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CONSULTANT'S CORNER

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What should I prescribe for this patient with panic disorder?

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You see a 28-year-old white male physical education teacher who has visited the emergency department (ED) twice in the past 10 days for episodes of chest pain and shortness of breath, which the ED physician attributed to stress. He tells you he had three or four other less severe episodes during the past month, and he describes several associated symptoms including dizziness, feeling his heart racing, and nausea. He admits that at times he actually thinks he may be going crazy.

What is the likely diagnosis?

This patient most likely suffers from panic disorder, a kind of anxiety state. Panic attacks, as defined in the *Diagnostic and Statistical Manual, Fourth Edition (DSM-IV)*, are manifested by the sudden onset of overwhelming fear accompanied by feelings of impending doom for no apparent reason. Four of 10 possible cardiac, neurologic, gastrointestinal, and respiratory symptoms must be present that develop abruptly and reach a peak within 10 minutes. These symptoms are the consequences of autonomic nervous system hyperactivity. Shortness of breath, dizziness or faintness, palpitation, accelerated heart rate, and sweating are the most common symptoms, although patients also experience trembling, choking, nausea, numbness, flushes, chills, or chest discomfort. Cognitive symptoms such as fear of losing control, fear of dying, and derealization also occur. *DSM-IV* recognizes three types of panic attacks: unexpected (uncued), situationally bound (cued), and situationally predisposed. Unexpected panic attacks are required for a diagnosis of panic disorder, while situationally bound attacks are most characteristic of social and specific phobias.

To meet the diagnostic criteria of panic disorder a person must experience full-blown discrete attacks of anxiety, followed by at least 1 month of persistent fear of another attack and persistent concern, worry, or behavioral changes related to the attacks. The fear of the impending panic attack produces more distress and disability than the attacks themselves. Between attacks, patients have anticipatory anxiety characterized by inhibition, fear of medical illness, role dysfunction, and feelings of helplessness or humiliation. One third develop agoraphobia, a fear of places where escape may be difficult such as bridges, trains, buses, or crowded areas, which usually means more severe panic disorder. The symptoms are not due to medication, drugs of abuse, or a general medical condition.

What is the differential diagnosis of panic disorder?

The differential diagnosis of panic attacks includes hyperthyroidism, hypoglycemia, congestive heart failure, cardiac arrhythmias, pheochromocytoma, audiovestibular dysfunctions, complex partial seizures, caffeinism, excessive use of bronchodilators, or substance abuse, all of which may produce panic-like symptoms and complicate the treatment of patients with panic disorder. The onset of anxiety symptoms after age 40, lack of personal or family history of anxiety disorders, absence of significant life events triggering or worsening anxiety symptoms, lack of avoidance behavior, and poor response to antipanic agents

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may all suggest that panic symptoms are related to organic disease. Treatment should include correction of the underlying medical condition and removal of provocative treatment agents.

What nonpharmacologic measures are helpful in treatment?

It is important to approach panic disorder patients with a calm, reassuring manner. The goals of pharmacotherapy are to inhibit the attacks, address comorbid psychiatric conditions, and get the patient into remission or recovery. Sometimes the goal is to decrease the intensity and frequency of attacks.

Medications are less effective in treating anticipatory anxiety, but they can reduce chronic arousal, diminish reactivity, and blunt or block climactic extremes of self-escalating arousal processes that can lead to panic attacks.

Caffeine consumption—including coffee, tea, other caffeinated beverages, cold medications, and analgesics—should be stopped or reduced. Alcohol use poses a particularly insidious problem. The person may drink to alleviate the panic, then as the effects of alcohol wane, may experience a rebound of panic that precipitates more drinking. Finally, I often recommend a book, *The Anxiety Disease*, by David Sheehan, MD, to my panic disorder patients.

What is the drug of choice in panic disorder?

