Prescribing Medications for Anxiety and Depression (without getting anxious and depressed)

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Disclosures

- None
Learning Objectives

• At the end of this session you will be able to:
  – Use first and second-line treatments for depression and anxiety, including medications for augmentation of partially effective meds.
  – Manage common side effects of medications for depression and anxiety.
  – Develop a differential diagnosis for reasons why treatments are not working as expected for anxiety and depression.
Psychopharmacology ATTACK!

- Lots of info in next 30 minutes!
- We will process more in the breakout session!
Session Structure

- First line treatments for anxiety and depression (15 minutes)
- Augmenting/second line treatments for anxiety and depression (10 minutes)
- Why is my patient not getting better? (5 minutes)
First Line Treatments for Depression and Anxiety
Anxiety and Depression First Line Treatment

• Mild-to-Moderate
  – Based on symptoms or PHQ-9/GAD-7 Score
    • PHQ-9 under 10 for Mild, under 20 for Moderate (15-19 Mod-Severe)
    • GAD-7 under 10 for Mild, under 15 for Moderate
  – Cognitive Behavioral Therapy is a good option
  – Medications often are not required for MILD anxiety or depression

• Moderate-to-Severe Medications:
  – SSRIs first line medication treatment
  – Try one at a good dose, give it at least 4-6 weeks
  – Partial response: increase dose and/or Augment
  – No response: go to 2nd SSRI

https://aims.uw.edu/sites/default/files/Exampleprovidertool.pdf
Anxiety and Depression First Line Treatment

- **KEY RESOURCE:**
  - University of Washington AIMS Center
  - [https://aims.uw.edu/sites/default/files/ConcisePsychotropicMedicationPrescribingDirections.pdf](https://aims.uw.edu/sites/default/files/ConcisePsychotropicMedicationPrescribingDirections.pdf)

- **Treat to Target!**
  - Value of care management (collaborative care)
  - What is remission?
    - Many use PHQ9<5 for depression as remission.
    - Antidepressant that is partially effective (>25% but <75% reduction on PHQ9/GAD7 score), consider increasing dose or augmenting with another medication.
    - Antidepressant that has not been effective (<25% reduction on PHQ9/GAD7 score) after an adequate dose/time (usually 4-8 weeks), consider changing antidepressants.
    - Ask the patient
BRIEF MEDICATION PRESCRIBING DIRECTIONS

50 mg qday. Max: 200 mg qday. Discontinuation: Taper slowly to minimize withdrawal symptoms. MONITORING: Weight. Consider posttreatment BMP to rule out hyponatremia in older adults. GENERAL INFORMATION: Mechanism of Action: Selective serotonin reuptake inhibitor. FDA Indications: MDD, OCD, panic disorder, PTSD, social phobia, premenstrual dysphonic disorder. Off-Label Indications: Other anxiety Pharmacokinetics: T 1/2 = 26hr. Common Side effects: Nausea (25%), insomnia (21%), diarrhea (20%), sexual side effects (14%), sweating (14%), dizziness (12%), fatigue (12%), somnolence (12%), dry mouth (7%), tremors (8%). Warnings and Precautions: Suicidality, manic switch, serotonin symptoms or NMS, abnormal bleeding, hyponatremia, discontinuation syndrome. Contraindications: Known hypersensitivity reaction to the product. Use of MAOI or within 14 days of stopping a MAOI or pimozide. Black Box Warning: Increased SI in patients < 25 y/o. Pregnancy: Category C. Breastfeeding: Safest, Use caution. Significant drug-drug interactions: Minimal; Check all drug-drug interactions Generic available: Yes, Moderate price.
SSRI Pearls

• Higher than FDA-recommended may be needed
  – Maximum benefit up to 250 mg equivalents of imipramine in metaanalysis\(^1\)
  – 250 mg of imipramine=300 mg of sertraline=250mg of fluvoxamine=50 mg of paroxetine or fluoxetine=83.25 mg of citalopram=41.75 mg of escitalopram

• Anxiety disorders – start really low dose

• Blunting of affect at higher doses

• Bruising (platelets have 5HT receptors!), hyponatremia in elderly

• STAR-D trial showed maximum benefit after TWELVE weeks!

