Hot Topics in Psychiatry 2018

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Disclosures

All planners, presenters, reviewers, and ASHP staff of this session report no financial relationships relevant to this activity.
Objectives

• Discuss clinical scenarios that might not be widely used or published within psychiatric pharmacy.
• Identify novel practice options for patient care in various psychiatric pharmacy settings.
• Describe medication management strategies in difficult or controversial psychiatric patient care situations.
• Identify clinical information that can be applied to your work setting.
No Benzos? Now What?
Non-Benzodiazepine Agents for Anxiety

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Assistant Professor of Pharmacy
Wingate University School of Pharmacy

Clinical Pharmacy Specialist – Internal Medicine
Carolinas Medical Center – Main
Background

- Anxiety disorders are most common mental health concern in the U.S.
  - Nearly 1 in 5 adults have an anxiety disorder

- Anxiety can be exacerbated inpatient
  - Stress
  - Disturbances in routine
  - Psychotherapy often limited/unavailable

- First and second line agents may not be appropriate in all patients
  - Special populations: elderly, history of substance abuse

https://www.nami.org/Learn-More/Mental-Health-Conditions/Anxiety-Disorders
### Pharmacotherapy Options

- **First line:** SSRIs/SNRIs
- **Second line:** SSRIs/SNRIs, Benzodiazepines

<table>
<thead>
<tr>
<th>SSRI/SNRI Limitations</th>
<th>Benzodiazepines Limitations</th>
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<tbody>
<tr>
<td>• Delayed onset efficacy</td>
<td></td>
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<tr>
<td>• Increased anxiety at initiation of therapy</td>
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<tr>
<td>• Adverse effects: sexual dysfunction, weight gain, nausea, insomnia, SIADH, discontinuation symptoms</td>
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<tr>
<td>• Drug-drug interactions</td>
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<td>• Short-term treatment only (&lt; 8 weeks)</td>
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<td>• Cognitive impairment</td>
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<td>• Sedation</td>
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<tr>
<td>• Risk of dependence and abuse</td>
<td></td>
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<tr>
<td>• Rebound anxiety</td>
<td></td>
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<tr>
<td>• Withdrawal symptoms</td>
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SIADH: syndrome of inappropriate antidiuretic hormone secretion

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Other Pharmacotherapy Options

- Buspirone
- Pregabalin
- Mirtazapine
- Hydroxyzine
- Quetiapine
- Propranolol
## Pharmacotherapy Options

<table>
<thead>
<tr>
<th>Medication</th>
<th>Advantages</th>
<th>Time to Efficacy</th>
<th>Dose</th>
<th>Limitations</th>
</tr>
</thead>
<tbody>
<tr>
<td>Buspirone</td>
<td>• FDA approved for GAD&lt;br&gt;• Short and long term efficacy data&lt;br&gt;• Ameliorates sexual dysfunction caused by SSRIs&lt;br&gt;• Lack of sedation, withdrawal, dependence</td>
<td>2-4 weeks</td>
<td>Starting: 5 mg TID&lt;br&gt;Range: 15-60 mg/day in divided doses (BID-TID)</td>
<td>• Delayed onset efficacy&lt;br&gt;• Ineffective as a PRN&lt;br&gt;• Frequency of dosing&lt;br&gt;• Dizziness&lt;br&gt;• Headaches</td>
</tr>
</tbody>
</table>

GAD: generalized anxiety disorder | BZDs: benzodiazepines | PRN: as needed

References:
- Brain Research 2012; 1461: 111-116
- BMJ 2012;345:e7500
# Pharmacotherapy Options

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<tr>
<th>Medication</th>
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</thead>
</table>
| Pregabalin | • Significantly decreased HAM-A scores in trials  
• Short and long term efficacy  
• Low risk for DDIs  
• Minimal withdrawal symptoms and rebound anxiety | • Within 1 week  
• Delayed response in elderly (2 weeks) | • Starting: 50-75 mg BID-TID  
• Range: 150-600 mg/day in divided doses (BID-TID) | • Sedation  
• Dizziness  
• Dry mouth  
• Weight gain  
• Abuse potential (low) |

