Antipsychotic Utilization – A Review of the Evidence

The most common prescribed atypical antipsychotics in ND Medicaid are risperidone (34%), aripiprazole (29%), quetiapine (20%), and olanzapine (6%). Antipsychotics are commonly used off-label, either due to good clinical evidence or because it is common clinical practice.

Common clinical practices should be closely looked at for evidence. For example, by 2011, more than $1 billion in settlements had been paid by the manufacturer of Seroquel® (quetiapine) for fraudulently marketing through false and/or misleading messages related to the drug's efficacy in unapproved conditions, to minimize concerns of certain side effects, and to conceal the potent nature of the drug.[4] Despite these settlements, quetiapine continues to be used off-label for indications with very low or negative evidence.

Antipsychotics differ in safety, tolerability and efficacy and are not interchangeable. **[1]**

When are antipsychotics used?

- Evidence for use in antipsychotics is strongest for schizophrenia.[1,5]
- Substantial evidence exists for use of antipsychotics in bipolar disorder, psychotic depression, severe aggression, and Tourette's syndrome. [5]
- There are severe or refractory circumstances where antipsychotics may be used for obsessive compulsive disorder (OCD) or self-injurious behaviors. [5]
- Antipsychotics do not have evidence supporting use for ADHD, sedatives, or eating disorders.[2, 5]

What is the evidence for common indications?

Pervasive developmental disorders (PDD) including autism

- Risperidone has the most evidence and consistently has shown improvement in aggression, irritability, self-injurious behavior, temper tantrums, and quickly changing moods. It is FDA approved for this use. **[1,3]**
- Aripiprazole has significantly improved irritability in patients aged 6 to 17. It is FDA approved for this use. **[1,3]**
- Olanzapine: may provide benefit in disruptive behaviors.**[1,3]**.
- Quetiapine has demonstrated suboptimal effectiveness in patients with PDD. **[1,3]**

Dementia and severe geriatric agitation

Warning: Cerebrovascular adverse events (stroke, transient ischemic attack) including fatalities have occurred in elderly individuals who received treatment of dementia-related psychosis with antipsychotics. Antipsychotics with a high binding affinity of alpha 2-adrenergic and M1 muscarinic receptors may be associated with a greater risk of stroke than the use of other types of antipsychotics

- Risperidone has the most evidence and is effective and well tolerated. **[1]** It has moderate affinity for alpha 2-adrenergic receptors.[2]
- Aripiprazole has favorable evidence and does not have affinity for alpha-2 adrenergic or M1 muscarinic receptors. [2]
- Olanzapine: has some trials showing safe and significant superior efficacy to placebo. Data is inconsistent. Olanzapine has a high affinity for M1 muscarinic receptors. [2]
- Quetiapine has not shown statistically significant improvement in agitation. [2]

Disruptive Behavior Disorders (DBDs)/Aggression

- Risperidone: There is substantial evidence for youths with disruptive behaviors in children with sub-average intelligence and impulsive aggression in conduct disorder and disruptive behavior disorders. [1]
- Aripiprazole: There is good evidence showing evidence for aggression in conduct disorders. [1]
- Olanzapine: has demonstrated effectiveness in disruptive behaviors.
- Quetiapine: There is low quality evidence showing evidence for aggression in conduct disorders.[1]

Antipsychotic use in children under age 6:

- Use of antipsychotic medications should only be considered in extraordinary circumstances, such as disruptive aggression in autism.[5]
- Only risperidone and aripiprazole have evidence for use.[5]

Assessing risk-benefit ratio of continuing medications:

Start with medications:[5]

1. Without indication, or if it is unclear what symptoms are being targeted
2. With the least evidence of efficacy for treatment of targeted symptoms or indication or are being used outside of guidelines recommending their use.
3. That were ineffective for targeted symptoms or symptoms have resolved
4. Without benefit to justify harms, or have the greatest risk of adverse effects
5. That are part of a prescribing cascade, treating side effects that have been misdiagnosed as another disorder or to counter side effects of another drug.

References

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3. Weissman L, Bridgemohan C. Autism spectrum disorder in children and adolescents: Pharmacologic Interventions. UpToDate. Waltham, MA: UpToDate Inc. https://www.uptodate.com (Accessed on January 18, 2019.)
4. Nutt AE, Keating D. (March 2018). One of America's most popular drugs – first aimed at schizophrenia – reveals the issues of 'off-label' use. [Electronic Version]. *Washington Post*.
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