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Editor-in-Chief

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IN THIS ISSUE

Focus of the Month:
Anxiety

Learning Objectives
After reading these articles, you should be able to:

1. Evaluate the current role of benzodiazepines for patients with anxiety disorders.
2. Describe the impact of the anxious distress specifier in diagnosing and treating patients with depression and anxiety.
3. Summarize some of the current findings in the literature regarding psychiatric treatment.

Benzodiazepines for Anxiety: Where They Fit In

Michael Posternak, MD. Psychiatrist in private practice, Boston, MA

Dr. Posternak has disclosed that he has no relevant financial or other interests in any commercial companies pertaining to this educational activity.

Benzodiazepines (BZDs) are widely used, rarely studied, and much maligned. So where exactly do they fit in today's medication arsenal for treating anxiety? In this article, I will discuss when BZDs are appropriate and when they are not, and how to choose among the various BZDs.

But before doing so, let's first address the elephant that always seems to be lurking in the BZD room: their addictive potential.

In Summary

- With the exception of current opioid users, benzodiazepines can be a safe and effective anxiety treatment for most patients.
- Studies show that the abuse potential of BZDs is greatly overstated.
- Which BZD to prescribe, and the dose, should be based on the patient's specific anxiety disorder.

"I've heard that benzodiazepines are highly addictive; are they?" It's one of the most common concerns patients share with me. While BZDs can be abused, the

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Q&A With the Expert

Anxious Distress: A New DSM Diagnosis

Mark Zimmerman, MD

Director of the Partial Hospital Program and Adult Outpatient Psychiatry at Rhode Island Hospital

Dr. Zimmerman has disclosed that he has no relevant financial or other interests in any commercial companies pertaining to this educational activity.

There's a new diagnosis in the DSM-5 called anxious distress. But is this truly a new diagnosis, or just another way of defining depression? This month, we spoke with Mark Zimmerman, MD, a clinician and leading researcher on the topic of anxious distress, to get some answers.

TCPR: We've been learning about a new understanding or new diagnosis of combined anxiety and depression, which the DSM-5 is calling anxious distress. Can you give us your take?

Dr. Zimmerman: Well, it's a new specifier. Is it a new diagnosis? That's something that research is being done on right now. To what degree does it agree with other ways of defining anxious depression? Details on that are just beginning to emerge. We just published a paper looking at the concordance between the DSM anxious distress specifier and the Hamilton Depression Scale (HAM-D) anxiety somatization factor, and that approach toward identifying anxious distress (Zimmerman M et al, *J Nerv Ment Dis* 2018;206(2):152–154). We found that, while they're significantly related, the degree of co-occurrence between the two is rather modest, if not poor. But the research into this is just beginning.

TCPR: Can you tell us more about depression with anxious distress? How do you diagnose it exactly, and what are the criteria?

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research shows that the vast majority of those abusing BZDs are also concurrently abusing other substances (Busto UE at al, *J Clin Psychopharmacol* 1996;16(1):51–57).

A task force assembled by the American Psychiatric Association that looked at BZD abuse concluded that the number of patients actually abusing BZDs is "relatively small"—perhaps less than 1% (Rifkin A et al, *Am J Psychiatry* 1989;146(10):1331–1332). Even most former substance abusers do not appear to be at greatest risk for abusing BZDs (Posternak MA and Mueller TI, *Am J Addict* 2001;10(1):48–68).

Opioid use, however, presents a clear exception to this rule: Opioid users often report utilizing BZDs specifically to enhance the opioid "high," and the co-use of opioids with BZDs has negative consequences for general health, treatment outcome, and overdose lethality (Jones JD et al, *Drug Alcohol Depend* 2012;125(1-2):8–18). BZDs are therefore contraindicated in current opioid users.

What about the fear that BZDs may trigger relapse of other substance use disorders, such as to alcohol? Most research suggests that just the opposite is true. If anything, BZD use may lead to lower rates of substance relapse (Caplan RD et al, *Soc Sci Med* 1985;21(8):887–898).

