RESISTANT DEPRESSION AND CHALLENGING CASES: What To Do When The Medicines Aren’t Working

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• No financial disclosures

• Will discuss off-label use of medications
OBJECTIVES

• Define, diagnosis, and strategize for Treatment-Resistant Depression (TRD)

• Describe the clinical course of depression with a focus on resistant and challenging cases

• Formulate a patient-centered and evidence-based treatment plan

• Focus on issues of particular importance to the PCP such as prevention, therapeutic lifestyle changes and health maintenance

• Q & A
MAJOR DEPRESSIVE EPISODE

- **S** - SLEEP (more or less)
- **I** - INTERESTS (less)
- **G** – GUILT/WORRY (more)
- **E** – ENERGY (low)
- **C** – CONCENTRATION/MEMORY (low)
- **A** – APPETITE (up or down)
- **P** – PSYCHOMOTOR (agitation or retardation)
- **S** – SEX (low)
- **S** – SUICIDAL THOUGHTS
- **OTHERS** – hopelessness, helplessness, worthlessness, irritability, crying, pessimism, cynicism
Statistics of Major Depressive Disorder

- 20% prevalence in women; 12% in men
- 15-20% mortality by suicide; >42k in 2014
  - 2nd leading cause – ages 10yo-34yo
  - 4th leading cause – ages 35yo-54yo
  - 10th leading cause – all ages

- Highest rate= men >75yo
- White men complete 78% of suicides
- Men use firearms; Women use poisoning/OD

CDC. 2014.
Phases of Major Depressive Disorder

Figure 1. Treatment Phases of Major Depression

Treatment phase begins at identification of MDD episode, continues to full remission, and followed by long-term maintenance.

TREATMENT RESISTANT DEPRESSION: What is it?

• No standard definition
• In general: “inadequate response to adequate antidepressant therapy”
• Adequate??????
WHY IS DEPRESSION HARD TO TREAT?

• A disease with varying stages of severity
• Antidepressant are “blunt instruments”
• High placebo rates in studies
• No cure, only treatment
• Non-compliance with medicine
Non-compliance with treatment

• Study - PCP’s prescribing, over 6 months

– FINDINGS:
  • At 6 months, only 19% taking the meds
  • 9% never filled the 1st prescription
  • 50% did not take med as directed
  • 89% of those who stopped meds never consulted the physician who prescribed the med
Results from STAR*D

• What was STAR*D trial?
Results from STAR*D

- What was STAR*D trial?

- After 4 steps, roughly 66% effective
- If keep going, can achieve ~90%
  - Long-time fact: 10% never get better
- After full remission, 68% relapse
Results from STAR*D

Figure 1. STAR*D: Treatment Step Remissions

% Remitted after:
- Step 1
- Step 2
- Step 3
- Step 4
- Still depressed

33
37
19
6
5

After 4 therapies in a controlled clinical trial environment, one-third of patients failed to achieve remission.

Why a relapse?

• **R** – rhythm disturbances
• **E** – ending treatment
• **L** – life change
• **A** – additional meds
• **P** – physical health changes
• **S** – substance abuse/withdrawal
• **E** – end of med response

ARE WE MISSING SOMETHING ELSE?

• Co-Morbidities:
  – BIPOLAR – type 1 or 2
  – OCD - Obsessive Compulsive Disorder
  – PTSD - Post Traumatic Stress Disorder
  – GAD - Generalized Anxiety Disorder
  – PANIC DISORDER
  – DYSTHYMIA
  – MEDICAL CONDITIONS
Anything else...before we treat the TRD?

• RATING SCALES
  – PHQ9 – Patient Health Questionnaire
  – BDI – Beck Depression Inventory
  – QIDS – Quick Inventory of Depressive Symptomatology

Anything else...before we treat the TRD?

• RATING SCALES
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• GENE TESTING – useful or not?
  – It depends…
TREATMENT

BUT FIRST, DO **THE BASICS**: 
TREATMENT

BUT FIRST, DO **THE BASICS**:

SLEEP
TREATMENT

BUT FIRST, DO **THE BASICS:**

SLEEP

NUTRITION
TREATMENT

BUT FIRST, DO **THE BASICS**:

SLEEP

NUTRITION

EXERCISE
TREATMENT

BUT FIRST, DO **THE BASICS**:

SLEEP
NUTRITION
EXERCISE

PSYCHOTHERAPY !!!!!
TREATMENT

Psychotherapy (CBT) alone: 52% improvement

Medication alone: 55% improvement

Psychotherapy + Medication: 85% improvement

Case study

47yo WF, married, 2 kids, employed as office administration assistant. Depression on and off for 15 years.

