Using and Managing Antipsychotics In the Primary Care Setting

Karen Blackman, MD
Amy Odom, DO
Primary Care Collaboration
Traverse City, MI 8/28/10
Objectives

- Identify the potential needs for prescribing anti-psychotics in a primary care setting

- Use a systematic approach to following patients on anti-psychotics to improve safety
Agenda

- Review of antipsychotic nomenclature
- Tour of antipsychotic use in the primary care setting
- Risk profiles of antipsychotics
- Safety tool for monitoring patients on antipsychotics
Handouts

- Bipolar dosing charts
- Materials for dosing of APs in dementia with agitation or psychosis
  - Cover of APA Quick Reference Guide to treating patients with Alzheimer’s Disease and other dementias
  - Copy of page #21 from guide - dosing atypical APs
- TRUSSt Big BeLts
  - Antipsychotic Monitoring Form
  - Antipsychotic Patient Education Form
Why Learn About Antipsychotics

- Primary care providers are prescribing them

- A great deal of psychiatry is done in the primary care office
  - Patients may not have psychiatry access
  - Patients may avoid psychiatry even if they do have access

- These drugs can be a blessing and a curse
Antipsychotic Nomenclature
First Generation (FGA) =Typicals=Conventional

- Examples:
  - Chlorpromazine (thorazine)
    - “Low potency”
  - Perphenazine (Trilafon)
    - “Medium potency”
  - Haloperidol (Haldol)
    - “High potency”
Second Generation Antipsychotics (SGA) = Atypicals

- Aripiprazole (Abilify)
- Asenapine (Saphris)
- Clozapine (Clozaril)
- Iloperidone (Fanapt)
- Olanzapine (Zyprexa)
- Quetiapine (Seroquel)
- Risperidone (Risperdal)
- Ziprasidone (Geodon)
Clinical Antipsychotic Trials of Intervention Effectiveness
- Published in NEJM in 2005

Compared efficacy and tolerability of FGA perphenazine (Trilafon) with several SGAs in schizophrenia

Majority discontinued their assigned medications (~1000/~1500)
CATIE continued

- Olanzapine (Zyprexa) most efficacious?
  - Longest time to all cause discontinuation
  - Refuted later

- Olanzapine worst weight gain, glucose, lipids

- Perphenazine worst re: neurologic side effects

- Efficacy and tolerability more similar than expected
When do YOU use Antipsychotic medications?
When to Consider AP Use

- Bipolar Disorder
- Depression
  - Augmentation in treatment resistant depression
  - Psychotic depression
- Psychosis
  - Acute
  - Chronic
- Dementia with psychosis or agitation
- Delirium
- Special cases
Antipsychotics in Bipolar Disorder

- Nearly all atypical antipsychotics are efficacious in mania, FDA approved and work quickly
  - Iloperidone not FDA approved for bipolar

- Can also be effective for bipolar depression
  - FDA approval for quetiapine (Seroquel)
  - FDA approval for olanzapine with fluoxetine (Symbyax)
How to Approach Bipolar Disorder

- Determine phase patient is in
  - 2\textsuperscript{nd} and 3\textsuperscript{rd} rows in page 1 of Bipolar Medication Chart give FDA indicated phase and other efficacy information

- Judge how ill the patient is
  - Urgent vs. non-urgent
  - Row labeled “acuity” in charts addresses time till onset of action
How to Approach Bipolar Disorder, cont.

- Then look at the patient (and yourself) in light of side effects and ease of monitoring medication.

