Applications of EBP and Psychiatric Medication Management for Anxiety

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Disclosures

Margaret R. Emerson APRN, PMHNP-BChas no financial relationships with commercial interests to disclose

Any unlabeled/unapproved uses of drugs or products referenced will be disclosed

Objectives for Anxiety:

- *Discuss EBP medications used in the management of anxiety disorders in the primary care setting*
- *Describe appropriate use of benzodiazepines in primary care setting and EBP with this medication class*
- *Identify management strategies for benzodiazepine use in the primary care setting*

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Common Anxiety Disorders…

- Generalized Anxiety Disorder (GAD)
- Social Anxiety Disorder
- Obsessive Compulsive Disorder (OCD)
- Panic Disorder

https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5840911/

Anxiety Disorders in Child/Adolescent Population

- Anxiety disorders affect about 15-20% of youth
- Anxiety disorders are among the most prevalent psychiatric conditions in the child and adolescent populations

https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5840911/

Presentations in children

- School refusal
- Somatic symptoms
  - GI symptoms
  - Headaches
  - Abdominal complaints.
- Rituals
- Reassurance-seeking
- Agitation
- Aggression
- Insomnia/refusal to sleep alone
- Perfectionism

https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5840911/

Fear

Is this normal fear?
Is this appropriate worry?

https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5840911/

Diagnostic Workup

- Medical workup
  - Substance use
  - Hyperthyroidism
  - Hyperglycemia/Medical workup
  - Seizure disorder
- Trauma screen
- Measures

https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5840911/

Screening Tools

Screening Tools for identification and progress tracking in patients >8 years of age:
- •Multidimensional Anxiety Scale for Children
- •Screen for Child Anxiety and Related Emotional Disorders (SCARED)
- •Spence Children's Anxiety Scale (SCAS)

The Preschool Anxiety Scale
- Parent report adapted from the SCAS
- Allows for screening for anxiety in young children (ages 2.5 to 6.5).

The Screen for Childhood and Anxiety Related Disorders (SCARED) (ages 8-11)
- Free
- Available online

The Spence Children's Anxiety Scale (SCAS) (ages 8-15)
- Free
- Available online

Clinician rated measure: Pediatric Anxiety Rating Scale

Specific Phobias or Social Anxiety Tools:
- Social Anxiety Scale
- Social Worries Questionnaire,
- Social phobia subscale of SCARED

https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5840911/

Current Practice Recommendations

1)Screening for anxiety symptoms
2)Rating the severity of the anxiety symptoms
3)Identifying functional impairment in youth with anxiety disorders
4)Carefully assessing for co-morbid psychiatric conditions as well as for general medical conditions (e.g., hyperthyroidism) that may mimic anxiety symptoms.

The American Academy of Child & Adolescent Psychiatry [32]

When should you treat?

When the anxiety is causing **functional impairments:**

- Disruptions in social relationships/activities
- Disruptions in academic performance
- Disruptions IADLs
- Impact on peer and family relationships
- Attempts at self-medication

https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5840911/

Best Practice for Treatment

Multimodal:

1)education of the parents and the child about the anxiety disorder
2)consultation with school personnel and physician providers
3)cognitive-behavioral interventions
4)family therapy
5)pharmacotherapy

https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5840911/

Treatment for Child/Adolescent Anxiety

- Treatment Options:
  - First Line:
    - Parental psychoeducation
    - Cognitive Behavioral Therapy (CBT)
  - Second Line:
    - Medication

https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5840911/

Anxiety Medications

Medications best supported by evidence
- POTS study (sertraline)
- CAMS study (sertraline)

https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5840911/

What did the POTs study tell us?

POTS

- CBT and sertraline were both superior to placebo
- CBT and sertraline combined showed the best efficacy

Remission rates in order of effectiveness:
1.) Combined treatment
2.) CBT
3.) Sertraline
4.) Placebo

https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5840911/

What did the CAMs study tell us?

CAMS
- At 12 weeks:
  - CBT > placebo
  - Sertraline > placebo
  - Combination > all

https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5840911/

Take home message…

- Individual CBT significantly reduced rates of anxiety diagnoses when compared with controls
- CBT was equally effective or superior to comparison psychotherapies.

