Opioid Alternatives Urged Postoperatively

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LAS VEGAS — Opioids maintain an important role in the treatment of certain types of pain, but clinicians typically have far more options than they realize to address chronic or acute noncancer pain ways that are potentially safer and equally effective, one expert says.

Speaking at PAINWeek 2013, James B. Ray, PharmD, CPE, clinical pharmacy coordinator for pain and palliative care at the University of Virginia Health Center in Charlottesville, urged clinicians to consider some of those other options.

"The way opioids are currently being prescribed reminds us of the old Mark Twain saying — 'If all you have is a hammer, everything looks like a nail'," Dr. Ray told colleagues here.

"Opioids are great and I have had great success with them in my career, but there are clearly some really scary things we're learning about overuse, particularly with ongoing chronic therapy, and we need to be thinking more about that," he said.

Synergistic Combinations Can Reduce Toxicity Risk

A good place to start is even rethinking the approach suggested in the title of his talk, "Rational Polypharmacy," replacing "polypharmacy" with the more appropriate term "multimodal."

"In acute, postoperative pain we call it taking a multimodal approach, which doesn't have as much of a pejorative tone, so I would suggest we use that term in treating chronic pain as well."

In a multimodal approach, the emphasis is centered on "achieving optimal pain relief with minimum toxicity" and combing drugs that have different mechanisms of action to produce a more synergistic effect.

"We want to promote a synergistic effect by potentiating the action of one agent with another — one plus one equals three," Dr. Ray said.

Acetaminophen, for instance, has been shown definitively in studies to work synergistically with opioids, enhancing pain relief in a way that is opioid sparing.

It can also be combined with nonsteroidal anti-inflammatory drugs (NSAIDs) such as ibuprofen for acute postoperative pain, provided that patients don't have comorbidity, such as cardiovascular conditions, that can place them at risk from NSAID toxicity.

But despite the well-known effects of acetaminophen and NSAIDs on their own or synergistically, and the potential benefit for acute, postsurgical pain, opioids are far too commonly the go-to drug, Dr. Ray said.

"There are patients who are much more sensitive to doses of opioids than you would expect postoperatively; that's why you need to use these agents," he said.

"Yet, I can't tell you how many times I ask a staff member, every day — 'Do you have the patient on acetaminophen around the clock?' 'No,' they respond. 'Do you have them on an NSAID?' 'No.' 'Are you giving them opioids?' 'Yes.' 'Is that all you're giving them?' 'Yes,' they say."

"We need to change that paradigm," he asserted. "We need to use other tools in our bag. These drugs can make significant differences in postoperative pain situation and reduce the overall morbidity that opioids cost."

Among the most concerning of opioid adverse effects are respiratory depressive effects, Dr. Ray said. "I am seeing more and more disordered breathing syndromes associated with chronic opioid use."

"Back in the 80s and early 90s we didn't have as many patients on chronic opioid therapy as we do now, and it's kind of a phenomenon that we need to put on our radar and think about more and more."

In terms of the treatment of chronic pain, Dr. Ray noted that data on the combination of acetaminophen and NSAIDs is not as clear, and the effect on renal function would be among the concerns with longer-term use.

Opioid Recommendations

Despite the many concerns about long-term opioid use, the drugs are highly valued as a cornerstone for handling malignant pain, but even in such cases, Dr. Ray cautioned that some opioids should simply be avoided.

Agonist-antagonists, for instance, are among these. "I have no regard for agonist-antagonists and I don't understand why they would ever be used either for acute and certainly not chronic pain," he said. "As far as I'm concerned they shouldn't be in anyone's bag or on anyone's formulary."

Of meperidine (*Demerol*), he says, "there is no reason to use this drug. None whatsoever."

Codeine, he notes, "is a pro drug that needs to be converted by the cytochrome P450 isoenzyme 2D6 to morphine and we have removed it, as well as any Tylenol-codeine products, from our formulary due to FDA [Food and Drug Administration] alerts of ultra-rapid metabolism. Why would you want to use a drug not reliably knowing whether it's going to work or if it is going to cause toxicity?"

Tramadol, he says, has "unreliable analgesic activity and you have to worry about side effects such as serotonin syndrome."

Despite acetaminophen's synergistic effect with opioids, Dr. Ray said he is not a fan of fixed combination products.

"In addition to codeine, we've taken Percocet (which combines acetaminophen and oxycodone) off of the formulary and the reason is that you're basically hamstrung when you use fixed combination products," he said.

"You cannot titrate the opioid up when you use the fixed combination."

Instead, Dr. Ray says postoperative orders at his center have a default setting for acetaminophen to a 3-g per day limit, with 1 g every 8 hours on a limited routine schedule.

"Surgeons generally order these drugs for PRN [as-needed] pain, but if acetaminophen is going to work, it needs to be given on a regular basis — you can't give it PRN if you want good analgesic effect."

"So it makes more sense to just give it by itself on a routine basis and then use the opioid as a single entity and titrate to effect."

Whether it's acute postoperative pain or chronic pain such as fibromyalgia, Dr. Ray echoed the common advice to "Start low and go slow."

Other key strategies should include frequent assessments and monitoring of side effects. Rotate drugs if needed but, importantly, with chronic pain, start with 1 drug at a time.

"With chronic pain, you're not going to win any race — you're in for the long haul, so take your time," he urged.

"If you throw a lot of drugs at a patient, you won't know what is responsible for pain relief and what is producing side effects. This will make it difficult to know how to sequentially move from one drug to another."

Start Low, Go Slow

Raj Kalra, MD, who is the medical director of Chronic Pain Management with Kaiser Permanente, Union City, California, commented that his approach in the treatment of chronic pain is to often start with NSAIDs or acetaminophen and topical agents and to move on to alternative pain medications such as tricyclic antidepressants or serotonin norepinephrine reuptake inhibitors (SNRIs) as well as anticonvulsants if necessary.

In a 2012 study reported by *Medscape Medical News*, Dr. Kalra and his colleagues reported that tricyclic antidepressants showed superiority over SNRIs in the treatment of chronic pain related to neuropathic pain and fibromyalgia.

If those treatments fail, he may consider the use of opiates. "The only time we use opiates is if the nonopioid and alternative pain medications are not as beneficial as we expected and patients continue to show functional limitations," he told *Medscape Medical News*.

"When opioid medications are prescribed, the 'start low and go slow' approach is recommended; however, if a patient develops intolerable side effects or shows an inadequate response to multiple dose escalations, we recommend either an opioid rotation or reduction."

Dr. Ray is a consultant and on the speaker's bureau for Millennium Laboratories and consultant to Cadence Pharmaceuticals. Dr. Kalra has disclosed no relevant financial relationships.

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