- If using antipsychotic, consider another product (like an anticonvulsant mood stabilizer) to take its place over time!
Antipsychotics in Treatment Resistant Depression

- 59 year old female
- Elderly demented mother
- Financial ruin due to divorce
- Moved out of “dream” home to small apartment
- Recurred on citalopram 60/d, fluoxetine, venlafaxine, sertraline,
- Failed bupropion and buspirone augmentation

Sparrow/MSU FMRP Behavioral Science Team
2010
Antipsychotics as Adjuncts to Antidepressants in Depression

- Aripiprazole (Abilify) FDA approved as augmenting agent
- Quetiapine (Seroquel) FDA approved as augmenting agent
- Olanzapine/fluoxetine (Symbyax) FDA approved for treatment resistant depression
- Other augmenting agents may pose less dangers
  - Direct to consumer advertising, look out!
  - Patients may be desensitized to danger statements
Antipsychotics in Psychotic Depression

- 55 year old female teacher
- Severely depressed and not responding to multiple antidepressant trials
- When psychiatrist closes blinds, she asks if psychiatrist is afraid of “him” too
  - Reveals paranoia
Antipsychotics in Psychotic Depression

- Add antipsychotic to antidepressant regimen
  - Won’t remit without this
  - Start low, go slow till symptoms addressed
- Treat for at least 3 months with the AP
  - Then can consider discontinuing
- Treat depression long term to help prevent further episodes
Antipsychotics in Acute Psychosis

- 45 year old woman
- Brought in by her sister
- Making no sense
- Moved recently from another state
- Stopped medications she was on
- Thinks she is important part of a government strategy to stop terrorism; suspects neighbors
Antipsychotics in Acute Psychosis

- Patient does not seem depressed, but distressed
- Diagnosis per se not known
- Consider hospitalization, psychiatry referral, trying to get back story (talk to previous treating provider if possible)
- This is the individual for whom antipsychotics were designed!
Antipsychotics in Chronic Psychosis

- 48 yo male seen for annual physical exam
- Lives in AFC
- Schizophrenia since age 26
- Goes to CMH for psychiatric care
- On olanzapine
- FBS 160, TG 400
Antipsychotics in Chronic Psychosis

- PCPs often provide care for chronically mentally ill
- May not be the prescriber of AP’s in these cases
- Need to monitor side effects and take action when necessary
- Communication with CMH to decide plan of action
Antipsychotics in Dementia

- 91 year old retired professor
- Alzheimer’s Disease
- At home with ill, 88 year old wife
- Up much of the night agitated and seemingly responding to people who are not there
Antipsychotics in Dementia With Psychosis or Agitation

- Non pharmacology first!
  - If can calm psychosis, agitation no need to treat
- Re: pharmacology: data best support atypical antipsychotic efficacy
  - though side effects minimize benefit potential!
- Less evidence that benzodiazepines, antidepressants, cholinesterase inhibitors, anticonvulsants benefit
- Once controlled, try to taper off antipsychotics

Use of Atypical Antipsychotics for Dementia Related Psychosis and Agitation

**TABLE 3. SECOND-GENERATION ANTIPSYCHOTICS**

<table>
<thead>
<tr>
<th>Medication</th>
<th>Usual Starting Dose (mg/day)</th>
<th>Usual Maximum Dose (mg/day)</th>
<th>Side Effects</th>
</tr>
</thead>
<tbody>
<tr>
<td>Aripiprazole</td>
<td>Unknown(^a)</td>
<td>15</td>
<td>Mild to moderate effects include akathisia, parkinsonism, sedation, peripheral and central anticholinergic effects, delirium, postural hypotension, cardiac conduction defects, urinary tract infections, urinary incontinence, and falls. Serious effects include tardive dyskinesia, neuroleptic malignant syndrome, hyperlipidemia, weight gain, diabetes mellitus, cerebrovascular accidents, and death.</td>
</tr>
<tr>
<td>Olanzapine</td>
<td>1.25–5</td>
<td>10</td>
<td></td>
</tr>
<tr>
<td>Quetiapine</td>
<td>12.5–50</td>
<td>200–300</td>
<td></td>
</tr>
<tr>
<td>Risperidone</td>
<td>0.25–1</td>
<td>1.5–2</td>
<td></td>
</tr>
<tr>
<td>Ziprasidone</td>
<td>Unknown</td>
<td>Unknown</td>
<td></td>
</tr>
</tbody>
</table>

\(^a\)Available evidence suggests that 5 mg/day of aripiprazole may be a safe starting dose for most patients.

