Don't Head for the Hills:
Managing psychotropic side effects in the primary care setting

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Disclosures

- None

Goals and Objectives

- Discuss commonly prescribed psychotropic medications and the common occurring side effect profiles
- Discuss significant drug-drug reactions that can occur when primary care patients are also on psychiatric medications
- Side effect management in the primary care setting
- Therapeutic drug monitoring strategies

Case #1

- 45 y/o CF with history of major depressive disorder , GERD and PVCs presents to clinic after being prescribed Celexa by the local community service board at 40mg daily. She is complaining of feeling emotionally numb, diarrhea and decreased sexual desire.

SSRIs

- Work by blocking serotonin reuptake pump increasing serotonin in the synapse
- Most common side effects:
  - Emotional flattening
  - Cognitive slowing
  - GI dysfunction: nausea, diarrhea, dry mouth
  - Sexual dysfunction: delayed ejaculation, decreased sexual desire and erectile dysfunction
  - Insomnia or sedation
  - Activation or agitation

SSRI drug specific side effects

- Fluoxetine: due to antagonism at 5HT2C can increase agitation, anxiety and activation
- Citalopram: should not be prescribed over 40mg per day due to risk of arrhythmia
- Paroxetine: has mild anticholinergic properties, and anti muscarinic side effects (dry mouth, constipation, transient bradycardia then tachycardia)
- Sertraline: has some ability to block dopamine reuptake pump

Management Strategies

- Insomnia: Trazodone 50-200mg qhs
- Sexual side effects: Bupropion, Sildenafil
- Many side effects are dose dependent or time dependent. Often side effects will remit by 4 month mark
- Patients with MDD who were told about specific adverse events were 1.5x more likely to have mild to moderate side effects.

Case 1: Management strategies

- Could wait to see if symptoms decrease over the next few months
- Could reduce the dose of Celexa to 20mg
- Could add Bupropion to address sexual side effects and potentially the emotional numbing
- Suggest patient taking medication with food and night time dosing to decrease nausea

SNRIs

- Dual serotonin and norepinephrine reuptake inhibitor.
- Increases dopamine transmission in the frontal cortex

SNRI side effects

- N/D, constipation
- Increased appetite
- Increased blood pressure
- Urinary retention
- Sweating
- Rare risk of seizures
- Increased suicidal ideation in patients up to age 24
- Can cause bleeding when combined with any anticoagulant.

Side effect management

- Urinary retention: α1 blocker like tamsulosin
- Insomnia: Trazodone
- Sexual dysfunction: can use Bupropion or Sildenafil

Unique issues with specific SNRIs

- Duloxetine: Metabolized by CYP1A2 and 2D6. Can increase TCA levels and cause serotonin syndrome when combined with MAOIs
- Venlafaxine: Headaches, nervousness, SIADH, sweating, hyponatremia. Discontinuation syndrome.
- Pristiq (Desvenlafaxine): more potent at serotonin receptor than norepinephrine.

Bupropion

- NDRI: norepinephrine and dopamine reuptake inhibitor.
- Takes 2-4 weeks to work
- Used to augment partial responders
- Can increase tremors, insomnia, agitation, headaches and dizziness.
- Increased risk of seizures when dosing over 450mg total per day of IR , SR or XL form or over 522 mg of Bupropion hydrobromide

Bupropion Side effects/management

- Inhibits CYP2D6:
- Interferes with codeine efficacy, increases levels of beta blockers and atomoxetine
- Don't use with other Dopamine increasing meds
- Don't use with patients with eating disorders
- Be very cautious when combining with any other med that will decrease seizure threshold

Case # 2

- 65 y/o male with hx of Bipolar disorder, GERD, hypothyroidism and HTN. He has been treated with Lithium chronically with stable drug levels of 0.8. No changes to his medications including his beta blocker. Over the past 3 years you notice that his WBC steadily climbing at his yearly visits with no correlating infection.

Lithium

- Unknown total mechanism of action
- Alters sodium transport across cell membranes
- Metabolized only through the kidney

Monitoring of Li

- Prior to initiation check: Cr, urine specific gravity, TSH and EKG
- Check Cr and BUN every 6-12 months
- Test therapeutic level every 3-6 months on stable dose. 4 days after dose increase. Trough level

Li Side effects

- Weight gain
- Polyuria, Polydypsia, Diabetes insipidus
- Diarrhea and Nausea with short acting forms and dose increases
- Goiter
- Acne, Rash
- Leukocytosis
- Arrhythmias, heart block

Managing Li Side effects

- To reduce risk of renal insufficiency- once daily dosing
- Tremor: propranolol, primadone or methazolamide
- Have patient take with food
- Avoid caffeine to control tremor

Drug interactions with Li

- Diuretics, NSAIDs, COX2 inhibitors and ACE-I can increase Lithium levels
- Metronidazole, Carbamazepine, Phenytoin, Ca Channel blockers and Methyldopa can increase levels
- Lithium can unmask Brugada syndrome: consult cardiology if pt develops syncope or palpitations.

