Treatment Resistant Depression: Challenges in Care for Hispanic Americans

Event Type
Home Study Webcast

freeCE Expiration Date
10/31/2013

ACPE Expiration Date
3/28/2016

Credits
1 Contact Hour

Target Audience
Nurses, Pharmacists, Pharmacy Technicians

Program Overview
Major depressive disorder is a severe and pervasive condition that requires a complex and strategic balance of approaches for treatment. While this condition is present in a variety of populations, some are particularly hard hit. As of 2012, Hispanics are now the largest minority group in the United States, constituting over 16% of the population. The American Psychiatric Association has found that older Hispanic adults and younger Hispanic youth are especially vulnerable to MDD due to the pressures of acculturation after immigration. In order to prevent Hispanics from suffering silently with MDD or TRD, we must focus adequate attention on overcoming barriers specific to their population.

Nurse Educational Objectives
• Review the etiology and prevalence of major depressive disorder (MDD) and treatment resistant depression (TRD) within the Hispanic community
• Outline treatment strategies for MDD patients who do not respond to first-line therapies (monotherapy vs augmentation)
• Evaluate current pharmacological treatment of TRD, including efficacy, safety, and tolerability profiles
• Update medical professionals on newer models of care and management of depression, including an awareness of common barriers that exist between the medical community and Hispanic patients
Pharmacist Educational Objectives

- Review the etiology and prevalence of major depressive disorder (MDD) and treatment resistant depression (TRD) within the Hispanic community
- Outline treatment strategies for MDD patients who do not respond to first-line therapies (monotherapy vs augmentation)
- Evaluate current pharmacological treatment of TRD, including efficacy, safety, and tolerability profiles
- Update medical professionals on newer models of care and management of depression, including an awareness of common barriers that exist between the medical community and Hispanic patients

Pharmacy Technician Educational Objectives

- List medications that are used to treat major depressive disorder (MDD)
- List common barriers that exist between the medical community and Hispanic patients

Activity Type

Knowledge

Accreditation

Nurse N-817
Pharmacist 0798-0000-13-127-H01-P
Pharmacy Technician 0798-0000-13-127-H01-T

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Faculty

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University of Maryland School of Pharmacy
Financial Support Received From
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LEARNING OBJECTIVES

• Review the etiology and prevalence of major depressive disorder (MDD) and treatment resistant depression (TRD) within the Hispanic community

• Update medical professionals on newer models of care and management of depression, including an awareness of common barriers that exist between the medical community and Hispanic patients, with an emphasis on increasing patient knowledge in order to increase patient participation in self-management.

CASE 1

• CC: “I am very sad today”

• HPI: CS is a 28yo Hispanic female who complains of sadness which has persisted for at least 6 weeks. She has had a poor appetite (resulting in a 10lb weight loss), difficulty sleeping (<5 hrs/night), daytime fatigue, and difficulty concentrating. (+) SI-no plan.

• PMH: None.

CASE 1 CONTINUED

• PSH: Has felt sad on and off for the last year. Never sought treatment.

• Medications: None. NKDA.

• Laboratory: WNL.

• SH: Feels unnecessarily guilty about the fact that she has been away from her country for years. She feels isolated and sad. Works as a receptionist but has received warnings about possible dismissal due to excessive absences. Denies alcohol and drug use.

• Clinical Impression: Major Depressive Episode
US Census 2010

- Population: 308.7 million
  - Non-Hispanic Whites: 74.5%
  - Hispanics: 16%
  - Blacks: 13.6%
  - Asian/Pacific Islander: 5.6%
  - American Indian/Alaska Native: 1.7%
- Hispanic population increased 15.2% from 2000 to 2010
- Foreign-born are 10% of the population
- As of July 2002, Hispanics surpass non-Hispanic blacks to become the largest minority group
- 55.4 million speaks a language other than English at home

Prevalence of Depression in Hispanic Americans

- Difficult to determine for resistant depression
- Data from CDC estimates that 9.1% of the US population (adults) data is from 2006-2008

Etiology of Depression in Hispanics

- Isolation
- Unemployment
- Lack of health insurance
- Legal Status
- Health Literacy

Cultural Considerations for the Diagnosis and Treatment of Depression

- Symptoms may not be specific (Cultural idioms of distress)
- Use of validated scales for diagnosis and treatment may be an issue
- Language and Cultural barriers
- Stigma of mental health

Cultural Issues in Depression Barriers to Care

- Religious beliefs
- Healing practices
- Use of home remedies and folk medicines
- Acceptance of diagnosis and prognosis
- Role of the family in treatment and healing
- Faith in western medicine
Treatment Resistant Depression Challenges in Care For Hispanic Americans

CULTURAL ASSESSMENT

**DIAGNOSIS - MEANING AND BEHAVIOR**

- Does the patient understand the diagnosis?
- How does the patient interpret the illness?
- How can she/he adapt to the illness?
- How does he/she think others view /feel about illness?
- What motivates the patient to recover?

