Federal Study to Probe Heart Risk in ADHD Drugs

BY MARY ELLEN SCHNEIDER
New York Bureau

Officials at the Food and Drug Administration and the Agency for Healthcare Research and Quality are launching a large-scale study to determine whether the medications used to treat attention-deficit hyperactivity disorder expose patients to an increased risk for cardiovascular problems.

The study is a retrospective review of about 500,000 children and adults who took ADHD medications before the end of 2005. Of the 500,000 patients included in the analysis, about 80% represent pediatric use and 20% adult use, according to the FDA. The evaluation will build on preliminary work performed by the FDA that included information from large health care databases on prescription drug use, outpatient treatment, health outcomes, and death.

The study will include all drugs being marketed for ADHD treatment and is expected to be completed in about 2 years.

Its launch follows reports of sudden death in treated patients with underlying serious heart problems, and reports of stroke and heart attack in treated adults with certain risk factors. In 2006, the agency directed ADHD drug manufacturers to revise their product labeling for physicians to include concerns about cardiovascular problems.

Earlier this year, FDA officials also directed drug manufacturers to develop patient medication guides to alert patients to possible cardiovascular risks from ADHD medications. The agency also recommended that physicians obtain a health history and assessment of possible cardiovascular problems before starting patients on ADHD medications.

The main question will be whether children with an underlying structural heart disease or an arrhythmia are at increased risk for cardiovascular problems when on these medications, said Dr. Martin T. Stein, professor of pediatrics at the University of California, San Diego. He is the recipient of unrestricted educational grants from Eli Lilly and Co., maker of Strattera, and a member of the Strattera Pediatric Advisory Board.

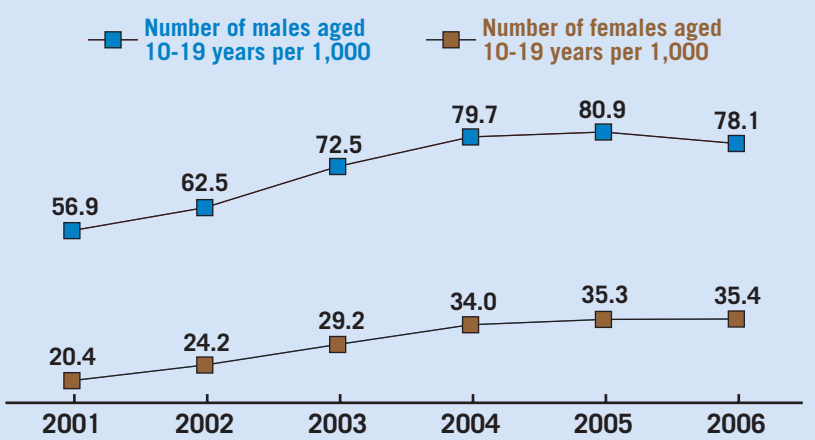
The 2006 reports of sudden death have raised public awareness, but the jury is still out on the risks of taking medications for ADHD. The federally funded study could lay some of these concerns to rest, he said.

But for most physicians who treat a lot of ADHD, there is no doubt about the safety of these medications, said Dr. Steven R. Pliszka, chief of the division of child and adolescent psychiatry at the University of Texas at San Antonio. Despite increases in prescriptions for these drugs among children, there has been no documented increase in cardiovascular disease, said Dr. Pliszka, who has conducted research for McNeil Pediatrics, Shire, and Eli Lilly and Co., which manufacture ADHD drugs.

ADHD affects 3%-5% of school-age children and about 4% of adults in the United States, according to estimates from the National Institute of Mental Health. Three ADHD drugs (Concerta, Strattera, and Adderall) were among the top five drugs prescribed for children 17 years and younger in 2004, according to the Agency for Healthcare and Research Quality. The national price tag for the three medications was about $1.3 billion in 2004. ■

DATA WATCH

Rate of ADHD Medication Use Higher in Young Males



Source: Medco Health Solutions Inc.

ELSEVIER GLOBAL MEDICAL NEWS

Naltrexone Is Less Effective In Women Than It Is in Men

BY MICHELE G. SULLIVAN
Mid-Atlantic Bureau

CHICAGO — Naltrexone may have little positive effect either on drinking behavior in older women with alcoholism comorbid with depression or on drug-using behavior in women with alcoholism and comorbid cocaine dependence.

Data presented at the annual meeting of the Research Society for Alcoholism—a subanalysis of a 2005 drug trial and a preview of a trial in press—hint that naltrexone may have very different effects in women than men, according to William Dundon, Ph.D., of the University of Pennsylvania, Philadelphia.

