Complex Medication Management

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Severe Mental Ilness

- Schizophrenia, Bipolar Illness, Schizoaffective disorder
- SMI have 20-25 year decreased life expectancy compared to the general population
- Majority of this is due to cardiovascular disease.

Eye Popping Stats

- 80% of schizophrenics worldwide smoke
- 30% of known diabetics, 62% of hypertensives and 88% of hyperlipidemics were **not** receiving treatment at enrollment in CATIE trial.
- 20% SMI are infected with HCV
- Between 1988 and 2002 rates of obesity and diabetes in schizophrenics increased 6% to 19%

Complex Med Management

- Polypharmacy should be minimized
- Generally no indication for >1 SSRI/SNRI, >1 atypical antipsychotic, or >1 BZD
- In Bipolar illness often need medications from multiple classes and can use multiple mood stabilizers.

Tx Resistant Depression Rational Polypharmacy

- Treatment Resistant Depression
  - Addition of WBT to an SSRI
  - Addition of atypical antipsychotic to SSRI
  - Addition Thyroid hormone
    - Cytomel (liothyronine) 12.5-25 mcg
  - Addition low dose Lithium
  - Addition Folate
  - Addition SAMe
  - Addition Lamotrigine

Medication Tx Bipolar d/o

- Mood Stabilizers
- Antipsychotics
- Antidepressants

Medication Tx Schizophrenia

- Typical (First Generation) Antipsychotics
- Atypical (Second Generation) Antipsychotics
- Mood Stabilizers
- Antidepressants

Atypical Antipsychotics

- Clozapine (Clozaril), Olanzapine (Zyprexa)> Quetiapine (Seroquel), Risperidone (Risperdal)>Aripiprazole (Abilify)> Ziprazidone (Geodon)
- Metabolic side effects- wt gain, diabetes, hyperlipidemia listed above in decreasing order of risk for these complications

Screening Recs for Atypical Antipsychotics

- November 2003 ADA, APA, AACE, NAASO came up with consensus guidelines for atypical antipsychotic screening (see next slide).
- FDA recommendations
  - Diabetics started on atypical antipsychotics monitored for worsening glucose control
  - If RF for DM get baseline and periodic fasting glucose if starting atypical antipsychotic
  - Any pt placed on atypical antipsycotic monitored for sx's of hyperglycemia if sx's get fasting glucose

Table 1: ADA Monitoring Recommendations for Patients on SGAs

	Baseline	4 weeks	8 weeks	12 weeks	Quarterly	Annually	Every 5 years
Personal/Family History	X					X	
Weight (BMI)	X	X	X	X	X		
Waist Circumference	X					X	
Blood Pressure	X			X		X	
Fasting Plasma Glucose	X			X		X	
Fasting Lipid Profile	X			X			X

Typical Antipsychotic Side Effect's

- Haldol, Prolixin, etc (but remember atypicals also can cause these SE's at a lower rate)
- Extra Pyramidal Symptoms (EPS)
  - Dystonic rxn within hours (treat with IM/IV benadryl)
  - Akithesia within days to weeks (Treat with propranolol)
  - Parkinsonism within months to years (treat with cogentin)
- Tardive Dyskinesia
  - May not resolve with d/c of med

More SE's of Antipsychotics

- Neuroleptic Malignant Syndrome
  - fever, muscular rigidity, altered mental status, and autonomic dysfunction
  - 90% cases occur within 10 days of initiation of med
- QT prolongation
- Hyperprolactenemia
  - Gynecomastia, decreased libido, amenorrhea
  - Most commonly from Risperidone/Invega/typical antipsychotics
- Orthostatic Hypotension
- Anticholinergic side effects

Clozapine (Clozaril)

- Leukopenia/Agranulocytosis- weekly CBC for 6 months then q2wk CBC for 6 months then monthly CBC.
- Drooling (Sialorrhea)
- Siezures
- Similar to Zyprexa in metabolic effects

Lithium

- Probably most effective tx for classic Bipolar I
- Renally cleared only
- Narrow therapuetic window
- Initial labs: BMP, TSH
- BMP, TSH, Li level q6-12 months
- Therapuetic serum level 0.6-1.2 (check 12h after last dose)
- Common maintinence doses 600-1500mg/day
- QHS dosing optimal

Lithium-cont

- Common Side Effects
  - Tremor
  - Polyuria
  - GI (nausea/diarrhea)

Lithium Complications

- Toxicity- continued use of lithium with renal insufficiency most common cause, lithium levels above 1.0 can cause toxicity
- Sxs of toxicity: ataxia, confusion, nausea/vomiting
- Toxicity requires hospitalization for telemetry
- Hypothyroidism
  - Generally not severe, often will treat with synthroid and can keep on lithium.
- Diabetes Insipidus
- Hypercalcemia
- Renal Failure?