Case 2 Management

- Patient from case 2 is experiencing Lithium induced leukocytosis
- This is typically a benign leukocytosis.
- Very unlikely to be dose dependent
- Could consider switching to another mood stabilizer

Valproate (Depakote, Depakene)

- Anticonvulsant and mood stabilizer
- Blocks voltage sensitive sodium channels
- Increases GABA
- Metabolized by the liver

Valproate : Side effects and monitoring

- Weight gain
- Sedation
- Alopecia
- Hyperinsulinemia
- Teratogenic – neural tube defects
- Check platelet count and LFTs prior to initiation
- Monitor for pancreatitis and hepatotoxicity

Lamotrigine

- Works on voltage sensitive sodium channels
- Decreases Glutamate and Aspartate
- Maintenance treatment of bipolar disorder and bipolar depression

Lamotrigine Side effects

- Binds to melanin containing tissues – encourage regular ophthalmic checks
- Benign rash in 10%, watch out for Stevens-Johnson Syndrome
- Low risk of wt gain or sedation
- OCPs will decrease plasma level of Lamotrigine
- Actually one of the safest mood stabilizers in pregnancy.

Case 3

- 35 y/o CM with hx of schizoaffective disorder comes in for his preventative care visit. He is currently on Zyprexa (Olanzapine) 20 mg daily in addition to Synthroid, Prevacid and Lisinopril. His weight is up 20lbs in the past year and his total cholesterol is now 220.

Antipsychotics

- Primary mechanism of action is the blockade of Dopamine 2 receptor (D2)
- Except Abilify (Aripiprazole) and Rexulti (Brexpiprazole) which are also D2 partial agonists
- Vraylar (Cariprazine) is a D3 preferring D3/D2 partial agonist
- 2nd generation agents (atypical antipsychotics) also bind to serotonin 5HT2 receptors
- For patients with CYP 2D6 genetic variants do not use Aripiprazole, Brexpiprazole, Fanapt (Iloperidone) or Clozaril

Side effects

- Metabolic Syndrome: Highest risk with Clozaril and Zyprexa. Lowest risk with Geodon, Abilify and Latuda
- Anticholinergic effects (dry mouth, constipation): Clozaril, Seroquel and Zyprexa
- Qt prolongation: Highest risk with Geodon and Fanapt. Lowest risk with Latuda, Abilify, Rexulti, Vraylar

Side Effects Cont.

- Clozaril: Associated with myocarditis and cardiomyopathy.
  - Typically occurs in the first few weeks to month of treatment. Thought to be a hypersensitivity reaction
- Changes in HR and BP (orthostatic hypotension and tachycardia): highest association with Clozaril, Fanapt, Seroquel and Invega
- Increased Prolactin level: Risperdal, Invega
  - Can lead to gynecomastia and lactation
- Sedation with all antipsychotics

Side effects/Management

- Increased risk of sudden death in dementia patients with psychosis
- Agranulocytosis: Clozaril. Monitor ANC weekly for 6 months, biweekly for 6 months then monthly
- Manage EPS, Dystonia or Parkinsonism with Cogentin 1-2 mg daily in divided doses

Monitoring

Monitoring for metabolic side effects of antipsychotic drugs

	Baseline	4 weeks	8 weeks	12 weeks	Quarterly	Annually	At least every 5 years
Personal or family history	X					X	
Weight (body mass index)	X	X	X	X	X		
Waist circumference	X			X		X	
Blood pressure	X			X		X	
Fasting plasma glucose	X			X		X	
Fasting lipid profile	X	*		X			X

* For patients taking olanzapine, quetiapine, clozapine.

Case 3 Management

- May add Topamax or Metformin to help with the weight gain from Zyprexa in addition to diet and exercise
- Add Statin for high cholesterol.
- If patient's symptoms of psychosis not well controlled on Zyprexa can switch to a more weight neutral agent like Latuda, Geodon or Abilify.

Thank You

References

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