Individualizing Antidepressant Therapy

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Overview

- The number of individuals receiving treatment for depression has increased significantly in the recent years.
- Most of them are treated by their PCP.
- One in 10 individuals older than 12 yrs now take antidepressants.
- The use of AD has increased by almost 400% for all ages by 2008 (2010 report released by the CDC).
Overview

- Major depression is the leading cause of disability worldwide among persons aged 5 years and older—according to the World Health Organization.
Overview

- AD were the most frequently prescribed prescription drug between 2005-2008 for adults aged 18-44 and the third most commonly used drugs for all ages
  - 10.8% of all Americans older than 12 years take antidepressants
  - More common in females and whites
  - No variation in use was found in different income groups
Overview

- More than a dozen of antidepressants have been demonstrated effective for the treatment of depression in the U.S.
- The American Psychiatric Association guidelines for the treatment of depression conclude that antidepressants are generally equally effective.
- The APA suggests to choose based on the
  - Side effects
  - Tolerability
  - Patient preference
  - Family response
  - Cost
  - Coverage...
Other factors to consider

- Bipolar depression
- Presence of anxiety or psychosis
- Atypical features
- Melancholic depression
- Symptom severity
- Presence of personality disorders
- Presence of medical problems or drug use
Tx Recommendation for depression with...

- Anxiety - SSRIs, SNRIs, avoid bupropion
- OCD sx-s - SSRIs, clomipramine
- Severe sx-s - SNRIs, augmentation
- Melancholic - SNRIs, TCAs
- Atypical - SSRIs, MAOIs
- Low energy - bupropion
- Insomnia - mirtazapine
- Sexual side effects - bupropion
Comorbid Disorders

- Generalized Anxiety Disorder
- Panic Disorder
- Post Traumatic Stress Disorder
- Obsessive Compulsive Disorder
- Social Phobia
- Attention Deficit Hyperactivity Disorder
- Impulse Control Disorder
- Bulimia Nervosa
- Substance Abuse
Other Indications

- Irritable Bowel Syndrome- TCA or SSRI
- Enuresis- TCA (clomipramine)
- Neuropathic pain- SNRI or TCA
- Migraine headache- TCA
- ADHD- bupropion
- Autism- SSRI
- Late luteal phase dysphoric d/o- SSRI
- Borderline personality d/o
- Smoking cessation- bupropion
SSRIs- Selective Serotonin Reuptake Inhibitors

- Similar spectrum of efficacy
- Broad spectrum of action
- Similar side effect profiles
- Structurally different
- Clinically distinct
- Different tolerability
- Different response
- Different pharmacokinetic properties
- Different half life
Common Side Effects

- Mild nausea
- Loose bowel movements
- Restlessness
- Headaches
- Insomnia or sedation
- Increased sweating
- Sexual problems
- Weight changes
- Vivid dreams
Other Side Effects

- Serotonin Syndrome-
  - Lethargy, restlessness, confusion, flushing, tremors, jerks, then, hyperthermia, rhabdomyolysis, renal failure
- Apathy
- Increased risk of seizures with tramadol
- Might increase TCA plasma eves
- Severe interactions with MAOIs
- Category C in pregnancy
- Discontinuation syndrome- flu like sx, paresthesias, electric shock feeling
Fluoxetine (Proza, Serafem)

- 20-80mg
- FDA approved for
  - MDD, OCD, PMDD, Bulimia and Panic d/o
- More activating
- Long half life
- Less weight gain
- Less sedation
- Liquid form and weekly formulation
- Better for atypical features, bulimia, and OCD
- Generic
- Symbyax- combination of Prozac and Zyprexa. Approved for bipolar depression
Fluvoxamine (Luvox)

- 100-300mg
- FDA approved for
  - OCD and social anxiety d/o (not for MDD)
- Better for anxiety in general
- More sedating
- Approved for children 8-17 for OCD
- Generic
- More GI side effects
- Less sexual side effects
- Might be better for depression in psychotic disorders
Paroxetine (Paxil, Paxil CR)

- 20-60mg
- FDA approved for
  - MDD, OCD, Panic d/o, Social anxiety, PTSD, GAD, and PMDD
- Also mild anticholinergic and norepinephrine reuptake inhibition
- More sedating
- More weight gain
- More sexual dysfunction
- More gastrointestinal side effects
- Shorter half life (more WD sx, bid dosing, need to taper down)
Citalopram (Celexa)

- 20-80mg
- FDA approved for 
  - MDD
- Mild antagonist of H1 histaminic receptors
- More insomnia and low energy
- More tolerable
- Good for the elderly
- Generic
Escitalopram (Lexapro)

- 10-20mg
- 10mg of escitalopram is equivalent to 40mg of citalopram
- FDA approved for MDD and GAD
- Less side effects
- Very well tolerated
- Less sexual side effects
- Less GI side effects
- Recently generic
Sertraline (Zoloft)

- 50-200mg
- FDA approved for
  - MDD, PMDD, Panic, PTSD, Social phobia and OCD
- Can also block dopamine reuptake
- More activating
- Well tolerated
- More safety studies during pregnancy
- More safety studies after MI or stroke
- Better for atypical symptoms
- Generic
Bupropion (Wellbutrin, Zyban)

- 150-450mg
- FDA approved for
  - MDD, Seasonal affective disorder
  - Nicotine addiction (Zyban)
- Less likely to induce manic symptoms in bipolar depression
- Better if comorbid ADHD, Parkinson’s or sexual dysfunction
- More activating and better to improve motivation, energy and cognitive problems
- Very good augmentation to SSRIs
- Works on NE and DA
Bupropion (cont.)

