

Pharmacological Management of Mania in the Adult Person with Mental Retardation and Developmental Disabilities (MR/DD)

1. Overview of Mania

Isolated mania is an uncommon psychiatric problem that can occur in the person with MR/DD; however, mania in bipolar patients is common. Mania is more commonly seen as a component to bipolar disorder. The assessment and management of mania in the person with MR/DD depends upon the patient's ability to communicate and their overall intellectual competency. The first step in treatment of mania is accurate diagnosis and identification of target symptoms for therapy. The treatment team must assess health problems to prevent unnecessary complications for medical therapy. Treatment of mania may reduce other behavioral problems (1).

The optimal therapy for mood disorders combines pharmacological and behavioral interventions. Behavior analytic procedures can be included with other treatment modalities for a person who has both mania 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 selected manic or hypomanic 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 of 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.

This section deals with the treatment of mania in the adult person with MR/DD and elderly populations. Psychiatric and behavioral problems are common in children; however, this section does not contain material that is appropriate to this age population. The assessment and management of psychiatric or behavioral problems in a small child

or young teenager requires the attention of a child psychiatrist and a pediatrician. Dosing schedules and medication recommendations are not applicable to the child and early adolescent populations. Clinicians should refer to appropriate pediatric references for advice on medication prescription and monitoring.

2. Management of Medical Mania

Medical mania, i.e., manic symptoms produced by medications such as antidepressants, steroids, etc., is best treated by elimination of the causative drugs. Drugs like angiotensin converting enzyme inhibitors, steroids, antidepressants, and others can elevate the mood. Antipsychotic medications with mood stabilizing properties may be used for short-term management of medical mania until the medical problem is corrected (2).

3. Symptom Targeting for Mania

Three clusters of symptoms may occur in persons with MR/DD and mania: 1) elation and chronic mood instability, 2) psychosis, and 3) acute agitation. Manic patients may demonstrate one or all of these symptoms (2).

Behavioral scales can be used to assess manic symptoms; especially in moderate or severely retarded persons. Once there is reasonable certainty that there are no medical explanations for the behaviors/symptoms of concern, an assessment of manic symptoms should be conducted. Individuals with intellectual disabilities are more likely to have behavioral manifestations of manic symptoms 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 mania and which behaviors are a result of learning. Functional behavioral assessments need to be conducted for the latter when identified.

4. Management of Acute Mania

Patients with acute mania may demonstrate dangerous behaviors that require immediate stabilization with pharmacological agents. Injectable antipsychotics can be administered to stabilize the patient (**See Table 1**). Stabilization of severe, potentially dangerous symptoms is best achieved through injectable medications. IM olanzapine, ziprasidone, or haloperidol can be used to quiet the acutely agitated patient to assure their safety and that of the unit. Injectable benzodiazepines such as Ativan in the dose range of 0.25 to 0.5mgm can be used when antipsychotic medications are not sufficient

to control symptoms. The benzodiazepines may produce confusion in some patients and disinhibition in others. The use of injectable benzodiazepines requires careful monitoring to avoid excessive sedation, falls, or aspiration.

Manic patients with MR/DD may develop psychosis and require antipsychotic therapy. Second and third generation antipsychotic medications also exhibit mood stabilization and these drugs are first choice in the treatment of mania-induced psychosis (**See Table 2**). Antipsychotic medications can be introduced along with mood stabilizers; however, the antipsychotics should be slowly tapered when the patient's psychotic symptoms are resolved and the patient appears adequately controlled.

Table 1

Common Dosing Ranges of Injectable Medications for Acute Mania in the Adult MR/DD Patient Produced by Psychosis (3),(4),(6)

(Dosing Range in Milligrams)

MEDICATION	FRAIL or OLD (mg)	HEALTHY (mg)	CAUTION See PDR
Haldol (haloperidol) ¹	0.5 to 2.5	1 to 5	Acute EPS
Zyprexa (olanzapine) ²	2.5 to 5	2.5 to 10	Hypotension
Geodon (ziprasidone) ³	5 to 10	10 to 20	Cardiac Toxicity

¹ May give Haldol every two hours for a total of four doses in 24 hours. ² May give a total of three doses of Zyprexa per 24 hours. Second dose may follow first dose by 2 hours and the third dose may be administered four hours after the second. ³ May repeat Geodon once in 2 to 4 hours for a total of two doses in 24 hours.

These values are suggested guidance. Each patient should be individually assessed and dosing adjusted to that individual's clinical circumstances. Consult a child psychiatrist for treatment of children and adolescents. All IM dosing is individualized. See PDR for complete information.

