Treating Anxiety Disorders

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Outline

- Michelle's Case
- Types of anxiety disorders
- Goals of therapy
- Treatment options and guidelines
- Pharmacological options
- Benzodiazepines and Buspirone
- Discussion

Learning Objectives

After completion of this session, participants will be able to:

1. List the treatment options for 6 types of anxiety disorders
2. Compare and contrast the efficacy and safety of antidepressants, buspirone and benzodiazepines for anxiety disorders
3. List monitoring parameters for assessing efficacy and toxicity of antidepressants, buspirone and benzodiazepines for anxiety disorders

Matthew's case

- 28 yo male, 64kg, lawyer who complains of feeling "anxious"
- *When you ask what his concerns are, he says* "I'm a worrier…my mind is always thinking about something that might happen and I can't relax"
- "Before, it would come and go…but now it is worse. I worry about money, my friends, my diet, my health, you get the picture. I can't seem to quiet my mind"
- Also complains of restless sleep, fatigue and has missed 10 work days in the last month, which makes him feel worse...

Matthew's Case Cont'd

- PMHx:
  - GAD x 1 year
  - Type 1 DM
- Current Meds:
  - buspirone 10 mg po bid for 6 weeks with not a big effect on symptoms
  - Insulin Lispro (Humalog) and Glargine (Lispro)

Occasional EtOH, caffeine, smoking

- Checks BG 7 times daily, HgA1C = 8%

Individual/Group Activity (~10 min)

1. Discuss the case and briefly list the goals of treatment
2. What are the treatment options for Matthew?
   - What are the pros and cons of the different treatment options? (e.g., what is the role of buspirone for treating anxiety disorders)
3. Write a prescription for Matthew
4. What will you be monitoring and how often?
5. Fill in the types of anxiety disorders

Types of Anxiety Disorders

1. Panic Disorder (+/- agoraphobia)
2. Social Anxiety Disorder (Social Phobia)
3. Obsessive-Compulsive Disorder (OCD)
4. Generalized Anxiety Disorder (GAD)
5. Post-Traumatic Stress Disorder (PTSD)
6. Phobic Disorders - specific phobias
7. Separation Anxiety Disorder (SAD)
8. Anxiety Disorder due to a Medical Condition
9. Anxiety Disorder due to a Substance
10. Anxiety Disorder Not Otherwise Specified

Goals of Therapy

- Short term (over 6-12 weeks)
  - Reduce or resolve symptoms
  - Improve functioning
  - Minimize side effects
  - Discuss realistic goals: Note: difficult to achieve total remission in OCD and PTSD
  - Education about treatment options and side effects

Goals of Therapy

- Long term (>12 weeks)
  - Aim for return to normal functioning (remission) where possible
  - Adherence to treatment
  - Manage side effects
  - Education (e.g. techniques on how to prevent or minimize future episodes)

