Dynamic Chiropractic

Antidepressants and Children: A Dangerous Combination

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Only a few months ago, a senior executive at one of the world's largest drug manufacturers admitted that most of his company's products work in less than half of the people who take them.[1] Based on that revelation, it should come as little surprise that research published in the April 10, 2004 issue of the *British Medical Journal* indicates that an entire class of drugs - antidepressant medications - do not work as well as advertised, and can be unsafe, especially when given to children.[2] This fact is even more disturbing when one considers that a separate study released in a psychiatric journal last month[3] indicates that children below age 5 are the fastest growing group of antidepressant users in the United States.

In the *BMJ* study, officials reviewed six published trials of newer antidepressants in children, analyzing each study's methods and the extent to which an author's conclusion was supported by the data provided in the research. Pharmaceutical companies paid for four of the trials, and either paid or provided services to the authors of at least three of the larger studies. Among the reviewers' revelations:

The researchers conducting the drug trials routinely "exaggerated the benefits" of the drugs they were investigating, while downplaying the negative side-effects. In one study of paroxetine, 11.8% of children in the drug group experienced a serious adverse event, and seven patients were admitted to a hospital during treatment. Only 2.3% of children in the placebo group experienced an adverse event. Despite this wide difference, the trial's authors concluded that paroxetine "was generally well tolerated in this adolescent population, and most adverse effects were not serious." In another trial on the antidepressant sertraline, more than three times as many children in the drug group withdrew because of adverse events compared to the placebo group, and no details of the adverse events were included in the published study. Nevertheless, the authors of that study concluded that sertraline is "effective, safe, and well tolerated."

Depression scores in many of the control groups showed "strong" improvement compared to the drug groups. In one study of the antidepressant fluoxetine, researchers found that children given a placebo showed at least 70% improvement in depression scores compared to children taking the drug. In the previously mentioned sertraline study, the reviewers discovered that "87 percent of the improvement in the sertraline group was reproduced in the placebo group," and that while the authors of the study did find a significant difference in scores at 10 weeks, "it was very small in size and unlikely to be clinically important."

"In discussing their own data, the authors of all of the four larger studies have exaggerated the benefits, downplayed the harms, or both," said the reviewers. They added that while some small benefits were seen among patients using some of the newer antidepressants, the risk of suffering an adverse event documented in the trials "raises serious concerns about their potential for harm."

"The magnitude of benefit is unlikely to be sufficient to justify risking those harms, so confidently

recommending these drugs as a treatment option, let alone as first line treatment, would be inappropriate," they concluded. "... It is vital that authors, reviewers, and editors ensure that published interpretations of data are more reasonable and balanced than is the case in the industry-dominated literature on childhood antidepressants."

Given the results of the *BMJ* study, one would think that parents would be more concerned about their children's mental health, and less inclined to put them on antidepressant medications. Yet evidence suggests just the opposite is happening.

Antidepressant Use, 1998-2002	
Age/Gender	Increase in Use
0-5 years of age	
Girls	100 %
Boys	64.3 %
6-10 years of age	
Girls	47.3 %
Boys	32.2 %
11-14 years of age	
Girls	63.9 %
Boys	21.9 %
15-18 years of age	
Girls	70.0 %
Boys	41.0 %

In the second study, published in the April 2004 issue of *Psychiatric Services*, researchers examined the prevalence of antidepressant use among children and adolescents from 1998 to 2002, using prescription claim information from a random, nationwide sample of approximately 3 million people with pharmacy benefits and their beneficiaries. Children ages 18 and younger were included in the sample if they were continuously eligible for pharmacy benefits during the year data were analyzed. Age categories for the children ranged from preschool (0-5 years) to elementary school (6-10 years), middle school (11-14 years) and high school (15-18 years).

For the entire sample, antidepressant use increased 49% in the five-year period, from 1.59% of the general population in 1998 to 2.37% in 2002. Use of antidepressants increased an average of 9.2% per year; the largest single-year increase took place between 2001 and 2002.

Over the course of the study, the growth in use was twice as great among girls (68%) as in boys (34%). While increases along all age levels were seen, preschool children represented the fastest-growing group: Antidepressant use among preschool girls doubled between 1998 and 2002; in preschool boys, antidepressant use increased more than 64%.