Similarly, while it is true that long-term BZD use can induce physiological dependency and withdrawal symptoms, this is not the same as having a substance use disorder. If it were, then paroxetine, venlafaxine, and lithium, among others, would also have to be considered "addictive" medications. Rather, it just means that BZDs need to be tapered off slowly—as is done with many antidepressants and mood stabilizers. For patients who remain hesitant to even try using BZDs, I suggest a limited supply (eg, 10–25 pills per month). I then reassure them, "You can't get physically dependent on a medication you don't take every day."

How to choose among the BZDs

BZDs all share the same mechanism of action: increasing GABA transmission, which has direct anti-anxiety effects, plus sedative effects at higher doses. The main distinction between BZDs is how quickly they work and how long they last. Typically, the faster they kick in, the sooner they wear off; the slower they kick in, the longer they last. The one exception to this rule is diazepam. Because it is lipophilic—meaning it enters fat cells and is slowly released from these cells over time—diazepam works quickly but lasts a long time (this dual feature makes diazepam particularly well suited for treating insomnia).

While there are over a dozen BZDs on the market, you probably will only ever need to use 5 or 6 of the most commonly prescribed ones. These can be ranked from fast-acting to longest-acting in the following order: *alprazolam -> lorazepam -> clonazepam -> alprazolam XR.*

Diazepam does not fit neatly into this chart because, as stated, it works quickly and lasts a long time. One other BZD that can come in handy is clonazepam wafers. These are taken sublingually and work even faster than alprazolam (alternatively, some clinicians have found that patients can bite traditional BZDs and chew them under their tongue, which allows them to be absorbed more quickly). We will see how these pharmacokinetic differences may affect our choice of BZD depending on the purpose. (For a table of frequently prescribed BZDs and their characteristics, see page 3.)

Prescribing BZDs for anxiety: The DSM matters!

Anxiety is a fear-driven state of internal distress. It is often useful to distinguish between mental anxiety (worries, ruminations, obsessions) and physical anxiety (chest pain, palpitations, sweating, etc). While patients typically know when they are "anxious," they don't necessarily distinguish between various anxiety states. The DSM-5 lists 6 distinct anxiety disorders, and I would argue that the role of BZDs in each specific anxiety disorder is distinct.

As a result, it is not sufficient to simply diagnose your patient as having "anxiety." Since each disorder may require a different treatment plan, you should always evaluate which anxiety disorders a patient suffers from. In fact, most anxious patients suffer from multiple anxiety disorders. For example, a recent large-scale epidemiological study found that about half of all patients with generalized anxiety disorder have at least 1 other anxiety disorder (Ruscio AM, *JAMA Psychiatry* 2017;74(5):465–475).

BZDs for each specific anxiety disorder

Panic disorder

Panic attacks are called "panic" for good reason: The sudden onset of overwhelming dread—accompanied by physical symptoms, such as chest pain, palpitations, and shortness of breath—is one of the most crippling experiences patients face. In these situations, patients typically want immediate relief, so the best choice is usually alprazolam (or clonazepam wafers). For many patients, just knowing they have an antidote in their back pocket goes a long way toward staving off future panic attacks. When panic attacks are infrequent, this will typically suffice. But

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Benzodiazepines for Anxiety: Where They Fit In

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when panic attacks occur more commonly, daily prophylactic medications may be necessary. In these cases, SSRIs may be part of a better long-term solution.

But SSRIs don't always work, and many patients either do not tolerate them or would prefer to avoid taking daily medications. If so, cognitive behavioral therapy (CBT) should be offered as an alternative. CBT teaches patients how to overcome panic attacks on their own, and therefore—in contrast to medications—can provide an actual cure for panic disorder.

There is one crucial point to keep in mind: CBT only works when patients experience their anxiety. When BZDs help, they actually may *prevent* the long-term benefits that CBT can offer (Marks IM et al, *Br J Psychiatry* 1993;162:776–787). Why? Because exposure—both to the feared situation *and* to the anxiety itself—is the mechanism by which CBT works. If BZDs eliminate patients' physiological anxiety, then they will not have the opportunity to gain mastery over their anxiety symptoms.

What about patients who want immediate relief from their panic attacks, but also want to engage in CBT so they can get off medications altogether? In these instances, you can offer BZDs now for immediate relief, and in coordination with their CBT therapist, you can plan to wean them off their BZDs. In these instances, the tapering off BZDs becomes the exposure exercise itself: The expectation is that the anxiety may increase during the tapering process. Thus, patients are now *choosing* to face their anxiety.

