

Patients Seek Natural Alternatives to NSAIDs

BY DOUG BRUNK
San Diego Bureau

LA JOLLA, CALIF. — The recall of Vioxx and safety warnings about Celebrex and Bextra created “a very insecure time for pain management,” Robert Bonakdar, M.D., said at a meeting on natural supplements in evidence-based practice sponsored by the Scripps Clinic.

But well before concern surfaced about the safety of those drugs, patients with inflammatory disease increasingly began to seek care from providers of complementary and alternative medicine (CAM) because they were dissatisfied with traditional care results.

“They thank their doctor for the NSAIDs, for the advice, for [the referral to] physical therapy, but they still have pain,” said Dr. Bonakdar, director of pain management at the Scripps Center for Integrative Medicine, La Jolla, Calif. “Also, people with higher pain intensity and duration, and those with a greater degree of self-care, are going to end up in more CAM offices.”

He discussed the following natural supplements, which have been found useful in treating pain associated with inflammatory disease:

► **Willow bark (*Salix spp.*)**. This agent contains multiple constituents including

phenolic glycosides, tannins, and flavanoids. In a double-blind, placebo-controlled trial of 21 patients who took 240 mg of salicin over a 2-week period, Western Ontario and McMaster Universities Osteoarthritis Index (WOMAC) pain scores were reduced 40%, compared with a 16% reduction among those on placebo.

At 2 weeks, the analgesic effect from willow bark was assessed to be about 40% of that from high-dose NSAIDs.

“There is a dose-response relationship,” Dr. Bonakdar said at the meeting, cosponsored by the University of California, San Diego. A randomized, double-blind placebo-controlled trial of 210 patients with low back pain who took 120 mg or 240 mg salicin demonstrated complete relief from pain in 21% and 39% of patients, respectively (Am. J. Med. 2000;109:9-14).

Only 6% of patients in the placebo group reported complete relief from pain.

The dosage used in trials varies, but it is typically standardized to 240 g salicin/day.

► **Phytodolor**. Available since 1963, this patented supplement is from Germany. It contains 1 mg salicin/mL, *Populus tremu-*

la, *Fraxinus excelsior*, and *Solidago virgaurea*. Of the nine randomized, controlled trials involving phytodolor, those with a placebo arm demonstrated superiority of phytodolor; six trials with a comparison group showed no benefit of phytodolor over NSAIDs.

One trial found a dose response to double-strength phytodolor vs. regular dosing at 2 weeks.

The typical dose in trials is 30 drops of standardized extract t.i.d.

► **Devil’s claw (*Harpagophytum procumbens*)**. This South African plant is

used for arthritis, myalgia, and as an external ointment for burns or sores. Its active ingredients are harpagoside and β -sitosterol.

There have been four double-blind, placebo-controlled trials involving 50-197 patients with osteoarthritis and low back pain. Patients were treated for 3-8 weeks with 50-100 mg harpagosides/iridoid content of 1.5%-3% (the typical dose in trials).

The treatments significantly improved the pain level and joint mobility in study participants. Side effects have included mild and infrequent GI symptoms (BMC

Complement. Altern. Med. 2004;4:13).

► **SAME (S-adenosylmethionine)**. This is an endogenous methyl donor that is a naturally occurring product of the reaction between methionine and adenosine triphosphate (ATP). It is postulated to have anti-inflammatory effects through inhibition of tumor necrosis factor- α and upregulation of proteoglycan synthesis and secretion into chondrocytes. SAME also appears to have a serotonergic effect that may support its pain-modulating abilities.

In a metaanalysis of 11 osteoarthritis trials, SAME appeared to be as effective as NSAIDs in reducing pain and improving functionality with fewer adverse effects than NSAIDs (J. Fam. Pract. 2002;51:425-30). SAME is typically initiated in the 200- to 400-mg range and titrated to between 600 and 1,200 mg with caution regarding its serotonergic effects.

Other natural supplements such as ginger (*Zingiber officinale*), boswellia (*Boswellia serrata*), turmeric (*Curcuma longa*), and essential fatty acids have also demonstrated anti-inflammatory activity in preliminary basic research or human trials. While these and other natural supplements have been documented for the treatment of pain, Dr. Bonakdar emphasized that “further well-done trials are required to advance understanding.” ■

Low-Dose Combos Top High-Dose Monotherapy for Sciatica

BY TIMOTHY F. KIRN
Sacramento Bureau

SNOWMASS, COLO. — Sciatica and low back pain respond best to low doses of medications used in combination as opposed to high-dose monotherapy, David G. Borenstein, M.D., said at a symposium sponsored by the American College of Rheumatology.

