The Suicide Epidemic in Youth and the FDA Black-Box Warning: Time to Reconsider

Andrew A. Nierenberg, MD

We are in the midst of a suicide epidemic. Increasing numbers of young people age 10 to 24 years have died by suicide from 2007 (6.8 per 100,000 persons) to 2017 (10.6 per 100,000 persons). Although the suicide rate for young people age 10 to 14 years declined from 2000 (1.5 per 100,000 persons) to 2007 (0.9 per 100,000 persons), it increased from 2007 to 2017 (2.5 per 100,000 persons). At the same time, decreasing numbers of young people have been treated with antidepressants, particularly since the 2006 US Food and Drug Administration (FDA) black-box warning, which linked the use of antidepressants to an increased risk of suicide in youth and extended the warning to those younger than age 25 years. One could reasonably conclude that the increasing rate of suicide is caused by the decreased use of antidepressants, but, as we all know, association is not necessarily causation. Nevertheless, the current tragic trend strongly argues against the hypothesis that antidepressants increase the risk of suicide in youth. So, let’s take another look at that FDA black-box warning and the arguments that it should be rescinded.

As has been reviewed, discussed, and dissected elsewhere, the FDA examined data from randomized clinical trials of antidepressants compared to placebo for youth for mostly major depressive disorder but also other disorders. With about 4,400 youth studied, and about 2,200 exposed to antidepressants, the rate of “suicide events” was about 2% for placebo and 4% for people currently taking antidepressants (with no deaths) with no advantage of antidepressants over placebo for the treatment of depression (with the exception of fluoxetine) coupled with high placebo responses. At the FDA hearings in 2004, parents who had lost their children to suicide provided moving testimony about how their children died after starting antidepressants. Critics of antidepressants (of which there are many) supported the black-box warning.

Subsequent reanalyses of the data showed that overall, antidepressants were not superior to placebo (except for fluoxetine) and had an equal effect on suicidal ideation and suicidal behavior compared to placebo (with the exception of venlafaxine), but few articles discuss that the high placebo response rates (over 50% in some studies) precluded finding a signal of efficacy if such a signal exists.

What would removing the black-box warning do? First, remember that a package insert black-box warning translates into action because it is the direst of warnings. Second, it could at least reopen the discussion about benefits and risks of antidepressants for youth. Third, if it led to increased (and hopefully appropriate) use of antidepressants for youth, then we would have the opportunity to reexamine the...
Editorial

trends and have a better sense of the relationship between antidepressants and suicide in youth.

REFERENCES