Matthew's Goals of Therapy

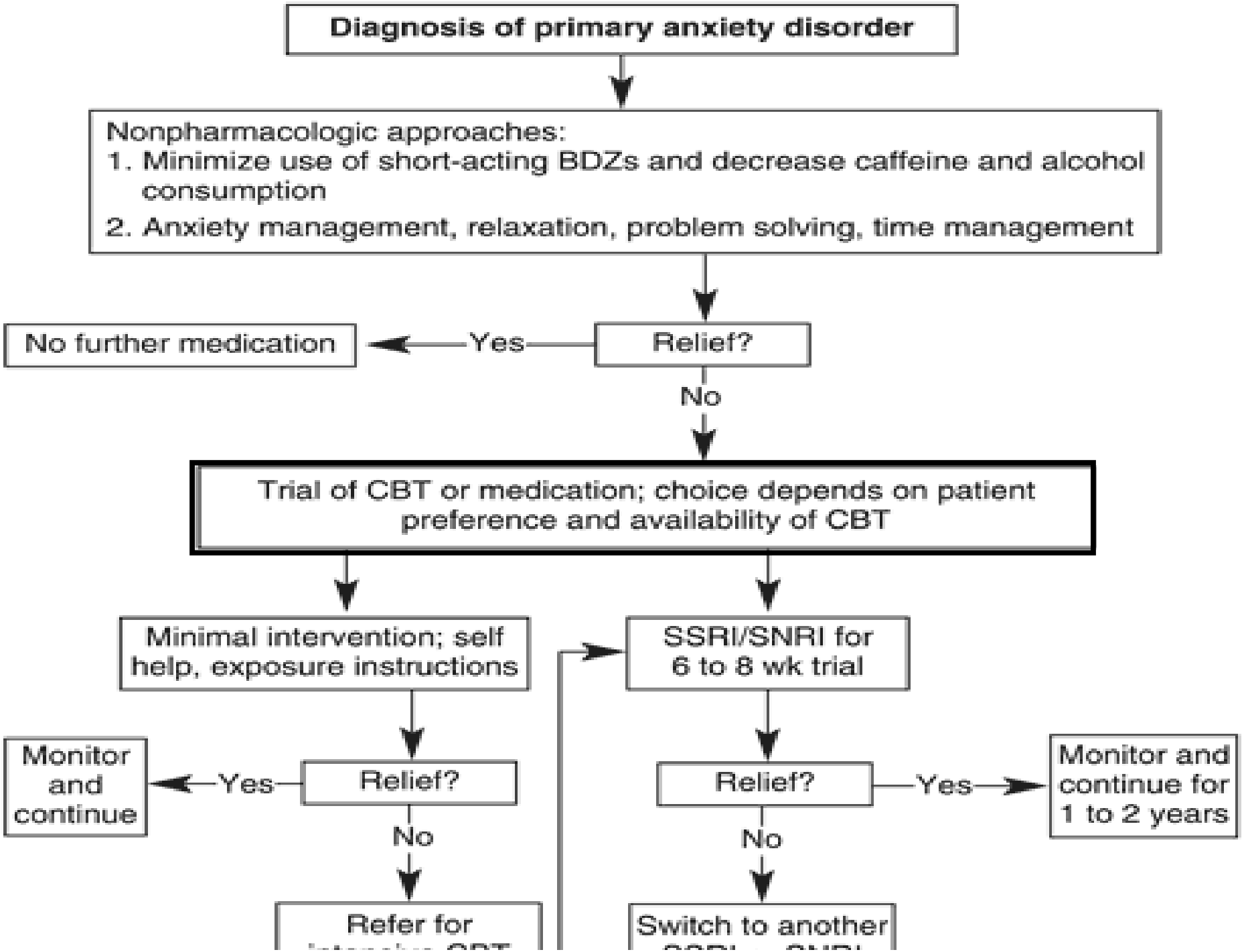
- Reduce or resolve his persistent worrying
- Decrease fatigue, improve sleep
- Improve functioning
- Education about GAD and various treatment options
- Minimize side effects
- Improve HgA1C?
- Reduce amount of monitoring of BG?

