Trauma and PTSD
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CPE Information and Disclosures
Janice Lee declare(s) no conflicts of interest, real or apparent, and no financial interests in any company, product, or service mentioned in this program, including grants, employment, gifts, stock holdings, and honoraria.

CPE Information
• Target Audience: Pharmacists & Technicians
• ACPE#: 0202-0000-15-216-L04-P/T
• Activity Type: Knowledge-based

Pharmacist Learning Objectives
• Compare and contrast the difference between post-traumatic stress disorder (PTSD) and a normal response to trauma
• State the symptoms of PTSD
• Describe the current clinical guidelines on the treatment of post-traumatic stress disorder or post-traumatic stress symptoms
• Discuss treatment strategies including medications and non-pharmacological interventions
• Explain how pharmacist and pharmacy technicians can be effective members of the treatment team

Pharmacy Technician Learning Objectives
• State the symptoms of PTSD
• Recall medication and counseling treatment options
• Explain how pharmacist and pharmacy technicians can be effective members of the treatment team

Self-Assessment Question 1
1. A patient is on a medication regimen consisting of paroxetine 60mg daily. He has previously tried sertraline and fluoxetine without adequate relief. States paroxetine has provided best relief in relieving his hypervigilance and flashbacks. He continues to experience sleep disturbance mainly due to frequent nightmares. Which therapeutic intervention would be the best approach in improving his sleep?
A. Initiate prazosin
B. Initiate valproate
C. Initiate low dose risperidone
D. Switch paroxetine to venlafaxine XR
Self-Assessment Question 2

2. The U.S. Food and Drug Administration approved which of the following drugs for treatment of post traumatic stress disorder (PTSD)?
   A. Venlafaxine
   B. Prazosin
   C. Sertraline
   D. Amitriptyline

Self-Assessment Question 3

3. The following are symptoms associated with Criterion E of DSM V Criteria for PTSD except:
   A. Hypervigilance
   B. Difficulty with concentration
   C. Flashbacks
   D. Reckless behavior

Background

• Lifetime prevalence of PTSD among adult Americans estimated to be 6.8%
• Prevalence of PTSD in Operation Enduring Freedom/Operation Iraqi Freedom in a study of 1,938 participants was 13.8%
• Women twice as likely to develop PTSD compared to men
• High rates of comorbid diagnoses (Alcohol/substance abuse, dysthymia, anxiety, etc.)

Pathophysiology

• Hippocampus: Memory
• Amygdala: Fear responses
• Medial prefrontal cortex: Modulation of emotional responses
• Two stress response systems
  – Hypothalamic-pituitary-adrenal (HPA)
  – Locus coeruleus-norepinephrine

Acute Stress Response - Public Speaking

Corticotropin-releasing factor (CRF)/Hypothalamic-pituitary-adrenal (HPA) axis

DSM-5 Criteria for PTSD

- Stressor (Criterion A)
  - Direct, witnessed, repeated or extreme indirect exposure
- Intrusion symptoms (Criterion B)
  - Recurrent memories, nightmares, flashbacks, intense distress after exposure to trauma-related stimuli
- Avoidance (Criterion C)
  - Persistent avoidance of trauma-related stimuli

DSM-5 Criteria for PTSD (cont.)

- Negative alterations in cognition and mood (Criterion D)
  - Dissociative amnesia
  - Persistent negative beliefs about oneself or world
  - Persistent distorted blame of self or others
  - Persistent negative trauma-related emotions
  - Diminished interest in activities
  - Feeling alienated from others
  - Constricted affect

DSM-5 Criteria for PTSD (cont.)

- Alterations in arousal and reactivity (Criterion E)
  - Irritable, aggressive behavior
  - Self-destructive, reckless behavior
  - Hypervigilance
  - Exaggerated startle response
  - Problems in concentration
  - Sleep disturbance

DSM-5 Criteria for PTSD (cont.)

- Duration (Criterion F): More than one month
- Functional significance (Criterion G)
- Exclusion (Criterion H): Not due to medication or other illness
- With dissociative symptoms: Depersonalization and derealization
- Delayed expression: Diagnosis not met until six months after trauma

Assessment Tools

- Post-Traumatic Stress Disorder Checklist (PCL)
- Clinician-Administered PTSD Scale (CAPS)
- Life Events Checklist (LEC)

Treatment Options

| Psychotherapy | • Exposure- and Cognitive-based |
|              | • Stress Inoculation Treatment |
|              | • Eye Movement Desensitization and Reprocessing (EMDR) |

| Medications   | • Antidepressants |
|              | • Sympathometics |
|              | • Mood stabilizers |

| Complementary and Alternative Medicine | • Acupuncture |
|                                         | • Yoga |
|                                         | • Mind-Body Medicine |
|                                         | • Energy Medicine |
Patient Case