Generalized anxiety disorder

Patients with generalized anxiety disorder (GAD) are chronic worriers. Worrying has its advantages, but it can also be extremely taxing. Although SSRIs/SNRIs and buspirone are FDA-approved options for GAD, CBT teaches people how to worry less. Because GAD patients have chronic, daily anxiety, BZDs are not an ideal choice since they would only offer sustained relief when taken daily over an extended period of time. BZDs then are best reserved as a last-resort option for the most severe GAD patients, who have failed on CBT, SSRIs, and buspirone. In these cases, and given its long half-life, alprazolam XR is usually the best option. It can sometimes be dosed once a day, but more often requires BID dosing (typical range 0.5 mg–2 mg QD or BID).

Characteristics of Commonly Used Benzodiazepines

Generic Name	Brand Name	Equipotent Dose (mg)	Typical Dose (mg)	Upper Limit Dosage (mg/day)	Onset of Action (mins)	Duration of Action (hrs)
Alprazolam	Xanax	0.5	0.5–1	4–6	20–30	2–3
Alprazolam XR	Xanax XR	1	0.5–2	4–6	30–120	8–12
Clonazepam	Klonopin	0.25	0.5–2	4–6	30–60	4–6
Clonazepam wafers	Klonopin Wafers	0.25	0.5–2	N/A	10–20	1
Diazepam	Valium	5–10	5	10–20	20–30	8
Lorazepam	Ativan	1	1–4	4–6	30–60	3–4

Obsessive-compulsive disorder

Patients with OCD have intrusive, distressing thoughts (obsessions) often associated with compensatory behaviors (compulsions). Despite the high level of anxiety OCD patients can display, BZDs have never been shown to be useful for OCD's core symptoms, and therefore have no role in treating this disorder.

Social anxiety disorder

Social anxiety disorder (SAD) can range from mild to debilitating, and it can be circumscribed (only manifesting in certain scenarios, such as public speaking) or generalized. Since it potentially limits social functioning and career advancement, more than perhaps any other anxiety disorder, SAD can affect one's quality of life. Once again, *unless* the social situation is circumscribed or predictable, CBT and SSRIs will typically be your first-line options. For example, a patient who gets very anxious in meetings may benefit from a BZD 30–60 minutes before that meeting. The same would apply for someone who gets anxious before going on a date (although the patient would need to careful about drinking alcohol) or giving a speech. If physiological symptoms are prominent (particularly palpitations), beta blockers, such as propranolol 20 mg–40 mg, may be a better choice; they are non-sedating and do not impair cognition.

Specific phobias

You may not typically screen for specific phobias. After all, how many patients come in looking for help with their fear of snakes or spiders? But there are two phobias that can be quite debilitating: flying phobias and driving phobias.

Patients presenting for depression (and even anxiety) often will not even mention these phobias unless asked directly. If you do elicit a history of such phobias, you will have the opportunity to make a significant difference in a patient's quality of life. Maybe a patient hasn't been able to travel abroad with family, or for years has taken back roads rather than highways to get to work.

CBT can address fear of flying (though SSRIs usually don't help). But if a patient flies only occasionally, as-needed BZDs are often the perfect solution. They provide consistent relief for most patients that will, at a minimum, allow them to travel wherever they want. For those with more severe anxiety, I use the "sledgehammer" approach: "Take as much medication as you need to reduce your anxiety. As long as you are not driving once you land, the worst that can happen is you will fall asleep during the flight." Due to its fast-acting nature, alprazolam will usually be the best choice for flying phobias.

In studies, alprazolam has routinely been dosed up to 6 mg/day and, in panic disorder trials, 10 mg/day, so even very high doses are safe. For patients who get anticipatory anxiety, I instruct them to "get ahead of their anxiety," much as pain patients are instructed to "get ahead of their pain." This could mean taking alprazolam the night before a flight or on the way to the airport. If the anxiety continues, the patient should keep taking alprazolam every 20–30 minutes.

Since BZDs sedate and affect coordination, driving phobias present a more difficult dilemma. Nevertheless, I

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Expert Interview

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Dr. Zimmerman: There are five criteria: feeling keyed up or tense, feeling unusually restless, impaired concentration, feeling that something awful will happen, and feeling that you might lose control. Regarding the concentration item, it's not just the major depressive disorder (MDD) criterion of impaired concentration; rather, the individual is supposed to attribute it to being anxious or worrying.

