

Pharmacological Management Of Aggression, Impulsivity Or Assaultiveness In The Adult Person With Mental Retardation and Developmental Disabilities MR/DD

1. Overview of Acute and Chronic Aggression

Aggression and impulsivity occur in 5-7% of the total patient population with MR/DD (1). No specific cause of mental retardation is more likely to produce aggressive or hostile behaviors. The pharmacological management of the aggressive or impulsive patient is usually the last option used to prevent dangerous behaviors. Some acute, dangerous behaviors require medication to sedate the patient until the problem can be properly assessed. Aggression and impulsive behavior are often the products of environmental stressors (2), health problems, pain, psychiatric morbidity or behavioral stressors (See Table 1), (3). These potential causes should be assessed prior to the initiation of medications by staff or family to reduce impulsive or aggressive behavior. Comorbid serious mental illnesses are common in patients with MR/DD and these disorders can increase the risk for dangerous behaviors (See Table 2).

Table 1
Common Causes of Agitation or Hostility in the Patient with MR/DD

1. Hunger
2. Pain
3. Thirst
4. Medical Problems
5. Rectal Impaction
6. Psychosis
7. Depression
8. Reaction to Abuse or Neglect

Table 2
Frequency of Serious Mental Illness in Adults with MR/DD* that can Produce Aggression

Diagnosis	%	Published Range
Schizophrenia	4.4	2-4.4
Mood Disorder	2.2	3.3-4.3
Anxiety	2.2	2.2-5.5

*Age 16 to 64 from total population

Several classes of medications are recommended by national consensus criteria to reduce the frequency or intensity of impulsive or aggressive behavior (4). Some medications have been used with great success while others have limited or minimal effectiveness, e.g., beta blockers, Klonopin, Naltrexone. A few medications such as Clonidine have substantial risk with limited benefit (4), (5), (6), (7).

Mood stabilizers, antipsychotics, and benzodiazepines are the three most commonly used drugs to manage impulsive or aggressive behavior. Benzodiazepines have limited efficacy aside from acute sedation in the management of persons with impulsive or aggressive behavior and these drugs are not recommended by national consensus guidelines. Benzodiazepines can cause sedation, confusion, and increased risk for falls. Some patients become intoxicated with these medications and demonstrate paradoxical excitation or disinhibition (8).

2. Management of Psychiatric Emergencies in Persons with MR/DD

Psychiatric emergencies can be divided into impulsive behavior, aggressive behavior or assaultive behavior (See Table 3). The term “assaultive” implies that the patient is physically attacking the staff or family through intentional behavior. Aggression can be verbal, physical, or sexual. Physical aggression may include resistiveness, property destruction, elopement, and other such behaviors. Assaultiveness may include direct physical attacks on staff or other residents. Verbal aggressiveness includes threatening behavior or verbal hostility that may provoke confrontations. Assaultiveness requires immediate interventions to safeguard patient and staff. Pharmacological interventions may be used as the first line of treatment when the patient’s hostility threatens serious harm. Aggressiveness may also require immediate psychopharmacological interventions; however, staff should carefully consider other options prior to use of medications, e.g., verbal de-escalation, stimulus reduction, etc. Patients with communication problems may not be able to explain causes of agitation and clinicians must exclude common psychiatric and medical disorders that can produce these behaviors (See Table 2). Medications are rarely necessary as the first option in verbal aggressiveness. Antipsychotics and benzodiazepines may be required to stabilize a dangerous patient but these medications rarely correct underlying causes for aggression or hostile behaviors. These medications simply sedate the patient until the staff can organize effective assessment and management of the underlying cause. Threat reduction is best accomplished by reduction of underlying causes. Under certain circumstances, mildly retarded patients should be advised that the assaultive behavior may produce an arrest and legal consequences. Assaultive behavior in persons with mild mental retardation may result in criminal charges as the term “assault” encompasses clinical and legal definitions.

Table 3
A Nomenclature System For Dangerous Behavior in Adult Persons with MR/DD

Type	Target of Behavior	Form	Risk Level
Impulsive	People, objects	Physical/verbal	Variable
Aggressive	People, objects	Physical/verbal/sexual	Variable
Assaultive	Towards people	Physical/sexual	High

3. Pharmacological Strategies for Acute Psychiatric Emergencies

The management of acute onset agitation or aggressiveness in a MR/DD patient may require the emergent use of injectable antipsychotic or benzodiazepine medications to stabilize the situation. The pharmacological management of acute, new onset hostility or aggression requires a delicate balance between administering sufficient medications to protect the patient or staff as well as caution to avoid excessive sedation or other complications. The pharmacological management of an acute psychiatric emergency begins with rapid assessment to determine the potential etiology for the hostility or aggression. Many types of problems can produce new onset acute combativeness, including pain, illness, fear, psychological distress, and post-ictal confusion.

