

MEDICATION UPDATES NAMI 2011

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ANTIPSYCHOTICS

PHARMACOLOGY OF ANTIPSYCHOTICS

- Antipsychotics (also called neuroleptics and dopamine antagonists) block receptors for dopamine, acetylcholine, histamine, and norepinephrine on the post-synaptic neuron. The current theory suggests that antipsychotic drugs suppress symptoms of psychosis by blocking dopamine₂ (D₂) receptors in the mesolimbic and mesocortical areas of the brain.

RECPETOR BLOCKADE AND SIDE EFFECTS OF ANTIPSYCHOTIC DRUGS

Receptor Type	Action	Treatment
D ₂ dopaminergic	EPS, prolactin release	Manage EPS.
H ₁ histaminergic	Sedation	None. Symptoms usually subside within 1 -2 weeks
Muscarinic anticholinergic	Tachycardia, anhydrases, dry mouth, urinary retention, constipation, impotence, and blurred vision.	Good dental hygiene, change medications, increase fluids and/or docusate sodium.
Alpha ₁ adrenergic	Orthostatic hypotension	Increase fluids
5-HT ₂ Serotonergic	Weight gain, impotence and anorgasmia	Reduce or change medication

WEIGHT GAIN & METABOLIC SIDE EFFECTS

- Evidence suggests that switching antipsychotic medication to one with lesser potential for causing weight gain or metabolic problems (aripiprazole or quetiapine) could be an effective way to manage these side effects
 - Mukundan A, Faulkner G, Cohn T, Remington G. Antipsychotic switching for people with schizophrenia who have neuroleptic-induced weight or metabolic problems. Cochrane Database of Systematic Reviews 2010, Issue 12.

ARIPIPRAZOLE

- Aripiprazole does not differ greatly from typical and atypical antipsychotics with respect to treatment response, efficacy or tolerability.
- No difference in efficacy compared to risperidone
 - El-Sayeh HGG, Morganti C. Aripiprazole for schizophrenia. Cochrane Database of Systematic Reviews 2006, Issue 2
 - Bhattacharjee J, El-Sayeh HGG. Aripiprazole versus typical antipsychotic drugs for schizophrenia. Cochrane Database of Systematic Reviews 2008, Issue 3.

ARIPIPRAZOLE

- Compared to other atypical antipsychotics:
 - Lower risk of akathisia,
 - Less risk of raised prolactin levels
 - Less risk of prolongation of the QTc interval
 - Komossa K, Rummel-Kluge C, Schmid F, Hunger H, Schwarz S, El-Sayeh HGG, Kissling W, Leucht S. Aripiprazole versus other atypical antipsychotics for schizophrenia. Cochrane Database of Systematic Reviews 2009

CLOZAPINE

- Twenty-seven studies compared clozapine with olanzapine, quetiapine, risperidone, and ziprasidone. Clozapine produced:
 - More sedation and hypersalivation than olanzapine, quetiapine and risperidone
 - More seizures than olanzapine and risperidone
 - A higher incidence of white blood cell decrease
 - More weight gain than risperidone
 - Fewer movement disorders than risperidone
 - Less prolactin increase than olanzapine and quetiapine
 - Asenjo Lobos C, Komossa K, Rummel-Kluge C, Hunger H, Schmid F, Schwarz S, Leucht S. Clozapine versus other atypical antipsychotics for schizophrenia. Cochrane Database of Systematic Reviews 2010, Issue 11

CLOZAPINE AND A SECOND ANTIPSYCHOTIC

- Clinical guidelines recommend a second antipsychotic in addition to clozapine in partially responsive patients with schizophrenia
 - Only one randomized controlled study
 - Inclusive evidence to show if any particular combination strategy was superior to the others
 - Cipriani A, Boso M, Barbui C. Clozapine combined with different antipsychotic drugs for treatment resistant schizophrenia. Cochrane Database of Systematic Reviews 2009, Issue 3

LURASIDONE

- One-daily, oral atypical antipsychotic
- 40mg/day demonstrated significant efficacy in the Brief Psychiatric Rating Scale
- Significant efficacy in positive and negative symptoms
- Weight gain
 - Short-term studies showed slight weight loss at low dose but slight weight gains at higher doses
 - Long-term (uncontrolled) studies showed slight weight loss
- Fasting lipids
 - Short-term studies showed slight decrease in fasting lipids
 - Long-term (uncontrolled) studies showed slight decrease in fasting lipids

LURASIDONE

- Glucose
 - Long-term (uncontrolled) studies showed increase in glucose levels
 - Elevates prolactin levels
 - Greater in females
 - Dose dependent in males
 - Risk for agranulocytosis
 - Risk for orthostatic hypotension, syncope and somnolence
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OLANZAPINE

- Olanzapine may be a somewhat more efficacious than aripiprazole, quetiapine, risperidone and ziprasidone
- No efficacy difference compared to clozapine
- Tends to cause higher weight gain and metabolic problems than most other second generation antipsychotic drugs, except clozapine
 - Komossa K, Rummel-Kluge C, Hunger H, Schmid F, Schwarz S, Duggan L, Kissling W, Leucht S. Olanzapine versus other atypical antipsychotics for schizophrenia. Cochrane Database of Systematic Reviews 2010, Issue 3.