TCPR: How are those symptoms related to the typical anxiety disorders or the discrete anxiety disorders? It sounds like they are similar to generalized anxiety.

Dr. Zimmerman: Absolutely; they are similar. Several of them are diagnostic criteria for generalized anxiety disorder. However, only two-thirds of the individuals who meet the anxious distress specifier are also diagnosed with generalized anxiety disorder, and one-third of the individuals who are not diagnosed with the anxious distress specifier are diagnosed with generalized anxiety disorder. So, it's not completely concordant. The other anxiety disorder that it seems related to is panic disorder—that fear of losing control.

TCPR: So, how is this new specifier helpful for practicing psychiatrists?

Dr. Zimmerman: I think its potential importance is in simplifying the assessment of anxiety. Rather than having to go through and assess all of the anxiety disorders, it would be much simpler to assess the five anxious distress criteria. There are a number of studies that show how comorbidity gets missed and is not diagnosed in routine clinical practice. We published one study that looked specifically at the issue of recognizing anxiety disorders in depressed patients and found that all anxiety disorders are under-recognized (Zimmerman M and Chelminski I, *J Psychiatr Res* 2003;37(4):325–333). Social phobia, by the way, is the most frequently underdiagnosed and under-recognized anxiety disorder—we learned that by comparing the frequency of diagnoses based on unstructured clinical interviews with diagnoses based on semi-structured interviews. So, in routine clinical practice, comorbid disorders get missed. Considering that, what may be most helpful with this specifier is that it is more clinically useful than assessing all the anxiety disorders.

"When the anxiety is uncomfortable and the patient is engaging in a lot of avoidance behavior, I'll use therapy to try and overcome that tendency to avoid. But when a patient's anxiety is overwhelming or more incapacitating, I'm more willing to add a medication."

Mark Zimmerman, MD

TCPR: Based on the five criteria you mentioned earlier, can you talk about how we would then assess whether patients are suffering from anxious distress?

Dr. Zimmerman: I'd start by assessing their mood state, and I would establish the negative mood states of depression—you know, the sadness, as well as establishing the presence or absence of anxiety and whether they tend to worry about things. I'd inquire about their ability to focus and concentrate, and if they say concentrating is an issue, then I'd ask them what they attribute that to, and to what degree they have problems concentrating. Is it because their mind is on the things that they are anxious about? So, I think it would be relatively straightforward like that.

TCPR: How prevalent is impaired concentration?

Dr. Zimmerman: Impaired concentration is one of the more frequent signs of MDD. Obviously, low mood is the most frequent, but impaired concentration is up there. In our research, we found that three-quarters of individuals within a major depressive episode reported experiencing impaired concentration due to worry (Zimmerman M et al, *J Nerv Men Dis* 2006; 194(3):158–163).

TCPR: Can you tell us how you assess for the criterion of feeling keyed up?

Dr. Zimmerman: We follow the typical approach used in semi-structured interviews, and that is to ask direct questions. So, we would ask, "Have there been times when you've felt keyed up or tense?" And then, because we are interested in rating severity, we would ask, "How often did you feel this way?" and, "How strong was the feeling?"

TCPR: What would you ask the patient to assess the criterion of feeling unusually restless?

Dr. Zimmerman: In that case, we would ask, "Have you felt restless? Is it hard to sit still?" And if it's not observed in the interview, we would inquire whether while at home the person often gets up just to walk around due to feeling so restless.

TCPR: And how about the fear that something awful might happen?

Dr. Zimmerman: We straightforwardly ask the patient, "Have you had a sense that something terrible might happen?" We then follow up and inquire, "Can you tell me anything in particular about that?"

TCPR: Finally, what should we ask to determine loss of control? What do you say to a patient who asks, "What do you mean by losing control?"

Dr. Zimmerman: What I ask is, "Have you felt like you were not going to be able to control your behavior and just lose it? Do you feel like you're having a nervous breakdown? Do you feel like you can't control your emotions?"

TCPR: To arrive at a diagnosis of anxious distress, do patients need to meet all 5 criteria?