Antipsychotics in Delirium

- 84 yo male has an acute mental status change
- Discovered to have a UTI
- Is aggressive with staff and family
- Not responding to redirection
Antipsychotics in Delirium

- Medical emergency
- Evaluate and treat medically
- Haloperidol 1-10 mg every 2-4 hours
  - Often 5 mg per dose is needed
  - Haloperidol 0.25 mg to 0.5 mg every 4 hours in elderly
Special Cases

- Transferred to primary care or discharged back to us on antipsychotics
  - What do we do when that patient is a child?
  - What do we do when patient depressed, just out of hospital, no diagnosis in papers of psychosis?

- Patient carries diagnosis of autism
  - Care transferred to pcp, stable on aripiprazole (Abilify) for last year

- Tourette Syndrome
Agenda

√ When to consider antipsychotic use in the Primary Care setting

- Review risk profiles of antipsychotics

- Safety tool for monitoring patients on antipsychotics
Antipsychotic Risks

- Cardiovascular
- Neurologic
- Metabolic
- Other
Antipsychotics: Cardiovascular Risks

Increased Mortality in Elderly Patients with Dementia-Related Psychosis

Elderly patients with dementia-related psychosis treated with atypical antipsychotic drugs are at an increased risk of death compared to placebo. Analyses of seventeen placebo controlled trials (modal duration of 10 weeks) in these patients revealed a risk of death in the drug-treated patients of between 1.6 to 1.7 times that seen in placebo-treated patients. Over the course of a typical 10 week controlled trial, the rate of death in drug-treated patients was about 4.5%, compared to a rate of about 2.6% in the placebo group. Although the causes of death were varied, most of the deaths appeared to be either cardiovascular (e.g., heart failure, sudden death) or infectious (e.g., pneumonia) in nature. RISPERDAL® (risperidone) is not approved for the treatment of patients with Dementia-Related Psychosis.
Antipsychotics
Cardiovascular Risks

- 2005 analysis of Tennessee Medicaid program reveals risk typicals = atypicals

- Recent study shows sudden cardiac death increased by about twofold amongst patients on APs, regardless of age*

Antipsychotic Risks

Neurologic

- Neuroleptic Malignant Syndrome
  - Incidence with atypicals .2%
  - Fever, encephalopathy, autonomic instability, elevated CPK, rigid muscles

- Acute dystonia
  - E.g., torticollis
  - E.g., oculogyric crisis

Sparrow/MSU FMRF Behavioral Science Team
2010
Antipsychotic Risks
Neurologic (cont.)

- **Akathisia**
  - Unpleasant sensations of "inner" restlessness
  - inability to sit still or remain motionless

- **Drug-induced Parkinsonism**
  - Tremor (resting)
  - Rigidity in movement, carriage
  - Postural instability

- **Tardive Dyskinesia**
  - Drug induced abnormal involuntary movements of face/jaw/mouth, trunk, limbs
  - Incidence on atypicals 0.8%, typicals 5.4%
Shades of Neurologic Impact

Higher Risk
- Most typicals
- Risperidone (Risperdal) especially as dose increases
- Note: Akathisia reported on aripiprazole (Abilify) even at low doses

Lower Risk
- Quetiapine (Seroquel)
- Clozapine (Clozaril)
Following Patients on Antipsychotics for Neurologic Risk

TRUSt Big BeLtS

- T remor
- Restlessness
- U nwanted movements
- St ifness
Antipsychotics Risks

Metabolic

- Increased weight
- Increased blood sugar and frank DM
- Increased lipids
  - Triglycerides
  - Cholesterol
  - LDL cholesterol
  - (↓ HDL cholesterol)
- Increased BP as part of metabolic syndrome
Shades of Metabolic Impact

Higher Risk
- Clozapine (Clozaril)
- Olanzapine (Zyprexa)

