

Letters

DISCONTINUATION SYMPTOMS

In “6 safety rules for tapering antidepressants” (Pearls, CURRENT PSYCHIATRY, November 2006, p. 89-90), Richard C. Shelton, MD, mentioned that discontinuation symptoms associated with serotonin reuptake inhibitors (SRIs) “appear to be more common and severe with short-acting drugs such as venlafaxine and paroxetine,” but occur with fluoxetine as well.

Although possible, this statement could be misleading because studies comparing discontinuation symptoms among SRIs have not shown clinically significant discontinuation symptoms with fluoxetine. The authors of these studies have hypothesized that the lack of discontinuation symptoms is because of the long half-life of fluoxetine (2 to 4 days) and its active metabolite, norfluoxetine (7 to 9 days).¹⁻⁴

Dr. Shelton also wrote, “infants born to mothers taking antidepressants can exhibit discontinuation symptoms.” The fact that these neonatal serotonergic symptoms occur equally with fluoxetine and shorter half-life SRIs argues against these being discontinuation symptoms.^{5,6}

Clinicians should recognize that this is a controversial topic and that experts are not comfortable characterizing such effects as discontinuation symptoms rather than symptoms secondary to serotonin exposure.

Scott A. Freeman, MD
Assistant professor of clinical psychiatry
University of Arizona
College of Medicine
Tucson, AZ

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Dr. Shelton responds

Dr. Freeman raises important issues. In fact, discontinuation symptoms with long-acting drugs such as fluoxetine—if they occur—are generally much milder than those observed with drugs with shorter half-lives. However, some studies examining comparative risks simply have been too short to pick up any discontinuation symptoms with longer-acting drugs. For example, in the Judge et al article cited by Dr. Freeman, the discontinuation periods were 3 to 5 days.

The Rosenbaum et al study of 242 patients on paroxetine, sertraline, or fluoxetine discontinued for 5 to 8 days was more informative. The total Discontinuation-Emergent Signs and Symptoms score between baseline and endpoint changed the most in paroxetine, the least in fluoxetine, and sertraline scored in the middle.

Although the total score comparing baseline to endpoint did not differ with fluoxetine, certain discontinuation symptoms were relatively frequent. For example, agitation was found in 25% of patients, emotional lability in 21%, and confusion in 19%. This suggests that discontinuation symptoms may indeed be “clinically significant.”

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Similarly, in the Zajecka et al study, patients treated with fluoxetine were randomly assigned to continuation fluoxetine or placebo for 6 weeks. There were few differences between the groups, suggesting that the discontinuation syndrome did not occur with cessation of fluoxetine. However, there was a small but significant increase in dizziness at 4 and 6 weeks and rhinitis at 6 weeks.

These studies yield at least 2 conclusions:

- Discontinuation reactions with fluoxetine tend to be very mild when they occur, an idea consistent with my recommendation to substitute fluoxetine to assist tapering other drugs.

- Reactions, when they occur, happen much later than with short-acting drugs, which is consistent with fluoxetine's long half-life.

Regarding neonatal discontinuation syndromes, I would refer the reader to a longer discussion in an earlier article.¹ The Moses-Kolko et al analysis cited by Dr.

Freeman was a review of 13 reports comprising 18 cases. The Oberlander et al citation described 46 exposures, with 14 showing post-natal problems. In the group exposed to an SRI alone, the rate was low with fluoxetine (n=3), paroxetine (n=3), or sertraline (n=1). A second group was exposed to both paroxetine and clonazepam, with a 39% total frequency of post-natal effects.

Regarding paroxetine, Sanz et al² reported that in the World Health Organization's database of adverse events, 64 of 93 cases of post-natal complications associated with SRI treatment were with paroxetine, compared to 14 with fluoxetine, 9 with sertraline, and 7 with citalopram. The authors described the problem as related to "discontinuation" after delivery. Haddad et al³ described some of the symptoms associated with neonatal complications as "serotonin syndrome."

Taken as a whole, however, the reported symptoms have been a combination of signs of acute toxicity—such as seizures, hypertonus, jaundice, and hypoglycemia—and more typical discontinuation symptoms, including respiratory distress and hyperventilation. The notion that these reactions are related to serotonin syndrome seems unsupported, given that they occur more often with short half-life paroxetine than with long half-life drugs.

Richard C. Shelton, MD
James G. Blakemore Research Professor
Professor of pharmacology
Department of psychiatry
Vanderbilt University
Nashville, TN

Studies indicate that discontinuation reactions with fluoxetine, when they occur, tend to be mild

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