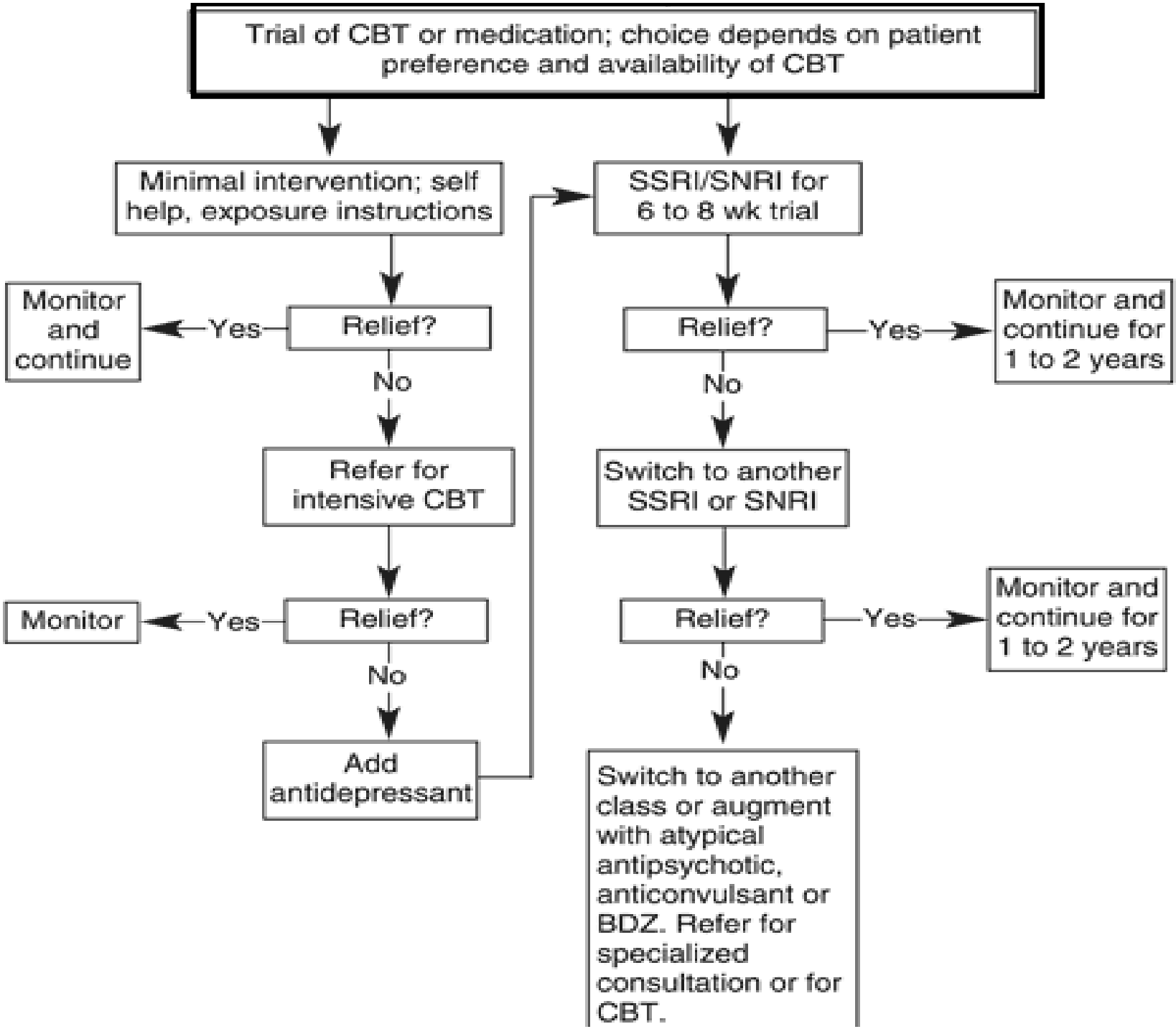
Initial Recommendations for Matthew

- Decrease caffeine, EtOH intake
- Regular aerobic exercise
- Quite smoking (if he's ready)
- Diet modification (regularly spaced meals)/ Improved glucose control
- Relaxation and breathing retraining techniques
- Good sleep hygiene – minimize use of sedatives or hypnotics where possible
- CBT
- SSRI

Treatment Options

- Pharmacotherapy
- Psychotherapy
- Self Management


Diagnosis of primary anxiety disorder
Nonpharmacologic approaches:
1. Minimize use of short-acting BDZs and decrease caffeine and alcohol consumption
2. Anxiety management, relaxation, problem solving, time management
Relief?
Yes
No further medication
No
Trial of CBT or medication; choice depends on patient preference and availability of CBT
Minimal intervention; self help, exposure instructions
SSRI/SNRI for 6 to 8 wk trial
Relief?
Yes
Monitor and continue
No
Refer for
Relief?
Yes
Monitor and continue for 1 to 2 years
No
Switch to another