Table 2

A Summary of Antipsychotic Medications Commonly Prescribed for the Adult Population with MR/DD Who Develop Manic Symptoms (3),(4),(6)

Drug	Healthy/Adult Daily Dose Range	Frail or Elderly Daily Dose Range	Major Advisory See PDR for full description (3)
1st Generation Medications			
Chlorpromazine	25-1000mg	10-500mg	Anticholinergic Side Effects
Thioridazine	25-500mg	10-250mg	Blackbox Cardiac Warning
Haloperidol	1.0-30mg	0.5-5.0mg	High Potential for EPS/TD
Fluphenazine	1-20mg	1-5mg	High Potential for EPS/TD
2nd Generation Medications			
Clozapine	100-600mg	25-300mg	Black Box for Agranulocytosis
Risperidone	1-6mg	0.25-2.0mg	Dose-related EPS
Olanzapine	5-20mg	2.5-10mg	Sedation and Metabolic Issues
Quetiapine	25-800mg	25-200mg	Sedation and Hypotension Possible
Ziprasidone	20-160mg	20-80mg	Cardiac Warning
3rd Generation Medications			
Aripiprazole	5-30mg	5-20mg	Akathisia and/or withdrawal Dyskinesia Possible

ABBREVIATIONS: EPS – Extrapyramidal symptoms like stiffness, tardive dyskinesia or akathisia.
 TD- Tardive dyskinesia or unwanted movements.

This table provides commonly prescribed dose information. Each patient requires individualized prescription to assure appropriate doses. Consult with a child psychiatrist for treatment of children and adolescents.

Table 3

Commonly Prescribed Doses of Mood Stabilizing Agents for Adults with Mental Retardation and Developmental Disabilities (2), (5), (6)

Medication	Daily Range Dose for Healthy/Young		Daily Range Dose for Frail/Elderly		Comments See PDR
	<i>Dose (mg)</i>	<i>Target Blood Level</i>	<i>Dose (mg)</i>	<i>Target Blood Level</i>	
Lithium	300 to 1200mg	0.5 to 1.5mEq/L	150 to 600mg	0.2 to 1.0 mEq/L	Multiple Drug Interactions Narrow Therapeutic Window
Valproic Acid	900 to 2400mg	50 to 125 mcg/ml	750 to 1500mg	50 to 100 mcg/ml	Hepato Toxicity Low Platelets
Carbamazepine	400 to 1200mg	4 to 10 mcg/ml	200 to 800mg	2 to 8 mcg/ml	Neutropenia Hyponatremia
Dose ranges are commonly prescribed for mood stabilization or anti-impulsive effect. All doses must be individually adjusted for the individual patient. Consult with a child psychiatrist for treatment of children or adolescents. Consult with PDR for complete information (3).					

5. Antipsychotic Medications as Monotherapy for Chronic Management of Mania

Antipsychotic medications can be used as monotherapy in stabilization of mood; however, these drugs have potential toxicity that requires careful evaluation and management. Zyprexa, Seroquel, Risperdal, Abilify, and Geodon have substantial mood stabilizing effects. Only second and third generation medications are useful as anti-manic agents for persons with MR/DD (See Table 1).

Long-term mood stabilization is best achieved through mood stabilizers. Lithium, valproic acid and carbamazepine have the best-developed data as mood stabilizers in the general population. Consensus guidelines rank lithium and valproic acid as the top choices as mood stabilizers in persons with mania or manic-depressive illness. Lithium has been proven effective for impulsive behavior in some individuals with MR/DD (7).

6. Lithium Therapy for Mania

Lithium is a complicated medication, which is a naturally occurring salt that affects noradrenergic and serotonergic systems as well as second messenger systems. Lithium has a relatively narrow therapeutic window and most patients with MR/DD are optimally managed with blood levels below 1.0mEq/L (See Table 3). Dosages should be initiated at the 150 to 300mg per day range and patients should be carefully monitored for evidence of toxicity including confusion, tremor, and gait instability. Large, younger patients with mild intellectual disability may require full therapeutic

doses at the 900 to 1200mgm per day range, while frail individuals or severely retarded persons may require very modest doses in the 150 to 450mgm per day range. Liquid preparations can be used for persons with swallowing problems or issues with compliance (3). The half-life of lithium is quite long – especially in patients with pre-existing renal disease. Blood levels should be obtained in 5 days after dose initiation or adjustment; when medication reaches steady state. Patients receiving lithium require regular monitoring of kidney function, thyroid function, and calcium levels. Non-compliant patients can receive the liquid form, which is more difficult to cheek or spit.

Patients receiving lithium can develop drug-drug interactions with specific medications including aspirin, non-steroidal anti-inflammatory medications, ACE inhibitors, thiazide diuretics, and several other medications. Concomitant administration of these agents may elevate serum lithium levels and produce toxicity (2), (3).

Lithium is generally safe to be used in conjunction with antipsychotics, antiepileptics, and antispasmodics. Patients with MR/DD who receive lithium may have a greater risk for developing delirium. Any patient treated with lithium who develops acute behavioral changes requires immediate therapeutic monitoring to exclude lithium toxicity (8).