Among children, the highest percentage of users was seen in girls and boys ages 15-18. More than 6% of the girls in this age group used antidepressants, as did 4.2% of the boys. If these figures were extrapolated to the entire pediatric population, it would mean that in 2002, one of every 16 high-school-age girls and one of every 23 high-school-age boys in the U.S. were taking some type of antidepressant.

Selective serotonin reuptake inhibitors (SSRIs) such as Prozac and Zoloft were the most popular form of antidepressant used by children in the study, followed by a specific SSRI, paroxetine. In fact, paroxetine use in the pediatric population doubled from 1998-2002. "This finding is of note given FDA's recent recommendation that paroxetine not be prescribed for depression among pediatric patients," the researchers emphasized.

The results of the survey led the researchers to two differing, but not mutually exclusive, views on the increasing use of antidepressants by young children and adolescents. As Dr. Tom Delate, the study's lead author, noted:[4]

"One is the concern that antidepressants are being prescribed to youths without adequate information about their safety and efficacy in this population. The second is the presumption that advocacy work to identify and treat depression among children and adolescents has begun to pay off. We realize that the use of antidepressants among youths is a critical issue that requires additional research to better understand."

... And They Don't Help Your Back, Either

Reading about the numbers of children who take antidepressants, and the fact that such drugs often do nothing to improve a person's mental state, is enough to make almost anyone feel, well, depressed. As if that information weren't enough, recent evidence also shows that most antidepressants provide very little in the way of making people with back pain feel better.[5]

A study published in *Spine* in November 2003 reviewed seven trials of antidepressants for the treatment of chronic low back pain and found that while "antidepressants that inhibit norepinephrine reuptake ... are mildly to moderately effective in reducing pain," in other types of antidepressants, such as paroxetine and trazodone, "no analgesic benefit was seen."The study was even more blunt in its assessment of using these drugs to treat acute back pain: "We found no adequate studies on the use of antidepressants for acute back pain. Given this lack of evidence, and the fact that acute back pain usually resolves in one to three months, antidepressants should not be used routinely for acute back pain."

In addition, none of the drugs used in the study was shown to improve low back function. The study concluded that "based on limited evidence, SSRIs and trazodone do not appear to decrease pain in patients with chronic low back pain."

FDA Suppressing Evidence?

As we go to press, members of the House Energy and Commerce Committee and the Senate Finance Committee have announced that they will launch an investigation into whether the Food and Drug Administration fully disclosed a disagreement among its scientists about whether antidepressants might be linked to suicide in children.[6,7] In particular, the committees intend to determine whether the FDA inappropriately suppressed crucial findings made by an agency scientist who believes a link between suicide and antidepressants has already been established.

"It would have been very wrong for the FDA to withhold any information it had about unintended consequences that might result from the use of antidepressants, especially for children and adolescents," said Iowa Sen. Charles E. Grassley, who chairs the Senate Finance Committee.

While recent studies have shown that children given antidepressants are more likely to become suicidal than those given placebos, many of those studies are funded by drug companies and are often left unpublished; furthermore, the results of some published studies have been interpreted

differently by psychiatrists and health officials. As a result, the FDA charged Dr. Andrew Mosholder, an epidemiologist, with analyzing 22 studies involving seven antidepressants and more than 4,200 children. In a 33-page memorandum, Dr. Mosholder concluded that children given antidepressants were almost twice as likely to become suicidal as children given placebos.

On Feb. 2, 2004, health officials convened a special advisory committee to discuss the Mosholder memorandum, and to offer guidance on how the FDA should respond to the studies. As the agency's principal reviewer, Dr. Mosholder was scheduled to speak at the meeting, but was removed from the meeting agenda because, according to one official, he failed to treat some reports of suicidal behavior in children "with the appropriate skepticism."

While the FDA insists that there is no clear link between antidepressants and suicidal behavior in children or teenagers, the agency has taken steps that suggest it knows more about a possible link than it is willing to reveal publicly. In March 2004, it sent a letter to the manufacturers of 10 popular antidepressants - Prozac, Zoloft, Paxil, Luvox, Celexa, Lexapro, Wellbutrin, Effexor, Serzone and Remeron - requesting that the labels of the drugs be changed to include warnings about possible suicide, worsening depression, anxiety, and panic attacks in adults and children. It has also hired investigators at Columbia University to examine reports from approximately 400 children in Mosholder's analysis, to determine independently what should be classified as "suicidal behavior."

The FDA also announced that it has launched its own investigation into any alleged links between antidepressants and suicide, the results of which will be published this summer.

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