Most effective:
- Combination of CBT and pharmacological management

https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5840911/

Pharmacologic Agents for Anxiety

Psychopharmacologic trial data in pediatric patients indicate:
Use SSRIs when:
- anxiety symptoms are moderate or severe
- impairment makes participation in psychotherapy difficult,
- psychotherapy results in a partial response

- Efficacy of benzodiazepines or buspirone in the treatment of youth with anxiety disorders not supported.

https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5840911/

Anxiety medications

Sertraline

FDA indications
OCD-ages 6 and up
Off Label:
GAD- ages 7 and up
Separation Anxiety Disorder –ages 7 and up
Panic Disorder-ages 8 and up
Social Phobia-ages 7 and up

Typical dosing start at 25mg po qday and titrate up to 200mg

Hepatic impairment: lower dose typically by 50%

https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5840911/

Anxiety medications

Fluoxetine

FDA indications
OCD- ages 7 and up
Panic Disorder-ages 8 and up

Off Label:
GAD- ages 7 and up
Separation Anxiety Disorder –ages 9 and up
Social Phobia
Typical dosing 60mg/day

Ages 6-12 studies have looked at dosing up to 60 mg po qday

Hepatic impairment: lower dose and less frequent dosing

https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5840911/

Anxiety medications

Escitalopram

FDA indications
GAD- ages 10 and up
Off Label:
Panic Disorder
Social Phobia

Typical dosing 10-20mg/day
Ages 6-11 safety and efficacy has not been established but medication has been used at doses up to 20mg/day

Hepatic impairment: lower dose and less frequent dosing
Typically if hepatic impairment dose should be kept at 10mg/day

https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5840911/

Anxiety medications

SSRI – best evidentiary support. Considered first line medication

- Cautions
  - Agitation / black box warning
    - **Clinical Point:** When prescribing SSRIs for pediatric anxiety, monitor patients for suicidality and routinely reassess suicide risk
  - Sleep disturbance
- SNRI – second line

https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5840911/

SSRI Side Effects

Side Effects for SSRI's:
- Restlessness
- Jitteriness
- Headache
- Fatigue
- Dizziness
- Nausea
- Anorexia
- Weight gain.
- Sexual dysfunctions
  - decreased libido
  - impotence
  - ejaculatory disturbances may be a problem in long-term treatment

https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5840911/

Other Considerations

- **Discontinuation syndromes have been observed**
- **Overstimulation**
- **Time**

https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5840911/

SNRI's

Duloxetine

FDA indications
GAD- ages 7 and up

Typical dosing 30-60 mg/day
Max dose 120mg/day

Hepatic impairment: Do not use with hepatic impairment

https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5840911/

SNRI's

Venlafaxine

- Has been used to treat anxiety disorders
- Not FDA approved
- Not sufficient data to establish the efficacy of venlafaxine ER in treating GAD in pediatric patients
- Off label indications:
  - Social phobia-ages 8 and up
  - GAD-ages 6 and up
- Dosing in pediatric patients should be weight based
  - Max doses per weight in kg.
  - Reduce with hepatic impairment

https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5840911/

Adult Anxiety

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Adult Anxiety

Escitalopram:
Indication: GAD
Off Label: has been used in panic disorder
Starting dose 10 mg by mouth daily
Max dose 20 mg by mouth daily
Fluoxetine:
Indication panic disorder, OCD
Starting dose 10 mg by mouth daily
Max dose 60 mg per day
Can go up to 80mg/day
Fluvoxamine:
Indication OCD
Starting dose 50 mg by mouth at bedtime
Max dose 300 mg. Doses above 100 mg to be given in 2 divided doses

https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5840911/

Adult Anxiety

Paroxetine:
Indication GAD, OCD, social anxiety disorder, panic disorder, PTSD
Starting dose to 10 mg by mouth daily
Typically increased by 10 mg by mouth weekly
Max dose 50-60 mg by mouth daily depending on indication
Sertraline:
Indication OCD, panic disorder, PTSD, social anxiety disorder
Starting dose typically 25-50 mg by mouth daily
Allow at least a week between dose increases
Max dose 200mg by mouth daily

https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5840911/

Adult Anxiety

Duloxetine:
Indication: Generalized Anxiety Disorder
Starting dose 30 mg.
Increase dose by 30 mg per day.
Max dose 120 mg by mouth daily
Venlafaxine ER
Indication generalized anxiety disorder, panic disorder, social anxiety disorder
Starting dose 37.5-75 mg by mouth daily
Can increase typically after 7 days
Max dose 225 mg by mouth daily with the exception of social anxiety disorder.
With Social Anxiety Disorder there is no evidence that doses above 75 mg provide additional benefit.

https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5840911/

Anxiety Measures

Hamilton Anxiety Rating Scale (HAM-)
- 14 items
- Clinician rating scale
- Available in public domain

Generalized Anxiety Disorder 7 Item Scale (GAD-7)
- 7 items
- Patient report
- Available for use in public domain and commonly used in primary care settings

https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5840911/

Anxiety and Pregnancy/Breastfeeding

SSRI's are the most frequently used medications in this population
- Why?