PALIPERIDONE

- Adverse effects similar to risperidone
 - Movement disorders, weight gain and tachycardia
- Associated with substantial increases in serum prolactin.
- Doses of 6 mg per day or higher, appears comparable in efficacy to olanzapine 10 mg/day.
- When dosed flexibly with other psychotropics available, it appears to be comparable in efficacy to flexible doses of quetiapine with other psychotropics available.

QUETIAPINE

- Effective for the treatment of schizophrenia, but not much different from first-generation antipsychotics and risperidone with respect to efficacy
- Higher risks of dizziness, dry mouth and sleepiness
 - Srisurapanont M, Maneeton B, Maneeton N. Quetiapine for schizophrenia. Cochrane Database of Systematic Reviews 2004, Issue 2.

QUETIAPINE

- Less effective than olanzapine
- Fewer extrapyramidal symptoms,
- Minimal prolactin increases
- Less weight gain than olanzapine but more than with risperidone and ziprasidone
- Lower risk of movement disorders
 - Komossa K, Rummel-Kluge C, Schmid F, Hunger H, Schwarz S, Srisurapanont M, Kissling W, Leucht S. Quetiapine versus other atypical antipsychotics for schizophrenia. Cochrane Database of Systematic Reviews 2010, Issue 1

RISPERIDONE CONSTA

- Risperidone depot compared with placebo:
 - Did not affect levels of anxiety
 - Decreased agitation
 - Did not substantially influence hallucinations
 - Higher depot doses to associated with higher incidence of movement disorders
- Questionable effectiveness in persons with SPMI
 - Hosalli P, Davis JM. Depot risperidone for schizophrenia. Cochrane Database of Systematic Reviews 2003, Issue 4

RISPERIDONE

- Favorable improvement of psychotic symptoms and mania
- Associated with movement disorders and sexual dysfunction
- Associated with more prolactin increase
- Compared to other SGA may cause more weight gain, metabolic problems, cardiac effects, sedation and seizures
 - Jayaram MB, Hosalli P, Stroup TS. Risperidone versus olanzapine for schizophrenia. Cochrane Database of Systematic Reviews 2006, Issue 2
 - Komossa K, Rummel-Kluge C, Schwarz S, Schmid F, Hunger H, Kissling W, Leucht S. Risperidone versus other atypical antipsychotics for schizophrenia. Cochrane Database of Systematic Reviews 2011, Issue 1.

ZIPRASIDONE

- May be a slightly less efficacious than olanzapine and risperidone
- Low propensity to induce weight gain and associated adverse effects
 - Komossa K, Rummel-Kluge C, Hunger H, Schwarz S, Bhoopathi PS, Kissling W, Leucht S. Ziprasidone versus other atypical antipsychotics for schizophrenia. Cochrane Database of Systematic Reviews 2009, Issue 4

SGA AND MAJOR DEPRESSIVE DISORDER

- Limited evidence suggests that aripiprazole leads to symptom reduction when added to antidepressants.
- Limited evidence suggests some benefits of olanzapine as additional treatment.
- Some evidence suggests that quetiapine alone or as additional treatment reduces depressive symptoms
- Some benefits of risperidone as additional treatment for MDD
- Treatment with second-generation antipsychotic drugs was associated with worse tolerability
 - Due to sedation, weight gain or prolactin increase
 - Komossa K, Depping AM, Gaudchau A, Kissling W, Leucht S. Second-generation antipsychotics for major depressive disorder and dysthymia. Cochrane Database of Systematic Reviews 2010, Issue 12

ANTIDEPRESSANTS

PHARMACOLOGY OF ANTIDEPRESSANTS

- The antidepressants fall into five major groups: tricyclic antidepressants, monoamine oxidase inhibitors (MAOIs), selective serotonin reuptake inhibitors, atypical antidepressants and tetracyclics. Their primary mechanism of action is to block reuptake of norepinephrine and serotonin in nerve cells. The MAOIs act by inhibiting the breakdown of norepinephrine, serotonin and dopamine in the synapse thereby preventing reuptake of those neurotransmitters.
- Takes 2 -3 weeks to start working.
- Might increase SI in adolescents but not quite empirically established.
- Used in conjunction with anxiolytics or alone to treat anxiety disorders (depression and anxiety coexist)
- Best method to treat depression is both pharmacology and psychotherapy.