**TREATMENT**

- Assess patient’s feelings and beliefs about the treatment
- Assess the role of the family in the treatment
- Assess the effect of the treatment in patients religious and/or cultural beliefs

Cultural Assessment

**RESOURCES**

http://www.hispanichealth.org/programs/depression.aspx

**POINTS TO REMEMBER**

- A tendency for greater somatization has been observed among Hispanics with depression. However, the level of recognition of somatic symptoms by their psychiatrists is low.
- Failure to detect somatic symptoms in depressed patients may have significant implications in the cost and outcome to treatment of treatment

**PROBLEM IDENTIFICATION**

- What symptoms does CS have which are consistent with major depressive disorder?

**DSM-IV-TR CRITERIA FOR MDD**

- Depressed mood or loss of interest/pleasure for ≥ 2 week period
- ≥ 4: weight change, appetite change, sleep disturbance, psychomotor agitation or retardation, ↓ energy, excessive guilt, difficulty concentrating, suicidal ideation
- Affects ability to function normally
- Not caused by medical illness or by an endogenous substance
- Hispanic patients more likely to present with somatic symptoms not depressed mood.
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**TREATMENT OPTIONS**

- Nonpharmacologic
  - Hispanic population may be more likely to want counseling
- Pharmacologic
  - Antidepressants (AD)

**ANTIDEPRESSANT MOA**

- Shitij Kapur, MD, PhD (presentation)

**SELECTIVE SEROTONIN REUPTAKE INHIBITORS (SSRIS)**

<table>
<thead>
<tr>
<th>Brand Name</th>
<th>Generic Name</th>
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<tbody>
<tr>
<td>Prozac®</td>
<td>Fluoxetine</td>
</tr>
<tr>
<td>Zoloft®</td>
<td>Sertraline</td>
</tr>
<tr>
<td>Luvox®</td>
<td>Fluvoxamine</td>
</tr>
<tr>
<td>Paxil® / Paxil CR®</td>
<td>Paroxetine</td>
</tr>
<tr>
<td>Celexa®</td>
<td>Citalopram</td>
</tr>
<tr>
<td>Lexapro®</td>
<td>Escitalopram</td>
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↑ SHT through selective serotonin reuptake inhibition

**SEROTONIN AND NOREPINEPHRINE REUPTAKE INHIBITORS (SNRIS)**

<table>
<thead>
<tr>
<th>Brand Name</th>
<th>Generic Name</th>
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</thead>
<tbody>
<tr>
<td>Effexor®</td>
<td>Venlafaxine</td>
</tr>
<tr>
<td>Pristiq®</td>
<td>Desvenlafaxine</td>
</tr>
<tr>
<td>Cymbalta®</td>
<td>Duloxetine</td>
</tr>
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- ↑ both SHT and NE
- Pharmacologic Advantages:
  - 3 drugs in one: low dose (SSRI), medium dose (add NRI), high dose (add DRI)
  - treatment resistance

**TRICYCLIC ANTIDEPRESSANTS (TCAS)**

<table>
<thead>
<tr>
<th>Brand Name</th>
<th>Generic Name</th>
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</thead>
<tbody>
<tr>
<td>Elavil®</td>
<td>Amitriptyline</td>
</tr>
<tr>
<td>Pamelor®</td>
<td>Nortriptyline</td>
</tr>
<tr>
<td>Tofranil®</td>
<td>Imipramine</td>
</tr>
<tr>
<td>Norpramin®</td>
<td>Desipramine</td>
</tr>
<tr>
<td>Anafranil®</td>
<td>Clomipramine</td>
</tr>
<tr>
<td>Silenor®</td>
<td>Doxepin</td>
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- Primarily ↑ NE through inhibition of reuptake at presynaptic neuronal membrane, to a lesser extent SHT
- TCAs differ mechanistically within class

