MASSACHUSETTS GENERAL HOSPITAL
PSYCHIATRY ACADEMY

Psychopharmacology of Panic Disorder

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Disclosures

If you have disclosures, state:

"My spouse/partner and I have the following relevant financial relationship with a commercial interest to disclose:

I am the author of the book "Almost Depressed" and have received payments from Harvard health Publications

Panic Disorder

- Common
- 12-Month Prevalence Rate 1.8%
- Minority of patients receive adequate care
  - Patients often don't seek help
  - When seeking help, probably due to predominance of physical symptoms often present to primary care, medical specialists or emergency rooms
  - Misdiagnosis is common too

Panic Disorder

- Course
  - Chronic or recurrent
  - Comorbid Disorders often present
  - Even when panic symptoms remit, other psychiatric pathology often present
- Impact
  - Negative on health, well-being, functioning
  - Associated with suicidal ideation & attempts
  - Associated with Medical Morbidity
  - Increases economic cost

Evidence Based Pharmacotherapy

- Selective Serotonin Reuptake Inhibitors (SSRIs)
- Serotonin Norepinephrine Reuptake Inhibitors (SNRIs)
- Tricyclic Antidepressants (TCAs)
- Irreversible Monoamine Reuptake Inhibitor (MAOI)
- Benzodiazepines

Efficacy in Short-term Treatment

- Demonstrated efficacy with
  - SSRIs (citalopram, escitalopram, fluoxetine, fluvoxamine, paroxetine IR and CR, sertraline)
  - SNRIs (venlafaxine IR and XR)
  - TCAs (IMI and CMI)
  - MAOI (phenelzine)

Antidepressant Dosages in Treatment of Panic Disorder

	Starting Dose (mg)	Mean Dose (mg)	Usual Max (mg)
Citalopram	10	20-30	60
Escitalopram	2.5-5	10	20
Fluoxetine	10-20	20	60
Fluvoximine	25-50	100-150	300
Paroxetine	10	20-40	60
Paroxetine CR	12.5	25-37.5	50
Sertraline	25-50	100	200
Venlafaxine	37.5	75-150	225
Clomipramine	25	100-150	250
Imipramine	25	100-150	300
Phenelzine	10	40-60	

Efficacy in Short-term Treatment

- Onset of Action
  - Relatively slow, usually on order of weeks
  - Symptoms may increase initially
  - May consider temporary addition of Benzodiazepine
- Drop Out Rates (estimates, not head to head)
  - Phenelzine >TCAs > SSRIs > paroxetine about same as venlafaxine
- Efficacy in Comorbid Conditions
  - These treatments have demonstrated efficacy in a range of anxiety disorders and depressive disorders

Common Adverse Events: SSRIs

- Headaches
- Gastrointestinal symptoms/complaints
- Insomnia
- Sexual dysfunction
- Weight gain
- Increased Anxiety
- Drowsiness
- Tremor
- Sweating

Common Adverse Events: venlafaxine

- Dry mouth
- Nausea
- Constipation
- Insomnia
- Anorexia
- Sexual dysfunction
- Somnolence
- Tremor
- Sweating
- Important to monitor blood pressure
- Discontinuation due to tapering or missed doses usually difficult

Common Adverse Events: TCAs

- Dry mouth, Constipation and other anticholinergic effects
- Cardiovascular Symptoms: palpitations, arrhythmia, exacerbating conduction anomalies
- Orthostatic Hypotension
- Dizziness
- Sexual dysfunction
- Somnolence
- Tremor
- Sweating
- Fatigue and weakness
- Cognitive disturbances
- Falls in the elderly
- Very dangerous in overdose and to DOGs
- Need to Monitor Baseline and Follow-up EKG; check 12 hour trough level

Common Adverse Events: MAOIs

- Hypotension
- Weight gain
- Sexual dysfunction
- Paresthesias
- Myoclonic jerks
- Dry Mouth
- Edema
- Sleeping disturbances
- Adherence to strict low tyramine diet required to avoid hypertensive crisis (usually give Rx for nifedipine if needed)

Efficacy in Long-term Treatment

- Demonstrated efficacy during follow-up study periods up to 2 years with
  - SSRIs: citalopram, fluvoxamine, paroxetine
  - TCAs: clomipramine, imipramine
- Time to relapse significantly longer in venlafaxine XR vs. placebo over course of 6 months
- No long-term studies with MAOI (phenelzine)

Benzodiazepines

- Efficacy in Short-term demonstrated with
  - Alprazolam, clonazepam, diazepam and lorazepam
- Efficacy in Long-term demonstrated with
  - Controlled studies up to 32 weeks with alprazolam and up to 1 year with clonazepam
- Drop-Out Rates in Panic Disorder
  - About 15%

Benzodiazepine Dosages in Treatment of Panic Disorder

	Starting Dose (mg)	Mean Dose (mg)
Alprazolam	0.5-1.5	4-6
Clonazepam	1	2-3
Diazepam	5-10	40-50
Lorazepam	1	2-4

- Fast Onset of Action
- Produce effects as soon as effective dose given
- Not usually helpful with comorbid disorder
- Often has a role early in treatment with antidepressant medications

Common Adverse Events: Benzodiazepines

- Sedation
- Fatigue
- Ataxia
- Memory Impairment
- Weakness
- Caution with Elderly due to risk of falls
- Dependence
  - Dose escalation
  - Withdrawal
  - Tapering

First-Line Pharmacotherapy

- Comparable efficacy between
  - IMI and Alprazolam and Clonazepam
  - Various SSRIs
  - SSRIs, SNRI, TCAs and Benzodiazepine appear effective over long-term
- Which to choose first? Please Consider…
  - Side effect profile
  - Drop-out rates
  - Onset of Action
  - Impact on Comorbid Conditions

SSRIs and Venlafaxine

- First-line Agents
- Given slow onset of action and possible increase in anxiety during initial treatment, consider temporary co-administration of a benzodiazepine

Benzodiazepines

- Fastest Onset of Action
- Usually well tolerated, especially in short-term
- Not usually helpful for comorbid depressive disorders or PTSD
- Monitor for
  - Drowsiness and cognitive side-effects
  - Dependence
  - Use of Other Substances

Duration of Treatment?

- Usual course of panic disorder is relapsing
- Long-term treatment goal is to reduce symptoms, impact and vulnerability to relapse
- Discontinuation often associated with relapse
- Maintenance treatment may prevent relapse
- Up to 50% of patients interrupted treatment
- Balancing tolerability and impact of disorder on patient's health and well-being

Discontinuing Medication

- Slowly over weeks to months
- Differentiate relapse and discontinuation symptoms
- If/when patient feels well on a lower dose should they continue on this dose? Will it be sufficient to prevent relapse?
- Psychotherapy
  - Effects of CBT in Panic Disorder often maintained over time
  - CBT Relapse Prevention Program

Treatment Refractory

- A substantial number of patients with Panic Disorder do not respond to initial treatment or experience only a partial response
- Strategies to use include:
  - Optimizing current treatment
  - Switching Medications
  - Augmentation
  - Consultation
  - More CBT

Panic Disorder is

- Prevalent
- Disabling
- Can be treated effectively