

Primary Care Guide To The Prescription Of Benzodiazepines For Adults With Mental Retardation and Developmental Disabilities (MR/DD)

1. Overview of Safe, Effective Prescription of Benzodiazepines

The consensus guidelines to the prescription of psychotropic medications to persons with MR/DD do **NOT** list benzodiazepines as first line medications of choice for any psychiatric or behavioral problem (1). Anxiety disorders or related symptoms may occur in up to 8% of patients with MR/DD (2), (3), (4). The patient with MR/DD may develop symptoms of anxiety as a primary disorder or in the setting of other medical or psychiatric problems. The use of benzodiazepines in the MR/DD patient requires careful prescription, dose titration, and monitoring for side effects. Most benzodiazepines have significant side effects in the patient with MR/DD and these drugs should be prescribed with great caution and precision (See Table 1), (5). Benzodiazepines are frequently prescribed for agitation, aggression, and sleep disorders; however, consensus guidelines do not support their use for these target symptoms. (1), (6).

Table 1
Appropriate Use of Benzodiazepine Medications in the Patient with MR/DD

1. Documented Anxiety Disorders
2. Anxiety Associated with Bereavement
3. Pre-op Procedure Sedation
4. Alcohol Withdrawal

Possible Use of Benzodiazepines

1. Acute Agitation or Aggression
2. Mania
3. Short-term Sleep Disorders

2. Indications for Benzodiazepines

The benzodiazepines can be used to treat anxiety disorders (7) including generalized anxiety disorder (GAD), post traumatic stress disorder (PTSD), and others when these symptoms are not produced by medical problems, depression or other conditions (See Table 1). These medications can be used to sedate patients for medical or dental procedures such as chest X-rays, EKGs, and such. In general, the benzodiazepine class of medications has very limited long-term efficacy for any condition except generalized anxiety disorders in persons with MR/DD. For this reason, nursing home regulations limit use of benzodiazepines for any indication besides a DSM diagnosis within the anxiety spectrum. The prescription of benzodiazepines has specific limitations for agitation, aggression, and other dangerous behaviors manifested by a person with MR/DD. Short-term use of these medications to sedate the patient may be the most effective way to defuse a potentially dangerous situation, e.g., Ativan 0.5 to 1mgm IM. Long-term use of a benzodiazepine may produce confusion, excitation, or disinhibition that will actually worsen agitation and aggression. The long-term use of benzodiazepines is not effective for insomnia or nocturnal agitation. Federal guidelines discourage the chronic, nightly prescription of these medications is not allowed for sleep in the nursing home setting beyond two weeks of continuous therapy. The benzodiazepines tend to lose efficacy as a hypnotic after 4-6 weeks of continuous nighttime

use and this class of medication is usually ineffective for long-term management of insomnia (8), (9).

3. Medication Characteristics

The benzodiazepines are generally divided into long, intermediate and short, half-life medications (10). Most older medications, e.g., Valium, Librium, etc., have a long half-life, while the newer drugs, e.g., temazepam, alprazolam, have intermediate half-life (See Table 2). The clinician should be familiar with the half-life of each medication. Most are hepatically excreted except for oxazepam and lorazepam and these medications may be better in patients with significant liver impairment. The clinician is encouraged to become familiar with one or two benzodiazepine medications and use these medications as the primary treatment.

Two benzodiazepines have special features of note for clinicians. Clonazepam is a long, half-life benzodiazepine, which may have some efficacy for seizure, mood stabilization, and myoclonic jerking. This medication can produce significant toxicity due to its long half-life and should be used with great care. Klonopin is specifically identified in nursing home regulations as problematic. Alprazolam (Xanax) is a second drug which is pharmacokinetically distinct from the other benzodiazepines. This medication can produce significant addiction and the potential for prolonged withdrawal with sustained use. Xanax has no parenteral formulation and patients who abruptly stop this medication, e.g., due to GI problems, can develop withdrawal. Cross-coverage with other benzodiazepines may not be effective in suppressing withdrawal for this medication. Because other benzodiazepines have fewer potential side effects, the clinician may wish to avoid Xanax in the mentally retarded. A brief course of Xanax, e.g., two weeks, for specific anxiety symptoms, such as bereavement may be quite beneficial; however, long-term therapy, e.g., over one month, can produce significant complications.