• Celexa over 40 mg (20 mg for geriatrics)
  – VA demonstrated worse outcomes when celexa doses lowered\(^2\)
  – UM study showing higher healthcare utilization and higher sedatives when dose changed\(^3\)
  – Baseline EKG if going over these doses and recheck EKG, keep K/Mg stable

SNRIs

- Co-morbid pain and anxiety/depression – consider 1\textsuperscript{st} line
- Cymbalta to 120 mg
  - Better outcomes with pain at 120 mg\textsuperscript{1}
- Effexor to 300 mg in XR, 375 in IR
  - Effexor does not hit NE until 150 mg and above (SSRI like before 150mg)
- Same time course as SSRIs
- May increase BP
- May be more effective for severe depression\textsuperscript{2}

Mirtazapine

• Sedating
  – More sedating at lower dose (higher dose NE kicks in)

• Increased appetite
  – Weight gain will not be subtle unlike atypical antipsychotics
Buspirone

- Can augment SSRI for depression and anxiety
- If it works, it works!
- Does not work well for people who have BDZ exposure already\(^1\)

Trazodone

- Approved for depression (higher doses)
- Mostly used for sleep
- SE: sedation, orthostatic hypotension/dizziness, priapism
- PEARL: 150 mg often scored in half one side, in thirds on other side (makes flexible dosing easy)
New(er) Agents

• Vilazodone
  – SSRI and 5HT1A partial agonist (Like Buspar and SSRI in one)
  – GI SE most common, headache

• Levomilnacipran
  – SNRI (enantiomer of milnacipran which is approved for fibromyalgia)
  – More heavy on norepinephrine, so more HR/BP/urinary hesitancy issues

• Vortioxetine
  – Trade name changed from Brintellix to Trintellix
  – SSRI, 5HT1A full agonist, 5HT3 antagonist
  – Increases dopamine, NE, Ach in prefrontal cortex
    • Could this be good for improved cognition in depression? 3 RCTs say so¹
    • Studied in geriatric patients and shows effect

Bupropion

- Great for low energy, smoking cessation, low concentration
- Off-label use for ADHD
- Does NOT help out generalized anxiety and may make anxiety worse
- THREE FORMULATIONS:
  - Immediate release (TID)
  - Sustained release (SR – BID)
  - Extended release (XR – qday)
- When dosing TID or BID, do not dose too close to bed
  - BID= qam and qdinner (9AM, 5 PM)
Tricyclic Antidepressants

- Effective – dirtier drugs re: receptor affinities
- More SE than SSRI and SNRI
  - Dry mouth, sedation, constipation, urinary retention, blurry vision, orthostasis
- Lethal in overdose (as few as 10 day supply can be lethal)
- Benefit with chronic pain
- Nortriptyline often tolerated better than amitriptyline
- Lower doses for pain; higher doses for depression
- EKG at baseline and annually if over 65 yo, cardiac diseases
- Can test blood levels!
Complementary and Herbals

- We are in Ann Arbor after all!
- Carlat Report Psychiatry July/August 2013 still one of best resources
- Depression effective and safe: Rhodiola rosea (300-900 mg), SAMe (200-800 mg BID)
  - St. John’s Wort as well, but interacts with SSRI-serotonin agents
  - 5-HTP may help but TID-QID
  - Methylfolate may help depression as adjunct
  - Fatty acids possible; 1-2 grams
- Kava helps anxiety but not safe (hepatotoxic)
- Valerian may help insomnia but poor studies
Augmenting Agents for Depression and Anxiety
Benzodiazepines

- Lipophilic - diazepam, alprazolam
- Hydrophilic – lorazepam, clonazepam
- Oxazepam, temazepam, lorazepam safer in liver disease
- Risk Assessment for BDZ Abuse:
  - Higher risk if h/o alcohol use DO, FH of alcohol use DO
  - Risk of accidental OD with Opioids
- Red Flags
  - Unwilling to try other treatments
- Urine GCS will catch alcohol metabolites!
- BDZ in depression may help patient stick with other meds short term\(^1\)
  - Lower risk if using PRN; Some patients use as back-up coping mechanism
- UK NICE guidelines recommend 2-4 week treatment, not for mild GAD

Atypical Antipsychotics

- FDA approved for augmenting depression (as of 7/2017):
  - Aripiprazole
  - Brexpiprazole
  - Olanzapine
  - Quetiapine XR

- None FDA approved for augmenting anxiety
  - Off-label use for quetiapine doses from qhs to even TID dosing
    - May be similar to SSRI effect BUT HIGHER SE PROFILE!