"Women metabolize alcohol differently than men, and respond to naltrexone differently as well," he said in an interview. Naltrexone blocks the mu-opiate receptors, moderating the sense of euphoria that alcohol provides, said Dr. Dundon, a researcher at the university's Center for the Studies of Addiction. Genetic makeup may also play a significant part in a given patient's response to the drug. Dr. David Oslin, also of the university, has recently identified a genetic variant—a polymorphism of the mu-receptor gene—that seems to predict naltrexone response (Addict. Biol. 2006;11:397-403).

Dr. Dundon presented a recent gender subanalysis of a 2005 study by Dr. Oslin, demonstrating a poor naltrexone response in older women with comorbid alcoholism and depression (Am. J. Geriatr. Psychiatry 2005;13:491-500).

This study comprised 74 older adults (mean age 63 years) with alcohol dependence and depressive disorder. Most subjects (59) were male; there were only 15 female subjects.

All patients received sertraline (Zoloft) 100 mg/day for their depression, as well as 10 sessions of therapy focused on both alcohol use and depression. They were also randomized to either placebo or naltrexone (50 mg/day). At the end of the 12-week trial, 42% of the patients were considered well, with no relapse to heavy drinking and with remission of depressive symptoms. An additional 24% remained depressed, but did not have a drinking relapse.

There were no significant differences between the placebo/sertraline group and the naltrexone/sertraline groups in terms of outcome measures: relapse to heavy drinking, abstinence, remission of depression, or overall improvement.

However, the gender subanalysis showed a slightly different picture. Men with positive outcomes did equally well on either regimen, with 40% of the placebo/sertraline and 45% of the naltrexone/sertraline groups considered well by 12 weeks. In women, only about 25% of those in the naltrexone/sertraline group were considered well by the trial's end, compared with 70% of those in the placebo/sertraline group.

Because so few women were in the trial, Dr. Dundon said it's impossible to make any clinical recommendations about naltrexone's suitability for older women with comorbid depression and alcoholism. ■

Paroxetine Doesn't Help Reduce Drinking in Anxious Patients

BY MICHELE G. SULLIVAN
Mid-Atlantic Bureau

CHICAGO — Paroxetine can take the anxiety out of the drinker, but it can't take the drinking out of the anxious person.

The drug did uncouple anxiety and drinking in patients who use alcohol to cope with severe generalized social anxiety, Dr. Sarah Book said at the annual meeting of the Research Society on Alcoholism. But compared with placebo, paroxetine (Paxil) had no effect on overall alcohol consumption.

Her 16-week randomized controlled trial pitted paroxetine (60 mg) against placebo in 42 patients with severe generalized anxiety and comorbid alcohol use disorders. The patients had no previous alcohol detoxification treatment. We wanted to see if we could intervene in the progression and prevent worsening of alcohol use, said Dr. Book, a psychiatrist at the Medical University of South Carolina, Charleston.

The patients' average age was 29 years; 50% were male. At baseline, their mean score on the Leibowitz Social Anxiety Scale (LSAS) was about 90, indicating severe social anxiety. Anxiety had its onset at age 12 years in these patients; the use of alcohol to cope with symptoms followed about a decade later. They were moderately dependent on alcohol, consuming about 15 drinks a week.

By week 16, the patients in the treatment group had a significantly greater decrease in their LSAS scores than did those in the placebo group (53% vs. 32%).

All of the patients completed a study-specific questionnaire on how often they drank to cope before and during social situations, and how often they would avoid such situations if they could not drink to cope. At week 16, those in the paroxetine group had significantly lower scores than did those in the placebo group, with 20% (vs. 40%) saying they still drank to cope with social situations, and 30% (vs. 70%) saying they would avoid such situations if they couldn't drink.

But when Dr. Book examined the total overall drinking, she found no differences between the groups in either frequency of drinking or quantity consumed. "We [also] saw no difference from baseline to week 1, a very important milestone in most alcohol treatment studies, and no change in drinking from baseline to end point."

A subanalysis confirmed that paroxetine uncoupled drinking and anxiety symptoms, Dr. Book said. When anxiety scores and drinking were plotted together for all patients, it was apparent that the drug reduced drinking to cope with social anxiety. "This relationship completely went away in the paroxetine group. Yet they continued to drink the same amount overall. For these people, something else is going on to maintain their alcohol use disorder."

GlaxoSmithKline Inc. provided the study medication; the study was funded by the National Institute of Alcohol Abuse and Alcoholism. ■