Varenicline for smoking cessation linked to increased risk of serious harmful cardiac events

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The use of varenicline to stop smoking is associated with a 72% increased risk of a serious adverse cardiovascular event, states an article in CMAJ (*Canadian Medical Association Journal*).

Heart disease is a common cause of serious illness and death in smokers and is often a reason for people to stop smoking. Varenicline is one of the most commonly used drugs to help people quit smoking worldwide. When varenicline was launched in 2006, the US Food and Drug Administration (FDA) safety reviewers reported that existing data indicated it could raise the risk of adverse cardiac events. The FDA recently updated the label for Chantix based on a small increased risk of cardiovascular events among smokers with heart disease.

A team of researchers from Johns Hopkins University School of Medicine, Baltimore, Maryland; the University of East Anglia, Norwich, United Kingdom; and Wake Forest Baptist Medical Center, Winston-Salem, North Carolina, sought to investigate the serious cardiac effects of varenicline in tobacco users (smokers or smokeless tobacco users) compared with placebos in clinical trials. They looked at 14 trials that included 8216 patients (4908 people on varenicline and 3308 taking placebos). All trials except one excluded people with a history of heart disease.

In the study, 52 of 4908 (1.06%) participants taking varenicline had

adverse events compared with 27 of 3308 (0.82%) participants on placebo. Seven of the 4908 people taking varenicline died compared with 7 of 3308 receiving placebo.

"Among tobacco users varenicline use was associated with a significantly increased risk of serious adverse cardiovascular events greater than 72%," writes Dr. Sonal Singh, Johns Hopkins University School of Medicine, Baltimore, Maryland, with coauthors.

"However, despite achieving more than twofold higher rates of abstinence in the trials, which should potentially induce a cardiovascular benefit, the participants allocated to varenicline experienced an increase in the risk of serious adverse cardiovascular events," they write. "These increased risks of adverse cardiovascular events are seen in smokers with or without heart disease," according to the authors.

They note additional risks of depression, agitation and suicidal thoughts which resulted in the FDA issuing a boxed warning - the highest level of warning - for the drug.

Despite study limitations such as variable data and lack of statistical strength, the researchers conclude that "clinicians should carefully balance the risk of serious cardiovascular events and other serious neuropsychiatric adverse events associated with varenicline against their known benefits on smoking cessation."

In a related commentary, Dr. Taylor Hays from the Mayo Clinic writes, "Although these results suggest a measure of caution should be taken in prescribing varenicline for tobacco dependence treatment, the small absolute risk of cardiovascular events associated with varenicline treatment is outweighed by the enormous benefit for reducing cardiovascular morbidity and mortality that can be achieved with successful smoking abstinence."

"The risk for cardiovascular events is low and is far outweighed by the benefits of diminishing the truly "heartbreaking" effects of cigarette smoking," he concludes.

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