Pharmacological Management of Anxiety Disorders in Adults with Mental Retardation or Developmental Disabilities (MR/DD)

1. **Overview**

   Extensive clinical research is not available on the pharmacological efficacy of specific anxiolytic medications for discrete types of anxiety disorders in persons with intellect disability. Four broad categories of medications are used in normal adults with anxiety syndrome: 1) antidepressants, 2) benzodiazepines, 3) other medications like Buspirone, and 4) antipsychotics for severe debilitating symptoms. Children and adolescents with anxiety should be referred to a child psychiatrist for management. **(1)**. Comprehensive therapy for anxiety disorders includes the documentation of specific target behaviors and use of behavioral interventions prior to initiation of medications **(2), (3).**

2. **Treatment of Medical Anxiety**

   The treatment of anxiety begins with a careful evaluation to exclude medical or psychiatric mimics for anxiety **(4), (5).** Anxiety can be produced by a variety of medications, such as bronchodilators, steroids, etc., and medical problems, e.g., thyroid disease, seizures **(5), (6).** Medical anxiety is treated by elimination of the causative medication or correction of the medical problem. Antipsychotic medications and selective serotonin reuptake inhibitors (SSRI's) can produce akathisia, which is a sense of restlessness that mimics anxiety.

3. **Pharmacological Strategy for Treatment of Anxiety**

   The pharmacological management of anxiety requires identification of target symptoms, initiation of therapy, and measurement of pharmacological efficacy. Medications should be prescribed in conjunction with behavioral interventions. Once there is reasonable certainty that there are no medical explanations for the behaviors/symptoms of concern, an assessment of anxiety symptoms should be conducted. Individuals with intellectual disabilities are more likely to have behavioral manifestations of anxiety when they occur and are less likely to be able to verbalize in a sophisticated way about what they are experiencing. Some assessment tools designed for aiding the identification of psychiatric symptoms in individuals with intellectual disabilities include the DASH-II (Diagnostic Assessment for the Severely Handicapped – II), the ADD (Assessment of Dual Diagnosis), and the REISS Screen. These instruments have taken symptoms for the various diagnostic categories in the DSM and translated them into descriptions of behaviors that have been associated with particular diagnostic categories. This kind of assessment can also help sort out which behaviors are manifestations of a psychiatric disorder and which behaviors are a result of learning. Functional behavioral assessments need to be conducted for the latter when identified.

4. Prescription of Antidepressant Medication for Anxiety

Consensus criteria identify second generation, selective serotonin reuptake inhibitor (SSRI) medications as first choice in treatment of anxiety disorders in the patient with MR/DD **(7), (8)**. Antidepressant medications can be effective in reducing the symptoms of generalized anxiety disorder, anxiety produced by depression, and panic disorder. The second and third generation antidepressants are the first drugs of choice in any person with MR/DD who manifests symptoms of anxiety. These non-addicting medications are shown to be effective for individuals with significant symptoms of anxiety **(9).** Multiple SSRI's have been demonstrated to be safe and effective in persons with MR/DD and no specific SSRI is recommended as superior for the management of anxiety. Dosing is adjusted for elderly or frail individuals. Patients require a 6-week course at therapeutic levels to determine the efficacy of antidepressant therapy. The typical dose for suppression of anxiety may be equivalent to the full antidepressant dose **(See Table 1)**. The dose range should be titrated to the lowest amount of medication that will adequately control target symptoms of anxiety. Sedating antidepressants such as Trazedone, Elavil, etc., should be avoided in the patient with MR/DD. Monoamine oxidase inhibitors are rarely prescribed because these complicated medications can produce serious side effects through drug-drug or drug-food interactions **(7), (8).**

Table 1
A Summary of Typical Doses of Antidepressant Medications Prescribed for Anxiety for the Adult Population with MR/DD

Drug	Healthy/Adult (Daily Dose Range)	Frail/Elderly (Daily Dose Range)	Comments (See PDR for Full Description)
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)			
Mirtazapine	15-45mg	7.5-45mg	Weight Gain/Sedate at Lower Doses (<30)
Venlafaxine	75-375mg	25-225	Monitor for Hypertension
A listing of antidepressant medications commonly prescribed for the patient with MR/DD. Each patient requires careful assessment and individualized dosing. This information provides general guidelines and does not represent prescriptive guidance. Consult with a child psychiatrist for children and adolescents. See PDR for additional information.			

The SSRI's 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 (1). Patients with a past history of bipolar disorder may develop mania and the use of an SSRI with other serotonergic agents can produce a serotonin syndrome that may resemble delirium (1). In general, these medications are safe and effective in this patient population.

5. Prescription of Benzodiazepine Medications for Anxiety

Benzodiazepines can be used in the treatment of anxiety for acute, severe symptoms or when other medications fail to improve symptoms. Long half-life drugs, such as diazepam (Valium) or clonazepam (Klonopin), can accumulate toxic serum levels over a period of days or weeks that produce delirium. Intermediate half-life drugs are preferential agents, especially lorazepam and oxazepam **(10).** Many clinicians perceive that Xanax is addictive with potentially dangerous symptoms of withdrawal. Intermediate half-life drugs, like Ativan, can be given three or four times per day to provide smoother blood levels. A short course, i.e., two weeks, can be prescribed for anxiety in reaction to a specific stressor, e.g., death of a caregiver. Long-term therapy can be used for severe, disabling anxiety when other pharmacological and behavioral interventions fail to adequately control symptoms. Caregivers should be advised about addiction and tolerance prior to initiation of therapy. Initial doses should be one-quarter to one-half the dose prescribed for intellectually normal individuals **(See Table 2).**

Table 2
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.			