**MONOAMINE OXIDASE INHIBITORS**

<table>
<thead>
<tr>
<th>Brand Name</th>
<th>Generic Name</th>
</tr>
</thead>
<tbody>
<tr>
<td>Eldepryl®</td>
<td>Selegeline</td>
</tr>
<tr>
<td>Nardil®</td>
<td>Phenelzine</td>
</tr>
<tr>
<td>Parnate®</td>
<td>Tranylcypromine</td>
</tr>
</tbody>
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- Inhibit monoamine oxidase, which is the enzyme that breaks down SHT, NE, DA
Miscellaneous AD MOA

<table>
<thead>
<tr>
<th>Brand Name</th>
<th>Generic Name</th>
<th>MOA</th>
</tr>
</thead>
<tbody>
<tr>
<td>Wellbutrin®</td>
<td>Bupropion</td>
<td>NE/DA reuptake inhibitor</td>
</tr>
<tr>
<td>Desyrel®</td>
<td>Trazodone</td>
<td>5HT2 antagonist, weak 5HT/NE reuptake inhibitor</td>
</tr>
<tr>
<td>Remeron®</td>
<td>Mirtazapine</td>
<td>↑ 5HT/NE due to alpha-2 antagonism, 5HT2/5HT3 antagonist</td>
</tr>
<tr>
<td>Viibryd®</td>
<td>Vilazodone</td>
<td>Inhibits presynaptic serotonin reuptake, partial 5HT1a agonist</td>
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Case 1 continued

- After seeing her MD, CS comes into your pharmacy with a RX for sertraline 50mg qam to treat her major depressive episode. She would like to know:
  - “How long is this going to take to work?”
    - Week 1: ↓ anxiety, improvement in sleep and appetite
    - Week 2-3: ↑ energy and libido. May be at higher risk for suicide
    - Week 4: improvement in mood
  - “How long am I going to have to take this?”
    - 1 MDD episode: 6-12 months
    - ≥ 2 MDD episodes: 18 months-5 years

Treatment Pearls for Antidepressants

- For the most part, AD are equally efficacious. Choose based on agent and patient-related variables
- 1-2 weeks for some effect and 4-8 weeks for full effect
- AD should be administered daily (not as needed)
- AD should be continued even after depression resolves to prevent recurrences

AD Issues in Hispanic Population

- Efficacy: limited literature comparing efficacy of AD in Hispanic population vs. others
- Side effects: > sensitivity to side effects
- Drug metabolism: ethnic differences in cytochrome P450 system
- Adherence: ↑ early nonadherence. PRN vs. daily

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Case 2

- **CC:** “I’m having problems with my nerves. This medication is not working.”

- **HPI:** JL is a 42yo Hispanic male with a 15 year h/o major depressive disorder. He has had at least 5 depressive episodes. He has been tried on fluoxetine and bupropion previously. He is currently taking Citalopram 10mg AM. He has noted no improvement with his current regimen.

- Would this patient meet the criteria for treatment resistant depression?

Assessment Issues

- Pseudoresistance: occurs when pt has not been tried on adequate dose or duration (4-8wks) of AD
  - Adherence
  - Adverse effects
- Assess for medical or psychiatric comorbidities (thyroid, substance abuse, anemia)
- Review for medications associated with depression (benzodiazepines, interferon)
- May require psychiatrist evaluation
  - Hispanic patient may be reluctant due to stigma associated with mental illness
  - Lack of insurance or coverage

What Is Treatment Resistant Depression (TRD)?

- No consistent definition
- Most accepted definition of TRD is failure to reach remission after 2 adequate AD trials from different classes
- Limited literature. Not specific for Hispanic population
- Does JL meet criteria for TRD?
  - Not enough information
  - 2 drugs different classes but unclear if failed AD trials

Pharmacologic Alternatives for TRD

- Augmentation
- Switching Antidepressants
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**Sequenced Treatment Alternatives to Relieve Depression Study**

- AKA STAR*D
- Landmark trial for TRD
- 1st RCT to investigate efficacy of switching and augmenting
- Real world management

**STAR*D Trial Design**

- Level 1 - citalopram monotherapy
- Level 2
  - Switch: bupropion SR, venlafaxine XR, sertraline, or CBT
  - Augmentation: citalopram+bupropion SR,
    citalopram+buspirone, citalopram+CBT
- Level 3
  - Switch: nortriptyline or mirtazapine
  - Augmentation: current antidepressant+lithium or T3
- Level 4
  - Switch: tranylcypromine, or venlafaxine XR+mirtazapine