Dr. Zimmerman: No, only 2 of the 5, which is why I suspect all studies have found that somewhere between 55% and 75% of individuals meet the criteria for anxious distress. In fact, in a recent *JAMA Psychiatry* issue, there is a report from the NESARC study of MDD in the community. This is the first community sample of individuals who were

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Expert Interview

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diagnosed with depression, and a little bit more than 70% of those in a major depressive episode met the anxious distress specifier (Hasin DS et al, *JAMA Psychiatry* 2018;10.1001.4602).

TCPR: So, anxious distress is a pretty prevalent thing, and my guess is that it will be diagnosed even more by psychiatrists going forward. Considering that, let's talk about treatment. What are your thoughts here, and what is the literature telling us about medications?

Dr. Zimmerman: Efficacy cuts across a lot of different medications. And obviously, all these meta-analyses and pooled analyses indicate that the medication under study was effective for the anxious depressed patient. It's important to point out that some of these trials could contain biases (Wang SM et al, *Expert Rev Clin Pharmacol* 2018;11(1):15–25). But there are a lot of medications to choose from, and there are reports on the effectiveness of vortioxetine, venlafaxine, imipramine, and mirtazapine, in addition to a report on quetiapine (Thase ME et al, *Depress Anxiety* 2012;29(7):574–586). There's a lot of research touting the efficacy of SNRIs, SSRIs, and the newer generation of antidepressants.

> **"Impaired concentration is one of the more frequent signs of MDD. Low mood is the most frequent, but impaired concentration is up there. In our research, three-quarters of individuals within a major depressive episode reported impaired concentration due to worry."**
>
> Mark Zimmerman, MD

TCPR: Was there any other interesting research you came across relating to medications?

Dr. Zimmerman: Yes. There was a study comparing bupropion and SSRIs, and they looked at the HAM-D anxiety somatization factor and found that SSRIs were better than bupropion. I don't think clinicians are all that enthusiastic about prescribing bupropion to highly anxious depressed individuals, so this study confirmed that clinical intuition (Papakostas GI et al, *J Clin Psychiatry* 2008;69(8):1287–1292). We also published a paper back in 2004 looking at what factors influenced antidepressant choice. Anxiety was the most common factor that influenced clinicians prescribing, and clinicians clearly were disinclined to prescribe bupropion when anxiety was a determining factor in choosing a medication (Zimmerman M et al, *Am J Psychiatry* 2004;161(7):1285–1290).

TCPR: What about some treatment alternatives to psychopharmacology? What's your view on psychotherapy for treating anxiety and depression?

Dr. Zimmerman: I'll often start by either doing therapy myself or referring patients to other therapists. It's only when the anxiety is overwhelming, more incapacitating, that I'm more willing to add a medication. But when the anxiety is uncomfortable and the individual is engaging in a lot of avoidance behavior, I'll use therapy to try and overcome that tendency to avoid. And I don't necessarily mean avoidance in the extreme phobic sense, but just avoiding things that are uncomfortable. I'll talk to patients about how life is often uncomfortable, but they can't run away from it. I tell them that it's more a matter of learning how to manage it. Rather than avoiding it, what skills can be taught to help cope with it? Mainly, they are just avoiding dealing with the usual things in life—they need to pay the bills and the mail is piling up, for example. When they are avoiding dealing with the reality of the situation, of course they are just digging a deeper hole for themselves.

TCPR: Are there any final thoughts on the subject that you'd like to leave us with?

Dr. Zimmerman: I'm happy we touched on the psychotherapeutic aspect of this—I think that's important. It's not just about prescribing medication or picking another medication. In fact, with a number of individuals, when they come in to our partial hospital program, I begin a negotiation with them and say, "Let's not start medication now. Let's wait a couple of days. Let's see how beneficial therapy can be and then we can reevaluate. I don't want to deprive you of the opportunity of learning that you're able to feel better without making any changes in medication."

TCPR: Thank you for your time, Dr. Zimmerman.

Research Updates IN PSYCHIATRY

ADHD

Neurofeedback and Adult ADHD

REVIEW OF: Schonenberg M et al, *Lancet Psychiatry* 2017;4(9):673–684

With neurofeedback, patients are hooked up to an EEG and shown images through various forms of media. The idea is that the EEG can detect brain waves that are associated with improvement in various symptoms, and then the patient can be taught to produce "healthier" brain waves. Some studies have shown that neurofeedback improves ADHD in children and adolescents. However, the results are controversial, and neurofeedback in general needs further research to prove its efficacy. (See *TCPR* April 2017 for a Q&A on neurofeedback.)