JR is a 29 year old male. He has recently been diagnosed with PTSD. He arrives to your pharmacy to pick up a new prescription for sertraline. He will begin exposure therapy with his psychologist. He is inquiring if he needs a medication if he is starting psychotherapy for his treatment of PTSD. The best response should be:

I. Medication should not be used when initiating psychotherapy as it may impede monitoring of progress.
II. Consider medication treatment prior to starting psychotherapy.
III. Advise JR to discuss treatment options with his provider. Patient preference often drives initial therapeutic approach.

Selection of Therapy

- Therapeutic options should be explained to all PTSD patients
- First line treatment: Psychotherapy or pharmacotherapy
- Recent studies show psychotherapy may have greater sustainable effect than pharmacotherapy
- Patient preferences often drive initial therapeutic approach

Psychotherapy

Significant Benefit
- Prolonged Exposure
- Cognitive Processing Therapy
- Eye Movement Desensitization and Reprocessing (EMDR)

Some Benefit
- Patient education
- Imagery Rehearsal
- Hypnosis
- Group Therapy
- Relaxation Techniques

Unknown Benefit
- Web-based
- Dialectical Behavioral Therapy

- Strongly recommended patients be offered psychotherapeutic interventions that include cognitive and/or exposure-based treatments
- Based on severity of symptoms and clinician expertise

Psychotherapy

- Relaxation techniques should be considered in alleviating physiological hyper-reactivity
- Imagery Rehearsal Therapy considered for treatment of nightmares and sleep disruption
- Hypnosis considered for other symptoms associated with PTSD including pain, anxiety, dissociation and nightmares
Pharmacotherapy

**Significant Benefit**
- Selective Serotonin Reuptake Inhibitors (SSRI), Serotonin Norepinephrine Reuptake Inhibitors (SNRI)

**Some Benefit**
- Mirtazapine, Prazosin (Nightmares), Tricyclic Antidepressants, Nefazodone, Monoamine oxidase inhibitors

**Unknown Benefit**
- Antipsychotics, Buspirone, Hypnotics, Bupropion, Trazodone, Gabapentin, Lamotrigine, Propranolol, Clonidine

**No Benefit**
- Benzodiazepines, Tiagabine, Guanfacine, Valproate, Topiramate, Risperidone

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**Pharmacotherapy**

- Discuss risks and benefits of pharmacotherapy
- Consider comorbidities and tailor medication choices to the individual patient
- Optimize monotherapy

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**Selective Serotonin Reuptake Inhibitors (SSRI)**

<table>
<thead>
<tr>
<th>SSRI</th>
<th>FDA approved</th>
<th>Significant improvement seen in multiple studies in noncombat-related PTSD</th>
</tr>
</thead>
<tbody>
<tr>
<td>Paroxetine 20 to 60mg</td>
<td>FDA approved</td>
<td>Significant improvement seen in multiple studies in noncombat-related PTSD</td>
</tr>
<tr>
<td>Sertraline 50 to 200mg</td>
<td>FDA approved</td>
<td>Significant improvement seen in multiple studies in both noncombat- and combat-related PTSD</td>
</tr>
<tr>
<td>Fluoxetine 20 to 60mg</td>
<td>FDA approved</td>
<td>Few studies showed no significant difference</td>
</tr>
<tr>
<td>Remission maintenance demonstrated</td>
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<td></td>
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**Serotonin Norepinephrine Reuptake Inhibitor (SNRI)**

<table>
<thead>
<tr>
<th>SNRI</th>
<th>Off label use recommended in guidelines</th>
</tr>
</thead>
<tbody>
<tr>
<td>Venlafaxine XR 37.5 to 300mg</td>
<td>Randomized trials found venlafaxine to be more effective than placebo</td>
</tr>
<tr>
<td>Duloxetine 30 to 90mg</td>
<td>Combat-related trials</td>
</tr>
<tr>
<td>Improvement in PTSD and comorbid depression</td>
<td></td>
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</tbody>
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**SSRI and SNRI**

- Recommended first line agents
- Caution with use in comorbid bipolar disorder
- Time to response: 3 to 8 weeks
- Avoid abrupt discontinuation
- Common adverse effects
  - Nausea, vomiting, diarrhea
  - Fatigue
  - Sexual dysfunction
**Mirtazapine**

- **Mechanism of action**
  - Alpha-2-adrenergic antagonist causing increase in release of norepinephrine and serotonin
  - High affinity for serotonin and histamine receptors
- **Common adverse effects**
  - Weight gain
  - Drowsiness
  - Less sexual adverse effects

