

Antidepressants and self-harm: For those under 24, initial dose matters

May 6 2014

About a decade after the Food and Drug Administration first warned that antidepressant medications increase the risk of suicidal thoughts and behaviors in children, new research has found that kids and young adults starting on high doses of antidepressants are at especially high risk, especially in the first three months of treatment.

Among patients 24 and younger, those who started treatment for depression or anxiety with a higher-than-usual dose of selective serotonin reuptake inhibitor, or SSRI, were more than twice as likely to harm themselves intentionally than those whose treatment began at the customary dose and increased slowly, the study found.

For every 150 such patients treated with high initial doses of SSRIs-antidepressants marketed under such commercial names as Zoloft, Paxil, Prozac, Celexa and Lexapro-the study suggests one additional suicide would be attempted. By contrast, young patients starting SSRI therapy at doses considered customary were at only slightly elevated risk of self-harm, about 12 percent above the level of their depressed peers not taking medication.

The latest research on depression treatment, conducted by epidemiologists at Harvard University and the University of North Carolina, was published Tuesday in *JAMA Internal Medicine*.

The researchers found no increased risk of suicidal behavior among adults older than 24 who started medical treatment for depression or



anxiety at larger initial doses.

About 18 percent of young people diagnosed with depression were prescribed an initial antidepressant dose that was higher than that recommended by clinical guidelines: For the antidepressant fluoxetine (better known by its commercial name, Prozac), for instance, a standard dose would be 10 milligrams daily for the first week, increasing to 20 milligrams for the next three weeks, and only then considering any increased dose.

Given that antidepressants appear to be less effective in <u>young people</u> than in older patients, and that higher doses do not appear to bring more or faster relief, the author of an invited commentary in *JAMA Internal Medicine* suggested that prescribing physicians should abide by the well-worn maxim "start low, go slow," and monitor patients closely during their first several months of treatment.

The study used medical records to track 162,625 U.S. residents, ages 10 to 64, who were diagnosed with depression and prescribed SSRI between 1998 and 2010. It found that more than half of antidepressants in that period were prescribed by primary care doctors, and about an additional quarter by practitioners not specialized in mental health. Even in children, fewer than 30 percent of antidepressant prescriptions were issued by psychiatrists.

The authors acknowledged that they could not discern why younger patients on high initial doses of antidepressant were more likely to try to harm themselves. Although it could have been the dose at which these young patients began their therapy, it is equally plausible that younger patients who are correctly perceived to be in a mental health crisis are more likely to be treated more aggressively, but not more likely to get better with SSRIs.



It might also be that those started on high-dose SSRIs are more likely to discontinue their therapy and to suffer from "discontinuation syndrome," which can bring physical symptoms of anxiety and is sometimes linked to unpredictable behavior.

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Citation: Antidepressants and self-harm: For those under 24, initial dose matters (2014, May 6) retrieved 10 April 2024 from

https://medicalxpress.com/news/2014-05-antidepressants-self-harm-dose.html

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