Warfarin users appear more likely to develop brain bleeding following stroke treatment

March 8 2010

Patients already taking warfarin who develop an acute stroke appear more likely to experience a brain hemorrhage following treatment with an intravenous clot-dissolving medication, even if their blood clotting function appears normal, according to a report posted online today that will appear in the May print issue of *Archives of Neurology*.

Intravenous tissue plasminogen activator (tPA), a clot-dissolving medication, is effective for acute ischemic stroke and generally results in improved clinical outcomes despite a slightly higher risk of brain hemorrhage, the authors write as background information in the article. Risk of hemorrhage is increased in some populations, including older adults and those with more severe strokes, high blood glucose levels, lower platelet counts and high blood pressure.

Use of anti-clotting medications, such as aspirin or warfarin, before having a stroke has raised further concerns about risk of hemorrhage. However, current American Heart Association/American Stroke Association guidelines permit the use of tPA in these patients as long as their results on blood clotting tests meet an international standard (described as an international normalized ratio of less than 1.7). Shyam Prabhakaran, M.D., M.S., of Rush University Medical Center, Chicago, and colleagues studied 107 patients (average age 69.2) with acute ischemic stroke who were treated with tPA between 2002 and 2009.

Of the patients, 13 (12.1 percent) were taking warfarin; all had an international normalized ratio of less than 1.7. "The overall rate of

symptomatic intracerebral hemorrhage was 6.5 percent, but it was nearly 10-fold higher among patients taking warfarin compared with those not taking warfarin at baseline (30.8 percent vs. 3.2 percent, respectively)," the authors write. "Baseline warfarin use remained strongly associated with symptomatic intracerebral hemorrhage after adjusting for relevant co-variates, including age, atrial fibrillation, National Institutes of Health Stroke Scale score and international normalized ratio."

Several mechanisms may explain this association, the authors note. The clot-dissolving effects of tPA may be enhanced by the clot-preventing effects of warfarin, even at low levels. In addition, the effects of warfarin last for an average of three days after the last dose, so the international normalized ratio may continue to increase following treatment with tPA.

Given the small size and other limitations of the study, it should "serve as a hypothesis-generating report that requires confirmation in larger cohorts," the authors conclude. "Further analysis including more extensive adjustment for confounding variables in larger data sets may prove useful."

More information: Arch Neurol. 2010;67[5]. doi:10.1001/archneurol.2010.25

Provided by JAMA and Archives Journals

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