Benzodiazepines and antipsychotic medications can be used in the acute management of the hostile or combative patient. Injectable antipsychotics are preferable as this class of medication will not produce the paradoxical excitation sometimes induced by benzodiazepines. Appropriate doses of Haldol, olanzapine or Geodon can be prescribed according to the patient's clinical circumstances, age, and body mass (See Table 4). Olanzapine injections often produce sedation. Lorazepam is an appropriate injectable benzodiazepine for use in these individuals. The combination of lorazepam with an antipsychotic can produce excessive sedation in some patients – especially frail and medically compromised individuals. The best choices for emergency medications are those medications that have previously controlled the dangerous behavior with minimum risk to the patient. Sedating drugs, such as hydroxyzine and diphenhydramine, are not effective.

Table 4
Common Dosing Ranges of Injectable Medications for Acute Agitation or Assaultiveness in the Adult MR/DD Patient
 (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. See PDR for complete information.			

For patients with no past clinical history of dangerous behavior or guidance, an injectable antipsychotic medication such as haloperidol, olanzapine, or ziprasidone can be administered. A benzodiazepine can be administered in 30 to 45 minutes if the patient appears to have no significant improvement with the antipsychotic medication. If the patient requires both an antipsychotic and a benzodiazepine for control of the symptoms, this information can be noted for future use. Behavioral interventions should continue while medications are administered. The use of acute sedation to control a dangerous behavior should be followed by a careful evaluation to determine the cause of the combative behavior as well as safeguard to prevent complications such as falls or choking. Physical restraint of the patient may be required until medications are effective.

4. Pharmacological Management of Persistent Impulsive Behavior

The treatment of persistent aggression begins with a meticulous evaluation to exclude medical, psychiatric, or environmental causes of the behavior. Once there is reasonable certainty that there are no medical explanations for the aggression, an assessment of psychiatric symptoms should be conducted. Individuals with intellectual disabilities are more likely to have behavioral manifestations of psychiatric 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 a psychiatric disorder and which behaviors are a result of learning. Functional behavioral assessments need to be conducted for the latter when identified.

Antipsychotics, mood stabilizers, and SSRIs are the three most commonly used classes of medications to reduce persistent impulsive behavior (**See Table 5**). The mood stabilizers are the first medications of choice, as the antipsychotic medications can produce significant side-effects (**See Table 5**). Lithium and anticonvulsant medications are the two most commonly used mood stabilizers for control of impulsive behavior. Lithium may reduce impulsive behavior in persons with normal intellect as well as those with intellectual disability (**9**). The typical dosing range is similar to that for the control of mania (**See Table 6**).

Several anticonvulsant medications have been demonstrated to reduce or diminish dangerous behaviors in the population with normal intellect. Valproic acid and

carbamazepine may be effective in some patients; however, these medications may also produce behavioral problems (10). Anticonvulsants may be helpful in persons with comorbid epilepsy and impulsive behavior. Other anticonvulsants such as dilatin and phenobarbital have little or no effect on these problem behaviors. The choice of anticonvulsant medications depends on the clinical features of the patient.

Therapeutic anticonvulsant levels may be required to control or reduce the frequency of aggressive behaviors. Among the anticonvulsants, valproic acid has the best data on safety and efficacy (11), (12), (13).

Table 5
Pharmacological Management of Persistent Impulsive or Aggressive Behavior
in Patients with MR/DD

Recommended Choices	Class	Medications	Comments
1^o	Anticonvulsants Mood Stabilizers	Valproic Acid Carbamazepine Lithium	Monitor blood levels May produce confusion or sedation
2^o	Antipsychotics Antidepressants	2 ^o or 3 ^o generation Antipsychotics SSRIs	Multiple potential side effects Low rates of effectiveness
3^o	Others	Beta Blockers Clonidine	Can produce significant side effects

All of the mood stabilizers have potential toxicity and side-effects. Blood monitoring is required for Valproic acid, carbamazepine, and lithium. Each of these medications has a specific toxicity profile. Drug-drug interactions are common with these medications and the prescribing physician should be familiar with potential side effects and interactions for each drug (15). Moderate to severely retarded patients are incapable of describing symptoms of adverse reactions, e.g., confusion with lithium, unsteadiness with Valproic acid, and clinicians must carefully monitor for these side-effects (See Table 6).