- First trimester considerations
- Third trimester considerations

Breastfeeding

Medication Decision making

Titration considerations

https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5840911/

Risk Factors for Anxiety in Pregnant and Postpartum Women

History of smoking
Single mothers
Young age
Lower level of completed education
Unplanned pregnancy
Low self esteem
Low marital satisfaction
Low social support
Presence of other mental health diagnoses, including depression

Common Symptoms of Anxiety in Pregnancy/Postpartum

Low self-esteem, low self-efficacy
Obsessions concerning contamination
Fear of harm to the fetus – intrusive thoughts
Examples:
- Contracting a serious illness
- Doubts about the baby's safety because of contamination
  - Sterilizing products aren't working
- Preparing the house, losing sleep over need to have house "perfect"
- Seeking reassurance from friends, family members, and healthcare providers

Pharmacologic Treatment for Anxiety

Selective serotonin reuptake inhibitors (SSRI)
- Most recent research does not indicate a need to choose one SSRI over another, but sertraline (Zoloft) is often chosen due to having the most information available on this medication
- In breastfeeding, may choose SSRI with shorter half-life due to concerns about plasma levels in the infant
  - Longer half-life: citalopram, fluoxetine

Perinatal Use of Benzodiazepines

Short half-life medications preferred (lorazepam)

Slight increase in risk of spontaneous abortion when used in first trimester

Increased rates of preterm birth

Prospective studies do not indicate low birth weight as compared to unexposed infants, but one retrospective study did associate early and late use of benzodiazepines with lower infant birth weight

Breastfeeding and Benzodiazepines

- Options that have low levels in breastmilk and short half-life are preferred:
  - Lorazepam, oxazepam, and temazepam good options if needed
- Monitor for effects of use on infant including sedation, difficulty feeding, and hypotonia
- "Pump and dump" not recommended

Neonatal Adaptation Syndrome

Chronic benzodiazepine use during pregnancy poses risk to infant:

- Low Apgar scores, apnea, hypothermia, hyperreflexia, hypertonia or hypotonia, irritability, lethargy, restlessness, tremor, diarrhea, poor feeding, and vomiting
- More common in preterm infants than term
- May last for up to 3 months

Prospective study promising that benzodiazepine use does not seem to negatively impact motor and cognitive development at 3 years of age in exposed infants

Resources - Websites

FDA Drug Information:
https://www.accessdata.fda.gov/scripts/cder/drugsatfda/

- New guidelines regarding use in pregnancy and breastfeeding no longer use the letter categories
- Now will have descriptive summaries, including use during pregnancy and lactation subsections

Postpartum Support International (PSI)– training for professionals, screening tools, certifications, resources for patients

- www.postpartum.net

Older Adults and Anxiety

Screening Measures:
Gold standard is the Geriatric Anxiety Inventory

Diagnostic Work-up
Neurological Conditions
Cardiovascular Conditions
GI Disorders
Metabolic/Endocrine Conditions
Deficiency States (Vit, B12, folic acid ect.)

Medication interactions

https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5840911/

Older Adults and Anxiety

Treatment of geriatric anxiety…
Focus on non-pharmacological approaches which are first recommended rather than pharmacological approaches.

These include:

- **Lifestyle modification**:
  - Sleep, diet, exercise, socialization –all in moderation.
  - Eliminate medical and non-medical triggers
- **Behavioral Therapy**
- **Cognitive Therapy**
- **Mindfulness**

https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5840911/

Older Adult Considerations

Clear diagnosis of anxiety…(2 options)

1.) Nonpharmacological treatment (recommended 1st line)
2.) Pharmacological options
First line drug trial 4-8 weeks
Second line drug trial 4-8 weeks
After 12 weeks if no improvement consider alternative strategies and/or augmentation.

https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5840911/

Medications in the Older Adult

Medications….

"Start low, go slow and titrate up to usually half of the adult dose."

