Drug Monitor

Resuming Continuous Antiretroviral Therapy After Episodic Treatment

An episodic approach to antiretroviral therapy for HIV, in which therapy is guided by CD4+ cell counts, has been proposed as a way to mitigate the risks associated with long-term exposure to antiretrovirals. Unfortunately, the multinational Strategies for Management of Anti-Retroviral Therapy (SMART) study group previously found an increased risk of opportunistic diseases, death, and serious nonopportunistic diseases with this episodic approach. Now, the group has published findings on the effects of restarting continuous therapy in patients who had been receiving episodic therapy—and the results are mixed.

In the SMART study, 5,472 patients with HIV infection and CD4+ cell counts above 0.35 x 10^9 were assigned randomly to receive episodic or continuous therapy. Patients in the episodic therapy group had antiretroviral treatment deferred until their CD4+ cell counts dropped below 0.25 x 10^9. Once begun, an episode of antiretroviral therapy aimed to achieve maximal viral suppression and was continued until the CD4+ cell count once more exceeded 0.35 x 10^9. Based on the results showing excess risks, however, episodic therapy was discontinued in January 2006, and those patients in the episodic therapy group who had been receiving antiretroviral therapy before the trial were advised to restart it. Follow-up of all study participants was conducted through July 2007.

As of January 2006, 35.6% of patients in the episodic therapy group and 94% of those in the continuous therapy group were taking antiretrovirals. By study's end, these percentages were 83.4% and 95%, respectively. Among episodic therapy patients who resumed antiretroviral therapy, HIV RNA levels dropped rapidly but CD4+ cell counts recovered more slowly. By July 2007, the mean CD4+ cell count in the episodic therapy group remained 0.12 x 10^9 cells/L below the mean count at baseline. The hazard ratio for opportunistic disease or death in the episodic versus the continuous therapy group decreased significantly but remained elevated at 1.4.

The researchers attribute the residual risk of opportunistic disease and death to the fact that CD4+ cell counts remained significantly lower and HIV RNA levels remained significantly higher in the episodic therapy group than in the continuous therapy group. They point out that some episodic therapy patients who previously had taken antiretroviral therapy did not resume it as advised. And, for those who did resume therapy, the follow-up time of 18 months was insufficient for CD4+ cell counts to recover fully. Additionally, the researchers cite previous findings that interruption of antiretroviral therapy induces activation of tissue factor pathways, thrombosis, and fibrinolysisx—which also may have played a role.

Source: *Ann Intern Med.* 2008;149(5):289–299.

Caffeine: A Gateway Drug?

Is caffeine abuse a real medical issue? Researchers from Northwestern Memorial Hospital and Illinois Poison Center (IPC), both in Chicago, say not only is it a problem but it may be a clue in some patients to abuse of other pharmaceuticals. They conducted a retrospective review of cases reported to the IPC between January 2002 and January 2004—and were surprised by the number of calls regarding caffeine, which increased yearly. The trend may reflect the increasing number of caffeine-enhanced products on the market: More than 500 new energy drinks were launched worldwide last year, they note.

During the study period, there were 254 reported cases of caffeine abuse that were determined not to be suicide attempts, unintentional ingestions, therapeutic errors, or ingestions involving only a coffee or tea product. The mean age of these patients was 20 years (range, 10 to 64 years). Caffeine abuse took the form of nondietary medications in 79% of patients, caffeine-enhanced beverages in 14%, and dietary supplements in 14%. A total of 32 patients abused more than one form of caffeine. Sixty-four patients reported abusing caffeine for energy, and 12 reported abusing it to get high.

Concomitant abuse of other pharmaceutical products was identified in 74 (29%) of the patients, alcohol in seven patients, and illegal drugs in six. Notably, the researchers found concomitant abuse of pharmaceuticals increased the need for hospitalization—whereas age, sex, concomitant abuse of alcohol or illegal drugs, and intention of ingestion had no effect.

Although no patient died, the researchers say "a 13% rise in hospitalization associated with supplemental caffeine use in an era of overcrowded EDs and hospitals is not insignificant." They suggest that clinicians routinely inquire about caffeine use in selected patient groups. And they caution against discharging a patient presenting for inappropriate caffeine ingestion, on the assumption that it can't be seriously harmful, without

Continued on page 31

Continued from page 28

thoroughly investigating the use of other pharmaceuticals and ensuring the patient's safety.

Source: *Am J Emerg Med.* 2008;26(7):799–802. doi:10.1016/j.ajem.2007.10.018.

Medication Reconciliation: A Safety Opportunity Not to Be Missed

It can happen all too easily: One physician is reluctant to question a medication prescribed by another, or a patient keeps taking a drug beyond the intended duration of therapy. Either way, the result can be continued use of a medication without a clear indication—a situation that can threaten patient safety and add to the problem of polypharmacy. According to researchers from West Virginia University School of Pharmacy and Care Partners, Inc., both in Morgantown, and South University School of Pharmacy, Savannah, GA, a good time to correct such problems is during a medication reconciliation performed at hospital admission.

They retrospectively reviewed randomly selected medical records of adults admitted to general medical units at a large, university medical center in Morgantown, WV between June and December 2005. They attempted to match all home medications listed in the admission note with an appropriate indication documented in the admission note or the preadmission paperwork.

Of the 121 records reviewed, 84 (69.4%) had at least one medication that could not be matched with an appropriate indication. Patients with such "unspecified medications" were taking significantly more medications at home than those without unspecified medications (10.2 versus 7.5, respectively). One quarter were receiving proton pump inhibitors or histamine type 2 antagonists without a clear indication, and 14% were receiving selective serotonin reuptake inhibitors without a clear indication. These medication classes have been "recurrently implicated as 'overprescribed,'" the researchers note.

They acknowledge that not all the unspecified medications identified necessarily represent inappropriate therapies. The lack of a clear indication also could result from omission errors by patients or history takers or poor physician-patient communication. But their findings highlight the need for clinicians to delve deeper as part of the history interview. The researchers advocate a rigorous medication reconciliation program to reevaluate the need to continue medications at admission and discharge—and they suggest that pharmacists could play an important role in this type of program.

Source: *Am J Geriatr Pharmacother.* 2008;6(3):161–166. doi:10.1016/j.amjopharm.2008.07.001.