HAM-A: Hamilton Rating Scale for Anxiety  
DDI: drug-drug interactions
# Pharmacotherapy Options

<table>
<thead>
<tr>
<th>Medication</th>
<th>Advantages</th>
<th>Time to Efficacy</th>
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<th>Limitations</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mirtazapine</td>
<td>• Significantly decreased HAM-A scores in trials</td>
<td>1-2 weeks</td>
<td>• Starting: 7.5-15 mg/day</td>
<td>• Sedation</td>
</tr>
<tr>
<td></td>
<td>• Effective for depression and anxiety</td>
<td></td>
<td>• Range: 15-45 mg/day</td>
<td>• Weight gain</td>
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<td></td>
<td>• Avoids common SSRI/SNRI adverse effects</td>
<td></td>
<td></td>
<td>• Constipation</td>
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<td>• Agranulocytosis</td>
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HAM-A: Hamilton Rating Scale for Anxiety
## Pharmacotherapy Options

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</tr>
</thead>
</table>
| Hydroxyzine | • Significantly decreased HAM-A scores in clinical trials  
• Absence of dependence/abuse | 1-4 weeks | • Starting: 12.5-25 mg TID  
• Range: 25-100 mg/day in divided doses (BID-QID) | • Sedation  
• Frequency of dosing  
• QTc prolongation |

**Notes:**
- HAM-A: Hamilton Rating Scale for Anxiety
## Pharmacotherapy Options

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<tr>
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</thead>
</table>
| **Quetiapine** | • Mixed data regarding efficacy; best data with XR formulation  
• Often used as adjunctive agent | 1-4 weeks | Starting: 50 mg/day*  
Range: 50-300 mg/day*  
*XR formulation | • Sedation  
• Weight gain  
• Increased BG and lipids  
• QTc prolongation  
• EPS  
• Increased mortality in patients with dementia |

BG: blood glucose | EPS: extrapyramidal symptoms

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## Pharmacotherapy Options

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</tr>
</thead>
</table>
| Propranolol | Decreases physical symptoms of adrenergic hyperactivation | 30-90 minutes for physical symptoms | Starting: 10-20 mg QID Range: 20-360 mg/day in divided doses (QID) | • Insufficient evidence to support use in most anxiety disorders  
• Frequency of dosing  
• Fatigue  
• Dizziness  
• Depression |

QID: four times a day
KEY TAKEAWAYS

1) Avoid use of benzodiazepines due to adverse effects

2) Choose alternative, non-benzodiazepine agents based on adverse effects and time to efficacy

3) Re-assess for effectiveness over time
   – Does dose need to be maximized?
   – Titrate off prior to discharge?
   – Non-pharmacological options?
   – Outpatient follow up?
Kratom Intoxication & Withdrawal Management

Dan McGraw, Pharm.D., BCPP
Clinical Specialist in Psychiatry
Medical University of South Carolina
Background – What is Kratom?

• “Kratom” is a common name for *mitragyna speciosa* plant indigenous to Southeast Asia
  – Traditionally consumed as a tea brewed from tree leaves
  – Dosage forms such as capsules, powders, gums also widely available
  – Gaining popularity in North America

• Pharmacology of primary alkaloids (i.e., mitragynine, 7-OH-mitragynine)
  – Partial agonist at µ-opioid receptor
  – Competitive antagonist at δ and κ-opioid receptors
  – Post-synaptic α²-receptor agonist
  – 5-HT²A-receptor antagonist

Background – Uses & Legality

• Purported uses
  – Pain management
  – Treatment or prevention of opioid withdrawal

• Industry group estimates 3 – 5 million kratom users in United States

• CDC has reported year-over-year increases in kratom-related cases reported to U.S. poison control centers

• Currently legal for sale/possession in U.S. with exception of select states and municipalities

Kratom Intoxication

• Sequelae of kratom intoxication are poorly understood
  – Most reported cases occurred in context of polysubstance use
  – Product adulteration or mislabeling adds confusion

• Mild symptoms
  – Altered mental status, constipation, insomnia, agitation, tachycardia, nausea/vomiting