SSRI's first line:

Escitalopram
- Recommend to keep dose at 10mg po qday
- Drug interactions especially other agents which prolong QT
- Hyponatremia

Sertraline
- Doses can go up to 200mg/day
- Make adjustments for hepatic impairment

1. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5840911/
2. Clinical Pharmacology. (2019). Drug Monograph. Tampa, FL: Elsevier. Retrieved from https://www.clinicalkey.com/pharmacology/

Ending Treatment

Duration of treatment
- Minimum of 12 months starting from the time of remission (and up to 2 years).

If the decision is made to stop medication, the dose should be reduced over several months with monitoring for relapse.

Monitoring should be done every 3-6 months keeping two things in mind:
- 1.) Remission/and or exacerbation of anxiety
- 2.) Emergent cognitive symptoms

https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5840911/

Benzodiazepines

- **Discuss benzodiazepine use in psychiatric disorders, specifically as they pertain to anxiety and depression**
- **Examine concerns related to benzodiazepine misuse**

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Anxiety Disorders and Benzodiazepines

"In the U.S. anywhere from 55-94% of patients with anxiety disorders are treated with benzodiazepines."

https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5840911/

Benzodiazepines

Benzodiazepines (BDZs)
- One of the most commonly prescribed psychotropic medications
- Seeking benzodiazepines is common
- 1 in 20 adults filled a benzodiazepine prescription in the last year
- Majority of benzodiazepine prescriptions are written by non-psychiatrists

Prescribers…
- should employ BDZs as primarily ***a short-term, stabilizing intervention***
- require significant monitoring of a range of possible adverse side-effects, including the potential for tolerance, dependency, rebound symptoms and withdrawal.

https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5840911/

Benzodiazepines Side Effects

BZD Side Effects:
- Sedation
- Dizziness
- Decreased reaction time
- Impaired driving skills
- Fatigue
- CNS Depression: Worse if combined with EtOH
- Behavioral Disinhibition
- Irritability
- Aggression

- Overdose: Rare fatalities if BZD alone
  - Severe CNS & Respiratory Depression if combined with: Alcohol, Opiates, Heroin, Barbiturates, Narcotics, and/or Tricyclic Antidepressants
- Most people will become dependent after > 6 weeks continuous use
- Only 30% of benzodiazepine dependent people ever get off them completely
- Methadone patients at high risk of benzodiazepine abuse (25 - 65%)

https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5840911/

	Advantages	Disadvantages
SSRIS	No dependency Sufficient evidence from clinical studies for all anxiety disorders Relatively safe in overdose	Latency of effect 26 weeks, initial jitteriness, nausea, restlessness, sexual dysfunctions and other side effects. Some risk of discontinuation syndromes.
SNRI's	No dependency Sufficient evidence from clinical studies Relatively safe in overdose	Latency of effect 26 weeks, nausea, possible increase in blood pressure and other side effects. Some risk of discontinuation syndromes.
Benzodiazepines	Rapid onset of action Sufficient evidence from clinical studies Relatively safe in overdose	Dependency possible; sedation, slow reaction time and other side effects. Paradoxical reactions in elderly patients
Buspirone	No dependency Relatively safe in overdose	Latency of effect 2-6 weeks; efficacy proofs only for symptoms of GAD; include lightheadedness, nausea and other side effects

https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5840911/

Co-morbid Disorders & Benzodiazepines

When treating comorbid anxiety disorders, benzodiazepines were not found to be effective in treating comorbid conditions, such as depression or OCD.

https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5840911/

BZDS Withdrawal Considerations

Dependence/Withdrawal, cont.

- • Rarely -seizures, delirium, confusion, psychosis
- • Triggering of depression, mania, OCD
- • 90% of long-term users (>8mo-1yr) experience significant withdrawal
- • Insignificant withdrawal if used less than 2 weeks
- • Mild-moderate if used >8 weeks
- • Slow taper (>30days) with +/- carbamazepine, valproic acid, trazodone, imipramine
- • CBT effective in discontinuing benzos and controlling panic/anxiety

https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5840911/

Predictors of Withdrawal

1. High-potency-quickly eliminated medications (e.g. alprazolam, lorazepam, triazolam)
2. Higher daily dose
3. Rapid rate of taper (last 50%)
4. Diagnosis of panic disorder (not GAD)
5. High pre-taper levels of anxiety and depression
6. ETOH or other substance dependence/abuse
7. Personality pathology -e.g. neurotic or dependent
8. Not motivated to discontinue use

https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5840911/

Why is it so hard to come off BZDS?