Benzodiazepines can also be prescribed for alcohol withdrawal. A seven-day course of tapering dosages is often used to prevent DT's.

4. Prescription of Benzodiazepine Medications for Specific Indications

Management of Acute Agitation with Benzodiazepine Medications. Injectable benzodiazepines are often given to calm acutely agitated patients. The typical dose of Ativan, ranging from 0.25mgm to 1mgm, will usually calm the average patient with MR/DD. Larger, healthy adolescents or young adults may require more medication. Treatment alternatives to benzodiazepines include IM atypical antipsychotics such as Zyprexa – 2.5-10mgm depending on patient features or older medications, such as Haldol-0.5 to 5mgm.

Management of Anxiety with Benzodiazepine Medications. Four broad classes of medications have been used for the treatment of anxiety in the population with MR/DD: antidepressants, benzodiazepines, antipsychotics, and other miscellaneous medications (11). A variety of sedating medications including antihistamines, barbiturates, and other sedatives such as meprobamate have been prescribed for symptomatic management. Similar medications are also prescribed to assist with sleep problems. These “all-other” drugs are included on both the old and the new “Beers” list of prohibited medications in nursing homes

and the use of these medications under OBRA regulations draws specific scrutiny by the nursing home surveyors (13).

The pharmacological management of anxiety in the patient with MR/DD depends on the severity of disability, underlying disease, associated health problems and psychiatric comorbidity (9). Anxiety is a fairly common symptom in the person with MR/DD for both children and adults. Individuals with mild to moderate MR should be capable of explaining core symptoms of anxiety; however, severely retarded individuals may lack the ability to describe these symptoms. The symptoms of anxiety or panic disorder should prompt a search for behavioral or medical explanations, as well as other underlying psychiatric comorbidity including depression, bereavement, response to environmental stressors, and abuse/neglect. The prescription of benzodiazepines should be limited to patients with a clear definitive diagnosis and precise target symptoms that allow clinicians and staff to determine whether sufficient improvement is present to warrant this use in high risk population. The use of benzodiazepines in moderate to severely retarded individuals who are unable to explain their emotional state requires careful consideration and follow-up.

Lorazepam and oxazepam are relatively safe benzodiazepine medications with intermediate duration half-life, rapid speed on onset and minimal sensitivity to liver disease (See Table 2). Dosing should begin at low range, low frequency, and occur three or four times per day. "As needed" medications are acceptable ways to treat anxiety when dosing occurs once or twice per week. Dosing ranges must be adjusted for each patient. Addiction may occur after three or four months of daily use and abrupt cessation of benzodiazepine medications should be avoided. Medications should be titrated to the lowest dosing range required to control symptoms. As tolerance develops, the patient may require larger doses of medications.

Benzodiazepines can be used in selected situations for brief periods of time, e.g., adjustment reactions, bereavement, etc. A brief, i.e., 2-weeks, course of low-dose, short half-life benzodiazepine is generally considered to be safe for most persons with intellectual disability.

Hypnotics. Sleep disturbance can occur in persons with MR/DD. Insomnia is caused by many medical, psychiatric, environmental and behavioral problems that will not respond to hypnotics. Short-acting hypnotic agents, such as zolpidem or eszopiclone, can be prescribed for brief periods of time or episodically, such as every third night (See Table 2). Tolerance and rebound insomnia are common problems of chronic usage.

Other Indications. Benzodiazepines are sometimes prescribed as anticonvulsants and antispasmodics. These medications have limited efficacy as anticonvulsants.

