Anxiety & Depression

“Anxiety & depression are different sides of the same coin...they coexist.”

Labwork

- Fasting labs -
  - Thyroid Profile (TSH, T4)
  - Treat subclinical hypothyroidism?
    - 4.5-10 mU/L (mild)
    - 10-20 mU/L (severe)
  - T4 is normal in subclinical hypothyroidism
- Other initial labs: CBC w/diff, multichem, liver profile.
  - Low folate levels associated w/TRD & increased rate of relapse.
  - Vitamin D level
  - Hormone levels

Insights on Neurotransmitters
- Psych meds work in the brain in & around the synapse.
- Neurotransmitters are housed in storage vesicles on the neuron's presynaptic terminals. Neurotransmitter deficiency & excess are related to mental disorders. Meds are effective because they cause > or < in the brain's ability to use a specific neurotransmitter:
  - Serotonin = worry/obsessions & compulsions
  - Dopamine = attention, pleasure, motivation, reward
  - Norepinephrine = alertness & energy
- Most psychotropic DDIs are related to interference with cytochrome P-450 enzyme system.

Treatment of Anxiety & Depression
- Up to 16 million Americans take antidepressants.
- All take 4-6 weeks to be effective.
- All have BBW for potential to induce suicidal thinking.
- Continue medication for 6-12 months in first episode depression.
- SSRIs are recommended treatment for anxiety disorders, not benzodiazepines.
- Start with small dose & increase slowly.

Selective Serotonin Reuptake Inhibitors (SSRIs)

**Celexa** - QTc prolongation > 40 mg/day. Best for those that worry/ruminate. Inexpensive.

**Lexapro** - QTc prolongation > 20 mg/day. Similar to but cleaner than Celexa.

**Prozac** - 10-120 mg/day. Long t ½ , numerous DDIs, 4 weeks to be effective, adds an energy component. Inexpensive.

**Paxil** - Discontinuation symptoms common, several DDIs.

**Zoloft** - Good for anxiety, OCD in high doses, can cause n/v & diarrhea, hyponatremia, helps w/energy. Inexpensive.

**Viibryd (SPARI)** - n/v & diarrhea. May not need 40 mg/day dose to be therapeutic. No generic.
SSRI Side Effects

- Weight gain or loss
- Sweating
- Hyponatremia*
- QTc Prolongation*
- Increases t½ of caffeine
- Worsens restless leg syndrome
- REM Sleep DO
- Discontinuation Syndrome
- Antidepressant Apathy
- Serotonin Syndrome/Toxicity

*See Index at end of slides

Anxiety Disorders/OCD

- Anxiety Disorders - SAD, GAD, OCD
- APA Guidelines for OCD (2007)
- Cognitive Behavioral Therapy (CBT) & SSRI together are best practice for OCD treatment
- High doses of SSRIs used to treat OCD –
  - Prozac up to 80-100 mg/day
  - Zoloft up to 300 mg/day
  - Luvox/Fluvoxamine up to 300 mg/day
  - Anafranil/Clomipramine up to 250 mg/day

APA Treatment Guidelines for OCD

Dual Serotonin & Norepinephrine Reuptake Inhibitor (SNRI)

- SE Profile same as SSRIs + alopecia, dose dependent HTN, > liver enzymes, > discontinuation symptoms.
- Effexor XR/IR/ER - 37.5-300 mg/AM XL formula; good for low energy/motivation/fatigue & worry. Hyponatremia risk. Monitor BP starting at 150 mg/day. Affordable.
- Prialtiq - 50-100 mg, AM.
- Cymbalta - 30-120 mg/AM; neuropathic/fibromyalgia pain; can elevate liver enzymes (AST), monitor ETOH use.
- Fetzima - 40-120 mg/AM. 20 mg initial x 2-3 d then increase to 40 mg/day. Expensive, requires PA.
Newest Antidepressants

Trintellix - 5-20 mg/AM  Increases release of SE, NE, dopamine, glutamate, acetylcholine & histamine. < GABA. Weight neutral, no sexual SE, helps cognitive symptoms. Okay in elderly population. Long t½. SE include n/v, constipation, agitation, akathisia. Metabolized by CYP450. Expensive but coupons available.

ForfivoXL - equivalent to Wellbutrin XL 450 mg/day in one tablet. Same SE as Wellbutrin. Expensive, requires insurance PA.

