

Prescription of Antipsychotic Medications for the Adult Person with Mental Retardation or Developmental Disabilities (MR/DD)

1. Overview

Antipsychotic medications are commonly prescribed for persons with intellectual disability. The prevalence of psychiatric disorders that may respond to antipsychotic medications is higher in the population with MR/DD than in the general population (See **Table 1**). Patients with schizophrenia and psychotic mood disorders often benefit from treatment with antipsychotic medications. Consensus guidelines define the role of these medications (1), (2).

Specific antipsychotic medications are not identified as uniquely beneficial in patients with specific causes of mental retardation. Autism commonly produces behavioral and psychiatric problems that require the use of antipsychotic medications. Antipsychotic medications are beneficial for some individuals

(See **Tables 2 and 3**) and studies have examined the clinical effectiveness of many of the old, first generation and new, second generation antipsychotics in this disorder (1), (2). Autism was selected for drug trials because this condition is common and is defined by specific DSM criteria. Mental retardation is caused by over 200 disorders and the clinical heterogeneity of mental retardation limits the ability of clinical investigators to examine the efficacy of antipsychotic medications in persons with many specific diseases. Few randomized controlled studies examine the efficacy of these medications in large numbers of persons with MR/DD; however, most experts recommend their use for specific psychiatric disorders or symptoms (1), (2), (4), (5).

2. Indications for Antipsychotic Medication

Antipsychotic medication can be prescribed for three broad indications: 1) specific psychiatric disorders such as schizophrenia or mania that produce psychosis, 2) dangerous behaviors that produce imminent threat or harm to self or others, or 3) disruptive behaviors that fail to respond to behavioral interventions, and reduce the quality of life, or habilitative potential for the individual (5), (6). Behavioral problems are common and some individuals require antipsychotic medications to control dangerous, severely disruptive, or debilitating behaviors (7). Antipsychotic medications will not improve intellectual function and these drugs may worsen neurological problems such as gait problems. The prescription of antipsychotic medications should always balance the benefit for the patient versus the potential toxicity produced by the drug.

Table 1
SMI in Adult MR/DD*

| Diagnosis | % | Published Range |
|---------------------|-----|-----------------|
| Schizophrenia | 4.4 | 2-4.4 |
| Mood Disorder | 2.2 | 3.3-4.3 |
| Delusional Disorder | ? | 0-1.1 |

*Age 16 to 64 from total population

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(3)

Several studies have demonstrated the value of antipsychotics in autism (See Tables 2 and 3), (8).

Table 2

Psychotropic Medications in the Treatment of Autism

| Medication | Symptom | No. Studies | Improve | Comment |
|-------------|--------------------------|-------------|---------|--------------------|
| Olanzapine | Aggression | 1 | Y | Autism and PDD |
| Clozapine | Aggression | 1 | Y | 200-400 high doses |
| Quetiapine | Aggression | 1 | N | Sedation |
| Risperidone | Aggression, Irritability | 2 | Y | Good Results |
| Ziprasidone | Aggression | 1 | Y | High Side Effects |

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Table 3

Psychotropic Medications in the Treatment of Autism

| Medication | Behavioral Complications | No. Studies | Improve | Comment |
|-----------------|--------------------------|-------------|---------|-----------------|
| Haldol | Anger, Lability | 4 | Y | High EPS |
| Risperidone | Aggression, Irritability | 2 | Y | Good Results |
| Fluvoxamine | Aggression | 1 | Y | Unclear Data |
| Lamotrigine | -- | 1 | N | Same as Placebo |
| Methylphenidate | Hyperactivity | 1 | Y | Minimal |

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3. Efficacy of Antipsychotic Medications

The “new” or “atypical” second generation antipsychotic medications are more effective than the “old” or “typical” first generation medications in management of psychosis related to schizophrenia or the symptoms of bipolar disorder (2). The choice of an antipsychotic medication depends upon the desired clinical effects as well as the perceived risk for side effects. The medication should be initiated in low dose and the titration can last over several weeks to several months (See Table 4). The new medications are more expensive than older drugs; however, their pharmacological superiority has shown these newer drugs as cost-effective (9). Patients generally prefer the newer, expensive medications. Some pharmacy services have restrictions for availability of new antipsychotic medications and clinicians will need to check on availability of medications. Clinical studies demonstrate behavioral symptom improvement for persons with MR/DD treated with Risperidone (3), (4), (10), (11), olanzapine (12), (13), quetiapine (14), and ziprasidone (15). Clozaril also has supportive data (16).

