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Treatment of Anxiety Disorders: Panic Disorder

General information about Panic disorder

- Lifetime rate prevalence panic attack: ~33% population; lifetime prevalence panic disorder ~3%
- Twice as common in women as in men
  - Is most often adult onset (median age of 24)
  - Prevalence decreases significantly after age 60
- Is a recurrent or chronic illness in the majority of cases
- Most patients showed improvement over 15-60 months, but few had complete remission
- Suicide-most studies have shown a higher likelihood of suicide attempts among people with panic disorder compared with the general population

What is the cause of Panic disorder?

- **Not known**,

In general, what is the treatment approach?

- Panic disorder may be effectively treated **with cognitive-behavioral therapy, medication, or a combination of the two modalities**
- For most patients the initial selection can be made on the basis of patient preference and treatment availability (CBT). There is no evidence of a robust difference between the effectiveness of the two different treatment modalities (**CBT and medications appear to be equally effective**)
- For psychotherapy treatment, CBT is first line over other psychotherapies.
- For medication treatment, first line treatment are selective serotonin reuptake inhibitors (SSRI's)
  - SSRI's are most widely tested in clinical trials and shown to be efficacious
    - No evidence of superior efficacy of one SSRI versus another SSRI
- Other medications that have demonstrated efficacy in treating panic disorder
  - Serotonin-norepinephrine reuptake inhibitors (SNRI's)
    - Randomized trials support efficacy of Venlafaxine (Effexor);
    - Venlafaxine (Effexor) is second choice (due of hypertension risk, particularly at higher doses)
  - Benzodiazepines
    - Advantages
      - Helps reduce each of three components of Panic disorder **(attack frequency, anticipatory anxiety, and phobic avoidance)**
      - **Onset of anti-panic effect is very rapid, beginning within the first week** of treatment
      - All medications within benzodiazepine class appear to be equally effective
    - Disadvantages
      - Not recommended for patients who have history of substance abuse;
      - While not absolutely contraindicated, would require increased prescription monitoring, increased visit frequency, use of more long acting benzodiazepines with slower absorption and slower onset of action
  - Medications not supported by randomized trials
    - Trazodone, bupropion (Wellbutrin), buspirone (Buspar)

How is medication treatment approached?

- Starting doses of antidepressants in treatment of panic disorder
  - like depression, starting dose should be in the lower end of the recommended range so as to minimize/avoid initial overstimulation side effects (anxiety, jitteriness, insomnia)
- Time to onset of clinical efficacy
  - Varies from patient to patient but **time to onset is 2-4 weeks**
    - **Clinical response can take up to 8-12 weeks** for some patients
    - Therapeutic effects for anticipatory anxiety and phobic avoidance may continue over 6-12 months
  - While no clinical trials have been done to suggest the optimal duration, expert consensus is medication should be continued for at least a year beyond the time symptom control has been attained
- Combination treatment of antidepressants and benzodiazepine
  - Studies shows more rapid symptom resolution compared to antidepressants alone; however no difference in outcome by 8-12 weeks

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- Combination recommended for patients with severe symptoms (marked distress or impairment) that has not responded to SSRI/SNRI or who cannot wait the time required for antidepressant to work

More complex situations

- Co-occurring substance use disorder
  - In general, avoid treating with a benzodiazepine (see above on benzos)
  - Instead of a benzodiazepine, augment the antidepressant with gabapentin (Neurontin), pregabalin (Lyrica), or mirtazapine (Remeron)

Initial response to medication is poor

- Options
  - First choice: Augment with CBT
  - Try a different SSRI or try venlafaxine (Effexor)

Initial response is partial

- Options
  - First choice: Augment with CBT
  - If no substance issues, add benzodiazepine such as clonazepam (Klonopin)
    - Initiating a benzodiazepine after initiating CBT is not recommended
    - **Using "as needed" (PRN) dosing is not recommended**
      - Better outcomes from either standing dose of benzodiazepine or no benzodiazepines

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Treatment of Anxiety Disorders: Generalized Anxiety Disorder

General information about Generalized Anxiety Disorder

- **Twice as common in women as men (like Panic Disorder)**
- **Most common anxiety disorder in the elderly** (in contrast to Panic Disorder)
- Highly comorbid with other psychiatric disorders

Course

- Onset
  - typically gradual; subsyndromal anxiety symptoms before age 20
  - those with early age of onset tend to have more protracted course or more likely to have comorbid disorders
- Prolonged and fluctuating course of illness; potentially chronic

Treatment options

- Medications (Serotonergic antidepressants), CBT, or both
  - Are no head to head comparisons of CBT and serotonergic antidepressants; meta-analysis show roughly equivalent effect sizes

- Medications
  - **1st line medications**:
    - **SSRI's or SNRI's**
    - **No individual SSRI or SNRI is better than other members of that medication class**
    - Therapeutic doses are approximately the same as for the treatment of depression
      - Similar to panic disorder and depression, start at low dose and gradually titrate upward
    - Time to onset of clinical meaningful action:
      - Medication trial: 4-6 weeks at therapeutic dosing levels
  - 2nd line medication:
    - Buspirone (Buspar)
      - Advantages: Similar efficacy as benzodiazepine without risk of dependence
    - Pregabalin (Lyrica)
      - Has shown efficacy in treatment of GAD;
    - Benzodiazepines
      - Avoid in patients with history of substance use disorder
      - Otherwise use cautiously for acute, maintenance, or long term treatment;
        - **Use hydroxyzine (vistaril, atarax) instead of benzodiazepines for patients with substance history**

  - If treatment shows a robust response
    - Continue treatment for at least 12 months beyond time when medication judged to be effective
    - After discontinuing medication patient relapses, restart medication, again recommend for at least 12 months beyond time when medication judged to be effective
    - After 2 relapses, recommend maintenance treatment

  - If initial treatment shows a **partial response**
    - Adjunctive treatment with **buspirone (Buspar), pregabalin (Lyrica)**

  - If initial treatment fails
    - Try a different SSRI or SNRI

  - If medication treatment resistance
    - Benzodiazepines
      - If no history of substance use disorders; ~~if no depressive symptoms~~
      - Use low doses, avoid large doses
      - **avoid PRN or "as needed"** dosing regimen;
    - Mirtazapine (Remeron)
    - quetiapine (Seroquel); may be used as adjunct or as monotherapy