• Severe symptoms
  – Seizure, severe vomiting, severe agitation
  – Hepatotoxicity has been reported
  – Possible signal for QT prolongation

Kratom Intoxication Management

• Diagnosis difficulties
  – Kratom is not detected on most standard urine drug screens
  – Thorough medication reconciliation process can help
  – Determine if co-ingestion and manage accordingly

• Supportive care for mild symptoms
  – Anti-emetics for nausea/vomiting
  – Consider benzodiazepine for agitation/insomnia/anxiety

• Monitor for severe symptoms
  – Consider seizure precautions
  – Consider electrocardiogram (QTc interval monitoring)
Kratom Withdrawal

• Physical dependence in chronic users is fairly well-documented

• Withdrawal syndrome observed after abrupt cessation
  – Symptoms may begin as little as 6 hours after last dose
  – Expected duration of symptoms approximately 2 to 4 days

• Presentation is similar to opioid withdrawal syndrome
  – Muscle aches, diaphoresis, mydriasis, agitation, rhinorrhea, diarrhea, gastrointestinal cramping, nausea/vomiting, loss of appetite
  – Psychological symptoms such as anxiety and depression also observed

Kratom Withdrawal Management

• Supportive care for physical symptoms
  – Anti-emetics
  – Anti-diarrheals
  – Acetaminophen or NSAID for muscle aches
  – Consider benzodiazepine for agitation/anxiety

• Case reports indicate that $\alpha_2$-receptor agonists may ameliorate symptoms
  – Examples: clonidine, lofexidine

• Validated withdrawal scales to assess severity and guide management
  – Example: clinical opiate withdrawal scale (COWS)

KEY TAKEAWAYS

1) ASSESS FOR KRATOM USE
   • Assess for use during medication reconciliation process
   • Not detected on standard urine drug screens

2) INTOXICATION MANAGEMENT
   • Symptoms are poorly understood
   • May present as component of polysubstance intoxication
   • Seizure precautions and supportive care

3) WITHDRAWAL MANAGEMENT
   • Physical withdrawal can occur with cessation of chronic use
   • Often presents as opioid withdrawal syndrome; management is similar
     with emphasis on supportive care
Clinical Pearl: Psychiatry in Primary Care

Monitoring for Akathisia in the Treatment of Major Depressive Disorder

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Associate Professor
University of Colorado Skaggs School of Pharmacy and Pharmaceutical Sciences
Patient Case

• 42 year old female presents to her PCP for management of her depressive symptoms. Due to her insurance, she has a hard time getting in to see a psychiatrist. She has a long history of depression.
• Current Meds:
  – Bupropion XL 300 mg once daily
  – Escitalopram 20 mg daily
  – Verapamil 80 mg BID
  – Omeprazole 40 mg once daily
• Fortunately, the clinic has a clinical pharmacist and a Collaborative Practice Agreement for Mood Disorders
Add-On Agents for MDD

• PharmD decides to add aripiprazole 5 mg once daily as an adjunct agent for the treatment of MDD.

• This decision was made based on several factors, including patient reporting a trial of aripiprazole before with good results, but stopped taking it due to insurance reasons

• Question: What dose of aripiprazole is best suited for use as an adjunct in MDD?
  A. 2.5 – 5 mg
  B. 7.5 – 10 mg
  C. 15 – 20 mg
  D. > 20 mg
Patient returns...

• Three weeks later she comes back to clinic complaining of twitching in her legs. She is visibly distressed and squirming in her chair. She states this started about 10 days after starting aripiprazole. Her energy level and mood have improved.

• **What is she experiencing?**

• Movement disorders, particularly akathisia, is often not asked about by clinicians.
  – Incidence up to 25% with aripiprazole!
  – The incidence appears to be higher when used for MDD
Patient Continues..

- Dose is reduced to 2.5 mg at this point

- One week later, patient still reports same level of akathisia

- It is decided to discontinue aripiprazole and give propranolol 20 mg TID to help with residual symptoms

- Patient reports relief of symptoms with propranolol but symptoms linger for over 3 weeks after discontinuing!
Why was it worse this time?