4. Common Side Effects of Antipsychotic Medications

All antipsychotic medications have four broad categories of toxicity: 1) neurocognitive, 2) neurological, 3) autonomic, and 4) medical – including hepatic, hematological, and others. Physicians should not prescribe antipsychotic medication for the patient with MR/DD unless they are familiar with all of the common side effects produced by the medications as well as standard interventions for potential toxicity (17), (18).

Common neurocognitive effects of antipsychotic medications include sedation or diminished intellectual function (19). Old, first generation antipsychotic medications are more likely to produce neurocognitive deficits than newer drugs. The neurological complications produced by both the old and new medications include tardive dyskinesia, parkinsonism, akathisia, and neuroleptic malignant syndrome (20). The old antipsychotics produce greater likelihood of EPS than newer drugs (21). Clinicians should avoid the “older” medications such as fluphenazine (Prolixin), haloperidol (Haldol), and thioridazine (Mellaril) that have high rates of toxicity including neurological, cardiovascular, and gastrointestinal (22). Substantial numbers of patients with MR/DD (1/3 - 1/2) will develop some form of extrapyramidal syndrome when prescribed the old antipsychotic medications. Tardive dyskinesia, akathisia, dystonia,

and drug-induced Parkinson's disease are common complications (21). Each form of EPS can produce dangerous or disabling symptoms for the patient. Some forms of toxicity such as tardive dyskinesia may be irreversible and this damage can expose clinicians to litigation. Akathisia is an inner sense of restlessness that occurs in almost 1/2 of persons who receive older medications. Akathisia resembles agitation or anxiety (9).

Cardiovascular toxicity of antipsychotic medications includes orthostatic hypotension, electrical conduction abnormalities, and tachycardia. Low potency, older medications such as chlorpromazine (Thorazine) and thioridazine (Mellaril) can produce significant cardiovascular changes. Mellaril and Thorazine should be avoided in persons with MR/DD because of the significant side effect profile and better medications are available for control of symptoms. Mellaril has a black box warning for cardiac toxicity (9), (22).

Metabolic problems are common with new antipsychotic medications. Patients may develop obesity, glucose intolerance, diabetes or hyperlipidemia. The conditions should be assessed prior to initiation of medication and clinicians must monitor these potential side effects (15).

5. Evaluation Prior to Initiation of Antipsychotic Medications

The clinician should document a recent, basic, physical examination prior to the initiation of antipsychotic medication. The neurological examination should screen for parkinsonism and other forms of extrapyramidal symptoms. A baseline blood sugar and weight is appropriate. An EKG is not indicated in the younger patient unless the individual is: 1) receiving Mellaril, 2) has some past QTc abnormalities, 3) has metabolic syndromes or 4) has evidence of serious cardiovascular disease. Older patients, i.e., over age 45 or 50 should have baseline EKG (9), (17).

Patients beginning on antipsychotic medications should have annual blood sugars and lipid profiles. Weights should be monitored on a monthly basis except to those individuals who are predisposed to obesity. Obese patients should have dietary monitoring, dietary education, and frequent weights. Patients with mild mental retardation should have dietary counseling to reduce the likelihood of excessive weight gain. The prescription of antipsychotic medications requires careful follow-up. All patients should be evaluated for side-effects within a month or sooner (9).

Once there is reasonable certainty that there are no medical explanations for the behaviors/symptoms of concern, 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.

6. Initiation of Therapy

The choice of medication depends on the patient, the target symptoms, past response to medication, and concerns about toxicity. The clinician should begin medication after identification of target symptoms and determination of expected result. Baseline behavioral data or clinical observations are helpful when prescribing medication to manage behavioral symptoms. Young, healthy patients can receive a standard dose. Frail or elderly patients should receive 1/4 or 1/2 the customary starting dose (**See Table 4**).