Selective serotonin reuptake inhibitors (SSRIs) are an effective, well-tolerated alternative to earlier agents in treating panic disorder. In a meta-analysis of 32 randomized, double-blind, placebo-controlled studies with data from more than 2,300 patients, results showed that patients did better on SSRIs than imipramine (Tofranil)or alprazolam (Xanax).* All five SSRIs currently marketed in the United States, fluoxetine HCl (Prozac), fluvoxamine maleate (Luvox), paroxetine HCl (Paxil), sertraline HCl (Zoloft), and citalopram hydrobromide (Celexa), are effective antipanic medications. SSRIs lack the cardiac toxicity and the anticholinergic effect of triclyclic antidepressants (TCAs). To minimize increased anxiety, treatment must be initiated with a low dosage (fluoxetine, 5 mg/d; sertraline, 12.5 mg/d; paroxetine, 5 mg/d; fluvoxamine, 12.5 mg/d; citalopram, 10 mg/d).

The dose is then titrated upward on a weekly basis (for example, fluoxetine is increased by 5 mg every week) until the patient no longer experiences panic symptoms. Therapeutic dosages are generally comparable to and sometimes higher than those for depression.

*Boyer W. Serotonin uptake inhibitors are superior to imipramine and alprazolam in alleviating panic attacks: A meta-analysis: Int Clin Psychopharmacol 1995;10:45-49.

How long should SSRIs be continued?

The continuation phase of treatment aims to prevent the recurrence of symptoms and maintain the benefits of drug therapy. In general, patients should be maintained on the SSRI for 1 year. Some whose symptoms recur during or after tapering of medication are candidates for maintenance treatment. The overriding principle regarding discontinuation of medication is always to reduce the dosage slowly, not abruptly. The frequency of appointments should be increased during the period of tapering, both to provide guidance and support and to assess carefully for rebound anxiety, withdrawal phenomena, and the return of symptoms.

Does alprazolam still have a therapeutic role?

High-potency benzodiazepines, clonazepam (Klonopin), alprazolam, and lorazepam (Ativan), have been found effective for blocking panic attacks. The advantages of a benzodiazepine include rapid onset of therapeutic effect and a safe, favorable side-effect profile. The starting dose of alprazolam is generally 0.5 mg bid. Potential drawbacks of the benzodiazepines include concerns about abuse and dependency, withdrawal symptoms on abrupt discontinuation, early relapse after discontinuation, and interdose rebound anxiety. They are contraindicated in a patient with a substance abuse problem. Benzodiazepines can also worsen depressive symptoms and contribute to drug dependence. Alprazolam, first used in 1980, has been the most extensively studied. About 70% of panic disorder patients treated with alprazolam will experience a reaction of increased anxiety, agitation, and insomnia when the drug is tapered.

Clonazepam has a long duration of effect, reducing the need for multiple daily dosing. Initial

low dosages of 0.25 mg/d are titrated to the usual effective dose of 1.0-5.0 mg/d. Sedation and ataxia are usually transient. Patients with panic disorder do not generally abuse benzodiazepines; they are more likely to underutilize than overuse them.

Benzodiazepines are used in two main ways: as monotherapy for patients with mild panic symptoms and as adjunctive therapy for patients with moderate-to-severe symptoms, allowing the patient to gain control over the symptoms on an as-needed basis. Benzodiazepines are also useful with SSRIs in the start of therapy before the SSRI therapeutic effects set in.

What about tricyclic antidepressants?

The antipanic effects of TCAs were first noted more than 30 years ago, but their use in treating panic disorder is associated with a delayed onset of action and side effects, particularly anticholinergic side effects, orthostatic hypotension, and weight gain. These effects may compromise tolerance of and compliance with therapy. The starting dosage for a TCA such as imipramine is 10 mg/d to avoid potential early onset anxiety exacerbation. Tachycardia may be induced. There is a 63% short-term control of panic attacks and a 28% attrition rate—usually secondary to side effects. TCAs are most helpful with psychic symptoms such as dysphoria or negative anticipatory thinking. There is little potential for abuse. Up to 250 mg/d is an adequate dosage. TCAs are not first-line therapy for panic disorder due to their side effects and lethality in overdose, but are reserved for those who do not respond to SSRIs or who have both panic disorder and neuropathic pain.

Does psychotherapy have a role?

Psychotherapy can elucidate unconscious conflicts that may prompt avoidance behavior or panic-driven cessation of functioning. Psychotherapy is often useful in that many panic disorder patients have experienced a recent loss such as divorce, job switching, or death. If loss is a precipitating factor in the onset of panic disorder, psychotherapy can be useful. It is best used as adjunctive therapy, but some patients refuse psychotropic medication, and psychotherapy should be offered as a treatment option. ■