Safer Treatments for Anxiety and Insomnia

Maine Independent Clinical Information Service • 2019

MICIS
Maine Independent Clinical Information Service

Take Home Messages:

- Benzos are neither safe nor effective for long-term use
- Risk of death increases 4-10x when benzos & opioids co-prescribed
- 'Z-Drugs,' gabapentin/pregabalin & carisoprodol are also risky to co-prescribe with opioids
- Enlist Behavioral Health support & start benzo tapers
- Prescribe naloxone to all pts currently co-prescribed benzos & opioids

! Non sedative-hypnotic treatment of ANXIETY

- assure proper diagnosis; anxiety may be a symptom of multiple psychiatric conditions
- rule out underlying medical problems
- consider medication side-effects as a cause of anxiety-related symptoms
- initiate psychotherapy and behavioral treatments; many people must try more than one provider before finding a match
- exercise has benefit for all
- benzodiazepines may cause harm in PTSD, avoid prescribing
- SSRIs/SNRIs are first line pharmacologic treatments for anxiety, trauma and OCD
  - caution in patients with bipolar disorder if not on mood stabilizer
  - start at low doses, but increase to moderate to high doses
  - clinical response to SSRI/SNRI can take 12-16w; therapeutic effect can increase over 6-12mos

Evidence-based medication treatments for Anxiety & PTSD

Class/Medication	Anxiety	PTSD
SSRI	X	X
SNRI	X	X
TCA	X	X
mirtazapine	X	X
buspirone	X	
hydroxyzine	X	
pregabalin/gabapentin*	X	
propranolol	X	
prazosin/clonidine/guanfacine		X
nefazodone		X

*some abuse potential, but less than benzos; can potentiate respiratory depression when combined with opioids

Reference: SFNH, Table 8.

Non sedative-hypnotic treatment of INSOMNIA

- Treat co-morbidities (depression, pain, movement disorders, sleep study to assess for sleep apnea)
- Eliminate activating medications/substances
- Employ psychological (e.g. CBT specifically for insomnia) and/or behavioral treatments (e.g. sleep diary) to restructure maladaptive cognitions and promote healthy sleep habits/sleep hygiene
- Consider concurrent SHORT-TERM pharmacological treatment

Evidence-based medication treatments for Insomnia

Doxepin	3-10mg	avoid doses >10mg as anticholinergic SEs
Gabapentin	100-200mg	also helpful for neuropathic pain
Mirtazapine	7.5-45mg	lower doses more sedating, can increase appetite/weight/triglycerides
Ramelteon	8mg	melatonin agonist, mild therapeutic effect, variable insurance coverage
Trazodone	12.5-300mg	start at low doses, effects may persist into morning (*not FDA approved for insomnia)

What about additional medications/supplements for insomnia?

Amitriptyline	possible use for **insomnia combined with depression** (*not FDA approved for insomnia)
Melatonin	most **useful in elderly** (lower levels of exogenous melatonin), safe when used for 3 mos or less; useful in **jet lag** (combine w/daytime sunlight)
L-tryptophan	**2 of 3** published studies showed **positive** outcomes for sleep, possible GI upset
Trial of "true" placebo	True placebo=pts unaware they might receive a placebo; found **small to moderate effect**
Diphenhydramine	**little evidence** for insomnia, may cause next day sedation due to long half-life, multiple other side effects
Valerian	meta-anaylsis of 11 randomized trials found **no evidence of benefit**, other studies with conflicting results, can cause daytime sleepiness & vivid dreams, possible w/d sxs with chronic use

Sources: UTD & SFHN Table 11

Sleep Hygiene

- Limit daytime naps
- Go outdoors and experience natural light during the day
- Exercise at least 10 minutes a day, preferably in the morning
- Avoid stimulants (caffeine, nicotine) & food near bedtime
- Establish a regular bedtime routine
- Turn off all electronic devices one hour before sleep
- Keep sleep area comfortable, cool, quiet & dark

Controlled Substance Prescribing Best Practices

- Document informed consent and treatment agreement
- Discuss a clear plan
- Be explicit about length of rx
- Don't initiate co-prescribing of opioids & benzos/sedatives
- See patient regularly (at least every 90 days)
- Do PMP checks + urine drug screens + pill counts
- Monitor efficacy + side effects
- Document, document, document

SAMPLE:
Informed Consent for Benzodiazepines for Anxiety Disorders

prepared by the Bangor Area Controlled Substance Work Group (BACSWG), Adopted November, 2015

Uses: I understand that benzodiazepines (drugs like lorazepam or Ativan, diazepam or Valium, clonazepam or Klonopin, alprazolam or Xanax) are sometimes used to lower high levels of anxiety. Some people report improved levels of anxiety when they take these drugs, but I understand that these drugs may not help people with anxiety when taken for more than 12 weeks. There are no studies that have answered this question.

