Tricyclics Tied to 35% Higher Cardiovascular Risk

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A large population-based study has shown a link between tricyclic antidepressant medications and an increased risk of cardiovascular disease, adding to a growing body of evidence that the medications carry cardiovascular risks – both for people with and without existing disease.

In a cohort study of 14,784 adults without known CVD in Scotland, the use of tricyclic antidepressants for any amount of time and for any reason was associated with a 35% higher risk of being diagnosed with CVD within 8 years, even after accounting for potential confounders, including symptoms of anxiety and depression, which are also linked to CVD.

Tricyclic antidepressants have been shown to increase cardiac events, including myocardial infarction, in patients with CVD; however, few population-based studies have examined the effects on people without known CVD, said Mark Hamer, Ph.D., of University College London, the lead author of the findings published in the European Heart Journal (doi:10.1093/eurheartj/ehq438). Now, "the evidence is starting to become overwhelming," Dr. Hamer said.

Tricyclic antidepressants are an older class of medication whose psychiatric use has fallen off in favor of newer agents such as selective serotonin reuptake inhibitors. However, TCAs are still used widely to treat headache, Dr. Hamer said, citing a recent meta-analysis (BMJ 2010;341:c5222) revealing tricyclics to be more effective than SSRIs and placebo in preventing migraine and tension headaches, and also to be increasingly effective with longer-term use.

For their research, Dr. Hamer and his colleagues used data from the Scottish Health Survey, an ongoing cohort study conducted every 3-5 years in Scottish households. They combined data from surveys in 1995, 1998, and 2003 in adults aged 35 years and older (age 52.4 + 11.9 years, 43.9% men) without clinically confirmed CVD. Of the total study group, 2.2%, 2.0%, and 0.7% reported taking TCAs, SSRIs, or other antidepressants (including monoamine oxidase inhibitors), respectively.

Over a mean follow-up of 8 years, there were 1,434 CVD events in the study group, 26.2% of which were fatal, and 67.5% of the events were related to coronary heart disease. The risk of CVD events (including death, nonfatal myocardial infarction, coronary artery bypass, percutaneous transluminal coronary angioplasty, stroke, and heart failure) was elevated in TCA users, but this was not significant after adjusting for confounding factors. No associations were found between SSRI use and CVD. Dr. Hamer and his colleagues also found no significant associations between any antidepressant use and all-cause mortality.

However, the TCA users saw a 35% higher risk of CVD (multivariate-adjusted hazard ratio 1.35, 95% confidence interval 1.03-1.77) even after adjustment for confounding factors, which included physical activity, smoking status, alcohol use, socioeconomic status, body mass index, marital status, a history of psychiatric illness, and the presence of preclinical CVD risk factors as measured by the use of cardiovascular medication and antihypertension drugs.

The investigators noted that tricyclic antidepressants have been associated with weight gain and have been shown to have cardiotoxic effects. These "might explain the increased risk of CVD, including orthostatic hypotension, reduced heart rate variability, QT interval prolongation, and greater risk of hypertension," they wrote in their analysis.

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