Ease Patients' Fear of Painkiller Addiction Through Education

BY SHERRY BOSCHERT
San Francisco Bureau

SAN FRANCISCO — Talking to elderly patients with chronic pain about the differences between addiction, dependence, and tolerance of drugs may help them overcome some fears about using opioids, Kathryn Healey Keller, Pharm.D., said at a joint conference of the American Society on Aging and the National Council on the Aging.

Treatment with opioids is becoming more acceptable for persistent noncancer pain, despite the common fear of addiction, especially among older patients, said Dr. Keller of the University of California, San Francisco, and a medical liaison for Purdue Pharma LP, a pharmaceutical company that specializes in pain medications.

She recommended explaining to patients that physical dependence is inevitable with continuous exposure to opioids because of the characteristics of these drugs, but this is not the same as addiction and "it's not a moral, personal issue," she said.

Give examples of other drugs that cause dependence with chronic use, such as prednisone or clonidine, she suggested.

Tell patients that dependence means they will have a rebound or withdrawal reaction if they stop taking any of these drugs, and alert them to the potential consequences if they stop opioid use suddenly.

Tolerance to a drug means that patients need more of the drug to maintain the same level of response. Coffee is a good example—people need to drink more of it over time to maintain the same caffeine buzz. Tolerance to opioids is slow to develop when treating stable disease, Dr. Keller noted.

Explain to patients that physical dependence is inevitable but is not the same as addiction.

DR. KELLER

Addiction is a neurobiologic disease involving a genetic predisposition and environmental factors that promote addiction. She said that patients who fear they're becoming addicted to opioids can consider "the four Cs" that help define addiction: **C**ompulsive use, lack of **C**ontrol, **C**raving for the drug, and **C**ontinued use despite harm to oneself or others.

Properly managed patients on opioids rarely become addicted. Chronic pain can be treated successfully even in patients addicted to opioids if they have the stable support of family and pharmacists, Dr. Keller said.

She recommended that physicians consult guidelines produced by the American Geriatrics Society Panel on Persistent Pain in Older Persons (J. Am. Geriatr. Soc. 2002;50[suppl.]:S205-24), which contain information on nonopioid analgesics, opioid options, and more. ■

Migraineurs Often Delay Headache Medication

BY TIMOTHY F. KIRN
Sacramento Bureau

VANCOUVER, B.C. — At least half of migraine patients who are given a prescription for a medication to abort their attacks wait too long to take their medication, making it less likely to be effective, Roger K. Cady, M.D., reported at the annual meeting of the American Headache Society.

In a pharmacy-based study of migraineurs, 49% of patients with severe migraines and 51% of patients with moderate migraines said they waited more than 2 hours after the onset of the most recent headache before taking the medication, which was either rizatriptan or another oral nontriptan, said Dr. Cady, director of the Headache Care Center, Springfield, Mo.

"You tell patients to treat early, but you really have no idea what that means to them," Dr. Cady commented.

Rizatriptan is considered to provide effective relief only 35% of the time if a patient waits 2 hours, he said in an interview. "They set themselves up for failure."

The most common reason that patients gave for delaying their treatment was to see if their headache really was a migraine. Overall, 86% of the study patients had other headaches as well as migraine.

This is probably unrealistic thinking on the patient's part, Dr. Cady commented. Most migraineurs are familiar with their migraines and the signs of an impending migraine.

Patients who had migraines for less than 3 years were one and a half times more likely to delay using the medication than those who had a longer history of migraine, he said.

Other reasons given for delay were wanting to rely on medication only for a severe attack (reported by 46% of those who delayed), having concerns about side effects (37%), having concerns that the drug would become less effective if taken too often (34%), having concerns about becoming dependent (29%), facing limits on supply from the provider (15%), and being worried about cost (9%). Also, 3% of the patients said they had been instructed by their physicians not to take the medication too early. ■

Synthetic Marine Snail Toxin Receives FDA Approval as Intrathecal Analgesic

BY ELIZABETH MECHCATIE
Senior Writer

An intrathecal formulation of a synthetic version of a toxin used by a fish-eating marine snail to catch its prey has been approved as a treatment for severe, chronic pain.

The Food and Drug Administration approved ziconotide for intrathecal (IT) infusion for managing severe chronic pain "in patients for whom intrathecal therapy is warranted and who are intolerant of or refractory to other treatment, such as systemic analgesics, adjunctive therapies, or IT morphine." It is being marketed under the trade name Prialt by Elan Pharmaceuticals Inc.

Ziconotide, which is not an opioid, is a synthetic version of a conopeptide used by a species of marine snail, *Conus magus,* to sting fish. In nature the toxin "is so powerful it stops the fish dead in its track, and the snail eats it," said Mark Wallace, M.D., director of the center for pain and palliative medicine at the University of California, San Diego.

The synthetic version is an N-type calcium channel antagonist. N-type calcium channels are located mainly in the dorsal horn cells of the spinal cord, predominantly on the superficial layers, in the area of substantia gelatinosa where pain fibers synapse, Dr. Wallace explained. Ziconotide "blocks those calcium channels at the level where these pain fibers meet up," essentially shutting them down, he said.

The three trials that led to approval included patients with "really refractory" pain due to causes such as low back pain, cancer pain, neuropathic pain, pain from nervous system injuries, and HIV-related pain, said Dr. Wallace, an investigator in the studies and a consultant to the manufacturer.

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The drug is a synthetic version of a potent toxin that the snail *Conus magus* uses to sting fish.

The three pivotal trials used the Visual Analog Scale of Pain Intensity (VASPI), as the primary end point.

The most recent trial was a multicenter study in 220 patients with severe chronic pain, described by most as refractory to treatments including IT morphine. Patients were first taken off IT medications and stabilized on analgesics that included opiates and the treated with placebo or ziconotide. At 3 weeks, VASPI scores had improved by a mean of 12% from baseline vs. a 5% mean improvement for patients on placebo, a highly significant difference. During treatment, the use of non-IT opioids dropped by 24% among patients on ziconotide, compared with 17% among those on placebo.

Dr. Wallace said ziconotide is not associated with addiction, withdrawal, or tolerance, and it is not a controlled substance. The most common side effects are neurologic, including neurocognitive impairment and dizziness.

The drug comes with a black box warning about possible severe psychiatric symptoms and neurologic impairment during treatment, and it is contraindicated in people with a history of psychosis. ■

Migraine Role Seen For Metoclopramide

Metoclopramide is an effective migraine treatment for adults—as few as four patients need to be treated to enable one to achieve significant pain reduction. But other antiemetics may have more effect on pain and migraine-related nausea, according to Ian Colman, a postgraduate student at the University of Cambridge (England), and his colleagues.

Their metaanalysis included five studies of metoclopramide vs. placebo (263 adults); three studies of metoclopramide vs. other antiemetics (194 patients); two studies of metoclopramide vs. non-antiemetics (60 patients); and seven studies of metoclopramide combinations vs. other agents (211 patients).

The drug was almost three times as effective as placebo for pain and nausea reduction, but not as effective as other phenothiazine antiemetics (prochlorperazine and chlorpromazine). Metoclopramide compared favorably with ibuprofen and sumatriptan, but there was not enough evidence to determine relative effectiveness, the investigators said (BMJ 2004;329:1369-73).

The combination studies suggested that metoclopramide might also be effective as an adjunctive treatment. Several of those studies showed that metoclopramide combinations were similarly, and more, effective for pain relief than were the comparison regimens.

"Given its nonnarcotic and antiemetic properties, metoclopramide should be considered as a primary agent in the treatment of acute migraine in emergency departments," they said.

—Michele G. Sullivan