Primary Care Guide For Prescription Of Anxiolytic Medications For Persons With Mental Retardation and Developmental Disabilities (MR/DD)

Overview of Prescription

The DD/MR patient may develop symptoms of anxiety as a primary disorder or in the setting of some medical or other psychiatric problems, such as depression (1), (2). The use of benzodiazepines in the DD/MR patient requires careful prescription, dose titration, and monitoring for side effects. Most benzodiazepines have significant side effects in the DD/MR patient and these drugs should be prescribed with great caution and precision (3).

Four broad classes of medications have been used for the treatment of anxiety in the DD/MR population: benzodiazepines, antidepressants, antipsychotics, and other miscellaneous medications, such as buspirone (4). A variety of sedating medications including antihistamines, barbiturates, and other sedatives such as meprobamate have been prescribed for symptomatic management. These medications are also prescribed to assist with sleep problems but these medications should be avoided in the person with MR/DD. These drugs are included in both the old and the new Beers list of medications that are prohibited in the nursing home and the use of these medications under OBRA regulations draw specific scrutiny by the nursing home surveyors (5). The national consensus criteria identify SSRI's and buspirone as the first options in the treatment of anxiety disorders (6).

All benzodiazepines act in the same way; by altering to the gabanergic receptor (7). These medications can be used with safety in the mildly retarded patient with significant anxiety produced by specific syndromes including generalized anxiety disorders, depression with anxiety, and schizophrenia with significant anxiety symptoms (8).

Basic Principles for Prescription

The pharmacological management of anxiety in the DD/MR patient depends on the severity of disability, underlying disease, associated health problems and psychiatric comorbidity (9). Anxiety is a fairly common symptom in the DD/MR person for both children and adults (10). 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. Benzodiazepines can be prescribed for specific syndromes in which the published, medical literature identifies these conditions as responsive to this class of medication including various anxiety disorders. The symptoms of anxiety or panic disorder should prompt a search for behavioral explanations as well as other underlying psychiatric comorbidity including depression, bereavement, response to environmental stressors, and abuse/neglect. Benzodiazepines should be prescribed when precise target symptoms allow clinicians and staff to determine whether sufficient improvement is present to warrant the continued use of the medication.

Table 1. Commonly Used Dosing Ranges for Benzodiazepine Anxiolytic Medications for the Adult Population with MR/DD

DRUG	HEALTHY/ADULT DAILY DOSE RANGE	FRAIL/ELDELRY DAILY DOSE RANGE	COMMENTS See PDR for Complete Details
Long Acting (t1/2>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 (t1/2 = 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 (t1/2<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.

Prescription of Benzodiazepines

Clinicians should avoid the use of long, half-life benzodiazepines in persons with mental retardation. These long, half-life medications or their active metabolites are included in the Beer's list of contraindicated drugs for brain damaged persons (5). The long, half-life medications increase risk of toxic accumulation **(See Table 1).** Intermediate and short, half-life medications are preferable and these drugs should be administered on a regular basis when indicated. Once-a-day dosing of a short, half-life drugs such as Ativan may produce mini withdrawal at 12 hours following the last

dosage. Short, half-life medications should be avoided because of dosing/half-life considerations.

Benzodiazepines are addictive and abrupt cessation of medication can produce withdrawal syndromes. The addictive nature of these medications may produce drug-seeking behavior in some patients. Xanax is particularly addictive and produces a complex withdrawal syndrome. Patients who are prescribed long-term Xanax for a long period of time should have a slow, gradual, methodical taper that lasts over weeks to months based on the total daily dosing at the initiation of the taper. Cross-titration to other benzodiazepines could potentially produce withdrawal in some individuals.

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

Dose Adjustment

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 (6), (11). 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 even greater care in the aging MR person and further dose reductions should be considered.

Benzodiazepines can be used in specific 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.

Prescription of Antidepressant Medications

Antidepressant medications can be effective in reducing the symptoms of generalized anxiety disorder, anxiety produced by depression, and panic disorder (12). Second and third generation antidepressants like the SSRIs or the tricyclic antidepressants are the drug of choice in any person with DD/MR who manifests symptoms of anxiety (4). These non-addicting medications are shown to be effective for individuals with

significant anxiety symptoms. Multiple SSRIs have been demonstrated to be safe and effective in persons with DD/MR and no specific SSRI is recommended as superior for the management of anxiety **(See Table 2).**

The typical dose for suppression of anxiety is equivalent to the full antidepressant dose. Sedating antidepressants such as trazedone, Elavil, etc., should be avoided in the DD/MR patient. Patients with seizure disorder often receive antiepileptic medications that can produce drug-drug interactions produced by alteration of drug metabolism.