Trial of CBT or medication; choice depends on patient preference and availability of CBT
Minimal intervention; self help, exposure instructions
SSRI/SNRI for 6 to 8 wk trial
Relief?
Yes
Monitor and continue
No
Refer for intensive CBT
Relief?
Yes
Monitor
No
Add antidepressant
Relief?
Yes
Monitor and continue for 1 to 2 years
No
Switch to another SSRI or SNRI
Relief?
Yes
Monitor and continue for 1 to 2 years
No
Switch to another class or augment with atypical antipsychotic, anticonvulsant or BDZ. Refer for specialized consultation or for CBT.

Factors to Consider:

1. Patients in trials may not be like the patient you are treating
   - Exclusions e.g. comorbid depression, substance use
   - Outpatient psychiatric clinics or academic centres
2. Endpoints are typically a decrease in symptoms (e.g. by 50%) and not total remission
3. Initial treatment may require both a BZD & antidepressant depending on patient factors

Non-Pharm: Psychotherapy

- Cognitive Behaviour Therapy (CBT)
  - Cognitive: change thinking patterns that keep people from overcoming fears
  - e.g. panic symptoms do not mean a heart attack
  - Behaviour: change peoples reactions to anxiety provoking situations
  - Slower onset of response vs. pharmacotherapy but may be longer-lasting
  - Improved outcomes if used with pharmacotherapy

Factors that Favour CBT over Pharmacotherapy

- Avoidance behaviours
- Clear ability to concentrate
- Capacity to understand and address psychological factors
- Willingness to try self-help assignments
- Previous failure of pharmacotherapy
- Preference for CBT/Non pharm approach
- Access to CBT
- Previous success with CBT

Non-Pharm: Psychotherapy

- Exposure & response prevention
  - E.g. OCD patient with fear of dirt and germs may be encouraged to wait before hand washing
  - Therapists provide strategies to cope with anxiety
- Desensitization, breathing retraining, relaxation techniques, biofeedback
- Supportive counseling
  - To assist patient with dealing with stress/anxiety
- Psychoeducation

Non-Pharm: Self Management

- Relaxation techniques
  - Massage, meditation, yoga
- Non prescription meds & herbs
- Exercise
- Mental health support groups
- Self-help books
- Internet
- Personal journals

Factors to Consider When Selecting a Medication

- Patient characteristics and preferences
- Past history of treatment/response
- Presence of comorbid psychiatric or medical condition
- Family history
  - previous response of a family member
- Financial status/coverage of meds
- Sensitivity to side effects
- Clinician experience

Reasons for a Muted Response

- Early age of onset
- Inadequate duration of therapy
- Comorbidity – personality disorders
- Biological markers
  - high systolic BP and heart rate
- Substance abuse
  - Alcohol or stimulant abuse

Drugs used for Managing Anxiety Disorders:

Anxiety disorder	First choice	Second choice
•OCD	•SSRIs	•NaSSA , Clomipramine, SGA[X]
•Panic disorder	•SSRIs, BDZ[X] (clonazepam, lorazepam, alprazolam)	•Clomipramine, SNRI
•Social phobia (aka Social anxiety disorder)	•SSRIs, SNRIs	•RIMA, Gabapentin[X], Propranlol
•Generalized anxiety	•SSRIs, SNRI, Buspirone, +/- BDZ[x]	•TCAs
•PTSD	•SSRIs, Clonidine	•NaSSA, SGA[X]
•Specific phobia	•Benzodiazepines[x]	•Propranolol

Antidepressant Dosing for Most Anxiety Disorders

DRUG	STARTING DOSE	DOSE RANGE
Citalopram	10-15 mg daily	20-30 mg
Fluoxetine	5-10 mg daily	20-80 mg
Fluvoxamine	25 mg daily	50-300 mg
Paroxetine	10 mg daily	40-60 mg
Sertraline	25-50 mg daily	50-200 mg
Venlafaxine XR	37.5 mg daily	75-**150** mg
Clomipramine	50-75 mg daily	75-200 mg
Desipramine	10-25 mg daily	150-300 mg
Imipramine	10-25 mg daily	150-300 mg