Benefits Expected: Improved function and lower levels of anxiety

Alternatives: I understand that benzodiazepines are not the first choice of treatment for anxiety disorders. There are safer drugs that work better called selective serotonin reuptake inhibitors (SSRIs) and serotonin norepinephrine reuptake inhibitors (SNRIs), as well as cognitive behavioral therapy (counseling that teaches skills to manage anxiety).

Risks: It has been explained to me and I understand that the use of benzodiazepines can cause: Slowed thinking and reaction times, poor focus, confusion, and memory loss. Less control of my emotions and actions. Depression. Weakness. Falls and fractures (broken bones), especially in the elderly. Car accidents. Breathing problems (particularly with lung disease such as asthma, COPD, or sleep apnea). Excessive sedation (sleepiness). Intoxication. Tolerance, withdrawal sickness. Dependence (of the body and mind), substance abuse, and addiction. Increased risk of all side effects when used with alcohol. Accidental overdose, especially when taken with certain pain drugs known as opioids. Higher doses of these drugs cause even greater risks. These drugs may increase my risk of being the victim of a crime. These drugs create a greater risk if I have a history of addiction (especially to opioids and alcohol).

I also understand: That using alcohol, along with benzodiazepines, is dangerous and that I must not use alcohol while I am taking benzodiazepine drugs. That using marijuana, along with benzodiazepines, is dangerous as both may delay my reactions and increase my risk of accident. That using opioids, along with benzodiazepines, is dangerous. I should avoid using opioids while I am taking benzodiazepine drugs. That all of these risks are especially high in those age 65 and older.

My provider and I have tried other more effective and safer treatments such as Cognitive Behavioral Therapy (counseling), SSRIs, SNRIs, and exercise. I understand the risks described here and I know that by taking benzodiazepine drugs I accept all of these risks. I will continue to work with my providers to explore other safer options to manage my excessive anxiety.

Treating anxiety:
Medications/Supplements in Addition to SSRI/SNRI/TCA

(see also table bottom of page 1)

Medication/Supplement	Daily Dose Range	Comments
Buspirone	10-60 mg	Best in conjunction w/SSRI/SNRI. Onset of effect 2 weeks, thus scheduled is better than PRN.
Hydroxyzine	25-400 mg	Can be used for short term/prn. Anticholinergic at high doses.
Pregabalin*	150-600 mg	Can use when tapering long-term benzo therapy. Taper over at least a week when discontinuing.
Gabapentin*	100-1200 mg three times daily	
Propranolol	10-240 mg in divided doses	Caution in reactive airways. Watch HR/BP.
Prazosin	1-15 mg	Trauma/PTSD related nightmares. Titrate carefully watching BP (esp 1st dose).
Clonidine	0.1-0.6 mg	Decreases CNS sympathetic outflow. Helps agitation & hyperarousal. Watch BP/HR.
Guanfacine	1-4 mg	Decreases CNS sympathetic outflow. Helps agitation & hyperarousal. Watch BP/HR.
Nefazodone	200-600 mg in divided doses	Take on empty stomach. Avoid in liver disease & monitor LFTs.
Chamomile	1100 mg	One small randomized trial showed modest efficacy. Minimal SEs.
Kava	125-250 mg	Several studies found benefit over placebo but inconsistent. Can cause hepatotoxicity, multiple other SEs.
L-theanine	200-400 mg	Possible benefit in psychotic d/o related anxiety, but no evidence in GAD. Minimal SEs.
Inositol	12-20 g	Limited evidence, small studies for panic d/o & OCD. Possible flatulence & mania.

*some abuse potential, but less than benzos; can potentiate respiratory depression when combined with opioids

Reference: SFHN Tables 9 & 11; Prescriber's Letter

Disclaimer

These are general recommendations only; specific clinical decisions should be made by the treating healthcare provider based on an individual patient's clinical condition.

References

- San Francisco Health Network Behavioral Health Services: Medication Use Improvement Committee, "Safer Prescribing of Sedative-Hypnotics Guideline," Approved May 2018, accessed online.
- Bangor (Maine) Area Controlled Substance Work Group documents, obtained from Committee Chair Noah Nesin, MD, October 2018.
- UpToDate online database, accessed September 2018.
- Prescriber's Letter online database, accessed November 2018.

Funding Statement/Disclosure

MICIS is administered by the Maine Medical Association with funding from Maine DHHS. MICIS does not accept compensation from pharmaceutical companies. Not all medications referenced in this document have FDA indications for the discussed conditions ('off-label use disclosure'). This monograph was created in support of accompanying live educational activities. Change to: This monograph was created to support live educational activities.

FMI Maine Independent Clinical Information Service (MICIS) c/o Maine Medical Association, MICISMaine.org, 207.622.

Maine Medical Association

MICIS
Maine Independent Clinical Information Service

Department of Health and Human Services
Maine People Living Safe, Healthy and Productive Lives
Paul R. LePage, Governor Ricker Hamilton, Commissioner