- **Drug interactions**
  - Verapamil / aripiprazole interaction via CYP 2D6 inhibition

- **Combination with bupropion**
  - Antidepressants themselves can cause akathisia as well
  - Bupropion PI lists akathisia as <2%
  - The combination of bupropion + aripiprazole could increase this risk
  - However, per patient, she had been on bupropion & aripiprazole combination before
Usual Course of Akathisia

• Defined as restlessness, fidgeting of the legs, rocking, pacing, and the inability to sit or stand still

• Usually occurs in the first few weeks of treatment
  – Could be up to 3 months
  – Appears to occur more often at higher doses

• Usually resolves within days to a week of discontinuing offending agent

• Can be misdiagnosed as agitation due to psychiatric condition leading to inappropriate treatment

Akathisia in Newer SGAs

- Akathisia is being seen commonly with newer SGAs
  - Aripiprazole, asenapine, lurasidone
    - RR: 2.01 compared to placebo and active controls
    - RR: 1.75 when compared to older SGAs alone (risperidone, olanzapine, ziprasidone)
  - In a meta-analysis, aripiprazole had a 49% higher risk of akathisia than older SGAS, however this was with doses between 10-30 mg/day

SGA: second generation antipsychotic

More about the interaction

• Verapamil is a moderate CYP3A4 inhibitor, while aripiprazole is a substrate of 3A4

• Per Lexicomp:
  – Recommended to consider reducing initial aripiprazole dose to as little as 25% of the usual dose
  – Risk Rating: C (monitor therapy)
  – Severity: Moderate
  – Reliability: Fair

• Be mindful of aripiprazole with any 3A4 or 2D6 inhibitors
What happened next?

- Patient was rechallenged with aripiprazole without verapamil

- Still experienced akathisia, but only lasted 5 days after discontinuation
  - It had lasted over 3 weeks when she was still taking verapamil
  - This drug interaction helps to explain the long duration of the symptoms
• Ask patients about akathisia symptoms!
  – Although this case was severe, many patients may experience less severe symptoms and not report them

• SGAs can cause akathisia even at low dosages
  – Even if they claim to have low EPS!
  – Certain promotional materials will separate akathisia from EPS

• Antidepressants can cause akathisia too
  – Be mindful when using in combination with SGAs

SGA: second generation antipsychotic
Assessment Question #1

1) DK is a 72 YOF with HTN, T2DM, and COPD admitted to the hospital for COPD exacerbation. It is day 3 of admission and she complains of occasional symptoms of anxiety, including worrying, insomnia, and agitation. She has previously been on an SSRI and is not interested in starting one at this time, but is willing to consider other options. Which of the following would be the most appropriate agent to consider for DK?

a. Lorazepam 1 mg QHS
b. Buspirone 5 mg TID PRN
c. Pregabalin 50 mg BID
d. Hydroxyzine 12.5 mg PRN
Assessment Question #2

2) True or False:

Kratom is structurally similar to morphine and is thus present on standard urine drug screens.
Assessment Question #3

3) Which of the following side effects should be routinely monitored while taking aripiprazole due to its high incidence?

A. Pseudoparkinsonism
B. Akathisia
C. Hyperprolactinemia
D. Migraines
Hot Topics in Psychiatry 2018
Catatonia

Shauna S. Garris, Pharm.D., BCPP, BCPS
Clinical Pharmacy Consultant, Psychiatry/Neurology
Catatonia includes...

A. Abnormality of movement and behavior caused by an underlying acute psychiatric condition

B. Can be considered overactivity or underactivity

C. Non-convulsive status epilepticus

D. All of the above
Catatonia: Brain Storm

- High glutamate in parietal cortex
- Low GABA in frontal cortex
- Low dopamine in basal ganglia