Meets criteria for MDD (major depression-severe- recurrent type)

Never seen psychiatry before
Case study

“Nothing works.” “The meds stop working.”

Can’t remember doses or lengths of time on meds. Tells me she has tried Zoloft, Lexapro, Paxil, Cymbalta, Wellbutrin, Abilify, Klonopin, and Xanax.

“Help me.”
Case study

• Substance use discontinuation
• Sleep, Nutrition, Exercise, Psychotherapy
• Get labs IF there is a reason
• Gene testing – NO!
• Start from scratch…and pick ANY anti-depressant medicine

• “Give me 90 days to begin to make a difference.”
Case study

• Prozac 20mg to 40mg to 60mg
  – Side effects but some benefits
Day 60
Case study

- Prozac 20mg to 40mg to 60mg
  - Side effects but some benefits

- Augment – Wellbutrin XL 150mg to 300mg
Case study

• Check labs – TSH
  CBC
  CMP

• Get Physical
Case study

• Prozac 20mg to 40mg to 60mg
  – Side effects but some benefits

• Augment – Wellbutrin XL 150mg to 300mg
  – No added effect
Day 90
Case study

• Time to discuss other options:
  – Atypicals
  – Lithium
  – Cytomel
  – TCA’s (tricyclics)
Case study

• Time to discuss other options:
  – Atypicals
  – Lithium
  – Cytomel
  – TCA’s (tricyclics)

• **WE** picked Abilify – 2-5mg in morning
Case study

• “MAYBE” per patient
  – Increase Abilify to 10mg per day
Case study

• “MAYBE” per patient
  – Increase Abilify to 10mg per day
  – So I leave it going…for now.

• Add lithium
Case study

• Better…so she is now on:
  – Prozac 60mg in morning
  – Abilify 10mg in morning
  – Lithium 600mg at night
Day 135
Case study

• Better…so she is now on:
  – Prozac 60mg in morning
  – Abilify 10mg in morning
  – Lithium 600mg at night

• 3 months later – “I’m getting worse.”
  – Increase lithium – now up to 1200mg at night with level of 0.9
Case study

• Not better

• NEW TALK:
Day 225
Case study

• Not better

• NEW TALK:

ECT

vs

Switch in Meds (i.e. start from scratch)
Case study

WE are now at Day 839
TREATMENT

• SWITCH to another medication

• AUGMENT by adding another medication
TREATMENT

• SWITCH to another medication
  – Which one?
TREATMENT

• SWITCH to another medication
  – Which one?
  – It actually does not matter:

  – STAR*D showed ~equal improvement with:
    • Another SSRI – 26.6%
    • SNRI – 25%
    • Wellbutrin – 25.5%
TREATMENT

Figure 2. STAR*D: Level 2 Remission Results

The practitioner should decide between using adjunctive treatment or switching therapy when 2 treatments have not produced a remission.  
TREATMENT

- SWITCH to another medication

- AUGMENT by adding another medication
TREATMENT

- AUGMENTATION (lots of options)
  - Wellbutrin (bupropion)
  - Remeron (mirtazapine)
  - Effexor (venlafaxine)
  - Buspar (buspirone)
  - Tricyclics: nortriptyline, desipramine, clomipramine
  - Lithium
  - Cytomel (thyroid supplement)
  - Provigil/Nuvigil (modafanil/armodafanil)
TREATMENT

- AUGMENTATION (lots of options)
  - Atypical Antipsychotics
    - New ones: Latuda (lurasidone)
      Rexulti (brexpiprazole)
      Vraylar (cariprazine)
    - Old ones: Abilify (aripiprazole)
      Geodon (ziprasidone)
      Seroquel (quetiapine)
      Zyprexa (olanzapine)
TREATMENT

- AUGMENTATION (lots of options)
  - Deplin (L-methylfolate)
  - Creatine
  - SAMe
  - St Johns Wort
  - Ketamine
OTHER TREATMENT OPTIONS:
- ECT – electroconvulsive therapy
- TMS – trans-magnetic stimulation
- Ketamine
THE “I’ve got 5 minutes” PLAN
THE “I’ve got 5 minutes” PLAN

• Patient as part of the decision - build a TEAM
  – What are the goals of patient vs provider
  – Patient preferences for medications