Table 4
A Summary of Antipsychotic Medications Commonly Prescribed for the Adult Population with MR/DD
(2), (17), (22), (23)

| Drug | Healthy/Adult Daily Dose Range | Frail or Elderly Daily Dose Range | Major Advisory See PDR for full description |
|--|--------------------------------|-----------------------------------|---|
| 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 |
| <p>ABBREVIATIONS: EPS – Extrapyramidal symptoms like stiffness, tardive dyskinesia or akathisia. TD- Tardive dyskinesia or unwanted movements.</p> <p>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.</p> | | | |

Most antipsychotic medications reach steady state after one week; however, their antipsychotic benefit may require 4-6 weeks of continuous therapy. The most immediate beneficial effect from neuroleptic medications is derived from sedation. Younger, healthy patients may require the full recommended dose for adults while elderly or frail patients may require 1/4 to 1/2 the total dose (**23**). The physician should avoid “loading doses” that may produce sedation.

7. Switching the Patient to a Newer Medication

Patients who are presently receiving old, first generation antipsychotic medications should be considered for cross-titration to newer medications. The old, first generation

antipsychotic medications including Haldol, Prolixin, and Mellaril can produce multiple toxicities and permanent side effects such as tardive dyskinesia. Mellaril has an FDA “black box” warning for cardiac abnormalities. The cross-titration should be accomplished with the appropriate second or third generation medication being initiated at a very low dosage, while the old antipsychotic is reduced in a proportionate dose. The cross-titration should be accomplished over a minimum of 6-8 week period of continuous therapy. The patients who receive antipsychotic medications should have appropriate documentation of target symptoms, beneficial effect, and potential side effects. For those individuals without clear indication for the medication, a dose reduction should be considered. The antipsychotic medication can be titrated downward at a dose range of approximately 10% per month or the nearest possible increment. The patient should be assessed on a regular basis and monitored for the emergence of psychotic symptoms, behavioral problems, or other clinical symptoms that initially warranted the use of the medication. Following successful discontinuation of the medication, the patient should be re-checked every 6 months for several years to exclude the re-emergence of psychotic symptoms.

Most new antipsychotic medications are demonstrated to be safe and effective in persons with mental retardation. Clozaril is effective; however, the potential toxicities, including worsening of seizures, suppression of white blood cell count, and orthostasis reduce the practicality of this medication (16), (17).

8. The Use of Antipsychotics For Acute Agitation

Any person with MR/DD may develop acute agitation or aggression that requires immediate administration of medication to protect the patient and others (24), (25). The clinician has several options based on the availability of medications and the relative compliance for the patient. Benzodiazepines are a second line drug because they can produce paradoxical excitation with intoxication and disinhibition (26). The clinician should determine which medication has worked best in the past and start with that previously successful intervention. Oral medications can include Risperdal liquid, Risperdal M-tab, or Zydys to assure compliance with the oral dose of medication (See Table 5). The dose must be adjusted according the level of threat, body size, past reactions to the medications and risk for toxicity. The addition of other medications, e.g., Ativan and Haldol, is discouraged unless monotherapy has failed in the past. Staff may want immediate sedation; however, the use of injectable medications should be coupled to behavioral interventions to maximize the benefit of the medication.

Table 5

Common Dosing Ranges for Injectable Medications for Acute Agitation in the Adult Patient with MR/DD (Dosing Range in Milligrams)

| MEDICATION | FRAIL/ELDERLY (mg) | HEALTHY/YOUNG (mg) | CAUTION |
|-----------------------------------|-----------------------|-----------------------|------------------|
| 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 Every two hours for a total of four doses. ² May give a total of three doses of Zyprexa per 24 hours. Second dose may follow first by 2 hours and third dose can be given four hours after the second. ³ May repeat Geodon once in 2 to 4 hours.

These values are suggested guidance. Each patient should be individually assessed and dosing adjusted to that individual's clinical circumstances. All IM dosing is individualized.

The use of PRN medication should be followed by a careful assessment to determine the precipitants of the behavior and exclude other underlying causes that may be producing the symptoms such as medical delirium with behavioral complications. The continuous use of PRN medications in the absence of aggressive behavioral intervention is discouraged by most clinicians (1), (2). Patients often develop tolerance to the psychotropic medications and the definitive treatment of the abnormal target behavior is identification and treatment of the underlying cause.

9. Course of Therapy

The duration of antipsychotic therapy depends on the clinical indication and severity of symptoms (See Table 6). The person with MR/DD and schizophrenia may require years of therapy. The patient with psychosis from delirium can have dose reductions within weeks or months after resolution of the underlying cause to determine the need for ongoing therapy. Patients with persistent, severe SIB may require long-term therapy, while an acute flare of SIB in a previously stable patient may require brief pharmacological therapy. All patients should be re-evaluated every three months regardless of cause and response to therapy.