**Tricyclic Antidepressants (TCA)**

- **Mechanism of action**
  - Inhibits reuptake of serotonin and norepinephrine
- **First antidepressants to be used for PTSD**
- **Randomized controlled studies show benefit**
- **Adverse effects limit use**
  - Arrhythmia, orthostasis
- **Second-line agent**

**Sympatholytic agents**

- **Decrease sympathetic nervous system hyperactivity**
- **Prazosin, clonidine, guanfacine, propranolol**
- **Common adverse effects**
  - Postural hypotension
  - Syncope

**Prazosin**

- **Open-label studies and placebo-controlled trials showed improvements in sleep-related symptoms of PTSD**
- **Recent study in combat-related PTSD patients showed improvement in daytime symptoms with additional daytime dose**
- **Dosage range:** 1 to 20mg/day
- **Titrate dose as tolerated**

**Atypical Antipsychotics**

- **Mechanism of action**
  - Blocks 5HT2A and dopamine receptors
- **Common adverse effects**
  - Weight gain
  - Diabetes
  - Hyperlipidemia
  - Postural hypotension
  - Extrapyramidal Symptoms
**Atypical Antipsychotics**

<table>
<thead>
<tr>
<th>Atypical Antipsychotic</th>
<th>Relevant Studies</th>
</tr>
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</table>
| Risperidone 1 to 6mg    | • Improved psychotic symptoms  
                          • Adjunct to sertraline showed no difference  
                          • Guidelines do not recommend use |
| Olanzapine 5 to 20mg    | • Improved CAPS mainly due to improved sleep quality ratings  
                          • Weight gain |

**Anticonvulsants**

- Anticonvulsants with mood-stabilizing properties that have been studied  
  - Gabapentin, lamotrigine, topiramate, valproate and tiagabine  
- Most studies showed no significant difference  
- Comorbid bipolar disorder

**Topiramate**

- Two randomized-controlled trials in civilian PTSD using topiramate as monotherapy  
  - Mixed results  
- Randomized-controlled trial in combat-related PTSD using topiramate as adjunct  
  - No significant difference  
- May benefit patients with alcohol use disorder

**Benzodiazepines**

- Enhances activity at GABA receptor  
- Currently not recommended by VA/DoD clinical practice guideline  
- Studies showed poorer outcome  
- Concern regarding use in comorbidities of substance abuse disorder and traumatic brain injury

**D-cycloserine**

- Mechanism of action  
  - NMDA partial agonist  
  - Facilitates extinction of conditioned fear in animal studies  
- Currently being studied as adjunct to exposure therapy  
- Not available at this time in the US
Future Areas of Research

- Cortisol
- Memantine
- Ketamine
- Early intervention

Patient Case

JR returns to your pharmacy after a month to pick up medications. He states therapy is ongoing and difficult. He experiences guilt and detachment. He avoids crowded places and mainly stays in his room. Denies use of alcohol. He is picking up the following medications:
- Sertraline 100mg daily
- Diazepam 5mg three times daily as needed

Patient Case (cont.)

What recommendations can you make to his psychiatrist regarding his medication regimen?
A. Increase frequency of diazepam to four times daily as needed
B. Increase dose of sertraline to 150mg daily
C. Taper and discontinue use of diazepam

\[ \text{Answers B and C} \]

Complimentary and Alternative Medicine

- Acupuncture
- Mind-Body Medicine
  - Yoga, Tai Chi, meditation, biofeedback
- Energy Medicine
  - Reiki, therapeutic touch

Pharmacy Role

- Pharmacy consults for medication evaluation and management
- Drug information for healthcare providers
- Patient education and counseling
- Review of medication compliance

Pharmacy Role

- Discuss medication expectations
  - Expected onset of effect from medication
  - Potential adverse effects
  - Withdrawal effects with abrupt discontinuation
- Provide tools to improve compliance
  - Pillbox
  - Smartphone apps
  - Medication lists
Additional Resources

- Defense Centers of Excellence: http://dcoe.mil
- National Center for PTSD: http://www.ptsd.va.gov/professional/treatment/overview/clinicians-guide-to-medications-for-ptsd.asp
- Veterans Crisis Line: 1-800-273-8255

Key Points

- Medication choices should be tailored to the individual patient.
- Treatments should be given sufficient trial of time to see benefit.
- Further studies needed for other medication treatment options.
- Pharmacists and technicians can have a big impact on enhancing medication regimens, increasing adherence and managing expectations.

Answer to Self-Assessment Question 1

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Closing Remarks

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