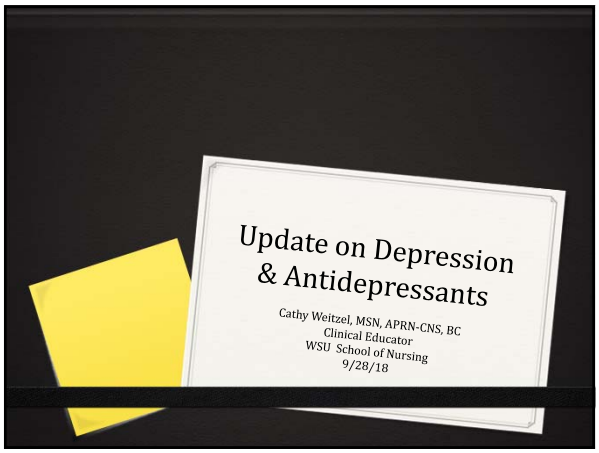

Anxiety & Depression

"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.
< folate levels associated w/TRD & increased rate of relapse.
- Vitamin D level
- Hormone levels

Raj, Y. Subclinical hypothyroidism: monitor or time to treat? Current psychiatry. 2014; 8(2): 47-48.

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 8-12 months in first episode depression.
- SSRIs are recommended treatment for anxiety disorders, *not* benzodiazepines.
- Start with small dose & increase slowly.
- Classes of Antidepressants:

National Institute of Mental Health Research Data 2018

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.

Stahl, Stephen, Essential Psychopharmacology Prescriber's Guide, 6th Ed., 2017, Cambridge University Press.

SSRI Side Effects

Weight gain or loss
Sweating
Hyponatremia*
QTc Prolongation*
Increases t ½ of caffeine
Worsens restless leg syndrome
REM Sleep DO
Discontinuation Syndrome
Antidepressant Apathy
Serotonin Syndrome/Toxicity
Sexual SE
Bruxism
Excessive yawning
Hyperreflexia

* 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 SSRI + alpoecia, 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.

Pristiq - 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 t ½. 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 EPSE, 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 Hgb A1c 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 sx of irritabilty/anger & anxiety worse if used by itself. SEs = HAs, 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); + arrthymias, numerous DDIs. Inexpensive.

Serotonin Syndrome/Toxicity

Neuromuscular hyperactivity -

Akathisia	Untreated EPSE
Tremor*	
Clonus	
Myoclonus	
Hyperreflexia*	
Rigidity	
Nystagmus	
Shivering	

Serotonin Syndrome (con't):

Autonomic hyperactivity -
- Diaphoresis
- Temp. > 100.4 F
- Tachycardia
- Tachypnea
- Dilated pupils

GI symptoms -
- Nausea
- Diarrhea

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 Nortryptyline (200 mg/day)
- Li+ most studied medication for TRD
- Li+ plasma levels = 0.4-0.8 mEq/L

Preskorn, S. Treatment options for the patient who does not respond well to initial antidepressant therapy. Journal of Psychiatric Practice. 2015; 15(3): 202-210.

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

Rexulti augmentation - 3rd generation antipsychotic & potent mood stabilizer. Onset of action 2-4 weeks. Up to 2.0 mg/daily for depression. SE: HA, tremor, weight gain. Monitor weight, FBS, lipids, BP. Monitor for EPSE. BBW for use in elderly. Expensive.

Stahl, Stephen M. Essential Psychopharmacology Prescriber's Guide, 6th Ed. Cambridge University Press, 2017.

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):

- Methlyphenidate/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

Spiegel, D. et al., Disorders of Diminished Motivation: What they are & how to treat them. Current Psychiatry, Jan. 2018, Vol. 17, No 1, p 11-18.

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 - Staphen Stahl's Neuroscience Education Institute
- psychiatry.org - American Psychiatric Association Clinical Practice Guidelines, coding & reimbursement, CPT changes, EHRs
- Stahl's Essential Psychopharmacology Prescriber's Guide 6th Ed. by Stephen Stahl
- uptodate.com - UpToDate medication database

Q & A

Review & Questions

Evaluations

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Index

1. Hyponatremia/SIADH
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: DC SSRI or offending meds., H20 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.
- Get a baseline EKG
- Can lead to fatal arrthymias, 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

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