- Possible side effects
  - Insomnia, tremors, agitation, headaches, dizziness, constipation, nausea, anorexia, hypertension, and tinnitus
  - It can also lower seizure threshold, although not as much with the XL formulation
- Avoid in patients with panic d/o or irritability
- Category C in pregnancy
- Partial contraindication in patients with eating disorders, head trauma or seizures
Mirtazapine (Remeron)

- 15-45mg
- Blocks alpha 2 adrenergic pre-synaptic receptors
- Also blocks histamine H1 receptors
- Modulates serotonin and norepinephrine
- FDA approved for MDD
- Most common SE are sedation and weight gain
- Good augmentation for venlafaxine
- Other side effects
  - Dry mouth, constipation, increased appetite, and hypotension
- Advantages
  - Less sexual side effects
  - Comorbid anxiety
  - Less drug to drug interactions
Venlafaxine (Effexor)

- 37.5-225mg
- SNRI
- Serotonin, norepinephrine and dopamine
- FDA approved for MDD and GAD
- Considered more effective for atypical or treatment resistant depression, comorbid anxiety and panic disorder
- Also for fibromyalgia and neuropathic pain
- Can be helpful for hot flashes
- Common side effects
  - Headaches, insomnia, sedation, nausea, diarrhea, changes in appetite, sexual dysfunction, sweating, and hyponatremia..
  - Dose dependent increase in blood pressure
  - Can be lethal in overdose
  - More withdrawal symptoms
Desvenlafaxine (Pristiq)

- 50-150mg
- FDA approved for MDD
- SNRI
- Modulates serotonin, NE and dopamine
- Benefits and side effects similar to venlafaxine
- More consistent plasma levels
  - Better side effect profile
  - Less increase in blood pressure and less withdrawal symptoms (compared to venlaxafine)
Duloxetine (Cymbalta)

- 60-120mg
- SNRI
- FDA approved for
  - MDD, Diabetic Peripheral Neuropathic Pain, Fibromyalgia, and GAD
- Also used for stress urinary incontinence and other anxiety disorders
- Side effects
  - Nausea, diarrhea, decreased appetite, dry mouth, constipation, insomnia, sedation, dizziness, sexual dysfunction, sweating, increased blood pressure, and urinary retention
- Better for severe depression, comorbid anxiety and somatic symptoms
Vilzodone (Viibryd)

- New
- 10-40mg
- Dual acting serotonergic antidepressant
- SSRI and 5-HT1A receptor partial agonist activity
- Side effects: diarrhea, nausea, somnolence
- Less sexual side effects
Tricyclic Antidepressants (TCAs)

- Amitriptyline (Elavil)
- Clomipramine (Anafranil)
- Doxepin (Sinequan)
- Imipramine (Tofranil)
- Desipramine (Norpramine)
- Nortriptyline (Pamelor)
- Amoxapine (Asendin)
- Maprotiline (Ludionil)
TCAs

Mechanism of action
- Block muscarinic receptors
- Block histamine H1 receptors
- Block alpha one adrenergic receptors
- NE reuptake blockade
- Serotonin reuptake inhibitor

- More side effects compared to the SSRIs
- Gradual titration
- Can be lethal in overdose
- Might be better for depression with melancholia
- Desipramine and protriptyline are more activating
- Nortriptyline is the least likely to cause orthostatic hypotension
- Amoxapine can antagonize D2 dopamine receptors so it can cause extrapyramidal symptoms
TCAs- side effects

- Anticholinergic
  - Dry mouth, constipation, urinary retention, blurred vision, tachycardia, cognitive impairment and confusion
- Sedation
- Cardiovascular effects
  - Orthostatic hypotension, tachycardia, cardiac conduction delays
  - In OD can cause life threatening arrhythmias
  - Do not use in pre-existing heart blocks
  - Order EKG before starting in patients with heart dz
- Seizures
- Weight gain
TCAs in overdose

- Neuropsychiatric impairment
- Hypotension
- Serious arrhythmias
- Seizures
- Delirium
- Agitation
- Hallucinations
- Death
Monoamine Oxidase Inhibitors (MAOIs)

- Phenelzine (Nardil)
- Tranylcypromine (Parnate)
- Better for atypical depression
- Side effects
  - Orthostatic hypotension, insomnia, weight gain, sexual dysfunction, and peripheral edema
- Hypertensive crisis
- Many drug to drug interactions
- Dietary restrictions
  - Aged cheeses, fava beans, wine, fermented meats, sauerkraut, soy sauce, tap beer...
- Serotonin syndrome
- Wash out periods
- Fatal in overdose
Other Interventions

- Psychotherapy
- Electroconvulsive therapy
- Transcranial Magnetic Resonance
- Deep Brain Stimulation (not FDA approved for depression)
Augmentation
APA guidelines

- I- Psychotherapy
- II- Add another antidepressant
- II- Atypical Antipsychotics
- II- Thyroid Hormone
- II- Mood Stabilizers
- III- Anticonvulsants
- III- Psychostimulants
- III- Omega-3 Fatty Acid
- III- Folic Acid
- III- Anxiolytic or Sedative/Hypnotic
Caution

- **Suicidality**
  - Transient increased risk after initiation of treatment
  - Antidepressant induced

- **Mania**
  - Look for excessive energy decreased need for sleep agitation aggression elevated mood...
  - Start a mood stabilizer and/or stop the antidepressant

- **Psychosis**
  - Add second generation antipsychotic

- **When in doubt...** refer to a psychiatrist