'Unacceptable' Pain Levels Common After Knee Arthroplasty
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February 14, 2012 (Miami Beach, Florida) — A "disproportionately large number" of patients participating in postoperative pain studies after knee arthroplasty receive inadequate analgesia and experience "unacceptable" levels of pain, according to a study presented here at the 6th World Congress of the World Institute of Pain.

In a meta-analysis of more than 12,000 patients who participated in pain studies from 2002 to 2011, as many as 3000 had unacceptable levels of pain, reported Kenneth Jensen, MD, and colleagues, from the University of Copenhagen, Bispebjerg Hospital, in Denmark.

The majority of undermedicated patients were in the control groups of studies, and were therefore receiving placebos or "no active comparator," which included systemic opioids — either alone or with other systemic analgesics, such as nonsteroidal anti-inflammatory drugs (NSAIDs), gabapentinoids, acetaminophen, and other weak nonopioid analgesics, Dr. Jensen told Medscape Medical News.

"We find this result problematic because current ethical standards dictate that we should not render patients in control groups less [optimally managed] than patients in intervention groups," he said.

"According to the Helsinki II declaration, no patients participating in clinical studies should receive inferior treatment for painful conditions because of randomization to treatment arms with placebo or regimens providing less analgesia than the best available standard," the researchers write.

The meta-analysis involved 376 cohorts of patients from 170 studies, and focused on "treatment failures" in the first 24 hours after surgery. Three criteria were used to define treatment failures: a visual analog scale (VAS) score of 5 or more out of 10 for maximal pain at rest; a VAS score of 7 or more out of 10 for maximal pain with movement; and an intravenous morphine (or equivalent) demand of more than 20 mg/day.

The Danish team found that of the postsurgical patients randomized to placebo or no active comparators, 43% had a VAS score of more than 5 at rest, 35% had a VAS score of more than 7 with movement, and 64% required more than 20 mg/day of morphine. That compares with 25%, 20%, and 41%, respectively, in patients in "active comparator" groups. Active comparators were defined as femoral nerve block, epidural analgesia, local infiltration analgesia (LIA), or combinations thereof.

"We find the use of systemic opioids as a control group questionable by today's scientific and ethical standards," the authors write.

The researchers were surprised at the percentage of patients receiving active comparator analgesics who also experienced "treatment failure."

Among patients receiving LIA, 31% had a VAS score of more than 5 at rest, 28% had a VAS score of more than 7 with movement, and 45% required more than 20 mg/day of morphine.

For patients who received femoral nerve block, these numbers were 22%, 19%, and 40%, respectively; for those who received epidural analgesia, they were 24%, 13%, and 39%, respectively.

"We find that new methods of pain relief, such as local infiltration analgesia, do not compete well against older methods, such as epidurals or peripheral nerve blocks."

"Opioids alone or in combination with systemic adjuvants are pretty lousy, by any standard," said Dr. Jensen. "LIA fares only slightly better than systemic opioids."
LIA, which was introduced in Australia and then popularized in several European countries, spread "almost overnight...basically without the proper documentation," said Dr. Jensen. "Despite good-quality studies and intermittently excellent results, many studies are, in fact, disappointing."

"The problem with the alternatives — nerve blocks and epidurals — is that "they impede mobilization considerably, and carry the risk of deep venous thrombosis or urinary bladder paresis, respectively," he noted.

What about the addition of adjuvant nonopioid analgesics to control breakthrough pain with LIA or systemic opioids?

Using the same data, the researchers looked at pain levels in patients who received adjuvant NSAIDs, gabapentin/pregabalin, paracetamol (acetaminophen), or any combination of these.

They found that the addition of these drugs "only marginally" reduce pain in the subgroup of patients with severe postoperative pain at rest.

The finding "supports our view that nerve blocks are pivotal for adequate pain management, systemic opioids are a troublesome but necessary default analgesic, and other systemic drugs are largely expendable in this clinical setting. Some of these results were really an eye opener for us," said Dr. Jensen.

Asked to comment on the findings, James Paul, MD, associate clinical professor, research chair, and director of the acute pain service at McMaster University in Hamilton, Ontario, Canada, told Medscape Medical News that "total knee arthroplasty is one of the most painful operations that we put our patients through, and the management of postoperative pain following this procedure is both challenging and vital to facilitate mobilization and rehabilitation."

"While control groups with placebos are necessary, in properly designed randomized controlled trials of new therapies, that doesn't mean that the placebo arms should receive substandard care or inadequate analgesia," he stressed.

He said his team recently studied gabapentin as an analgesia adjunct, in addition to patient-controlled analgesia (PCA) morphine, for knee surgery. Both the treatment and placebo groups received multimodal analgesia with acetaminophen and NSAIDs.

"It's true that gabapentin did not turn out to have a significant impact on analgesia outcomes for this surgery, but both acetaminophen and NSAIDs have been shown to improve the analgesia outcomes for many surgeries, including joint replacement," said Dr. Paul.

"Both epidurals and femoral nerve blocks with concurrent PCA opioids have been shown to provide good analgesia after knee surgery, with a fairly low incidence of severe pain," he added.

"In the case of epidurals, there is some evidence that they reduce the incidence of deep vein thrombosis. LIA followed by PCA opioids has had some promising results in a few small studies, but it is too early to say if it is effective. Larger studies are necessary."

The high incidence of poor pain scores and increased morphine consumption in the meta-analysis might be due to the fact that "many of the trials may have studied only the analgesia options, without also providing multimodal analgesia," said Dr. Paul.

These results "should serve as a reminder to investigators that placebo groups should get the best-known analgesia treatment minus the study drug. If the study drug is known to be effective, then the trial is likely not necessary."

Additionally, he cautioned that 20 mg/day of morphine "isn't necessarily too much; there is wide variability in opioid requirements, and some patients require larger dosages to have sufficient analgesia."
Dr. Jensen and Dr. Paul have disclosed no relevant financial relationships.


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