



Office of the Ombudsman for Mental Health and Developmental Disabilities



Behavioral Side Effects of Benzodiazepine Medications in People with Mental Retardation



This Medical Alert should be posted prominently. The Office of the Ombudsman for Mental Health and Developmental Disabilities works to improve the services provided to people with disabilities by communicating important information found in the Medical Review Subcommittee's reviews of deaths and serious injuries. Thank you for promptly reporting deaths and serious injuries. You are helping us to meet our mission.

Preface

This Alert was written for the Office of the Ombudsman for Mental Health and Developmental Disabilities by Thomas E. Hanzel, M.A., Licensed Psychologist – Retired, New Prague, Minnesota, and John E. Kalachnik, M.Ed., Director of Integrated Services, Iowa Department of Human Services, Woodward Resource Center, Woodward, Iowa.

The Alert is adapted from the following original research article: “Benzodiazepine Behavioral Side Effects: Review and Implications for Individuals with Mental Retardation,” by John E. Kalachnik, Thomas E. Hanzel, Robert Sevenich, and Stuart R. Harder, which was published in the American Journal on Mental Retardation, Volume 107, Number 5: 376-410, September 2002. Please refer to the original article for further information and additional references.

Introduction

Behavioral side effects associated with benzodiazepines such as clonazepam (Klonopin[®]), diazepam (Valium[®]), and lorazepam (Ativan[®]) can be an easily overlooked and under-recognized problem for people who have mental retardation and can be inadvertently confused with other behavioral or psychiatric conditions. This is especially important because many individuals with mental retardation cannot effectively communicate the presence of these side effects and are, for the most part, dependent upon others for detecting and recognizing these side effects.

The intent of this Alert is not to suggest that benzodiazepines should never be prescribed. Rather, the intent is to inform clinicians, families, and providers about the possibility of benzodiazepine behavioral side effects, discuss implications if these side effects are not correctly identified, and provide clinical profiles suggesting the need for review by appropriate health care professionals.

Please note that under no circumstances should a client’s benzodiazepine medication be reduced or discontinued without a thorough evaluation by, and under the guidance of, the client’s psychiatrist/neurologist and the client’s primary care physician.

Benzodiazepines and Their Uses

Benzodiazepines are generally prescribed for anxiety, epilepsy, and insomnia. Other uses include treatment for alcohol withdrawal, skeletal muscle spasms, akathisia, tardive dyskinesia, and sedation prior to dental, diagnostic, or medical procedures.



Examples of benzodiazepines prescribed for anxiety include alprazolam (Xanax[®]), clorazepate (Tranxene[®]), chlorthalidone (Librium[®]), clonazepam (Klonopin[®]), diazepam (Valium[®]), halazepam (Paxipam[®]), lorazepam (Ativan[®]), oxazepam (Serax[®]), and prazepam (Centrax[®]).

Examples of benzodiazepines prescribed for sleep include estazolam (ProSom[®]), flurazepam (Dalmane[®]), quazepam (Doral[®]), temazepam (Restoril[®]), and triazolam (Halcion[®]).

Examples of benzodiazepines prescribed for treatment-resistant epilepsy include clonazepam (Klonopin[®]), diazepam (Valium[®]), and lorazepam (Ativan[®]). In addition, Ativan[®] or diazepam (Diastat[®]) may be prescribed within the context of a seizure protocol for seizures exceeding a certain frequency (e.g., two seizures within four hours) or duration (e.g., seizures lasting longer than three minutes).

Finally, other benzodiazepines such as midazolam (Versed[®]) may be prescribed for conscious sedation as part of dental, diagnostic, or medical procedures.

Prevalence of Use

Although the use of benzodiazepines in the general population has declined since the late 1970s and early 1980s, a substantial number of individuals are still prescribed benzodiazepines. Five benzodiazepines continue to be listed in the top 200 prescriptions dispensed in the United States in 2004. Alprazolam (Xanax[®]), lorazepam (Ativan[®]), and clonazepam (Klonopin[®]) are listed in the top 50.

Benzodiazepine use with persons with mental retardation is generally 5%, but may vary between approximately 3% and 13% depending on variables such as the living location, the specific benzodiazepines, and the diagnostic uses surveyed.

Behavioral Side Effects of Benzodiazepine Medications

For purposes of this Alert and based upon several authorities, benzodiazepine behavioral side effects are considered to be:

- Aggression
- Agitation
- Anger
- Depression
- Hostility
- Hyperactivity
- Irritability
- Property destruction
- Self-injurious behavior
- Socially inappropriate behavior (e.g., disrobing in public)
- Temper tantrums

Please Note: This list does not include other benzodiazepine side effects which some authorities consider to be behavioral. Some of these include concentration difficulties, confusion, sedation, and motor incoordination.

The display of benzodiazepine behavioral side effects can take one of two forms. First, an item listed above may increase or worsen. This is often referred to as “behavioral exacerbation.” Second, an item listed above may occur for the first time. This is often referred to as “behavioral disinhibition.”

Risks for Benzodiazepine Behavioral Side Effects

There are a number of groups which may be at higher risk for benzodiazepine behavioral side effects. These include children, the elderly, people living in frustrating environments, people with poor impulse control, people with borderline personality disorder, people with a history of behavior problems, and people with mental retardation, autism, or brain injury. It is critical to remember this does not mean that a specific individual in these groups will actually develop benzodiazepine behavioral side effects.