Phobia Treatment

- Simple phobias: Exposure therapy (90%) CBT
- Performance phobia:
  - Alprazolam 0.25 mg prn
  - Lorazepam 0.5 mg prn
  - Propranolol 10-20 mg prn

Benzodiazepines (BDZ)

- Relatively quick acting (1-5 days)
- Generally used for short term treatment of insomnia or anxiety
- Quick response may help to build relationship
- Usually well tolerated in the short term
- Evidence for efficacy, but first line use is not recommended except as an adjunct during onset of treatment
- May be useful for those who don’t respond to antidepressants alone
- Use lowest effective dose for shortest period of time where possible

BDZs Cont'd

- BDZs considered 'targeted substances' in Canada
- Can interfere with CBT treatment or driving if patient is too sedated
- Some patients are concerned about long term use while others are concerned about withdrawing a medication that has helped them in the past
- Tolerance to sedation may be seen by 2-3 weeks, however tolerance to anxiety/ "anti-seizure" effect is highly variable
- Use should be avoided (where possible) in patients with a previous history of alcohol or drug abuse

Benzodiazepine Adverse Effects

1. Drowsiness/tiredness
2. Incoordination
3. Headaches
4. Cognitive impairment
5. Anterograde amnesia
6. Dizziness
7. Respiratory depression
8. Paradoxical effects
9. Muscle weakness

Pharmacokinetic Comparison

Generic Name	Elimination half-life (hr)	Active Metabolite	Pathway of metabolism	Rate of Onset of Action	Indication/Uses
Alprazolam	12 - 15	N	Oxidation	Intermediate	A, PA
Chlordiazepoxide	> 100	Y	Oxidation	Intermediate	A,AW,SE, PS
Clonazepam	20 - 80	N	Oxidation	Fast	A,E
Clorazepate	> 100	Y	Oxidation	Fast	A, AW, E
Diazepam	> 100	Y	Oxidation	Very fast	A,AW,MS,PS,SE
Flurazepam	> 100	Y	Oxidation	Fast	S/H
Lorazepam	10 - 20	N	Conjugation	Intermediate	A, AW, S/H, SE
Oxazepam	5 - 14	N	Conjugation	Slow	A, AW, S/H
Temazepam	10 - 20	N	Conjugation	Intermediate	S/H
Triazolam	1.5 - 5	N	Oxidation	Intermediate	S/H

A = Anxiety, AW = Alcohol withdrawl, E = Epilepsy, MS = Muscle spasms, PA = Panic attacks, PS = Perioperative sedation, SE = Status Epilepticus, S/H = Sedative/Hypnotic

Buspirone

- Anxiolytic & weak antidepressant properties
- Useful for GAD
- Less drowsiness and psychomotor impairment than BZD
- Mode of action is dose dependent
  - Low doses (5-30 mg):
    - presynaptic partial agonist at 5-HT_{1A} receptors
  - High doses (30-60 mg):
    - postsynaptic partial agonist at 5- HT_{1A} receptors

Comparison of Anxiolytics

BZD	BUSPIRONE
Potentiate GABA	Modulates serotonin
Variable onset; Effective PRN	Slow onset (3-5 weeks); Not effective PRN
Anxiolytic, sedative, muscle relaxant, anticonvulsant	Chronic anxiety disorders, depression, irritability, aggression
S.E.: sedation, ataxia fatigue, depression memory impairment	S.E.: dizziness, nausea, nervousness, headache, paresthesias
Tolerance, withdrawal	No abuse potential
Interacts with alcohol	No alcohol interaction

Efficacy of Anxiolytics

Many of these listed are adjunctive and imply that they are not often used first line for these indications and have little evidence to support their use. Hence, data on this table may differ from the other tables.

