Drug Monitor

ONLINE EDITION

Managing Postoperative Pain in Older Adults

"The common belief that acute pain is merely a symptom, will resolve as healing occurs, and is not harmful in itself relegates the relief of acute pain to a minor level of priority" for many health care providers, say researchers from Mount Sinai Medical Center, Manhattan, NY and the James J. Peters VA Medical Center, Bronx, NY. This can be detrimental to the patient who is trying to recuperate from lower extremity orthopedic surgery, since uncontrolled pain can impede functional recovery, they point out. In fact, their study findings suggest that aggressively managing pain in the immediate postoperative setting may reduce the development of chronic pain.

The study, of a generalizable interdisciplinary pain management program, is the largest to show that better pain control results in better rehabilitation for older adults after surgery, the researchers say. The intervention was a standardized pain management protocol that included daily comprehensive pain assessments by nursing and physical therapy (PT) staff, daily feedback of pain scores to all clinical staff, and a standardized analgesic protocol that included guidelines to help physicians treat adverse effects of opioids. The overall protocol called for analgesia to be administered based on patients' reports of pain on standing and, preemptively, one hour prior to each in-hospital rehabilitation PT session. Analgesia was adjusted for breakthrough pain and was titrated in order to prevent opioid withdrawal symptoms and adverse effects.

The intervention was implemented on one acute rehabilitation unit. Two other units, on which pain was assessed and treated according to "usual care" standards, served as control units. For their study, the researchers prospectively enrolled 248 patients aged 50 and older who had undergone hip fracture repair or unilateral total hip or total knee arthroplasty—150 from the intervention unit and 98 from the two control units. All study patients were interviewed daily about their pain, had physical performance testing conducted on days four and seven of postsurgery rehabilitation, and received follow-up telephone interviews every six weeks for 24 weeks after discharge to assess pain and walking ability. The researchers employed one-to-many matching, using propensity score, to match 88 control patients with 129 intervention patients. To confirm the findings of the propensity score analyses, they also employed multivariable modeling using data from all study patients.

Patients in the intervention group reported significantly less pain at rest and with PT than did control patients. They also were significantly less likely to report moderate to very severe pain during their last PT session before discharge and at discharge.

Additionally, intervention patients had significantly faster 8-ft walk times at rehabilitation day four than did the control patients (9.3 seconds versus 13.2 seconds, respectively); were significantly less likely than control patients to miss a PT session or to have a session cut short; and had a significantly shorter length of stay (10.1 days versus 11.3 days, respectively).

At six months postdischarge, only 4% of the intervention patients reported moderate to very severe pain when walking, 7% reported that pain interfered with walking, and 35% reported taking analgesics—compared with 15%, 18%, and 51%, respectively, of the control patients.

During the immediate, in-hospital recovery period, patients in the intervention group received 8 mg more oral morphine sulfate equivalents per day (23.6 mg/day versus 15.6 mg/day in the control group) and were significantly more likely to receive regularly scheduled opioid analgesia (98% versus 48% in the control group). As it is hypothesized that chronic pain stems from extended sensitization of the peripheral and central nervous systems, the researchers suggest that providing effective analgesia in the immediate postoperative period may prevent the development of central nervous system sensitization.

Source: *J Am Geriatr Soc.* 2009;57(1):1–10.

Anti-TNF-α Agents and Herpes Zoster

Drugs that inhibit tumor necrosis factor-α (TNF-α) may be effective therapy for patients with rheumatoid arthritis (RA) who do not experience relief from their condition from conventional disease modifying antirheumatic drugs (DMARDs). Unfortunately, anti-TNF-α agents make patients more vulnerable to bacterial infection. There also is concern that patients may be similarly at risk for viral infection since herpes zoster is one of the most common adverse events reported by patients taking anti-TNF-α agents and retrospective data suggest that herpes zoster occurs more often in patients with than in those without RA. To prospectively evaluate the risk of reactivation of the varicella zoster virus in patients taking varying RA treatments (with different mechanisms of action), researchers

from German Rheumatism Research Centre and Charité-University Medicine, both in Berlin, Germany, analyzed data on 5,040 patients.

The patients were identified from 150 outpatient clinics or private practices between May 2001 and December 2006. They were enrolled in the German biologics register RABBIT (a German acronym for Rheumatoid Arthritis—Observation of Biologic Therapy) when they started new DMARD treatment with one of two monoclonal anti-TNF-α antibodies (infliximab or adalimumab), new DMARD treatment with the anti-TNF-α receptor fusion protein etanercept, or new treatment with the biologic response drug anakinra. Patients who changed their DMARD treatment after experiencing at least one treatment failure with another conventional DMARD were enrolled as a control group.

During a three-year follow-up, 82 patients had 86 episodes of herpes zoster. Of these episodes, 39 could be attributed to one of the monoclonal anti-TNF-α antibodies, 23 could be attributed to etanercept, and 24 could be attributed to a conventional DMARD. Both older age and glucocorticoid use were found to increase patients' risk of developing herpes zoster. After adjusting for these two factors and for RA severity, the researchers found a significantly higher risk of herpes zoster in patients taking a monoclonal anti-TNF-α antibody than in those receiving conventional DMARDs—although this risk was lower than the threshold for clinical significance. No significant associations with herpes zoster were found for anti-TNF-α agents as a class or for etanercept.

Although major complications from any of the herpes zoster cases were rare in their study, the researchers recommend monitoring patients receiving treatment with infliximab or adalimumab for early signs of the infection.

Source: *JAMA.* 2009;301(7):737–744.