- Reducing causes increased excitation throughout the brain which causes the symptoms of withdrawal, including agitation, anxiety, and insomnia.
- The number of GABA receptors is slowly restored in response to benzodiazepine cessation or dose reduction.
- The rate of withdrawal of treatment needs to allow time for GABA receptors to regenerate if withdrawal symptoms are to be minimized.

https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5840911/

How long do withdrawal symptoms last?

- Up to 15% of people develop protracted withdrawal symptoms (months or years)
- Anxiety Symptoms
- Insomnia Symptoms
- Depression Symptoms
- Cognitive Impairments
- Perceptual Symptoms:
- Motor symptoms
- Gastrointestinal Symptoms

https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5840911/

Benzodiazepine Tapers

- Slow Taper: (3-6 Months)
- Fast Taper: (2-6 Weeks)

Slow Taper

1. Calculate the total daily dose. Switch from short acting agent (alprazolam, lorazepam) to longer acting agent (diazepam, clonazepam).
2. Follow up 1 week after initiating the taper to determine need to adjust initial calculated dose.
3. Reduce the total daily dose by 5-10% per week in divided doses.
4. Once ½ of the original dose has been reached, the taper can be slowed further by decreasing the dose each month thereafter.
5. Consider an adjunctive agent to help with symptoms or to replace the benzodiazepine such as: buspirone, vistaril, clonidine, SSRIs, and/or sleeping aids.
6. Educate patient on nondrug therapies available to assist with symptoms such as: relaxation techniques, deep breathing, exercise, psychotherapy, etc.

https://www.jpshealthnet.org/sites/default/files/prescribing_and_tapering_benzodiapines.pdf

Fast Taper

1. Use an equivalent dose replacement with Diazepam two times daily for 1-2 weeks.
2. Add an anticonvulsant (carbamazepine, valproate, gabapentin) at a maintenance dose. These work on the same GABA receptors and help to facilitate a faster taper.
3. Consider an adjunctive agent to help with symptoms or to replace the benzodiazepine such as: buspirone, vistaril, clonidine, SSRIs, and/or sleeping aids. After 1-2 weeks decrease the dose of diazepam to once daily.
4. Then cut the diazepam to ¼ of the initial dose once daily for 1-2 weeks
5. Discontinue the Diazepam.
6. Continue the anticonvulsant for 2-3 months after discontinuing the benzodiazepine.
7. Educate patient on nondrug therapies available to assist with symptoms such as: relaxation techniques, deep breathing, exercise, psychotherapy, etc.

https://www.jpshealthnet.org/sites/default/files/prescribing_and_tapering_benzodiapines.pdf

Dose Equivalency To Valium 5mg

- Alprazolam 0.5mg
- Chlordiazepoxide 10–25mg
- Clonazepam 0.5–1 mg
- Lorazepam 0.5–1
- Oxazepam 15mg
- Temazepam 10–15mg

https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5840911/

Case Study Review

Applying the content

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Example 1.

Common patient scenario…

45-year-old female comes in for appointment after having worsening in depression and anxiety symptoms. Prior to seeking out psychiatric consultation patient was recently switched from Fluoxetine 10 mg by mouth daily to Vilazodone HCL 10 mg by mouth once a day by her primary care provider.

– Additional Details…

Example 2.

30-year-old patient presents for treatment of depression and anxiety. Patient has had several medication trials all resulting in what was determined to be medication failure by primary care provider.

In review of medication history patient has trialed:

- Sertraline 25 mg by mouth once a day for 3 weeks
- Paroxetine 10 mg by mouth daily for 2 weeks
- Escitalopram 10 mg by mouth once a day for 4 weeks
- Fluoxetine 10 mg by mouth once a day for a week

Example 3.

A 25 y/o patient with anxiety disorder was recently started on buspirone 5mg po qday. The patient called the primary care clinic after a week to inform the provider that the medication has not done anything for their anxiety.

The provider decided to stop the buspirone and inquired from psychiatric provider how to proceed.

Example 4.

Patient comes into clinic with symptoms of anxiety. Patient doesn't "really feel depressed," they just want something for anxiety.

Provider prescribes benzodiazepine to take up to three times daily prn anxiety.

Concerns?

THANK YOU!

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