Benzodiazepines can produce paradoxical excitation or disinhibition in persons with MR/DD. These gabanergic medications share some pharmacological features with alcohol and may produce similar complications to alcohol intoxication, including unsteady gait, confusion, and increased risk for GERD. Mildly retarded persons may be unable to drive or operate dangerous equipment while taking these medications **(11).**

6. Other Medications for Anxiety, e.g., Buspirone

Buspirone is a unique medication that is effective in the long-term management of some individuals with anxiety. Several published reports document the usefulness and effectiveness of Buspirone in a variety of clinical conditions in persons with mental retardation. The precise biochemical effect of this medication is unknown; however, the pharmaco-dynamic shows that the medicine must be given for 4 to 6 weeks to determine whether the patient is improved. Most healthy patients with MR/DD can tolerate a full therapeutic dose of 60mg per day; however, frail or elderly individuals should receive lower doses. This medicine may not totally eliminate symptoms of anxiety; however, symptoms may be significantly reduced by the drug.

A variety of other medications have been discussed as useful in the treatment of anxiety in the MR/DD patient. Mood stabilizers, anticonvulsants, antihistamines, etc., have been considered for this usage. None of these medications have proven efficacy in the reduction of anxiety symptoms. Many sedative medications such as diphenhydramine or hydroxyzine can produce confusion, sedation and unsteady gait.

7. Prescription of Antipsychotic Medications for Anxiety

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 for the treatment of anxiety disorders in the patient with MR/DD unless the symptoms are so severe as to be life-threatening or disabling **(18).** 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 and the drugs can produce akathisia that mimics anxiety.

The prescription of old, first generation antipsychotic medications, such as Haldol or Prolixin, should be avoided for severe, disabling anxiety in the patient with MR/DD. Almost one-third of these individuals would be expected to develop akathisia or tardive dyskinesia which may mimic worsening of anxiety **(12).** These medications have such significant side effects as to render them inappropriate in the treatment of anxiety disorder in the patient with MR/DD except as a last option.

8. Psychological Interventions for Anxiety

Psychotherapy is the mainstay of therapy for chronic anxiety in the intellectually normal individual **(5), (7).** This intervention is helpful in the person with borderline or mild MR; however, these interventions may be less valuable in the moderately impaired patient **(2), (8).** These interventions are rarely helpful in the severe to profoundly retarded individual who lacks the capacity to understand the process. Insufficient clinical data is available to identify a specific type of psychotherapy that is most effective in persons with mental retardation.

Behavior analytic procedures can be included with other treatment modalities for a person who has both a psychiatric diagnosis and intellectual disabilities. Behavioral specialists can determine appropriate training strategies to assist a person with intellectual disabilities to gain better coping skills for dealing with their anxiety symptoms. Triggers for the symptoms can be identified and strategies taught to staff, family members, and the individual to prevent escalation of the behavioral symptom. Counseling can be provided, keeping in mind that discussions need to be geared toward the level of understanding of the individual. Most counseling should take the form skill-building and include the chance for positive reinforcement during the learning process. For example, if an individual becomes angry easily due to an impulse control problem, anger management training may be successful when presented in simplistic terms, modeled by the clinician, and practiced repeatedly by the individual in more than one or two sessions. As the person learns the management techniques, positive reinforcement should be delivered to assist with the acquisition and maintenance of the skills.

9. Assessment of Outcome

The therapeutic goal for treating anxiety disorders is maximum reduction of symptoms. Total elimination of symptoms may be impossible.

The therapeutic endpoint in the treatment of anxiety is reduction of symptoms as described by the patient and caregiver or as measured by behavioral monitoring. Mildly retarded patients can describe symptoms. The clinician must depend on behavioral symptoms to determine efficacy in severely retarded persons. Minimal behavioral monitoring requires consistent measurements over a minimum of several days of observation **(See Table 3).**

Table 3
Methods of Assessing Therapeutic Benefit of Mood Stabilizer Medications

Severity of Mental Retardation	Self-Reporting	Caregiver Reporting	Behavioral Monitoring
Mild	R	R	H
Moderate	H	R	R
Severe/Profound	U	R	R

R=Required **H**=Helpful, but not always required **U**=Unreliable

10. Conclusion

The prescription of anti-anxiety medications should follow a thorough, meticulous evaluation to exclude medical, psychiatric, behavioral, and environmental precipitants of this symptom. Psychological or behavioral interventions should be considered in all patients with anxiety disorders. Anxiety disorders do occur in the intellectually disabled person and the drugs of choice for these individuals are second generation antidepressants such as the SSRI's. Benzodiazepines should be used with great caution to avoid toxicity and side effects. Antipsychotic medications are a treatment of last resort. Other sedating medications such as antihistamines should be avoided **(13).**

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