Table 2
Common Dose Ranges for the Prescription of Antidepressant Medications for the Adult Population with MR/DD

Medication Class	Healthy/Adult Daily Dose Range	Frail/Elderly Daily Dose Range	Comments (See PDR for full description) (13)
1st Generation (TCA's)			
Nortriptyline	25-150mg	10-100mg	Therapeutic Level (50-150ng/ml)
2nd Generation (SSRI's)			
Fluoxetine	10-80mg	5-40mg	Generic Available. May be Activating
Paroxetine	10-60mg	5-30mg	Generic Available. Anticholinergic
Sertraline	50-200mg	25-200mg	GI Side Effects. Take With Food
Citalopram	20-60mg	10-20mg	Few Significant Drug Interactions
Escitalopram	10-30mg	5-20mg	Few Significant Drug Interactions
3rd Generation (SNRI's, Others)			
Buproprion	75-450mg	75-300mg	Use Caution With Seizure Disorders
Mirtazapine	15-45mg	7.5-45mg	Weight Gain/Sedate at Lower Doses (<30)
Trazodone	50-300mg	25-150mg	Monitor Priapism and Orthostasis
Venlafaxine	75-375mg	25-225	Monitor for Hypertension
Duloxetine	40-60mg	20-40mg	Dual Re-uptake Inhibitor, All Doses
This table contains common dose ranges of antidepressant medications that are commonly prescribed for persons with MR/DD. Each patient requires an individualized prescription based on medical and psychiatric features. This information is not a prescriptive guidance. Consult a child psychiatrist for pharmacotherapy in children and adolescents.			

The SSRIs have relatively few side effects in patients; however, drug-induced akathisia can resemble worsening of anxiety. Akathisia is an inner sense of restlessness that resembles anxiety and produces agitation or excessive motor activity. Some patients may develop hyponatremia. The combined use of an SSRI with other serotonergic agents can produce a serotonin syndrome that resembles delirium. In general, these medications are safe and effective in this patient population (4).

Prescription of Buspirone

Buspirone is a unique medication that is effective in the long-term management of anxiety. Several papers document the effectiveness of buspirone in a variety of clinical conditions in persons with mental retardation. The precise biochemical effect of this medication is unknown; however, its pharmaco-dynamic shows that Buspar must be given 4 to 6 weeks to determine efficacy. Most patients with DD/MR can tolerate a full therapeutic dose of 60mg per day. This medicine may not totally eliminate symptoms of anxiety; however, symptoms may be significantly reduced by the drug (6).

Prescription of Antipsychotic Medications

Antipsychotic medications have been used for the symptoms of anxiety in demented patients and those with intellectual disability. In general, antipsychotic medications are not indicated at any dose for the DD/MR patient unless the symptoms are so severe that they are life-threatening or disabling. Antipsychotic medications will reduce symptoms of anxiety that are produced by psychosis through the reduction of psychotic symptoms. The antipsychotic medications have no specific anti-anxiety effect. The national consensus criteria do not include antipsychotic medications as a recommended therapy for anxiety (6).

Old antipsychotic medications such as Haldol or Prolixin should be avoided as antianxiety therapy in the patient with DD/MR. About 40% of these individuals would be expected to develop akathisia which may mimic worsening of anxiety. These medications have such significant side effects as to render them inappropriate in the treatment of anxiety disorder in the DD/MR patient.

Other Medications for Symptoms of Anxiety

A variety of other medications have been discussed as useful in the treatment of anxiety in the patient with DD/MR. Mood stabilizers, anticonvulsants, and others have been considered for this usage. None of those medications have proven efficacy in the reduction of anxiety symptoms.

Psychological Interventions

Psychotherapy is the mainstay of therapy for chronic anxiety in the intellectually normal individual. This intervention is quite helpful in persons with borderline or mild MR; however, these interventions may be less helpful in the moderately impaired patient. These interventions are not helpful in the severe to profoundly retarded individual who lacks the capacity to understand the process.

Conclusion

The prescription of anti-anxiety medications should follow a thorough, meticulous evaluation to exclude medical, psychiatric, behavioral, and environmental precipitants of this symptom. Anxiety disorders do occur in the intellectually disabled person and the drug of choice for these individuals is the SSRI. Benzodiazepines should be used with great caution to avoid toxicity and side effects.

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