

# Pindolol Use for Treatment-Refractory Panic Disorder

Melissa Vaz-Ayes, BS; Bernard Sarmiento, MD; Matthew Gunther, MD; and Shixie Jiang, MD

Panic disorder (PD) is described as recurrent, untriggered panic attacks with at least 1 of the attacks followed by 1 month or more of concern about future attacks and/or significant maladaptive behavioral changes in relation to the attacks.<sup>1</sup> PD is a chronic, recurrent disease that affects 1%–3% of the population; some individuals improve with treatment, but few achieve lasting remission.<sup>2–4</sup> There is no standardized definition of treatment-resistant PD; several authors utilize criteria of no response to at least 1 to 2 adequate 8-week treatment trials with medications effective for PD.<sup>5,6</sup> We present the case of a patient with treatment-resistant PD who when treated with pindolol experienced a significant reduction in the frequency and severity of his attacks.

## Case Report

A 36-year-old man with generalized anxiety disorder, major depressive disorder, and PD was seen as an outpatient in July 2020. The patient was reporting 2 to 3 moderate attacks per day and 2 to 3 severe attacks per week. He was being managed with nortriptyline 125 mg nightly, buspirone 30 mg twice/d, ziprasidone 40 mg twice/d, and lorazepam 0.75 mg twice/d. Previously, it had been attempted to increase lorazepam 1 mg twice/d, but the patient reported he was too sedated. The patient reported trials with several first-line medications but failed them, as well as several others that seemed to alleviate symptoms, but he was unable to tolerate the medications due to various side effects. Bupropion and venlafaxine successfully managed the patient's mood symptoms but heightened anxiety. Quetiapine was trialed, but

the medication was highly sedating. Aripiprazole was attempted as an augmenting agent for anxiety but tapered a few months later due to increased anxiety and depression. Hydroxyzine 25 mg was self-discontinued due to “mental foggy” and concentration issues. Temazepam 7.5 mg resulted in hypersomnia.

At the initial visit, pindolol 2.5 mg 3 times daily was initiated. This dose was increased to 5 mg 10 days later, as the patient reported a reduction in attack severity. One month after the initiation of pindolol (August 2020), the patient reported a decrease in the frequency of attacks to 1 to 2 times daily, and pindolol was titrated to 7.5 mg 3 times daily. In September 2020, the patient reported significant efficacy of pindolol in reducing the severity of his attacks. However, he continued to experience functional limitations. In October 2020, there was an increase in attacks from prior visits, as the patient noted he was regularly forgetting his midday dose of pindolol. Pindolol was thus titrated to 15 mg twice/d. Four months after initiation (November 2020), the patient reported a reduction in the frequency of attacks, and pindolol was increased to 20 mg twice/d. Following this titration, the patient experienced 4 severe panic attacks over the subsequent 2 weeks, with 1 day entirely free of panic attacks. Lorazepam was tapered gradually over months afterward. Titration of other medications is unknown. Over 1 year of this regimen, the patient demonstrated consistent improvement, ultimately achieving remission.

## Discussion

Pindolol is a  $\beta$ -adrenergic and 5-HT<sub>1A</sub> receptor partial agonist.<sup>7</sup> Its

role as an augmenting agent in antidepressant and treatment-refractory PD therapy has been investigated, with particular attention paid to pindolol's role as a serotonergic modulator.<sup>5,8–12</sup> Clinical effects have been theorized to be related to pindolol's antagonist activity at presynaptic and somatodendritic 5-HT<sub>1A</sub> receptors, which serve as inhibitory autoreceptors that inhibit serotonin release, of which pindolol appears to have a unique stronger preference compared to other  $\beta$ -blockers.<sup>8–11,13,14</sup> This preference may contribute to its effectiveness in alleviating symptoms of panic attacks. This case and the limited controlled trials analyzing pindolol efficacy in PD underscore the need for further research into pindolol as an augmenting panicolytic, with appropriate dosing guidelines.

## Article Information

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**Author Affiliations:** College of Medicine, University of Florida, Gainesville, Florida (Vaz-Ayes); College of Medicine, University of Central Florida, Orlando, Florida (Sarmiento); Department of Psychiatry, Stanford University, Stanford, California (Gunther); Department of Psychiatry, University of Florida, Gainesville, Florida (Jiang).

**Corresponding Author:** Melissa Vaz-Ayes, BS, College of Medicine, University of Florida, Gainesville, 1208 SW 16th Ave, Apt D, Gainesville, FL 32601 (melissavazayes@ufl.edu).

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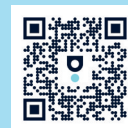
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