



UW PACC

Psychiatry and Addictions Case Conference

UW Medicine | Psychiatry and Behavioral Sciences

**I HAVE TRIED 3 DIFFERENT
ANTIDEPRESSANTS. SHOULD I TRY
LITHIUM, THYROID HORMONE, OR
ANTIPSYCHOTICS NEXT?**

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SPEAKER DISCLOSURES

- ✓ Any conflicts of interest-none

OBJECTIVES

1. Learn when to consider when choosing augmenting medications for depression
2. Develop competence around choosing an augmenting medication for depression
3. Improve skills in prescribing augmenting medications for depression

Q: OF THE FOLLOWING, WHAT IS YOUR FAVORITE MEDICATION FOR AUGMENTING ANTIDEPRESSANTS IN TREATMENT RESISTANT DEPRESSION?

- Bupropion
- Mirtazapine
- Lithium
- Thyroid hormone
- Antipsychotics

CASE

56yo F with MDD recurrent severe, non-psychotic. She has been in therapy for the past 4 months on a weekly basis with little improvement. In addition to her low mood she experiences poor sleep and poor energy. She is hopeless and has been having passive SI occasionally but not today.

Her medication regimen to this point has included-Escitalopram, then Venlafaxine, and now Fluoxetine. Bupropion had been tried but she could not tolerate it.

- PHQ9: 16/27 ← 20/27 (4 weeks earlier)
- PMH: HTN, Migraines
- NKDA
- Meds: Fluoxetine 80mg qday, HCTZ, Amlodipine, Sumatriptan prn

ANYTHING ELSE YOU WOULD LIKE TO KNOW?

- Adherence
- Adequate trials: 6 weeks or more?
- Substance use history?
- Medical comorbidity → sleep apnea, hypothyroid, low Vit D
- Correct diagnosis?
- What is going on in therapy?

WHEN WOULD YOU CONSIDER AUGMENTING TREATMENT FOR AN ANTIDEPRESSANT?

Most depression remits

– Use the PHQ9 to help determine this, look for scores < 5

- Adequate trials but no remission of symptoms
- Partial response or minimal response
- If psychotic depression → antipsychotic

CASE: TREATMENT REFRACTORY DEPRESSION (PHQ9 15 ON 3RD ANTIDEPRESSANT TRIAL)

Question: What would you consider augmenting her treatment with next?

1. Lithium
2. Thyroid Hormone
3. Antipsychotics
4. Something else

THE LITHIUM OPTION

- Lots of evidence to support use → NNT=5
- May reduce the risk of completed suicide
- Dosing-start 300mg bid or 300mg qhs
 - Serum trough level 0.5mEq/L-1.0mEq/L
 - Narrow therapeutic window-starts at 1.5mEq
 - Dosing all at night can reduce side effects
- Monitoring: Li level, Cr, TSH, ECG, Ca, CBC
- Response in 1-6 weeks
- Side Effects: n/d, fine tremor, polyuria/polydipsia, memory problems, wt gain, hypothyroidism, acne, worsening psoriasis, DI, cardiac dysrhythmia

THE LITHIUM OPTION

- Interactions:
 - Increase Li: **No ACE in the Hole** (NSAIDs, ACE inhibitors, HCTZ), fluid loss, low Na diet
 - Decrease Li: caffeine
- Duration: 1 year if responds
 - Rapid discontinuation increases the risk of relapse and possibly suicide → taper slowly over 3 months if it is to be discontinued after long-term maintenance
- Contraindications: renal impairment, hyponatremia, dehydration, significant CV disease
- Other Pearls?

THE THYROID (LIOTHYRONINE) OPTION

- Evidence is overall supportive but a little mixed
- Better tolerated than Lithium and Antipsychotics
- May help with
 - lethargy and fatigue
 - Stabilizing fluctuating mood
- Predictors of response: subclinical hypothyroidism?
 - Useful in euthyroid patients
- Dosing-T3 Start at 25mcg qday. (12.5mcg in elderly)
 - Titrate to 50mcg if needed after 1-2 weeks.
- Response: within days, full-in 4-6 weeks
- Monitoring: baseline TSH, 1mo and Q6
 - Reduce dose if TSH < lower limit of normal

THE THYROID (LIOTHYRONINE) OPTION

- Side Effects: well tolerated
 - **Think-hyperthyroidism**: tremor, palpitations, heat intolerance, sweating, inc bowel movements, arrhythmias
- Interactions: cholestamine binds T3 in gut
- Duration: 1 year if working
 - No taper needed
- Contraindications: adrenal insufficiency, unstable angina, recent MI, caution in elderly and DM (increase in insulin requirements?)
- Other Pearls?

THE 2ND GEN ANTIPSYCHOTIC OPTION

- Strong evidence for efficacy
 - May work better as treatment resistance increases
 - Aripiprazole, Brexiprazole, Cariprazole, Olanzapine, Quetiapine, Risperidone, Ziprasidone
 - Quetiapine vs Li → no difference in effects or discontinuation
- May help with
 - Aripiprazole: low energy
 - Quetiapine: sleep, anxiety
 - Olanzapine: anorexia and wt loss
- Dosing
 - Aripiprazole: start 2mg, max dose 15mg, titrate gradually to avoid agitation
 - Quetiapine: start 25-50mg, max dose 300mg
 - Risperidone: start 0.25mg, max dose 3mg
- Response: 2 weeks, if no reduction in symptoms by 25% (PHQ9 score) by 4 weeks, further treatment not likely helpful

THE ANTIPSYCHOTIC OPTION

Side Effects	Aripiprazole	Quetiapine	Risperidone
Wt gain/DM	+	+++	+++
Hypercholesterolemia	-	+++	+
EPS/TD	+	-/+	+++
Prolactin Elevation	-	-/+	+++
Sedation	+	++	+
Anticholinergic SE	-	++	+
Orthostatic	-	+	+
QTc prolongation	-/+	+	+

Other Notable Side Effects

- Aripiprazole: akathisia (dose dependent)
- Quetiapine: sedation, dry mouth, dizziness, hepatotoxicity (rare)
- Risperidone: dry mouth, EPS, hyperprolactinemia

THE ANTIPSYCHOTIC OPTION

- Monitoring: weight, waist circumference, blood pressure, fasting plasma glucose, fasting lipid profile, CBC (for baseline WBC), EKG (to assess QTc) and AIMS test.
- Interactions:
 - Aripiprazole: met by CYP3A4 and 2D6
 - Quetiapine: met by CYP3A4
 - Risperidone: met by CYP 2D6
- Duration: mixed evidence
 - Consider taper after response to 3-6 months to reduce exposure to side effects
- Cautions: may antagonize levodopa, increase effects of BP meds, Risperidone-may increase risk of stroke in elderly with afib
- Other Pearls?

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