Tricyclics (TCAs)

3rd line treatment for depression; numerous SE - dry mouth, weight gain, constipation, sexual SE, others. QTc prolongation. Fatal in OD

> 400 studies supporting TCAs  Inexpensive

Good for neuropathic pain -

Elavil/amitriptyline - 50-150 mg/day
Pamelor/nortriptyline - 75-150 mg/day
Anafranil/clomipramine - 100-200 mg/day; indicated for OCD

Abilify

Abilify - Dopamine partial agonist; atypical antipsychotic. FDA Approved as adjunct tx for depression. 2.5-10 mg, range; take in AM; pts start to feel better in a few days; metabolized by CYP450; < sedating; consider QTc prolongation. Monitor for akathisia; weight gain can be problematic. Generic formulation.

*Monitor for metabolic syndrome
*Risk for EPS, tardive dyskinesia
*BBW for risk of CVA in patients > 65 y/o
Required monitoring for antipsychotics

- Metabolic Syndrome – Any weight gain is concerning, esp. > 5% of initial wt. BMI monthly x 3 months, then quarterly. Monitor BP at office visits. Fasting lipids in 3 months then yearly. FBS or HgbA1c in 1 month, 3 months & then yearly. Evaluate cardiac risk.

Other Antidepressants

Wellbutrin XL/IR/ER - NDRI; up to 450 mg/d; used for Seasonal Affective DO; good for < energy/motivation; fast acting; augmentation for sexual SEs or to boost SSRI/SNRI effects. Can make us of irritability/anger & anxiety worse if used by itself. SEs = HA, tremor; avoid w/active ETOHism, hx of seizure DO. XL formulation ideal (once/day).

Remeron - 7.5-60 mg. HS. Moderate hyponatremia risk, no DDIs, low doses for sleep & to stimulate appetite. Weight gain (can be significant) within 1st six weeks, more likely in fe & before menopause. Not lethal in OD, safe LT use, good for elderly population. Generic inexpensive.

Trazodone - 50-300 mg. HS. Plasma levels increased by SSRIs. Older antidepressant found to have > sedative properties than antidepressant properties. Priapism, strong antihistaminic, best for initial & middle insomnia. LT use, not habit-forming. Can use w/other antidepressants (not MAOIs). > arrhythmias, numerous DDIs. Inexpensive.

Serotonin Syndrome/Toxicity

Neuromuscular hyperactivity -
- Akathisia
- Tremor*
- Gionus
- Myoclonus
- Hyperreflexia*
- Rigidity
- Nystagmus
- Shivering

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Serotonin Syndrome (con’t):

- Autonomic hyperactivity
  - Diaphoresis
  - Tachycardia
  - Tachypnea
  - Dilated pupils

- GI symptoms
  - Nausea
  - Diarrhea

- Temp. > 100.4°F
- Altered mental status
  - Agitation
  - Excitement
  - Confusion

**Hunter Serotonin Toxicity Criteria Scale

Antidepressant Black Box Warning

- Issued in 2004
- Increased suicidality in children, adolescents & young adults up to age 25
- NIMH pediatric trial results - benefits outweigh risks in both depression & anxiety
- No completed suicides
- 4% of those taking SSRIs
- Close monitoring

National Institute of Mental Health 2018

Depression vs. Bipolar Depression

- Early age of onset (childhood)
- Postpartum onset
- Hypersomnia
- Psychomotor slowing
- Depression with psychotic features
- Family history of bipolar illness
- History of antidepressant induced SI, mania or hypomania
Treatment-Resistant Depression (TRD)
- No response to at least 2 complete trials of 2 different classes of antidepressants.
- Switching between SSRIs of limited value (STAR-D)
- GeneSight Testing
- Wellbutrin augmentation - Abilify augmentation
- Level 3 treatments: add Lithium (450-600 mg/day) or Remeron (60 mg/day) or Nortriptyline (200 mg/day)
- Li+ most studied medication for TRD
- Li+ plasma levels = 0.4-0.8 mEq/L


Treatment-Resistant Depression (con't):
Combining SSRI with Tricyclic (TCA) - obtain serum tricyclic levels, monitor for Serotonin Syndrome or Hypertensive Crisis.
Lamictal augmentation - 100-200 mg/day
L-methylfolate 15 mg/day (Deplin)
Vitamin D