There are no magic bullets. Instead, “it’s trial and error and seeing what works with a patient,” said Dr. Borenstein, a textbook author and researcher who practices in a rheumatology group in Washington.

According to prescribing patterns, it appears that muscle relaxants are among the most effective medications for back pain, but they’re more effective when used in combination with other medications.

In a telephone survey of patients with acute low back pain contacted 1 week after an office visit, the best outcomes appeared to be associated with a combination treatment using a muscle relaxant and an NSAID together. Other respondents were taking no medication, or opioids, acetaminophen, and muscle relaxants alone (Spine 1998;23:607-14).

Dr. Borenstein said the survey findings are consistent with his own clinical experience using combination regimens, which he said can minimize side effects and have a synergistic effect. He added that providers could use a lot more guidance on how to use drugs in combination;

more dose-finding studies are needed.

In a report on two combined studies involving 1,405 patients with low back or neck pain, participants were randomly assigned to take the muscle relaxant cyclobenzaprine or placebo. Dr. Borenstein noted that the cyclobenzaprine outperformed placebo in three primary, patient-rated end points: relief from pain at the start of the day, assessment of medication helpfulness, and clinical global impression of change.

Interestingly, when the researchers looked at three doses—2.5 mg, 5 mg, and 10 mg—each taken three times daily, they found that all the doses were more effective than placebo. The 5-mg dose was no less effective than the 10-mg dose and was less likely to cause sedation, Dr. Borenstein said (Clin. Ther. 2003;25:1056-73).

Future strategies for treating low back pain may involve biologics such as infliximab, Dr. Borenstein said.

Yet to be published open-label trials of infliximab, conducted in Finland, have shown significant efficacy within hours of patients’ receiving a single injection, compared with controls that were given sham injections of saline.

Yet the only double-blinded, controlled trial reported to date found no benefit relative to placebo. The lack of efficacy seen in this unpublished trial may have been due to the high placebo response, Dr. Borenstein said. Another trial is underway. ■

Just 45% of Pain Patients Take OxyContin as Prescribed

BY BETSY BATES
Los Angeles Bureau

PALM SPRINGS, CALIF. — Just 45% of prescriptions for the opiate OxyContin (oxycodone HCl controlled release) are taken as directed by patients being treated for nonmalignant pain, according to a study of urine samples from approximately 5% of the nation’s outpatient pain clinics.

Fully 40% of the drug was recycled among other patients being treated for pain in 264 clinics whose combined case-loads exceeded 33,000 patients, Michael Kell, M.D., of the Labyrinth Institute of Smyrna, Ga., reported at the annual meeting of the American Academy of Pain Medicine.

Another 15% of OxyContin prescriptions were diverted to the black market, said Dr. Kell, who was chosen to present his poster in an oral format at the meeting. Dr. Kell, a toxicologist, collected his data using software technology that interprets highly specific urinalysis results that control for urine concentration and acidity and patient body mass index (BMI).

The urine from 55% of approximately 11,000 patients prescribed OxyContin either contained more of the drug, or less, than what would be expected based on the amount prescribed to them. To allow for time of day and other variations, Dr. Kell considered a patient com-

pliant if the level of OxyContin in his or her urine was within three standard deviations of the mean. Interestingly, about 15% of patients prescribed OxyContin had none of the drug in their urine.

At the same time, many patients being treated with alternative pain drugs in the clinics had OxyContin in their urine, suggesting that “most of the diversion was patient to patient,” Dr. Kell said.

“There is an incredible amount of diversion on the street [as well]. We tend to be in denial,” he added.

Funding for Dr. Kell’s study was provided by UD Testing Inc., a Marco Island, Fla., company that uses Dr. Kell’s software to monitor patient compliance with prescription medicine.

Another study presented at the meeting described very preliminary results from a novel oxycodone drug formulation called Remoxy. The formulation delivers a long-acting dose of the opiate in a gel cap designed to be impervious to efforts to extract the full dose to achieve a “spike” effect by crushing, freezing, heating, or dissolving it in various substances.

Current formulations of the drug can be manipulated in this way, adding to abuse and diversion.

Plasma concentrations were markedly lower in 20 subjects who took Remoxy after it had been tampered with, compared with concentrations among people who had taken crushed controlled-release formulations of oxycodone. ■