment of patients with anxiety disorder, a number of steps can help. If these steps are followed by the physician, they will aid in selecting the appropriate patients and reduce risks of therapy.

- Confirm the diagnosis of an anxiety disorder that is responsive to benzodiazepine treatment. Consider other treatments first, ie, buspirone for generalized anxiety disorder or tricyclics for panic disorder.
- Take a good history from the patient concerning past treatments and specifically ask about depression and past or present substance abuse. Seek collaborative evidence from other family members or previous doctors.
- Search for possible risk factors that put the patient at risk of abusing benzodiazepines, ie, antisocial or borderline personality disorders.
- If you have doubts about patient suitability for long-term therapy, refer the patient to an appropriate center or specialist.
- Discuss treatment options and the risks of long-term benzodiazepine therapy with your patient.
- Explain your expectations to the patient, ie, the need for close supervision initially, regular visits by the patient, and your reluctance to continue treatment if the patient is not willing to agree or comply with these rules.
- Fully educate the patient about how to use benzodiazepines properly and safely. This education should cover drug interactions, the need to keep the supply of medication safely hidden from others, and the necessity of medication charts, which should be brought with the patient to each consultation.
- Documentation is crucial. Explain the reasons for diagnosis and discuss alternative treatments. Keep thorough records of all prescriptions. ■

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