Negative Efficacy of Desvenlafaxine and Fluoxetine for Children and Adolescents With MDD

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Review of: Weihs et al, *J Child Adolesc Psychopharmacol* 2018;28(1):36–46

The debate about whether antidepressants work in children has been with us since the tricyclic era. A recent study evaluated the short-term efficacy and safety of a newer agent, desvenlafaxine (Pristiq).

This multi-center, randomized, double-blind, placebo-controlled study included 339 children and adolescents ages 7–17 who met DSM-IV-TR criteria for MDD. A fluoxetine 20 mg/day group was included as a reference for assay sensitivity, but not as a comparison to the study drug. Enrolled patients had a Children's Depression Rating Scale—Revised (CDRS-R) total score > 40 at baseline. Patients were excluded from the study if they had psychotic features, if they had a personal or family history of bipolar disorder or suicide, or if they were felt to be at significant risk of suicide.

Patients were randomly assigned (1:1:1) to placebo, desvenlafaxine, or fluoxetine. Desvenlafaxine dose was chosen by body weight: 20 to < 35 kg: 25 mg/day; 35 to < 70 kg: 35 mg/day; and ≥ 70 kg: 50 mg/day. The patients were assessed weekly for the first month and again at weeks 6 and 8. The primary endpoint, change in the CDRS-R score from baseline to week 8, did not differ statistically from placebo (-23.1) for either desvenlafaxine (-22.6) or fluoxetine (-24.8). Adverse events (AE) attributed to medications were present in all study groups (desvenlafaxine, 28.7%; fluoxetine, 32.1%; and placebo, 34.8%). The most common treatment-emergent AEs were headache, upper abdominal pain, and nausea. There were no deaths in the study, but 5 patients receiving either desvenlafaxine or fluoxetine experienced serious AEs—suicidal ideation, a suicide attempt, disinhibition, and postpartum hemorrhage.

CCPR's take

High placebo response rates in the pediatric population make it difficult to demonstrate the benefit of even established treatments such as fluoxetine, and clinicians should closely monitor for suicidal thoughts during initial stages of treatment with SSRIs and SNRIs. New-onset suicidal ideation was reported for 8, 10, and 7 patients in the desvenlafaxine, fluoxetine, and placebo groups, respectively; suicidal behavior was reported for 1 fluoxetine-treated patient, who reported suicidal ideation at baseline.

But more importantly, this landmark publication of a negative study, where neither desvenlafaxine nor fluoxetine were efficacious for treating MDD in children and adolescents, was conducted with financial and medical writing support from Pfizer Inc. As we go to press, another negative study for depression in children is being published on desvenlafaxine by the same journal. There appears to be a sea change happening on the heels of the final rule from the FDA, which severely penalizes (through fines) the suppression of negative studies.

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