Medium Risk
- Quetiapine (Seroquel)
- Risperidone (Risperdal)

Lower Risk
- Aripiprazole (Abilify)
- Ziprasidone (Geodon)
Following Patients on Antipsychotics for Metabolic Risk

TRUSt Big BeLts

Big = BMI (weight, waist circumference)
Blood pressure
Lipids
Sugar

Sparrow/MSU FMRP Behavioral Science Team
2010
Antipsychotics
Other Risks

- Somnolence
- Dizziness
- Hypotension
- Sexual dysfunction
- Dry mouth
- Lowering of seizure threshold
- Hyperprolactinemia
- Leukopenia
  - agranulocytosis with Clozapine (Clozaril)
Given the Risks
Don’t Prescribe Lightly

- Make sure patients need the AP medication
  - Discover prior diagnoses by phoning hospitals, psychiatrists, CMHs, therapists
  - Do NOT use for sleep when no other psychiatric diagnosis requiring AP exists
  - Consider other treatments for disruptive behaviors in children without a firm psychiatric diagnosis

- Partner with patient in making decision to use
  - Risk/benefit discussion
Given the Risks
What Do We Do When We Prescribe APs?

- Track neurologic and metabolic parameters
- Respond to neurologic and metabolic changes
  - Change antipsychotic or dose
  - Address metabolic changes medically
Agenda

√ When to consider antipsychotic use in the Primary Care setting
√ Review risk profiles of antipsychotics

Safety tool for monitoring patients on antipsychotics
Antipsychotic Monitoring Form and Patient Education Handout

TRUSt Big BeLts
Following Patients on Antipsychotics: TRUSt Big BeLts

- Tremor
- Restlessness
- Unwanted movements
- Stiffness
- Blood pressure
- Lipids
- Sugar

Sparrow/MSU FMRP Behavioral Science Team

2010
Following Patients on Antipsychotics: TRUSt Big BeLts

- **Tremor**: Ask, observe, document
- **Restlessness**: Ask, observe, document
- **Unwanted movements**: Ask, observe walking, ask if others have noticed, document
- **Stiffness**: Ask, observe, check for cogwheeling, document

**Big** = BMI (weight, waist circumference)

- **Blood pressure**
- **Lipids**
- **Sugar**

Sparrow/MSU FMRI Behavioral Science Team 2010
<table>
<thead>
<tr>
<th></th>
<th>Baseline</th>
<th>4 weeks</th>
<th>8 weeks</th>
<th>12 weeks</th>
<th>Quarterly</th>
<th>Annually</th>
<th>Every 5 years</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Personal/family history</strong></td>
<td>+</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Weight (BMI)</strong></td>
<td></td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td></td>
</tr>
<tr>
<td><strong>Waist circumference</strong></td>
<td></td>
<td>+</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>+</td>
</tr>
<tr>
<td><strong>Blood pressure</strong></td>
<td></td>
<td>+</td>
<td></td>
<td></td>
<td></td>
<td>+</td>
<td>+</td>
</tr>
<tr>
<td><strong>Fasting plasma glucose</strong></td>
<td>+</td>
<td></td>
<td></td>
<td>+</td>
<td></td>
<td></td>
<td>+</td>
</tr>
<tr>
<td><strong>Fasting lipid profile</strong></td>
<td>+</td>
<td></td>
<td></td>
<td></td>
<td>+</td>
<td></td>
<td>+</td>
</tr>
</tbody>
</table>

Antipsychotics in Primary Care: Summary

- Appropriate uses
- Remember risks
  - Neurologic
  - Metabolic
  - Cardiovascular
  - Other
- Can be a blessing when used appropriately, though these are serious drugs
- Systematize monitoring for safer use
Antipsychotic References


Antipsychotic References

- Stahl’s Essential Psychopharmacology: Neuroscientific Basis and Practical Applications; Third Edition
  - On-line version at neiglobal.com