Disorder	BZD	Buspirone
GAD	+	+ (first line)
Panic Disorder	alprazolam,lorazepam, clonazepam (adjunctive)	-
Social Phobia	alprazolam, clonazepam (adjunctive)	adjunctive
OCD	If SSRIs not helpful	adjunctive
PTSD	adjunctive	adjunctive

Choice of Antidepressant

1. Evidence: First line consideration for anxiety disorders given overall long-term effectiveness (except specific phobias)
2. Patient characteristics & preferences
   -E.g. Past response, drug interactions, current symptoms, age
3. Receptor and neurotransmitter activity define selectivity, potency and side effects
4. Aim to treat for year
5. Comorbid illnesses
6. Toxicity in overdose
7. Cost

Antidepressants Used in Anxiety Disorders

DRUG	GAD	PANIC DIS.	SOC. PHOBIA
SSRIs	+	+	+
Venlafaxine	+	2nd	+
Bupropion	-	-	-
Tricyclics	clomipramine imipramine	clomipramine	-
MAOI or RIMA	-	moclobemide phenelzine	moclobemide phenelzine
Mirtazapine	Prelim. Data	-	-

Antidepressants Used in Anxiety Disorders

DRUG	OCD	PTSD
SSRIs	+	+
Venlafaxine	-	-
Bupropion	-	-
Tricyclics	Clomipramine 2nd	amitriptyline imipramine
MAOIs	-	phenelzine
Mirtazapine	2nd	2nd

Monitoring Parameters

- Target symptoms
  - Have they been reduced? To what extent? What symptoms are still present and to what degree?
  - Symptom diary or checklist
  - Check q 3 months
- Overall functioning
- Adverse effects associated with treatment selected
- Possible drug interactions

Factors to consider…

Antidepressants prescribed? Consider:

- The time required to see a benefit (4-6 weeks); take as prescribed; treatment for a year or longer
- May initially worsen agitation (dose-related)
- Barriers to compliance
- Not addictive
- Don't discontinue suddenly
- Counsel on side effects (and some management strategies) & special precautions
- Drug interactions (if applicable)

Factors to consider...

Using Benzodiazepines? Consider:

- Not increasing dose without discussing with prescriber
- The intended length of treatment (initial treatment is usually 2-6 wks)
- Issues regarding the potential for physical dependence/abuse (their concerns, past history in family)
- Initial identification of patients at risk of bdz dependence/withdrawal
- Not discontinuing them suddenly
- Side effects (not driving initially, avoid alcohol)

Internet Websites on Anxiety Disorders

1. National Institute of Mental Health http://www.nimh.nih.gov/anxiety/anxiety.cfm
2. Anxiety Disorders Association of America http://www.adaa.org/
3. National Depressive and Manic Depressive Association http://www.ndmda.org/
4. Obsessive Compulsive (OC) Foundation http://www.ocfoundation.org
5. Social Phobia/Social Anxiety Association http://www.socialphobia.org/
6. National Center for PTSD http://www.ncptsd.org/

Guidelines for Assessing and Treating Anxiety Disorders

- Evidence-based guidelines for the pharmacological treatment of **anxiety disorders**: *J Psychopharmacol* 2005;19(6):567-96. http://www.bap.org.uk/consensus/Anxiety_Disorder_Guidelines.pdf
- Canadian Psychiatric Association. Can J Psychiatry 2006; 51 (8) Suppl 2; 9S-91S
- American Psychiatric Association Practice Guidelines (panic disorder)
  - http://www.psych.org/psych_pract/treatg/pg/pg_panic.cfm
- New Zealand Guideline Group
  - http://www.nzgg.org.nz/library/gl_complete/anxiety/index.cfm
- The Assessment and Treatment of Children and Adolescents With Anxiety Disorder
  - http://www.aacap.org/clinical/Anxtysum.htm