Antidepressant Medications for Children and Adolescents: Information for Parents and Caregivers

Depression is a serious disorder that can cause significant problems in mood, thinking, and behavior at home, in school, and with peers. It is estimated that major depressive disorder (MDD) affects about 5 percent of adolescents.

Research has shown that, as in adults, depression in children and adolescents is treatable. Certain antidepressant medications, called selective serotonin reuptake inhibitors (SSRIs), can be beneficial to children and adolescents with MDD. Certain types of psychological therapies also have been shown to be effective. However, our knowledge of antidepressant treatments in youth, though growing substantially, is limited compared to what we know about treating depression in adults.

Recently, there has been some concern that the use of antidepressant medications themselves may induce suicidal behavior in youths. Following a thorough and comprehensive review of all the available published and unpublished controlled clinical trials of antidepressants in children and adolescents, the U.S. Food and Drug Administration (FDA) issued a public warning in October 2004 about an increased risk of suicidal thoughts or behavior (suicidality) in children and adolescents treated with SSRI antidepressant medications. In 2006, an advisory committee to the FDA recommended that the agency extend the warning to include young adults up to age 25.

More recently, results of a comprehensive review of pediatric trials conducted between 1988 and 2006 suggested that the benefits of antidepressant medications likely outweigh their risks to children and adolescents with major depression and anxiety disorders. The study, partially funded by NIMH, was published in the April 18, 2007, issue of the Journal of the American Medical Association.[1]

What Did the FDA Review Find?

In the FDA review, no completed suicides occurred among nearly 2,200 children treated with SSRI medications. However, about 4 percent of those taking SSRI medications experienced suicidal thinking or behavior, including actual suicide attempts—twice the rate of those taking placebo, or sugar pills.

In response, the FDA adopted a "black box" label warning indicating that antidepressants may increase the risk of suicidal thinking and behavior in some

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children and adolescents with MDD. A black-box warning is the most serious type of warning in prescription drug labeling.

The warning also notes that children and adolescents taking SSRI medications should be closely monitored for any worsening in depression, emergence of suicidal thinking or behavior, or unusual changes in behavior, such as sleeplessness, agitation, or withdrawal from normal social situations. Close monitoring is especially important during the first four weeks of treatment. SSRI medications usually have few side effects in children and adolescents, but for unknown reasons, they may trigger agitation and abnormal behavior in certain individuals.

What Do We Know About Antidepressant Medications?

The SSRIs include:

fluoxetine (Prozac)
sertraline (Zoloft)
paroxetine (Paxil)
citalopram (Celexa)
escitalopram (Lexapro)
fluvoxamine (Luvox)

Another antidepressant medication, venlafaxine (Effexor), is not an SSRI but is closely related.

SSRI medications are considered an improvement over older antidepressant medications because they have fewer side effects and are less likely to be harmful if taken in an overdose, which is an issue for patients with depression already at risk for suicide. They have been shown to be safe and effective for adults.

However, use of SSRI medications among children and adolescents ages 10 to 19 has risen dramatically in the past several years. Fluoxetine (Prozac) is the only medication approved by the FDA for use in treating depression in children ages 8 and older. The other SSRI medications and the SSRI-related antidepressant venlafaxine have not been approved for treatment of depression in children or adolescents, but doctors still sometimes prescribe them to children on an "off-label" basis. In June 2003, however, the FDA recommended that paroxetine not be used in children and adolescents for treating MDD.

Fluoxetine can be helpful in treating childhood depression, and can lead to significant improvement of depression overall. However, it may increase the risk for suicidal behaviors *in a small subset of adolescents.* As with all medical decisions, doctors and families should weigh the risks and benefits of treatment for each individual patient.

What Should You Do for a Child With Depression?

A child or adolescent with MDD should be carefully and thoroughly evaluated by a doctor to determine if medication is appropriate. Psychotherapy often is tried as an initial treatment for mild depression. Psychotherapy may help to determine the severity and persistence of the depression and whether antidepressant medications may be warranted. Types of psychotherapies

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include "cognitive behavioral therapy," which helps people learn new ways of thinking and behaving, and "interpersonal therapy," which helps people understand and work through troubled personal relationships.

Those who are prescribed an SSRI medication should receive ongoing medical monitoring. Children already taking an SSRI medication should remain on the medication if it has been helpful, but should be carefully monitored by a doctor for side effects. Parents should promptly seek medical advice and evaluation if their child or adolescent experiences suicidal thinking or behavior, nervousness, agitation, irritability, mood instability, or sleeplessness that either emerges or worsens during treatment with SSRI medications.

Once started, treatment with these medications should not be abruptly stopped. Although they are not habit-forming or addictive, abruptly ending an antidepressant can cause withdrawal symptoms or lead to a relapse. Families should not discontinue treatment without consulting their doctor.

All treatments can be associated with side effects. Families and doctors should carefully weigh the risks and benefits, and maintain appropriate follow-up and monitoring to help control for the risks.

What Does Research Tell Us?

An individual's response to a medication cannot be predicted with certainty. It is extremely difficult to determine whether SSRI medications increase the risk for completed suicide, especially because depression itself increases the risk for suicide and because completed suicides, especially among children and adolescents, are rare. Most controlled trials are too small to detect for rare events such as suicide (thousands of participants are needed). In addition, controlled trials typically exclude patients considered at high risk for suicide.

One major clinical trial, the NIMH-funded Treatment for Adolescents with Depression Study (TADS)[2], has indicated that a combination of medication and psychotherapy is the most effective treatment for adolescents with depression. The clinical trial of 439 adolescents ages 12 to 17 with MDD compared four treatment groups—one that received a combination of fluoxetine and CBT, one that received fluoxetine only, one that received CBT only, and one that received a placebo only. After the first 12 weeks, 71 percent responded to the combination treatment of fluoxetine and CBT, 61 percent responded to the fluoxetine only treatment, 43 percent responded to the CBT only treatment, and 35 percent responded to the placebo treatment.

At the beginning of the study, 29 percent of the TADS participants were having clinically significant suicidal thoughts. Although the rate of suicidal thinking decreased among all the treatment groups, those in the fluoxetine/CBT combination treatment group showed the greatest reduction in suicidal thinking.

Researchers are working to better understand the relationship between antidepressant medications and suicide. So far, results are mixed. One study, using national Medicaid files, found that among adults, the use of antidepressants does not seem to be related to suicide attempts or deaths. However, the analysis found that the use of antidepressant medications may be related to suicide attempts and deaths among children and adolescents.[3]

Another study analyzed health plan records for 65,103 patients treated for depression.[4] It found no significant increase among adults and young people in the risk for suicide after starting treatment with newer antidepressant medications.

A third study analyzed suicide data from the National Vital Statistics and commercial prescription data. It found that among children ages five to 14, suicide rates from 1996 to 1998 were actually lower in areas of the country with higher rates of SSRI antidepressant prescriptions. The relationship between the suicide rates and the SSRI use rates, however, is unclear.[5]

New NIMH-funded research will help clarify the complex interplay between suicide and antidepressant medications. In addition, the NIMH-funded Treatment of Resistant Depression in Adolescents (TORDIA) study, will investigate how best to treat adolescents whose depression is resistant to the first SSRI medication they have tried. Finally, NIMH also is supporting the Treatment of Adolescent Suicide Attempters (TASA) study, which is investigating the treatment of adolescents who have attempted suicide. Treatments include antidepressant medications, CBT or both.

Complete list of all NIMH Clinical Trials.

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