Dysregulation of motor and autonomic function

Catatonia Diagnosis: DSM-V

- Stupor
- Catalepsy
- Waxy flexibility
- Mutism
- Negativism
- Posturing
- Mannerism
- Stereotopy
- Agitation
- Grimacing
- Echolalia
- Echopraxia
<table>
<thead>
<tr>
<th>Symptom</th>
<th>Description of Pathology</th>
</tr>
</thead>
<tbody>
<tr>
<td>Stupor</td>
<td>Decreased response to external stimuli, hypoactive behavior</td>
</tr>
<tr>
<td>Immobility</td>
<td>Akinetic behavior, resistance to being moved</td>
</tr>
<tr>
<td>Waxy flexibility</td>
<td>Slight resistance to being moved</td>
</tr>
<tr>
<td>Mutism</td>
<td>Verbally unresponsive, refusal to speak</td>
</tr>
<tr>
<td>Posturing</td>
<td>Purposely maintaining a position for long periods of time</td>
</tr>
<tr>
<td>Excitement</td>
<td>Frantic, stereotyped or purposeless activity</td>
</tr>
<tr>
<td>Echolalia</td>
<td>Senseless repetition of the words of others</td>
</tr>
<tr>
<td>Echopraxia</td>
<td>Mimicking the movements of others</td>
</tr>
<tr>
<td>Staring</td>
<td>Eyes fixed and open for long periods of time</td>
</tr>
<tr>
<td>Catalepsy</td>
<td>The passive adoption of a posture</td>
</tr>
</tbody>
</table>

Wilcox JA, Duffy PR *Behav Sci* 2016;5:576-88
Catatonia Diagnosis: Bush-Francis Scale

- Clinical objective rating scale
- Measures 22 symptom domains
- Absence, presence, severity (mild/moderate/severe)
  - Domains 1-14 presence or absence
  - Domains 1-22 indicate severity
- Presence of 2 or more items indicates catatonia
- Total score reflective of severity (0-66)

## Other Diagnostic Testing

<table>
<thead>
<tr>
<th>Basic</th>
<th>Advanced</th>
<th>Imaging</th>
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<tbody>
<tr>
<td>• MEDICAL and PSYCHIATRIC HISTORY</td>
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<td>• CMP</td>
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<td>• CK</td>
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<td>• LFTs</td>
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<tr>
<td>• D-dimer</td>
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<tr>
<td>• Ceruloplasmin</td>
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<td>• Autoimmune antibodies</td>
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<td>• EEG</td>
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<td>• MRI</td>
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<tr>
<td>• CT/SPECT</td>
<td></td>
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<td>• PET</td>
<td></td>
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<tr>
<td>• Pelvic ultrasound</td>
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</tbody>
</table>

Malignant Catatonia

Catalepsy
Stupor
Mutism
Waxy flexibility
Negativism
Posturing

Autonomic dysfunction
Rigidity
Fever
Muscle injury

Multi-organ dysfunction
Infection
DEATH

PROMPT diagnosis and treatment are necessary to avoid negative outcomes
Begin with benzodiazepines, DO NOT DELAY ECT

Catatonia: Treatment

• Plan A, part one
  – Benzodiazepines
• Plan A, part two
  – ECT
  – Seek primary cause and manage as appropriate
• Plan B
  – Alternative medication management of acute catatonic symptoms
  – Continue to seek primary cause
Benzodiazepines

Considered mainstay of treatment if ECT is not feasible
- Up to 30% non-response to benzodiazepines
- Untreated catatonia may become malignant
- Dosing ranges up to and beyond 16 mg lorazepam per day
- Reports of marked response with IM/IV administration
  - “Ativan challenge”= administer 1-4 mg IM/IV and observe for results
  - Single site describes protocol of 2 mg IM, repeat in 2 hours, then proceed to diazepam infusion
- Transition to oral medication at lowest effective dose
- Treatment may extend up to one year
  - Implications for continued outpatient and LTC management

Morrison, J. Hospital and Community Psychiatry 26, 2 Feb 1975
Electroconvulsive Therapy (ECT)

- Effective in 80-100% of catatonia cases
- First-line therapy
  - Malignant catatonia
  - Severe excitatory catatonia
  - All patients partially or non-responsive to pharmacotherapy
  - Neuroleptic malignant syndrome
- Should be initiated **WITHIN THE FIRST FIVE DAYS** of hospitalization
- Inefficacy may suggest neurologic illness or extrapyramidal effects
- Full index series typically required to extinguish symptoms
- Maintenance ECT may be required to sustain effect