Table 6
Common Diagnoses that Allow Continued Antipsychotic Therapy

1. Schizophrenia
2. Schizo-Affective Disorder
3. Bipolar Disorder
4. Behavioral problems that fail two dose reductions in the previous year

Patients with mood disorders may have antipsychotic medication dose reduction after the mood stabilizing medication has improved the patient's affective state and the patient has remained stable for a month or more.

The therapeutic endpoint for prescription of antipsychotic medications is reduction of symptoms as described by the patient and caregiver or as measured by behavioral monitoring. Mildly retarded patients can describe psychotic symptoms. The clinician must depend on behavioral manifestations to determine efficacy in severely retarded persons. Minimal behavioral monitoring requires consistent measurements over a minimum of several days of observation (See Table 7).

Table 7. 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. Management of the Non-Compliant Patient

Higher functioning patients may refuse to take medications or discontinue treatment once they reside in the community. Medication non-compliance is a common reason for relapse of psychotic symptoms. Serum levels can be monitored and patients should be checked for "cheeking". Liquid or injectable preparations can be used to manage the non-compliant behavior. Both Zyprexa and Risperdal have dissolvable preparations, i.e., Risperdal M-tabs and Zydys, which dissolve immediately on contact with moist mucous

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membranes. These medications are absorbed unless the patient self-induces vomiting or flushes their mouth immediately after consuming the medication. Liquid medications are harder to “cheek” and Haldol, as well as Risperdal, come as liquid preparations. The long-acting, antipsychotic injectable medications include Haldol decanoate, Prolixin decanoate, and Risperdal Consta. The long-term use of old antipsychotics such as Haldol and Prolixin produces significant risk for drug-induced toxicity. The Risperdal Consta is a preferable preparation; however, this medication is more expensive (See Table 8).

Table 8

Commonly Used Dose Ranges of Injectable, Long-Acting Preparations (Depot Preparations) of Antipsychotic Medications for the Adult with MR/DD
(Dosing Range in Milligrams- Given Every 2 Weeks)

| 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 |
| Prolixin (perphenazine 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. These values are suggested guidance. Each patient should be individually assessed and dosing adjusted to that individual's clinical circumstances. | | |

Non-compliance with medications can be a serious problem in mildly retarded persons or individuals who refuse to take medications. Paranoid or psychotic individuals may be hesitant to take any medication. Liquid, sol-tab, and injectable forms of second generation antipsychotic medications can improve compliance. The clinician should consider a serum level of antipsychotic medication for any patient receiving large doses of drugs with minimum obvious therapeutic benefit or sedation. Patients should receive a full therapeutic dose for at least 6 weeks prior to conclusion that medications do not produce the desired effect. Any beneficial effect from the medication warrants an additional 6 weeks at sustained dosage to assure the clinician has afforded the medication adequate time to work. Failure of one medication warrants trial with a second medication using the previous described method. Additional doses of medicine can be used on a PRN basis when acute behavioral episodes warrant. Polypharmacy as defined by the use of two or more antipsychotic medications is not recommended except where all other medications have failed to control symptoms (2).

11. The Role of Antipsychotic Medication in Management of the Person with MR/DD

Many psychotropic medications can be safely used in persons with MR/DD; however, all of these medications can produce adverse outcomes. The clinician can use antipsychotic medications for specific psychiatric conditions, e.g., schizophrenia. These medications are not a substitute for appropriate behavioral management. The antipsychotics should only be used as chemical restraints when all other options fail and the patient is in danger of harm to self or others. The use of antipsychotics requires informed consent from either

the patient of the caregiver. Antipsychotic therapy should accompany behavioral therapy for maximum therapeutic benefit to the patient.

Behavioral analytic procedures can be included with other treatment modalities for a person's psychotic symptoms 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 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.

12. Conclusion

Antipsychotic medications may be prescribed for persons with MR/DD and comorbid schizophrenia, mood disorders, delirium with agitation or severe, dangerous behavioral symptoms that are not managed with behavioral interventions. Newer, second or third generation medications are preferable to older drugs. Medication side effects are common and require careful monitoring. Polypharmacy, i.e., two or more antipsychotics should be avoided when possible.

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