Table 2
Commonly Used Dosing Ranges for Benzodiazepine Anxiolytic Medications for the Adult
Population with MR/DD

DRUG	HEALTHY/ADULT DAILY DOSE RANGE	FRAIL/ELDERLY DAILY DOSE RANGE	COMMENTS See PDR for Complete Details
Long Acting (t_{1/2}>24hrs)			
Diazepam (VALIUM)	5 - 20mg	2 - 10mg	Very Fast Onset of Action
Clonazepam (KLONOPIN)	0.5 - 4mg	0.25 - 2mg	No Active Metabolites
Chlordiazepoxide (LIBRIUM)	5 - 300mg	5 - 100mg	Useful Treating Alcohol Withdrawal
Intermediate Acting (t_{1/2} = 12-24hrs)			
Alprazolam (XANAX)	0.5 - 4mg	0.25 - 2mg	Fast Onset of Action
Temazepam (RESTORIL)	15 - 30mg	7.5 - 15mg	No Active Metabolites
Lorazepam (ATIVAN)	0.5 - 6mg	0.25 - 2mg	No Active Metabolites
Oxazepam (SERAX)	15 - 60mg	7.5 - 30mg	No Active Metabolites
Short Acting (t_{1/2}<12hrs)			
Zolpidem (AMBIEN)	5 - 10mg	5mg	Only Indicated for Acute Insomnia
Eszopiclone (LUNESTA)	1 - 3mg	1 - 2mg	Indication for Chronic Insomnia
All benzodiazepine medications may be addictive and produce delirium, falls, or excessive sedation. These medications are not recommended for children.			

5. Toxicity of Benzodiazepines

Clinicians should avoid the use of long, half-life benzodiazepines in persons with mental retardation. The long, half-life medications are included in the Beer's list of contraindicated drugs for brain damaged persons because of increased risk of toxic accumulation (13). Intermediate and short, half-life medications are preferable and these drugs can be administered on a regular basis when indicated. Once-a-day dosing of a short, half-life drug such as Ativan produces withdrawal at 16 hours following the last dosage. Most benzodiazepines are hepatically excreted producing problems for patients with liver failure. Oxazepam and lorazepam are benzodiazepines that are almost totally excreted by the kidneys (10).

Benzodiazepines are addictive and abrupt cessation of medication can produce withdrawal syndromes and drug-seeking behavior on the parts of patients. Xanax is particularly addictive and produces a complex withdrawal syndrome. Patients who are prescribed Xanax for months or years should have a slow, gradual, methodical taper that lasts over many weeks to months. The dose reduction schedule should be based on the total daily dosing at the initiation of the taper. Cross-titration to other benzodiazepines could potentially produce withdrawal in a small number of individuals. Addicted individuals receiving large doses, e.g., 6-8mgm per day, may require many months of dose tapering.

Benzodiazepines are potentially toxic in all persons with brain injury or developmental brain abnormalities. Benzodiazepines can produce considerable sedation, additional confusion, respiratory suppression, and functional deterioration because of the chronic intoxication. Some individuals develop a paradoxical effect to the medication and may become agitated or delirious. Individuals receiving benzodiazepines are at greater risk for falls, injury, and fractures. These individuals have a higher rate of GERD (See Table 3), (4).

Table 3
**Possible Complications of
 Benzodiazepine Therapy in Adults
 with MR/DD**

- **Hyperkinesia**
- **Paradoxical Excitation**
- **Confusion**
- **Accidents**

Psych Annals 1997;27(3):183-90

6. Dosing Ranges for Benzodiazepines

The initiation and maintenance dose of benzodiazepines depends on the age, size, and frailty of the person with MR/DD. Dosing with benzodiazepines should commence with one-half to one-quarter the recommended initial dose in persons with medical or neurological problems as well as those with severe intellectual disability (See Table 2). The younger patient with mild retardation and no significant health problems can tolerate a normal adult dose of a benzodiazepine; however, moderate or severely retarded individuals as well as those with comorbid medical problems require substantial dose reductions in the range of one-half to three-quarters the normal adult dose. Benzodiazepines should be used with great care in the aging MR person and further dose reductions should be considered. The sedating effect of benzodiazepines is additive with other medications that can depress level of alertness, such as antiepileptics.

7. Conclusion

Benzodiazepines are powerful, psychotropic medications with a relatively narrow therapeutic range and list of clinical indications for persons with MR/DD.

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