Underlying Diagnosis

Schizophrenia
Depression
Autism
Acute stress disorder

Neurosarcoidosis
Encephalitis
Astrocytoma

Ceruloplasmin-related neurotoxicity
Cocaine-induced leukoencephalopathy
Syphilis

Metabolic disorders
Fabry disease
Manganese neurotoxicity

RULE OUT:
Stroke
Seizure
Dementia/delirium
Alternative Treatments

- Anticonvulsants
  - Carbamazepine, valproate
- NMDA antagonists
  - Amantadine, memantine
- GABA agonists
  - Zolpidem
- Antipsychotics
  - Olanzapine reported successful
  - MUST consider risk of NMS vs benefit of treatment

KEY TAKEAWAYS

1) CATATONIA IS OR CAN QUICKLY BECOME A MEDICAL EMERGENCY
Prompt diagnosis and initial treatment are essential to patient care; look for acute PE, rhabdomyolysis, NMS, dehydration/starvation

2) IMPORTANT TO DISCOVER AND TREAT THE UNDERLYING CAUSE
Catatonic schizophrenia, while common, should not be the only diagnosis pursued

3) DO NOT UNDERESTIMATE THE UTILITY OF ECT
ECT the only effective management in many cases; rare/no contraindications, is also effective for NMS management
Tourette Syndrome: More To It Than Tics

Andrea Calvert, Pharm.D.
Children’s Mercy Hospital
December 2018
Tourette Syndrome (TS)

• Neuropsychiatric condition characterized by childhood or adolescent onset of motor and vocal tics

• Diagnosis: presence of ≥2 motor tics + ≥1 phonic tic over at least a year period of time prior to 18 years of age

• Tics are brief, stereotyped, repetitive movements or vocalizations
  – Often preceded by a premonitory urge
  – Suppressible, suggestable, distractible, variable

Epidemiology and Pathophysiology

• Prevalence: 0.3-1% of the population
  – Males > females (3/4:1)

• Pathophysiology is still unknown
  – Complex disorder with social and environmental factors along with genetic abnormalities
  – Dysfunction in the striatal-thalamic-cortical spinal system, leading to disinhibition of the motor and limbic system

Associated Comorbid Conditions

• 85.7% diagnosed with a second psychiatric disorder
  – Attention deficit hyperactivity disorder (ADHD) (60-80%)
  – Obsessive compulsive disorder (OCD) (11-80%)
  – Anxiety disorders (49%)
  – Learning disabilities (47%); Speech or language problems (29%)
  – Autism spectrum disorder (35%)
  – Behavioral disorders (26%)
  – Depression (25%)
  – Sensory processing issues, dysgraphia, sleep disorders, migraines, substance abuse, eating disorders

Pharmacotherapy Strategy

• Use a collaborative team approach
• Develop patient specific goals
• Give priority in treatment to conditions causing the most distress
• Choose medications that can improve multiple issues
• Titrate to effect, using the lowest effective dose to minimize unwanted side effects
Pharmacotherapy for Tics

- FDA Approved Medications
  - Haloperidol
    - Common adverse effects (AE): Hypersomnia, headache (HA), extrapyramidal syndrome (EPS), GI disturbances/N/V, emotional hypersensitivity, anticholinergic effects, dizziness, chest discomfort, hyperprolactinemia, prolonged QTc
  - Pimozide
    - Common AE: hypersomnia, HA, EPS, GI disturbances/N/V, emotional hypersensitivity, anticholinergic effects, weight gain, hyperprolactinemia, prolonged QTc
  - Aripiprazole
    - Common AE: Hypersomnia, N/V, EPS, HA, weight gain, hyperlipidemia

Pharmacotherapy for Tics

• Off-label medications used as first-line therapy: Alpha-2 Agonists
  – Guanfacine
    • Dosing: 0.5 mg/day up to 4 mg/day
    • Common AE: Sedation, orthostatic hypertension
  – Clonidine
    • Dosing: 0.025-0.05 mg/day up to 0.1-0.4 mg/day
    • Common AE: Sedation, orthostatic hypertension

Attention Deficit Hyperactivity Disorder

- Symptoms precede onset of tics by several years
- Hyperactivity/impulsivity
- Inattention

