No increased risk of serious cardiovascular events among adults who use ADHD medications: study

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Although there have been cardiovascular safety concerns about attention-deficit/hyperactivity disorder (ADHD) medications because of their ability to increase heart rate and blood pressure levels, an analysis that included more than 150,000 ADHD users found no evidence of an increased risk of heart attack, stroke or sudden cardiac death associated with current use compared with nonuse or rare use among young and middle-aged adults, according to a study appearing in *JAMA*. The study is being released early online because of its public health importance.

"Between 2001 and 2010, use of medications labeled for treatment of ADHD increased even more rapidly in adults than in children. According to a 2006 U.S. Food and Drug Administration (FDA) advisory committee briefing on the safety of ADHD medications, more than 1.5 million U.S. adults were taking stimulants in 2005, and adults received approximately 32 percent of all issued prescriptions," according to background information in the article. "Placebo-controlled studies in children and adults indicate that stimulants and atomoxetine [a medication used to treat ADHD] elevate systolic blood pressure levels by approximately 2 to 5 mm Hg and diastolic blood pressure levels by 1 to 3 mm Hg and also lead to increases in heart rate. Although these effects would be expected to slightly increase risk for myocardial infarction [MI; heart attack], sudden cardiac death (SCD), and stroke, clinical trials have not been large enough to assess risk of these events."

Laurel A. Habel, Ph.D., of Kaiser Permanente Northern California, Oakland, and colleagues examined whether medications used primarily to treat ADHD are associated with an increased risk of heart attack, SCD, or stroke in adults. The researchers used computerized health records from 4 study sites, starting in 1986 at 1 site and ending in 2005 at all sites, with an additional assessment using 2007 survey data. Participants were adults 25 through 64 years of age with dispensed prescriptions for methylphenidate, amphetamine, or atomoxetine. Each medication user (n = 150,359) was matched to two nonusers on study site, birth year, sex, and calendar year (total users and nonusers = 443,198).

During follow-up, there were 1,357 cases of heart attacks, 296 cases of sudden cardiac death, and 575 cases of stroke. After analyses of the data, the researchers found that current or new use of ADHD medications, compared with nonuse or remote use, was not associated with an increased risk of serious cardiovascular events, such as heart attack, sudden cardiac death, or stroke. "We also found little support for an increased risk for any specific medication or with longer duration of current use. Results were similar when users were restricted to new users. Rate ratios did not appear to be influenced by prior cardiovascular disease or by prior non-ADHD psychiatric conditions. They also were similar across age groups. As expected, event rates were substantially higher in the Medicaid population; however, the rate ratio for current use was similar to that in other sites," the authors write.

The researchers also found that among ever users of ADHD medications, the adjusted rate ratio of serious cardiovascular events was nearly the same during periods of current use as during follow-up periods more than 1 year after use ended. Cardiovascular diseases were similar or slightly more prevalent in new users than nonusers.

The authors note that a modestly elevated risk of serious cardiovascular

events cannot be ruled out, given limited power of the study and a lack of complete information on some potentially important risk factors and other factors related to use of these medications.

In an accompanying editorial, Philip Shaw, M.D., Ph.D., formerly of the National Institute of Mental Health (currently with the Human Genome Research Institute), Bethesda, Md., writes that the findings of this study raise several clinically important issues.

"First, the findings support the final decision by the FDA in 2006 not to place a black box warning of serious cardiovascular events on ADHD medications for all children and adults but to pursue further research. The findings, however, do not directly inform the current black box warning for psychostimulants, which is confined to patients with structural heart lesions. The study focused on very rare events, which prevented examination of specific subgroups such as individuals with cardiac disease. Joint care by cardiologists and other physicians remains necessary for these individuals. In addition, the study provides no evidence to support routine obtaining of electrocardiograms before starting treatment, certainly insofar as this recommendation was driven by concerns about serious cardiovascular events."

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