Prevalence of Benzodiazepine Behavioral Side Effects

The overall rate of benzodiazepine behavioral side effects in persons with mental retardation is approximately 13%. This figure is based upon a literature search which resulted in 43 references containing 446 people with mental retardation who were prescribed benzodiazepines for behavioral or psychiatric conditions, epilepsy, or medical conditions such as myoclonus or cerebral palsy. Benzodiazepine behavioral side effects occurred for approximately 17% of persons prescribed benzodiazepines for behavioral or psychiatric conditions, 15% of persons prescribed benzodiazepines for epilepsy, and 2% of persons prescribed benzodiazepines for other medical conditions such as myoclonus or cerebral palsy. The four most frequently reported behavioral side effects were aggression, irritability, hyperactivity, and agitation. Behavioral side effects for individual benzodiazepines for which data were available ranged from approximately 11% to 25%. These benzodiazepines were chlordiazepoxide (Librium®), clobazam (not available in United States), clonazepam (Klonopin®), diazepam (Valium®), lorazepam (Ativan®), and medazepam (not available in United States). In general, the data supported the view of some authorities that benzodiazepine behavioral side effects are a frequent side effect with persons who have mental retardation.

Implications for People with Mental Retardation

There are three major implications of not recognizing benzodiazepine behavioral side effects.

- 1. Benzodiazepine behavioral side effects may be inadvertently assigned to an underlying behavioral or psychiatric condition, especially in cases where an existing problem behavior varies over time.** This, in turn, could lead to the ongoing prescription of the benzodiazepine such that the individual continues to experience behavioral side effects. Complicating this situation is the possibility that a delay may occur between the initiation or dose increase of a benzodiazepine and the appearance or recognition of behavioral side effects. Benzodiazepine behavioral side effects may occur within two to seven days. However, the onset of behavioral side effects for specific benzodiazepines may be longer in some cases.
- 2. Other psychotropic medications such as antipsychotic medications, mood-stabilizing medications, and antidepressant medications may be started or doses increased in an effort to treat the unrecognized behavioral side effect.** This could result in additional medication, polypharmacy, or other side effects.
- 3. Quality of life may be compromised.** Cases have been reported of individuals who “went wild,” had to be withdrawn from school, became “animal-like,” or lost interpersonal relationships and emotional bonds. Aggression, agitation, hyperactivity, irritability, and property destruction could lead to the disruption of activities of normal daily living, the use of restraints, or the use of other restrictive or aversive procedures. Injuries requiring medical attention may also occur to both the individual and staff.

Clinical Profiles Suggesting Need for Review by a Healthcare Professional

A clinical difficulty is presented by the possibility of benzodiazepine behavioral side effects. If problem behavior emerges or increases, should the possibility of benzodiazepine behavioral side effects be considered and the benzodiazepine reduced? Or should other possibilities be considered such as environmental changes, relapse, or co-morbidity? While there are no simple answers or solutions to this situation, the following profiles may suggest review for possible benzodiazepine behavioral side effects by a healthcare professional.

- 1. An established psychotropic medication dose or a behavioral treatment program is no longer effective after the start or dose increase of a benzodiazepine.**

2. A typically variable problem behavior rate has been consistently high after the start or dose increase of a benzodiazepine.
3. A previously established psychotropic medication and dose level, when re-started, does not have the expected benefits within a reasonable amount of time, and a benzodiazepine has been added to the regimen since the discontinuation.
4. Psychotropic medication intraclass polypharmacy (i.e., two or more psychotropic drugs from the same class) or interclass polypharmacy (i.e., a total of three or more psychotropic drugs) is present, or additional psychotropic medication is being considered to treat an ongoing behavior problem.
5. An increase in problem behavior data is correlated with the 24-hour period after the use of a shorter-acting benzodiazepine such as lorazepam (Ativan[®]) for a dental or medical visit.
6. Little else seems to explain the behavior problem, and the behavior problem has continued despite great efforts to treat it.

Conclusion

The intent of this Alert is not to suggest that benzodiazepines should never be prescribed for seizures, anxiety, tardive dyskinesia, or spasticity for persons with mental retardation. Indeed, a benzodiazepine may be the only medication that provides successful treatment for some individuals. Not everyone prescribed benzodiazepines develops behavioral side effects, and problem behavior may not be explained by benzodiazepine behavioral side effects.

The intent of this Alert is to inform clinicians, families, and providers about the possibility of benzodiazepine behavioral side effects, especially for cases in which the clinical profiles are present. Because the risk of benzodiazepine behavioral side effects in people with mental retardation is frequent at 13%, the cautious use of benzodiazepines is warranted, and the use of empirical behavioral measurement methods is recommended. If benzodiazepine medications are prescribed, behavioral side effects may be less frequent or less severe if lower doses are used, for example, 3 milligrams per day or less of lorazepam (Ativan[®]).

To the degree possible, benzodiazepines should not be prescribed for anxiety for longer than three to four months, and benzodiazepines should not be prescribed for sleep for longer than 14 days. Finally, if a benzodiazepine is discontinued, the possibility of withdrawal effects or rebound effects should be considered. Depending on the specific case and duration of use, benzodiazepine dose reductions should be done gradually in the range of 10 to 25 percent approximately once every one to four weeks.

Again, please note that under no circumstances should a client's benzodiazepine medication be reduced or discontinued without a thorough evaluation by, and under the guidance of, the client's psychiatrist/neurologist and the client's primary care physician.

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