Lithium therapy should be adjusted to the severity of symptoms with a typical serum level in the 0.4 to 0.6MEq/L range. Some brain-damaged individuals respond to extremely low doses of medication and low serum levels in the 0.2 to 0.6mEq/L range (**See Table 3**). Dosing should be adjusted to provide full suppression of symptoms with the least possible medication.

7. Valproic Acid (VPA) for Mood Stabilization

Valproic acid is also recommended as a first line drug for mood stabilization. Valproic acid is a relatively safe medication that can stabilize mood and reduce the frequency of impulsive behaviors. The initial dose and titration schedule of valproic acid depends on the clinical features of the patient including age, size, level of intellectual disability and other health problems. Small, frail patients may begin as low as 250mg twice a day, while large, mildly retarded younger adults may require 500mg to 1000mg per day (**See Table 3**). Dosing should be titrated to symptom control or maximum antiepileptic level (9), (10).

Valproic acid is a relatively safe medication; however, some patients may have problems with drowsiness and gait at therapeutic levels. Abrupt, unexplained changes in level of sensorium for patients treated with valproic acid should cause the clinician to consider a serum level to exclude valproic acid toxicity as well as elevation of ammonia levels. Patients with pre-existing liver disease may be at higher risk for developing

confusion produced by elevated ammonia and pancreatitis has been reported in patients treated with this medication (11).

8. Carbamazepine for Mood Stabilization

Carbamazepine has been shown to exert mood stabilization effect and its close molecular relative, oxycarbamazepine, may also exert some mood stabilization as well. Dosing is adjusted to the age, body size, and neurological status of the patient. Dosing can begin at 50mgm to 100mgm per day and increased on a weekly basis until symptom improvement is detected or the patient achieves a maximum therapeutic, antiepileptic blood level. Blood counts should be monitored on a regular basis to monitor for neutropenia, e.g., every 6 months to a year. Side effects can include sedation, unsteady gait, and occasional hyponatremia (3).

9. Other Medications Used for Mood Stabilization

Many new, third and fourth generation anticonvulsants, e.g., Trileptal, are described as possessing mood stabilization properties in persons with bipolar disorder and normal intellect. The newer antiepileptic medications have not been adequately assessed in the population with MR/DD to confirm efficacy or superiority over older medications with published data or clinical experience (6).

10. Maintenance Therapy for Mania

The titration of mood stabilizing medication begins with documentation of measurable or observable target symptoms. Medications should be titrated to the lowest dose that reduces symptoms to an acceptable level as defined by patient comfort, function, and safety. Medications should be adjusted on a steady schedule, e.g., every week or two weeks, to allow symptom stabilization. Staff or family should be encouraged to have reasonable expectations for therapeutic end points. Staff should have specific rationale for enhancing target symptoms and the management team should not substitute behavioral therapy with medications.

The therapeutic endpoint 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 several days of observation (**See Table 4**).

Table 4

Methods of Assessing Therapeutic Benefit of Mood Stabilizing 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

Some patients with bipolar disorder may experience episodes of elation, irritability or hyperactivity that last for days or several weeks, followed by extended periods of stabilization. The treatment team may use several interventions to manage these mood or behavioral “blips” for the patient after excluding medical or environmental causes. Patients who receive concomitant antidepressant therapy may respond to holding the antidepressant for one or two weeks. Patients who are not sleeping can receive a sedative-hypnotic to assure eight hours of restful sleep for several days. Patients who are not receiving chronic antipsychotic therapy can receive a second generation medication for several weeks to stabilize the patient. Substantial changes in mood stabilizing medications are the last option for patients who fail other interventions.

11. Discontinuation of Mood Stabilizer Medication

Mood stabilizers can be slowly discontinued when the patient is determined to be stable for an appropriate duration of time. The decision to stop a mood stabilizer depends upon the clinical circumstance of each patient and the side effects produced by the medications. Mania is a recurring illness and severe bouts of mania may require long-term use of mood stabilizers. A single bout of mania in an otherwise stable patient may benefit from a slow dose taper after 6 to 12 months to assess vulnerability for repeat manic episodes. Many patients will require lifetime treatment with mood stabilizers to prevent debilitating relapses.

12. Natural History of Mania

The natural history of mood disorders in older persons includes lithium resistance and accelerated cycles. The natural history of mania in the older patient with MR/DD is unknown; however, it is likely that these patients will demonstrate more therapy resistance and sensitivity to medications. Long-term benzodiazepine usage should be avoided in the treatment of mania (4). Long-term use of old antipsychotics such as Haldol, Prolixin, etc., is discouraged because bipolar individuals have an increased risk of developing EPS.

Symptomatic relapse may not indicate therapeutic failure. Symptom relapse in a manic patient requires careful evaluation to exclude new medical causes of mania as well as an assessment to exclude non-compliance with medications. Non-compliance with long-term therapy is common in manic or bipolar patients.

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