This investigation tested neurofeedback treatment in adults. The triple-blinded, randomized, controlled study was conducted at Germany's University of Tubingen. Eligible participants met the DSM-IV-TR criteria for ADHD, were ages 18–60, and had no or stable use of medication.

Overall, 118 people were randomly assigned to neurofeedback (38), sham neurofeedback (39), or meta-cognitive group therapy (41). In the neurofeedback group, participants received 30 treatments, while the sham group underwent 15 sham sessions followed by 15 treatment sessions. In the therapy arm, patients attended 12 group therapy sessions. The primary outcome was scores on the Conners' Adult ADHD Rating Scale (CAARS), assessed before treatment, at mid-treatment (8 weeks), after treatment (16 weeks), and 6 months later.

Significant improvement on the CAARS from pre-treatment to the 6-month follow-up was observed for all treatments. For the neurofeedback group, scores dropped from 135 to 104. For sham neurofeedback, they decreased from 132 to 94. For meta-cognitive group therapy, they fell from 138 to 104. Clinical improvements were unrelated to EEG brain activity changes. No serious adverse events resulted from any treatment.

TCPR'S TAKE

These findings suggest EEG neurofeedback is not superior to a sham condition or group psychotherapy in adults with ADHD. Data supporting ADHD EEG neurofeedback remain sparse, but we're interested to see if further research proves it to be an option for adults who do not respond to medications, have significant side effects, or object to using medication. For now, though, we remain skeptical.

—Reban Aziz, MD. Dr. Aziz has disclosed that he has no relevant financial or other interests in any commercial companies pertaining to this educational activity.

ANTIDEPRESSANTS

Is SSRI Efficacy Real, or Just a Placebo Response?

REVIEW OF: Hieronymus F et al, *Molecular Psychiatry* 2017. doi:10.1038/mp.2017.147

Over the last several years, there's been a lively debate about the efficacy of antidepressants. Meta-analyses have shown that antidepressants do outperform placebo in most studies. However, active medications cause more side effects than placebo pills. Thus, it's possible that side effects lead patients to accurately guess that they've been assigned to the active drug group, and this positive expectancy alone could underlie any supposed efficacy of the drug.

But how would you structure a study to resolve this problem? You can't randomly assign patients to the active medication with side effects vs the same active medication without side effects. So, researchers have resorted to the artful use of statistical methods. One of these is called a "mega-analysis." In a mega-analysis, you combine the results of independent studies using data from the individual subjects. This differs from the more common meta-analysis, which combines the results of independent studies using summary data from groups of people.

In a new mega-analysis, the authors reviewed all industry-sponsored, FDA-registered, placebo-controlled trials of paroxetine and citalopram in adults with major depressive disorder. 2,759 patients were included from the paroxetine trials, and 585 patients formed the citalopram trials. The purpose was to compare the response of patients who reported side effects vs those who were side effect–free.

Focusing on the mood item of the Hamilton Depression Rating Scale (HDRS) as the outcome measure, researchers found that among patients who reported no side effects, patients assigned to paroxetine or citalopram did significantly better than those assigned to placebo ($p < 0.001$). Furthermore, looking at the entire sample, there were no significant differences in the reductions in the HDRS-17 depressed mood item at 6 weeks for paroxetine treatment with or without side effects, and for citalopram treatment with or without side effects.

TCPR'S TAKE

This study supports the hypothesis that both citalopram and paroxetine have genuine antidepressant effects caused by their pharmacodynamic properties, and more than just placebo effects.

—Adam Strassberg, MD. Dr. Strassberg has disclosed that he has no relevant financial or other interests in any commercial companies pertaining to this educational activity.

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Below are the questions for this month's CME/CE post-test. This page is intended as a study guide. Please complete the test online at www.TheCarlatReport.com. Note: Learning Objectives are listed on page 1.

