New Pain Guidelines Take Aim at NSAIDs

BY PATRICE WENDLING

CHICAGO — An updated guideline addressing persistent pain in older people takes a tough stance on the use of nonsteroidal anti-inflammatory drugs.

The American Geriatrics Society (AGS) guideline recommends that acetaminophen be considered for initial and ongoing treatment of persistent pain, particularly musculoskeletal pain. But in a significant departure from its 2002 guideline, the AGS recommends that nonselective NSAIDs and cyclooxygenase-2 (COX-2) selective inhibitors "be considered rarely, and with extreme caution, in highly selected individuals."

The AGS had recommended that seniors use over-the-counter or prescription NSAIDs (such as aspirin or ibuprofen) or COX-2 inhibitors before being prescribed an opioid. The current recommendation reflects recent good evidence that this is a risky strategy in older people, panel member Dr. James Katz said at the society's annual meeting, where the guidelines ("Pharmacological Management of Persistent Pain in Older Persons") were released.

Conventional NSAIDs are associated with adverse gastrointestinal events in 20% of patients, with 107,000 hospitalizations and 16,500 deaths attributed yearly to NSAID-related GI complications.

COX-2 inhibitors seem to produce fewer upper GI events than do other NSAIDs, but "all nonsteroidals, whether they are [COX-2 inhibitors] or not, have a significant portfolio of adverse effects that is noteworthy for the elderly population," said Dr. Katz, director of rheumatology at George Washington University in Washington. "They can aggravate hypertension, they can cause renal impairment by a variety of mechanisms, [they can cause] edema [and] gastrointestinal problems, and now we know cardiovascular and cerebrovascular disease can be attributed to nonsteroidal interaction."

Last year's study of 336,906 community-dwelling Medicaid beneficiaries by the VA Tennessee Valley Healthcare System extended concerns about COX-2 selective inhibitors to cerebrovascular disease, said Dr. Katz. The study suggested an increased risk of stroke with rofecoxib (Vioxx) and valdecoxib (Bextra), compared with the effects of nonselective agents (Stroke 2008;39:2037-45). The finding was not statistically significant, he noted, but both drugs have been withdrawn from the market.

Recent evidence also showed that combining a conventional NSAID with low-dose aspirin therapy increases the risk of GI bleeding beyond that of the NSAID alone (Curr. Opin. Rheumatol. 2008;20:239-45). In 2006, the Food and Drug Administration warned against taking aspirin and ibuprofen together because ibuprofen interferes with aspirin's acetylation effect.

More research is needed to determine whether other NSAIDs interfere with the cardioprotective benefits of low-dose aspirin, said Dr. Katz, who was part of a panel unveiling the guidelines at the meeting. Panel members also said that more data are needed on the safety of topical preparations of NSAIDs.

The revised guideline recommends the eradication of *Helicobacter pylori* prior to initiating NSAIDs for pain, and the use of a proton pump inhibitor or misoprostol for gastrointestinal protection in older persons taking nonselective NSAIDs or in patients taking a COX-2 selective inhibitor with aspirin.

The guideline recommends that physicians consider opioid therapy for patients with moderate to severe pain, pain-related functional impairment, or diminished quality of life because of pain. People with continual or frequent daily pain may be treated with around-the-clock, time-contingent dosing aimed at achieving steady-state opioid therapy, said Dr. Perry Fine of the pain management center at the University of Utah, Salt Lake City.

He noted the guideline's caution concerning methadone, and recommended that only clinicians who are well versed in its use and risks initiate and titrate the drug. "That doesn't mean you don't do it," said Dr. Fine, "but hook yourself up to someone who has a lot of experience

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Members of the American Geriatric Society panel on the pharmacologic management of persistent pain in older persons include (from left to right) Dr. Bruce Ferrell, Dr. Perry Fine, Dr. James Katz, Dr. F. Michael Gloth III, and Lori Reisner, Pharm.D., shown discussing the release of the guidelines at the AGS annual meeting.

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in this when you believe this drug is indicated, if you don't already have the experience."

Methadone-related deaths during pain treatment have risen up to eightfold in the past few years. This is largely because methadone is attractive as a relatively inexpensive drug, but it has an unpredictable and long half-life. That the drug stays active is a blessing, but that quality is also a problem because it accumulates in the body, Dr. Fine said.

Earlier this year, the American Pain Society and the American Academy of Pain Medicine released clinical guidance on the management of opioid therapy for chronic noncancer pain (J. Pain 2009;10:113-30). Like the AGS guidelines, that document stressed the need for clinicians to regularly assess patients for pain intensity, functional status, side effects, and safe and responsible use.

The updated AGS guideline gives new references and discussions on the use and limitations of newer adjuvant, topical, and other drugs for recalcitrant pain.

"Persistent pain isn't a normal part of aging and should not be ignored," Dr. Cheryl Phillips, AGS president, said in a statement. "As seniors become susceptible to more complex health ailments, the need for a clear and precise pain management plan is key."

The AGS published its first pain guideline in 1998. To arrive at the 2009 recommendations, a panel of experts conducted a systematic review of 2,400 abstracts and 240 data-based, full-text articles. The panel focused on pharmacotherapy because it is the most common strategy used for pain management among elderly people, as well as the area of greatest risk, said Dr. Bruce Ferrell of the University of California, Los Angeles, who chaired the panel. The 2009 update is to be published in an upcoming issue of the Journal of the American Geriatrics Society.

Dr. Katz disclosed that he has served as a paid consultant in the last 12 months for the American Academy of CME Inc. and for UCB Pharma Inc. Dr. Fine said he is a paid consultant or speaker for numerous pharmaceutical companies and has commercial interests in Johnson & Johnson and Cephalon Inc. Dr. Ferrell disclosed no relevant conflict of interest. ■