**STAR*D Results**

- 1/3 reached remission during the initial phase of the study. An additional 10-15% had partial response
- 1/2 became symptom-free after the first 2 treatment levels
- Remission is harder to achieve with each failed AD trial
- Over all 4 levels, ~70% of those who did not withdraw became symptom-free
- Demonstrates different people respond to different treatment strategies but does not determine what works best

**Augmentation Pearls**

- Good alternative for partial response after adequate dose and trial of AD. Do not lose benefit of current AD*
- Options
  - 2nd AD (other than MAOI) w/ alternative MOA
  - Alternative agents good support: thyroid supplementation, lithium, second generation antipsychotic (SGA)
  - Alternative agents less support: lamotrigine, omega-3 fatty acids, folate, stimulants


**Augmentation Pearls**

- SGA
  - Olanzapine (Zyprexa*), risperidone (Risperdal*), quetiapine (Seroquel*), aripiprazole (Abilify*)
  - ↑ 5HT action which enhances AD effects
  - ↓ dose compared with psychosis
  - Possibly faster improvement than with AD monotherapy
  - ↓ dropout rate due to side effects (wt gain, metabolic, EPS)
  - Associated with hyperglycemia and diabetes mellitus (DM).
  - FDA indication as adjunct for depression: quetiapine XR, aripiprazole, olanzapine+fluoxetine
Treatment Resistant Depression Challenges in Care For Hispanic Americans

**AUGMENTATION PEARSLS**

- Lithium (Lithobid®)
  - Lithium ↑ serotonergic function and enhances AD
  - 600-900mg/d
  - Lithium level ≥0.6 mEq/L. Do not exceed 1.2 mEq/L
- Thyroid supplementation-beneficial even if euthyroid
  - MOA
    - Treatment of subclinical hypothyroidism
    - Augmentation of beta-adrenergic system in euthyroid patients
  - T3 (Liothyronine -Cytomel®) most studied
  - 25-50 mcg/d
  - STAR*D suggests T3 better tolerated than Li

**SWITCHING PEARSLS**

- Good alternative for nonresponders. Option for partial responders*
- Advantages: ↓ cost and side effects
- Fail 1 AD: SSRI, SNRI, bupropion, or mirtazapine
  - Usually switch to another class
  - SSRI nonresponders may still respond to a trial of alternative SSRI
- Fail ≥2 AD: TCA, MAOI (must have a washout period of 4-5 drug half lives. ≥5 wks with fluoxetine.)

**CASE 3**

- HPI: TM is a 32yo Hispanic female with a 6 year h/o major depressive disorder. She has been tried on numerous antidepressants including fluoxetine, citalopram, and mirtazapine. Her venlafaxine XR was titrated up to 225mg qam and has been maintained at this dose for 6 weeks. She notes some improvement with this regimen but continues to complain of difficulty sleeping and lack of energy. She has gained 15 lbs and is prediabetic.
- As the consulting pharmacist, JL’s MD contacts you regarding her antidepressant therapy. What antidepressant regimen modification would you recommend?

**CASE 3 DECISION POINTS**

- Augmentation-partial responder
  - Liothyronine/T3
  - Aripiprazole (Abilify®)
  - Bupropion (Wellbutrin SR®) (antidepressant with alternative MOA)
    - On SNRI
    - Tried SSRI, mirtazapine (Remeron®)

**CASE 3 DECISION POINTS**

- What about the alternatives?
  - Pt gained 15lbs. Options associated with weight gain:
    - Mirtazapine (Remeron®)
    - Lithium (Lithobid®)
    - Quetiapine (Seroquel®)
    - Risperidone (Risperdal®)
    - Olanzapine (Zyprexa®)
  - DM 5th leading cause of death in Hispanic population. Options associated with ↑ risk for DM:
    - SGA: quetiapine, risperidone, olanzapine

**CONCLUSION**

- Most accepted definition of TRD is failure to reach remission after 2 adequate AD trials
- Most AD affect 5HT, NE, and/or DA However, they vary in exact MOA
- TRD pharmacologic alternatives are augmentation or switching
- STAR*D demonstrated that patients’ responses to AD vary
- No clear data on prioritizing pharmacotherapy
QUESTIONS

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