Treatment-Resistant Depression (con't):
- Seroquel/quetiapine - FDA approved as adjunct tx for depression. Used for severe treatment-resistant anxiety. Weight gain & lipid elevation can be significant.
- Latuda - FDA approved adjunct tx, 20-40 mg/day dose. Take w/at least 350 cal. meal. Potential for metabolic syndrome, akathisia, weight gain, sedation, elevated prolactin.
- Saphris - not FDA approved but could be used, structurally similar to quetiapine.
Treatment-Resistant Depression (con’t):

- **Methylyphenidate/Ritalin**: 10-40 mg/day divided doses
- **Modafinil/Provigil**: 100-200 mg/day
- Ketamine - approved 1970 as general anesthetic
- Transcranial Magnetic Stimulation (TMS) – FDA Approved 2008, done at Prairie View East Wichita
- Vagus Nerve Stimulation


Treatment-Resistant Depression (con’t):

Electroconvulsive Therapy (ECT) -
- Remission rates 50-70%
- Safe for pts w/pacemaker, other cardiac devices.
- Data suggest ECT should be recommended sooner.
- Use in pregnancy, bipolar disorder mania, pts > 65 years old, psychosis, SI.
- Stigmatized but in truth effective & backed by research.

Rosenquist P., McCall, W. & Youssef, N: Charting the course of electroconvulsive therapy: where have we been & where are we headed? 11/16; 46(11): 647-651.

Ruling Out Bipolar Disorder

- Misdiagnosed as Major Depression
- Definite mood swings
- Patient history - Family history
- History of insomnia/sleep issues occur in conjunction with mood symptoms.
- SSRIs, other antidepressants do not help the anxiety.
- SSRIs alone precipitate mania.
- Important to rule out PTSD, ADHD, OCD.
- Mood Disorder Questionnaire (MDQ) - self administered
Clinical Considerations
- Extended office visits
- One medication change/addition at a time & evaluate.
- Consider high risk groups for SEs, DDIs, BBW.
- Cranial Nerve & Motor Movement Assessment to substantiate findings.
- Pharmacist is an excellent resource.
- CBT effective for sleep disorders & is underutilized.
- When to refer to psych med provider.

Valuable Websites & Resources
- Audio-Digest Psychiatry Series
- Essential Pain Medication Prescriber's Guide by Stephen Stahl
- kumc.edu/parkinson - Rajesh Pahwa, M.D.; internationally known movement disorder clinic @ KU Medical Center, Kansas City
- neiglobal.com - Stephen Stahl's Neuroscience Education Institute
- psychiatry.org - American Psychiatric Association Clinical Practice Guidelines, coding & reimbursement, CPT changes, EHRs
- uptodate.com - UpToDate medication database

Q & A
Review & Questions
Evaluations
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2. QTc Prolongation
3. References

Hyponatremia/SIADH

- Mild: Na+ 125-130 mEq/L; nausea, HA, confusion starting, malaise, decreased DTRs.
- Moderate: Na+ 115-125 mEq/L; lethargy, psychosis, disorientation, agitation.
- Severe: Na+ < 115 mEq/L; seizures, respiratory arrest.
- Other labs = low BUN, chloride & uric acid. K+, TSH & cortisol levels WNL. Increased urine Na+.
- Treatment: DCSSR1 or offending meds., H2O restriction, slow IV replacement of Na+, other supportive measures.

QTc Prolongation: What’s the concern?

- Measured by 12-Lead EKG.
- Normal = 440 msec. or <
- Clinical relevant threshold = 500 msec.
- Can lead to fatal arrhythmias, Torsades de points, associated with risk of sudden cardiac death.
- Associated w/Celexa > 40 mg/day & Lexapro > 20 mg/day
- Other medications (including antidepressants) prolong QTc = diuretics, antipsychotics, antibiotics, antiarrhythmics.
- Physiologic states = hypokalemia, hypocalcemia, hypomagnesemia, bradycardia, heart block. • Age > 65 yrs
References

- Giffit, M. Management of depression & common comorbidities. Audio Digest Psychiatry Series. 7/21/18; 47(14).
- Koran, L. Update on obsessive-compulsive disorder. Audio Digest Psychiatry Series. 7/07/14; 43(13).

References (con’t):