**Treatment**
- Alpha-2 agonists
  - Clonidine: 0.025-0.05 mg/day to 0.1-0.4 mg/day
  - Guanfacine: 0.5 mg/day up to 4 mg/day
- Stimulants
  - Methylphenidate (various dosing depending on formulations)
- Norepinephrine reuptake inhibitor
  - Atomoxetine: 0.5-1.2 mg/kg/day (max initial: 40 mg)
- Atypical antipsychotic
  - Aripiprazole: 2.5 mg/day up to 10 mg/day

Obsessive Compulsive Disorder

- Arise anytime during the course of TS
- Compulsions > obsessions

Treatment
- SSRI
  - Fluoxetine: 5-10 mg/day up to 20-60 mg/day depending on weight
  - Sertraline: 25-50 mg/day up to 200 mg/day
- Atypical antipsychotics
  - Risperidone: 0.25-0.5 mg/day up to 6 mg/day divided BID
  - Aripiprazole: 2-2.5 mg/day x7 days to 5 mg/day, up to 20 mg/day
- Combination SSRI + atypical antipsychotic

Summary

• Comorbid conditions are commonly associated with TS and often have a greater impact on quality of life measures than tics.

• Pharmacotherapy frequently involves treatment of the comorbid conditions rather than the tics, themselves.

• Patient specific goals should be determined to guide pharmacotherapy by prioritizing complications causing the greatest impairment.

• Pharmacotherapy benefiting multiple concerns should be explored, when applicable.
KEY TAKEAWAYS

1) FDA approved medications for the treatment of tics in TS are rarely used as first line pharmacotherapy due to their intolerable side effect profile.

2) Clonidine and guanfacine are used as first line medications for the treatment of tics, as well as ADHD, in TS.

3) SSRIs ± atypical antipsychotics are used in the management of OCD in TS.
Gabapentinoids: Trends in Misuse and Abuse

Giulia Barlow, Pharm.D.
PGY2 Psychiatric Pharmacy Resident
UNC Health Care
**Gabapentinoids**

- Gabapentin (Neurontin®)
- Pregabalin (Lyrica®)

**Mechanism of action**

- Analogs of inhibitory neurotransmitter, 𝛾-aminobutyric acid (GABA)
- Block α2 subunit-containing voltage dependent calcium channels

**Pharmacokinetics**

- Oral bioavailability is not dose proportional
- Renal elimination

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FDA APPROVED INDICATIONS

Gabapentin

- Adjunctive antiepileptic for refractory partial seizure
- Post-herpetic neuralgia

Pregabalin

- Post-herpetic neuralgia
- Fibromyalgia
- Neuropathic pain

Schedule V

COMMON OFF-LABEL USES

- Anxiety
- Insomnia
- Migraines
- Mania
- Bipolar Disorder
- Alcohol Withdrawal
- Hot Flashes
- Restless Leg Syndrome
- Trigeminal Neuralgia
- Attention Deficit Disorder

RISING USE OF GABAPENTINOIDS

Increase in prescribing practices

- 165% increase in use from 2016-2017
- 2,950% increase since 2008

Major suppliers

- Physicians (52%)
- Drug Dealers (36%)

Inexpensive

- $1.00 per pill or tablet


ABUSE POTENTIAL

Why?
- Anticholinergic and GABAergic
- Additive euphoric and ‘blackout’ effects in combination with central nervous system (CNS) depressants

How?
- Use of higher than recommended oral dosages
- Intravenous injection
- Insufflation

Behavioral Effects
- Relaxation
- Stimulation
- Sedation
- Dissociation
- Euphoria
- Enhanced Sociability

The FDA and the Next Wave of Drug Abuse — Proactive Pharmacovigilance

Douglas C. Throckmorton, M.D., Scott Gottlieb, M.D., and Janet Woodcock, M.D.

In response to the opioid crisis, the Food and Drug Administration (FDA) has taken action on multiple fronts. We have approved better measures for treating opioid use disorder and preventing deaths...
As of April 2018, **46 States** have implemented initiatives to improve opioid prescribing practices to align with the CDC’s guidelines for the treatment of non-cancer pain.