Atypical Antipsychotic Pearls

- High Metabolic Risk: Olanzapine, Clozapine
- Medium Metabolic Risk: Quetiapine, risperidone, asenapine, iloperidone
- Low Metabolic Risk: Aripiprazole, Brexpiprazole
- Lowest Metabolic Risk: Ziprasidone, Lurasidone
- Ziprasidone and Lurasidone need to be taken with food (300 cal)
- Augmenting doses are on lower end of spectrum; bipolar doses mid-range; schizophrenia doses highest
Atypical Antipsychotic Pearls

• Most Sedating: Quetiapine, Olanzapine, Clozapine
• Don’t forget Akathesia (looking at you aripiprazole)
  – Reduce dose, add low dose BDZ or propranolol, switch agents
• METABOLIC MONITORING FOR ALL
Consensus Development Conference on Antipsychotic Drugs and Obesity and Diabetes

Table 3—
Monitoring protocol for patients on SGAs*

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* More frequent assessments may be warranted based on clinical status
Other Augmenting Agents

- Can mix and match MOST groups of antidepressants
  - SSRI/SNRI/TCA together to not make much sense (maybe low dose TCA)
  - We didn’t discuss MAOIs – do NOT mix serotonin meds with MAOIs!
- Mirtazapine for depression/anxiety
- Bupropion for depression (can worsen anxiety)
- Buspirone for depression/anxiety
- Low dose stimulants for geriatric depression\(^1\)
  - 5-10 mg of methylphenidate; up to 40 mg
- Gabapentin for Anxiety (off label use)
- Hydroxyzine for PRN use anxiety
- Lithium for unipolar depression (per STAR*D)
- Cytomel (T3) for depression (per STAR*D)
- STAR-D: https://www.nimh.nih.gov/funding/clinical-research/practical/stard/allmedicationlevels.shtml

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Why is My Patient Not Getting Better?
Reasons for Treatment Failure

• Is the dose high enough?
• Has the treatment been long enough?
  – Instant gratification does not work with SSRI/SNRIs
• Do you have the correct diagnosis?
  – Could this be bipolar depression? Hypomania often undiagnosed and unrecognized. Bipolar depression notoriously difficult to treat.
  – What are the refractory symptoms?
    • Attention? Irritability? Consider co-morbid ADHD
    • Irritability? Mood Swings? “0 to 60 in seconds”? Consider Personality DO
Reasons for Treatment Failure

- Chronic Pain
- Is there a medical cause?
  - Thyroid? Brain tumor?
  - Revisit your review of systems
- Are they taking their meds?
- Are meds affordable? (Donut Hole, loss of insurance)
- Culture – is mental illness accepted?
  - LARGE placebo effect in psychiatric medications
  - If you undersell meds, they will not work as well
Tools to Help

- PHQ-9 (depression)
- GAD-7 (anxiety)
- Mood Disorder Questionnaire (bipolar – not good universal screen)
- CIDI (Structured bipolar screening)
- PC-PTSD (Primary Care PTSD screen)
- PCL-5 (PTSD symptom scale – LONG)
- Adult ADHD Self-Report Scale
- AUDIT and AUDIT-C (alcohol screening)
- DAST-10 and DAST-20 (Drug abuse screening)
REFERENCES

- https://aims.uw.edu/sites/default/files/ExampleproviderTool.pdf
- https://aims.uw.edu/sites/default/files/ConcisePsychotropicMedicationPrescribingDirections.pdf


• Chessick CA et al. Azapirones for generalized anxiety disorder. Cochrane Database of Systematic Reviews 2006, Issue 3


REFERENCES


• STAR*D Summary Site: https://www.nimh.nih.gov/funding/clinical-research/practical/stard/allmedicationlevels.shtml

• https://www.integration.samhsa.gov/clinical-practice/screening-tools
Thank you!