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FROM THE FAMILY PRACTICE INQUIRIES NETWORK

What are effective treatments for panic disorder?

Deborah A. Sturpe, PharmDAlicia M. Weissman, MD

University of Iowa, Iowa City

EVIDENCE-BASED ANSWER

Selective serotonin reuptake inhibitors (SSRIs), tricyclic antidepressants (TCAs), benzodiazepines (BDZs), and cognitive behavioral therapy (CBT) are effective for panic disorder (PD) with or without agoraphobia (NNT5 for complete remission). SSRIs may be most effective, but BDZs work faster. Clomipramine is more effective than other TCAs. CBT improves response and decreases relapse rates when used with medication. Severe symptoms may warrant short-term use of a BDZ until other therapies take effect (Grade of recommendation: A, based on systematic reviews of randomized clinical trials (RCTs); high quality RCTs).

EVIDENCE SUMMARY

SSRIs were more effective than imipramine or alprazolam in a meta-analysis,[1] but equivalent to these drugs in an effect-size analysis.[2] The absolute difference in efficacy is difficult to determine; few studies directly compare SSRIs with other drugs. In 2 randomized head-to-head trials,[3,4] remission rates (eliminating symptoms) were 50%-65% for paroxetine, 37%-53% for clomipramine, and 32%-34% for placebo after 9-12 weeks of therapy; differences between the 2 active drugs were not significant. Clomipramine is serotoninergic and was more effective than other tricyclics in an RCT.[5] Adding a BDZ to an SSRI for the first 3 weeks can rapidly stabilize symptoms[6] (**Table**).

Two meta-analyses concluded that CBT is as effective as antidepressants or BDZs during acute treatment[7] and during long-term follow-up (31-121 weeks).[8] CBT and imipramine each reduce symptoms in 45%-48% of patients; combining them reduces symptoms in 60%.[9] Imipramine is more effective initially; CBT is more durable[9] but effects may be therapist-dependent. When used in conjunction with medication, graded exposure to panicinducing situations reduces agoraphobia[7] but does not improve relapse rates.[8] Behavioral therapy with exposure homework has good long-term results.[10]

An adequate trial of medication requires 6-8 weeks.[11] Before treating, evaluate patients for comorbid mood, anxiety, personality, substance use, or medical disorders, which affect 40%-50% of patients with panic disorder, and may influence the choice of treatment.[12] Current practice is to slowly taper and discontinue medication after 12-18 months of maintenance treatment[12] if there are no significant residual symptoms, no increased psychosocial stressors, and no history of severe or recurrent relapse.

Drugs used to treat panic disorder

Drug Class	Side Effects	Other Considerations
Selective serotonin reuptake inhibitors	Nausea (10-30%), drowsiness (7-20%), insomnia (< 10%), nervousness(< 10%), sexual dysfunction (< 10% but underreported).	All equivalently effective. Some patients may respond to lower than usual doses. Start at half the usual dose.
Tricyclic antidepressants	Dry mouth (> 45%), dizziness (2%), constipation (15%), sweating (15%), tremors (15%), fatigue (< 10%)	Requires more time to titrate to treatment dose. Clomipramine more effective. Some patients with panic disorder are extremely sensitive both to the therapeutic and adverse effects of TCAs. Start at very low doses.
Benzodiazepines	Somnolence (15-34%) and impaired coordination (6-22%). Potential for physical dependence and withdrawal symptoms, but psychological addiction has not been a significant problem in clinical trials.	Faster onset of action than antidepressants, but do not treat comorbid depression and are more difficult to discontinue.

RECOMMENDATIONS FROM OTHERS

The American Psychiatric Association Guideline states that CBT and pharmacotherapy are equivalently effective, and that SSRIs, TCAs, BDZs, and MAOIs are equivalently effective.[12] The International Consensus Group on Depression and Anxiety concludes that SSRIs, TCAs, and BDZs are effective. SSRIs and BDZs are tolerated better than TCAs, and BDZs act faster (1 week vs. 4-8 weeks).[11]

Read a Clinical Commentary by William A. Hensel, MD, at **www.fpin.org**.

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