• Realistic expectations of treatment
THE “I’ve got 5 minutes” PLAN

SSRI
THE “I’ve got 5 minutes” PLAN

SSRI ➔ Push the dose higher
THE “I’ve got 5 minutes” PLAN

SSRI → Push the dose higher → Keep pushing
THE “I’ve got 5 minutes” PLAN

SSRI → Push the dose higher → Keep pushing
Switch
Augment
THE “I’ve got 5 minutes” PLAN

SSRI → Push the dose higher → Keep pushing

Pick something → Switch

Augment
THE “I’ve got 5 minutes” PLAN

SSRI → Push the dose higher → Keep pushing

   ↑                        ↓

Pick something          Switch

   ↓                        ↓

Augment
THE “I’ve got 5 minutes” PLAN

SSRI ➔ Push the dose higher ➔ Keep pushing

Pick something

Switch

Wellbutrin or Buspar ➔ Augment
THE “I’ve got 5 minutes” PLAN

SSRI $\rightarrow$ Push the dose higher $\rightarrow$ Keep pushing

$\downarrow$

Pick something $\leftarrow$ Switch

$\downarrow$

Wellbutrin or Buspar $\leftarrow$ Augment

$\downarrow$

Atypicalss
THE “I’ve got 5 minutes” PLAN

SSRI → Push the dose higher → Keep pushing

Pick something

Switch

Wellbutrin or Buspar → Augment

Atypicals, Lithium, Cytomel, TCA’s
THE “I’ve got 5 minutes” PLAN

SSRI → Push the dose higher → Keep pushing

Pick something → Switch

Wellbutrin or Buspar → Augment

Atypicals, Lithium, Cytomel, TCA’s
THE “I’ve got 5 minutes” PLAN: Dosages of medications

<table>
<thead>
<tr>
<th>Medication</th>
<th>Dosage</th>
</tr>
</thead>
<tbody>
<tr>
<td>Zoloft</td>
<td>50-200mg</td>
</tr>
<tr>
<td>Prozac</td>
<td>20-80mg</td>
</tr>
<tr>
<td>Celexa *</td>
<td>20-40mg</td>
</tr>
<tr>
<td>Lexapro</td>
<td>10-40mg</td>
</tr>
<tr>
<td>Paxil</td>
<td>20-80mg</td>
</tr>
<tr>
<td>Effexor XR</td>
<td>150-300mg</td>
</tr>
<tr>
<td>Cymbalta</td>
<td>60-120mg</td>
</tr>
<tr>
<td>Remeron</td>
<td>30-60mg</td>
</tr>
<tr>
<td>Provigil</td>
<td>100-200mg</td>
</tr>
<tr>
<td>Nuvigil</td>
<td>50-250mg</td>
</tr>
<tr>
<td>Brintellix</td>
<td>10-40mg</td>
</tr>
<tr>
<td>Viibryd</td>
<td>10-40mg</td>
</tr>
<tr>
<td>Wellbutrin XL</td>
<td>150-300mg</td>
</tr>
<tr>
<td>Buspar bid</td>
<td>30mg bid</td>
</tr>
<tr>
<td>Lithium</td>
<td>300-900mg</td>
</tr>
<tr>
<td>Cytomel</td>
<td>25-75mcg</td>
</tr>
<tr>
<td>Latuda</td>
<td>20-40mg</td>
</tr>
<tr>
<td>Rexulti</td>
<td>1-2mg</td>
</tr>
<tr>
<td>Seroquel</td>
<td>50-300mg</td>
</tr>
<tr>
<td>Abilify</td>
<td>2-5mg</td>
</tr>
<tr>
<td>Geodon</td>
<td>20-60mg</td>
</tr>
<tr>
<td>Zyprexa</td>
<td>2.5-5mg</td>
</tr>
<tr>
<td>Fetzima</td>
<td>20-120mg</td>
</tr>
</tbody>
</table>

*FDA warning to not exceed 40mg/day
THE “I’ve got 5 minutes” PLAN

• Take home message:
THE “I’ve got 5 minutes” PLAN

• Take home message:

KEEP TRYING
THE “I’ve got 5 minutes” PLAN

• Take home message:
  
  KEEP TRYING

  OR

  REFER TO PSYCHIATRY
  (if you can find one)
QUESTIONS

UMG-PSYCHIATRY
864-522-5550

3 locations:
10 Patewood Dr (Patewood campus)
701 Grove Rd (main campus)
1409 W. Georgia Rd (Simpsonville)