SSRI'S AND CHILDREN

- Fluoxetine (Prozac)
 - FDA approved for major depression and OCD
 - Sertraline (Zoloft)
 - FDA approved for OCD
 - Paroxetine (Paxil)
 - No better than placebo for MDD
 - Fluvoxamine (Luvox)
 - FDA approved for OCD
 - Citalopram (Celexa)
 - No improvement in ASD
 - Escitalopram (Lexapro)
 - FDA approved for MDD in teens
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ADVERSE EVENTS WITH SSRI'S

- Nausea and vomiting
- Sedation and drowsiness
- Activation (up to 20% of patients treated with SSRI's)
- Agitation, insomnia, and increased activity
- Increased anxiety, mood lability
- Frequency of side effects not yet determined, but clinical experience suggests these events are more common in atypically developing individuals
- McCracken J. (2005) *Journal of Clinical Psychiatry*, 66, 32-37

MOOD DISORDERS: DEFINED

- Sleep
 - Decreased need for sleep with little to no fatigue (total sleep time)
 - Grandiosity
 - Elation, more bold, more energized than normal
 - Moods that are not tacked down to triggers or are clear, over responses to events
 - Racing thought/pressured speech
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MOOD DISORDERS: SHARED

- Hyperactivity/excitability
 - Lability/mood reactivity
 - Aggression (but different than with ADHD)
 - Anxiety
 - Depression, especially MDD
 - AH/some VH
 - Poor concentration/attention
 - High impulsivity
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MOOD DISORDERS: DIFFERENTIATING

- Sleep
 - Not just difficulty falling asleep but much less need
 - Aggression
 - Does not occur exclusively from “not fair”, “told no” moments (ADHD)
 - Does not occur exclusively from protective/reactive moments (PTSD)
 - Does not occur exclusively when routine is broken (ASD)
 - Change from previous functioning
 - Attention, activity level, thought process, sensory experiences, impulsivity (times/type) and mood
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MOOD SYMPTOMS: OTHER CAUSES

- ADHD: Comorbid in 50% - 60% of all mood disorders, but also has symptoms that can be misdiagnosed
 - PTSD: Especially if precipitating event is unknown, and/or occurred early in life
 - ASD
 - Prodromal schizophrenia
 - Learning disorders
 - Family chaos
 - Substance abuse
 - Adjustment disorders
 - Immaturity
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OTHER DISORDERS THAT MIMIC MOOD DISORDERS

- PTSD
 - Hyperactivity is more anxious (agitated)
 - Inattention may be dissociation or anxiety
 - Impulsivity may be unsafe actions/self-harm
 - AH/VH brief psychotic states
 - Change in functional level
 - Sexualized behavior
 - Increase in substance abuse
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MEDICAL ISSUES THAT MIMIC MOOD DISORDERS

- Seizure disorders
 - Lead exposure
 - Sensory impairments
 - Thyroid problems
 - Use of other medications
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STIMULANTS

STIMULANTS

- Stimulant use may be associated with unusual reactions, including confusion, possible psychosis and higher rates of treatment-emergent tic disorder
- No data on long-term treatment with stimulants in children with ASD
- Treatment guideline: To improve tolerance, use lower doses, longer titration periods and extended release preparations
 - McCracken J. (2005) *Journal of Clinical Psychiatry*, 66, 32-37

NONSTIMULANTS

ALPHA-2 AGONISTS

- Used to treat ADHD symptoms and tic disorders
 - Clonidine
 - Common adverse events
 - Dry mouth, drowsiness, irritability, weakness, fatigue and mid-sleep awakening
 - Hypotension and bradycardia possible but not common in children
 - Guanfacine
 - Common adverse events
 - Sedation and mid-sleep awakening
 - Rains & Scahill (2006). JCAPN, 19, 44-47

NONSTIMULANTS

- Strattera
 - Consider if family resistance to stimulants
 - Co-morbid substance abuse in patient or family
 - Consider if co-morbid anxiety or substance abuse
 - Watch for liver function
 - Not quite as good as stimulants-especially with inattention
 - Takes 3 – 4 weeks for full efficacy
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NONSTIMULANTS

- Wellbutrin
 - Moderate effect
 - Consider if mildly depressed
 - Careful if seizure history
 - Takes 3 – 4 weeks for full efficacy
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NONSTIMULANTS (NEW)

- Modafinil
 - Risk for Stevens-Johnson syndrome
 - Cholinergic agents
 - Research
 - Abilify
 - Some mixed evidence
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