Short-Acting Opioids Up Fracture Risk in Elderly

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DENVER – Elderly patients who are placed on a short-acting opioid analgesic for treatment of arthritis pain are twice as likely to experience a fracture during the subsequent year, compared with those on a long-acting opioid, according to a large cohort study.

The increased fracture risk was particularly strong during the first 2 weeks after initiation of therapy, when the relative risk was almost sevenfold higher in patients on a short-acting opioid, such as propoxyphene or oxycodone, than in those who were started on an nonsteroidal anti-inflammatory drug (NSAID) or long-acting opioid, including fentanyl or sustained-release hydrocodone. After that initial 2-week period, the fracture risk associated with short-acting opioid therapy dropped off but remained about threefold greater than with NSAID therapy, Dr. Matthew Miller reported at the meeting.

The fracture risk during the first 2 weeks on a long-acting opioid did not differ significantly from that in patients who were placed on an NSAID.

When 90% of opioids prescribed to the elderly are short-acting, we may be putting people at unnecessary risk.

DR. MILLER

Over the course of 1 year, however, the difference grew such that the cumulative fracture risk was 2.6-fold greater in the group on a long-acting opioid than in those on an NSAID. In contrast, the relative risk of fracture at 1 year was increased 5.1-fold in elderly arthritis patients on a short-acting opioid, added Dr. Miller, associate director of the Harvard Injury Control Research Center, Boston.

"Our findings indicate that opioids increase the risk of fractures among older patients with arthritis, and suggest that clinicians should be alert to the possibility that short-acting opioids pose a significantly greater risk of fractures among older adults than do equianalgesic doses of long-acting opioids, especially during the first 2 weeks after initiating therapy," he observed.

These results have the potential to change clinical practice by shifting prescribing in the direction of greater use of long-acting opioids in the elderly. At present, short-acting opioids are prescribed far more often than long-acting ones.

"Our findings, if borne out in other databases, could help inform safer prescribing practices consonant with the latest American Geriatrics Society guidelines on the pharmacological management of pain in older persons, which recommend that all patients with moderate to severe pain, pain-related functional impairment, or diminished quality of life due to pain should be considered for opioid therapy," the physician continued.

His study involved 12,436 Medicare beneficiaries with arthritis who initiated monotherapy with an opioid analgesic, and 4,874 who started on an NSAID. Participants averaged 81 years of age, and 85% were women. Osteoarthritis was the diagnosis in 90%; the rest had rheumatoid arthritis. None of the subjects had been on an opioid within the previous 6 months.

Not surprisingly, patients who were started on an opioid tended to be somewhat sicker, with a mean baseline Charlson comorbidity index score of 2.2 in the short-acting opioid group, 2.1 in those on a long-acting opioid, and 1.6 in the NSAID group.

The primary study end point was the 1-year incidence of fractures of the hip, radius, ulna, or wrist. The incidence rate was 25 fractures per 1,000 person-years in the NSAID group, 128 per 1,000 person-years in those on short-acting opioids, and 53 per 1,000 person-years in the group on long-acting opioids.

A dose effect was evident. Patients on a low-dose opioid had a 2.2-fold greater fracture risk than did those on an NSAID,

after adjustment for comorbid conditions and other potential confounding variables. Patients on a moderate-dose opioid had a 4.6-fold increased risk. And those on high-dose opioid therapy had a 5.1-fold increased risk.

Among high-dose opioid users, patients who were placed on a short-acting opioid had an adjusted 2.1-fold greater risk of a fracture than did those on a high-dose, long-acting opioid.

Asked why he thought short-acting opioids were prescribed 13-times more frequently than long-acting ones in the study population, Dr. Miller replied that although the study didn't address this question, it's his impression that many physicians believe that if they place a patient on a long-acting opioid, the patient may not get pain relief quickly enough. Hence, the patient might take another dose, and then another, perhaps getting into the overdose range. This belief about long-acting opioids' sluggish onset of action, he added, is erroneous.

The cumulative relative risk of fracture at 1 year was 5.1-fold higher in elderly arthritis patients on a short-acting opioid, such as propoxyphene or oxycodone, than in those on an NSAID.

"It's important to recognize that the modern formulations of these long-acting drugs can actually provide adequate analgesia in a time scale that's similar to that for short-acting drugs, because of the long-acting agents' biphasic distribution in the blood stream. Yet 90% of the drugs that we're prescribing when we're prescribing opioids in an elderly population are short-acting drugs, raising the question of whether we're putting people at unnecessary risk," Dr. Miller said.

The Food and Drug Administration recently removed from the U.S. market one of the short-acting opioids in this study – propoxyphene – because of an increased risk for fatal heart rhythm abnormalities associated with its use.

Dr. Miller declared having no relevant financial interests. ■