**Nociceptive Pain:** non-opioid analgesics are first-line treatment

**Neuropathic Pain:** gabapentinoids are first-line treatment

Inappropriate use of gabapentinoids

Co-prescribing of opioids and gabapentinoids

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Pregabalin classified as a Schedule V

Ohio added gabapentin to prescription drug monitoring program

Kentucky classified gabapentin as a Schedule V

FDA statement on the rise of gabapentinoid misuse/abuse

West Virginia classified gabapentin as a Schedule V

Tennessee classified gabapentin as a Schedule V

RISK FACTORS FOR GABAPENTINOID ABUSE

- Opioid Misuse
- Benzodiazepine Misuse
- Female Sex
- Chronic pain

## Abuse and Misuse of Pregabalin and Gabapentin

### Study Design
- A systematic review indexed through July 2016

### Methods
- Included 59 studies: 24 epidemiological, 3 clinical abuse liability, 16 abuse/misuse case reports/series, 17 acute overdose cases

### Results
- Gabapentinoid abuse prevalence ranged from 3% to 68% among opioid abusers versus 1.6% in the general population
- Risk factors for gabapentinoid abuse include a history of substance abuse and psychiatric co-morbidities

### Conclusion
- Gabapentinoids are increasingly being identified in post-mortem toxicology analyses
- Prescribers should be aware of high-risk populations and monitor for signs of abuse

IMPLICATIONS

**Fourfold** increased risk of respiratory depression with the concomitant use of gabapentinoids and opioids

Gabapentin doses greater than 900 milligrams per day have been shown to **increase the odds of opioid-related deaths 60%** as compared to opioids alone


KEY TAKEAWAYS

1. Recognize the dangers of concomitant use of gabapentinoids and CNS depressants

2. Evaluate patients for risk factors of gabapentinoid misuse

3. Reassess indication and continued need for gabapentinoids at every encounter
Assessment Question #4

4) True or False?

• Catatonia is a diagnosis of exclusion
• The most common cause of catatonia is psychiatric conditions
• Catatonia always presents with waxy flexibility
• Catatonia is an underdiagnosed condition
• It is important to confirm diagnosis prior to treating catatonia
Learning Assessment Question

1. FC is an 8 year old boy who is referred to the Tourette Syndrome Center of Excellence Clinic by his PCP for evaluation of abnormal movements concerning for tics. These movements started in October of 2016 and consist of neck rolling, throat clearing and eye squinting. The neck movement is very bothersome to him, but is not causing physical pain. The other movements are not bothersome or interfering with his quality of life. He describes an arm extending movement where he would lock his elbow that he no longer experiences. The movements happen more when he gets excited or upset.

FC struggles in school quite significantly. On recent testing, he was found to have ADHD. He displays some worrisome behavior, particularly in regards to school. He is very emotionally sensitive. He has significant sensory defensiveness for bright lights, loud noises, clothing textures/tags and is a remarkably picky eater. He does not appear to have significant obsessive-compulsive behaviors.
Learning Assessment Question Cont.

Which of the following should be considered for FC?

A. Pharmacotherapy is not necessary as his tics are not bothersome.
B. He should be started on guanfacine.
C. Methylphenidate should not be used as it is likely to make the tics worse.
D. He should be started on aripiprazole.
**Patient Case**

MB is a 22 yo F with a PMH of juvenile RA, anxiety, and substance use disorder (oxycodone, alprazolam) admitted after a MVC with sharp, shooting rib and chest pain. Due to the patient’s increasing anxiety, psychiatry was consulted and recommended initiating gabapentin for anxiety and additional pain control.

**Home medications:** buprenorphine/naloxone, methotrexate, meloxicam, ranitidine, multivitamin

**UDS:** positive for opioids

**Would you recommend initiating gabapentin for MB?**
Hot Topics in Psychiatry 2018

Jamie Sebaaly, Pharm.D., BCPS
Dan McGraw, Pharm.D., BCPP
Benjamin Chavez, Pharm.D., BCACP, BCPP
Shauna Garris, Pharm.D., BCPP, BCPS
Andrea Calvert, Pharm.D.
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