Table 6

Commonly Prescribed Dosing Ranges of Medications that Stabilize Mood or Diminish Impulsive Behavior for Adults with Mental Retardation and Developmental Disabilities (4), (14), (15)

Medication	Daily Dose Range for Healthy/Young		Daily Dose Range 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 (16).					

5. Use of Antipsychotic Medications

Antipsychotic medications are often used to control persistent, impulsive or hostile behavior. Chronic prescription of the old, first generation antipsychotics, e.g., Haldol, Prolixin, can produce severe side-effects in the patient with MR/DD. First generation antipsychotic medications can produce acute dystonic reactions that may be difficult to detect in patients with communication problems. Thorazine is quite sedating and can produce significant orthostatic hypotension (**See Table 7**).

Table 7
Summary of Common Doses of Antipsychotic Medications Prescribed for the MR/DD
Population with Impulsive Aggressive Behavior (15), (16)

Drug	Healthy/Adult Daily Dose Range	Frail or Elderly Daily Dose Range	Major Advisory
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 TD- Tardive Dyskinesia These values summarize typical dose ranges used for persons with MR/DD. Each patient should be carefully assessed and dosing adjusted to his or her clinical circumstances. See PDR for a complete description of possible side effects.			

Among the new antipsychotic medications, risperidone (17), (18) and olanzapine (19), (20) have published clinical data that supports their use for aggression. Quetiapine can produce sedation in some patients. No specific new antipsychotic medication has demonstrated superiority over other medications for management of acute or persistent aggressive or impulsive behavior. The recommended, maximum prescribed dose for these medications is equal to that of the standard dose for psychosis. Ziprasidone and olanzapine both have injectable forms that are helpful with acute agitation. Risperdal and olanzapine both have soluble preparation that reduce the likelihood of noncompliance, e.g., spitting, medication refusal, etc. Some patients will not take oral medications and long-acting, injectable medications can be used until the patient is stabilized. The injectable medication can be cross-titrated to the oral dose over time (See Table 8).

Dosing is recommended for the evening when the sedating side effects are less problematic. Patients require monitoring for EPS. Prophylactic use of

anticholinergics like Artane or Cogentin, is not recommended because of potential confusion produced by this class of medication.

Table 8
Summary of Injectable, Long-Acting Preparations (Depot Preparations) of Antipsychotic Medications for the Adult Patient with MR/DD (15), (16)
 (Dosing Range in Milligrams- Given Every 2 Weeks)

INTRAMUSCULAR MEDICATION	IM DOSE FOR FRAIL/ELDERLY (mg)	IM DOSE FOR HEALTHY (mg)
Haldol (haloperidol decanoate) <i>every two weeks</i>	12.5 to 25	12.5 to 75
Perphenazine (Prolixin decanoate) <i>every two weeks</i>	2.5 to 25	12.5 to 50
Risperdal Consta <i>every two weeks</i>	25	25 to 37.5
Dose frequency, i.e., duration between injections, can be titrated to every three or four weeks. Each patient should be individually assessed and dosing adjusted to that individual's clinical circumstances. Consult with a child psychiatrist for children and adolescents.		

6. Use of SSRIs for Aggression

The SSRI medications are variably effective for acute aggression or assaultiveness (See Table 5). Consensus guidelines recommend the use of SSRIs in chronic, episodic aggressive behavior as possibly effective. No specific medication within the SSRI class is recommended. Clinicians must be vigilant to identify akathisia produced by most SSRIs. Tricyclic antidepressants and monoamine oxidase inhibitors are not shown to be clinically effective for aggression. The dosing range of antidepressant medications for aggression is similar to that for depression.

7. Benzodiazepines

Benzodiazepine medications can be prescribed for acute aggression or impulsive behavior and for impulsivity produced by anxiety disorders. Long-term benzodiazepine therapy is not demonstrated to be effective for persistent impulsivity or aggression (See Table 5).

8. Behavioral Intervention for Chronic Aggression

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 psychiatric 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. Assessing Clinical Outcomes

The therapeutic endpoint is reduction of chronic or persistent 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 9).

Table 9
Methods of Assessing Therapeutic Benefit of Antipsychotic 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

Aggression, impulsivity or assaultiveness can be serious behavioral problems manifested by a small number of patients with MR/DD. The pharmacological management begins with acute stabilization followed by chronic therapy to suppress symptoms. Injectable antipsychotic medications are the best option in most acute aggression. Mood stabilizers, lithium, SSRI's, and antipsychotic medications are used for chronic symptoms (See Table 4).

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