Drug Monitor

HIV Treatment: Continuous or Episodic?

Continuous antiretroviral therapy is superior to episodic therapy, according to findings from the Strategies for Management of Anti-Retroviral Therapy, or SMART, trial funded by the National Institute of Allergy and Infectious Diseases and conducted at 318 sites in 33 countries. Enrollment in the trial was stopped earlier than anticipated—at 5,472 rather than the targeted 6,000 participants—because HIV-positive patients receiving episodic therapy had double the risk of progression to AIDS or death.

Researchers randomly assigned volunteers with HIV who had CD4 levels greater than 350 cells/mm^3 to either ongoing therapy, which did not take CD4 levels into account, or to a "drug conservation" (DC) strategy, in which patients received antiretroviral therapy (ART) only when their CD4 levels dropped below 250 cells/mm^3. In an effort to reduce adverse effects of ART and preserve treatment options, ART was stopped in the DC group when patients' CD4 levels rose above 350 cells/mm^3.

At the time of a review by an independent Data and Safety Monitoring Board, the average follow-up was approximately 15 months—though, for some patients, follow-up exceeded three years. Not only were participants in the DC treatment group at greater risk for disease progression but also for major complications (such as cardiovascular, kidney, and liver disease) that previously had been found to be associated with ART.

Patients assigned to the DC arm and currently receiving ART due to low CD4 levels are being advised to continue to receive treatment. Those who are currently not receiving ART are being advised to speak with their doctors about restarting it. While the long-term risks and benefits of the DC strategy remain uncertain, the NIH says the short-term information argues strongly for restarting ART.

Source: NIH News Release. January 18, 2006.

Aspirin Use and Stroke Prognosis

Results of a population-based study by researchers from Oulu University Hospital (OUH), Oulu and Helsinki University Central Hospital, Helsinki, both in Finland, suggest that taking regular, moderate doses of aspirin doubles the risk of death among patients experiencing spontaneous intracerebral hemorrhage (ICH).

The researchers studied the medical and death records of 208 patients admitted to OUH between January 2003 and September 2005 with a verified ICH. Of these patients, 44 used aspirin regularly, 26 used warfarin regularly, and 138 used neither drug regularly before their stroke. Other variables analyzed were age; sex; history of hypertension, ischemic or hemorrhagic stroke, cardiac disease, and cancer; bleeding disorders; current smoking; and ICH score. The ICH score was calculated based on the Glasgow Coma Scale (GCS) score on admission, volume, supra- or infratentorial location and ventricular extension of the hematoma, and the patient's age.

The mortality rates within three months were 73% for warfarin users, 43% for aspirin users, and 22% for nondrug users. The primary bleed was the cause of death for 18 of 19 (95%) of warfarin users, 17 of 19 (89%) of aspirin users, and 24 of 30 (80%) of nondrug users. In addition to aspirin use, warfarin use and an ICH score of greater than 2 on admission were independent predictors of death.

Of the 47 patients (n = 199) determined to have an ICH score of between 3 and 6, 55% had a GCS score of 3 to 4, 40% had a GCS score of 5 to 12, and 74% had a hematoma volume of greater than 30 cm^3. Most (89%) had intraventricular hemorrage and 13% had infratentorial hemorrhage. In addition, 28% were aged 80 or older; the older patients were more likely to be taking aspirin on a regular basis.

The researchers say the high mortality rate among warfarin users reflects the fact that most had large hematomas on admission (which were significantly larger than both aspirin users and nondrug users) and no effective measure to reverse the anticoagulant effect was used. They attribute the untoward effect of aspirin use on short-term outcome to early enlargement of hematomas caused by impaired hemostasis. They were unable to prove this hypothesis, however, because evaluation of a second CT scan, performed within a week after the ICH, was available for only 104 patients. On the other hand, they note, mortality during the first four days after the onset of ICH was higher in aspirin users (18%) than in nondrug users (11%), despite the fact that aspirin users did not have larger hematomas on admission than nondrug users.

If early hematoma growth is the real problem, using transfusions to reverse aspirin's antiplatelet effect might be beneficial, the researchers suggest, just as emergency reversal of anticoagulation is currently recommended for patients taking warfarin. ●

Source: *Stroke*. 2006;37:129–133.