1. Which of the following statements about benzodiazepine use is true? (LO #1)
   - [ ] a. Former substance users appear to be at greatest risk for abusing benzodiazepines
   - [ ] b. Benzodiazepine use may lead to lower rates of substance relapse
   - [ ] c. Approximately 5% of patients prescribed benzodiazepines develop a substance use disorder
   - [ ] d. Benzodiazepines are not contraindicated in current opioid users

2. According to a study conducted by Dr. Zimmerman, what percentage of patients within a major depressive episode reported impaired concentration due to worry? (LO #2)
   - [ ] a. 45%
   - [ ] b. 55%
   - [ ] c. 75%
   - [ ] d. 85%

3. You prescribe your patient 0.25 mg of clonazepam for her anxiety. She wants to know how fast she will "feel better" after taking her medication. You share with her that the average onset of action for clonazepam is _____. (LO #1)
   - [ ] a. Approximately 10 minutes
   - [ ] b. 20–30 minutes
   - [ ] c. 30–60 minutes
   - [ ] d. Up to 120 minutes

4. Which of the following criteria does not meet the "anxious distress" specifier within the DSM-5 diagnosis of major depressive episode? (LO #2)
   - [ ] a. Feeling keyed up or tense
   - [ ] b. Feeling that one's anxiety is excessive or unreasonable
   - [ ] c. Feeling that something awful may happen
   - [ ] d. Feeling that one might lose control

5. In a recent study on neurofeedback and adult ADHD, clinical improvements in patients based on the Conners' Adult ADHD Rating Scale were unrelated to EEG brain activity changes. (LO #3)
   - [ ] a. True
   - [ ] b. False

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do prescribe BZDs for driving phobias under the following conditions:

1. The patient is engaged in CBT for the driving phobia
2. The patient's anxiety is so impairing that even getting on the road to do CBT driving exercises is a challenge

What about the risk of an accident? You must discuss this with your patient and document it in your notes, but the reality is that the risk of getting into an accident is probably greater if a patient has severe anxiety than if the patient is taking a BZD that helps alleviate some of that anxiety. For driving phobias, a mid-acting BZD, such as lorazepam or clonazepam, usually works best. Because the risks associated with sedation while driving are inherently greater, it is best to begin with the lowest possible doses and gradually titrate up.

Insomnia

Insomnia is not an anxiety disorder per se, but in many patients who develop acute insomnia, it soon will sound like one. A patient might tell you, "If I don't get a good night's sleep tonight, I'm going to be exhausted tomorrow and won't be able to function at work. I haven't been able to sleep well in weeks. I don't know how much longer I can do this!" Here, it is crucial to educate patients about good sleep hygiene habits, with the main principle being to shift the focus away from how many hours of sleep they get, and to focus instead on sleep efficiency (Edinger JD et al, *JAMA Psychiatry* 2001;285(14):1856–1864). For example, instruct them to get out of bed when they can't fall asleep after

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THE CARLAT REPORT: PSYCHIATRY

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This Month's Focus:
Anxiety

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Neurobiology

Benzodiazepines for Anxiety: Where They Fit In

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a period of time. Due to the potential for tolerance to develop over time and the risk of dependency, for chronic insomnia it is preferable to avoid BZDs. Trazodone, gabapentin, clonidine, and amitriptyline are good first-line options instead.

But in some cases, such as when insomnia is due to a severe, time-limited stressor, BZDs are the ideal choice. A typical example is the patient who complains of work stress from a looming deadline, leading to late-night racing thoughts and sleeplessness. With such acute distress, there is no need to mess around with other agents: Use a BZD to reduce the nighttime ruminations, and dose it aggressively until adequate sleep is obtained.

Given its quick onset of action and long-acting effects, diazepam is often the ideal choice for insomnia. BZDs generally are pretty "clean" in that they don't cause much morning grogginess. Should grogginess occur, instruct your patient to take it earlier in the evening, decrease the dosage, or try a shorter-acting BZD. One thing to note, however, is that short-acting BZDs (such as alprazolam and lorazepam) can help patients fall asleep, but they can also induce middle-of-the-night awakenings as the medications begin to wear off. In these cases, switch to a longer-acting BZD.

TCPR VERDICT: Benzodiazepines are an invaluable tool for treating anxiety and insomnia. Their abuse and dependency potential are vastly overstated. Use them judiciously, and you can provide tremendous relief for your patients.