Lithium Complications

- Drug-drug interactions
  - Many medications can increase Lithium serum level and cause toxicity.
  - Avoid NSAIDs, diuretics, ACE/ARB unless you are carefully monitoring lithium level
  - Anything that decreases renal fxn can cause lithium toxicity.

Depakote (Divalproex)

- Treatment for Bipolar d/o
- Common maintenance doses 1000-2500mg/day
- Serum levels used for dosing; therapuetic serum level 60-125 (drawn 12h after last dose)
- Baseline labs: CBC, LFTs.
- Monitor CBC, LFTs, Valproic acid level q6-12 months
- Ammonia level if symptomatic (note ammonia level often elevated in asymptomatic patients on Depakote)

Depakote Side Effects

- Common
  - Nausea/diarrhea
  - Wt gain
  - Sedation
  - Thrombocytopenia
  - Alopecia

Major complications of Depakote

- Liver Failure
- Teratogenicity
  - Would not rec in women of child bearing age
  - If you do us it in this population put in an IUD
- Pancreatitis
- Polycystic ovary syndrome
- Pancytopenia
- Encephalopathy

Other Mood Stabilizers

- Carbamazepine (Tegretol)
  - Many drug-drug interactions
  - Autoinducer therefore levels will decrease over time
  - Lab monitoring: tegretol level, CBC, LFTs, sodium
  - Side effects: hyponatremia, SJS, liver tox, pancytopenia, teratogen
- Lamotrigine (Lamicital)
  - SJS, d/c med if develops rash, most common in asians
- Oxcarbazepine (Trileptal)
  - Hyponatremia
- Topiramate (Topamax)
  - Metabolic acidosis
  - Wt loss
  - “dopamax”

Antidepressants SSRIs

- Side effects as a class
  - Sexual side effects (anorgasmia, decreased libido)
  - Hyponatremia
  - Serotonin Syndrome (requires 3 of below)
    - Agitation
    - Diarrhea
    - Heavy sweating not due to activity
    - Fever
    - Mental status changes such as confusion or hypomania
    - Muscle spasms (myoclonus)
    - Overactive reflexes (hyperreflexia)
    - Shivering
    - Tremor
    - Uncoordinated movements (ataxia)
  - Initial anxiety (for first 2 weeks)
  - Mania/hypomania

SSRI Medication Specific SE's

- Paroxetine (Paxil)
  - Wt gain
  - Discontinuation syndrome
  - FDA warning for birth defects
- Mirtazapine (Remeron)
  - Wt gain
  - Sedation
- Venlafaxine (Effexor)
  - HTN
  - Discontinuation syndrome

Rates of SE's with different Antidepressants

- Wt gain: Mirtazapine>paxil>zoloft, celexa, lexapro, prozac, effexor>wbt
- Sedation: Mirtazapine>paxil, zoloft>celexa, lexapro>prozac, effexor, WBT
- Drug/Drug interactions: Prozac, Paxil have the most; Lexapro, Celexa, Zoloft have the least.
- Sexual side effects: Wellbutrin and Mirtazapine only two antidepressants without sexual SE's

Choice of Antidepressant in Particular Populations/Conditions

- Elderly: celexa, lexapro, zoloft, remeron
- Pregnant: zoloft (but probably would not change any antidepressant if pt is responding to it except maybe paxil)
- Children/Adolescents: Prozac, Lexapro
- Multiple medical problems: celexa, zoloft, lexapro
- Concurrent anxiety: SSRI
- Concurrent ADHD: WBT
- Chronic/Neuropathic Pain: Effexor, Cymbalta, Tricyclic Antidepressant

Tricyclic Antidepressants (TCA)

- Nortriptyline best choice in elderly due to least anticholinergic effects
- High side effect burden: dry mouth, sedation, wt gain, constipation, urinary retention
- Not a good choice in those with cardiac dz
- Good effectiveness for chronic pain syndromes

Monoamine oxidase inhibitors (MAOI)

- Tranylcypromine (Parnate), Phenelzine (Nardil), Isocarboxazid (Marplan), Selegiline (EMSAM)
- EMSAM transdermal patch 6mg and less no need for food restrictions
- Otherwise all MAOIs require adherence to low tyramine diet to avoid hypertensive crisis
- Never combine SSRI and MAOI
- Always check for drug/drug interations when prescribing a medication to a person on MAOI

Other Antidepressants

- Nefazodone
  - Black box warning for liver failure
- Fluvoxamine (Luvox)
  - SSRI but rarely used except sometimes for OCD
  - Many drug/drug interactions

Caution

- Use great care when combining TCAs and SSRIs the SSRI will increase the TCA level
- Tramadol and SSRI/WBT increase sz risk, and risk serotonin syndrome
- Never combine MAOI and SSRI
- Avoid TCAs in heart dz
- Avoid combining triptans and SSRIs