PRACTICAL PSYCHOPHARMACOLOGY

Ask About Pain in Initial Evaluations

Pain is a frequent concomitant of psychiatric disorders—depression, anxiety, and somatoform disorders in particular—and psychiatric difficulties are common among the estimated 86 million Americans who suffer from chronic pain.

"In many cases, you can't treat one effectively without treating the other," said Dr. Rollin M. Gallagher, professor of psychiatry at the University of Pennsylvania, Philadelphia. "The relationship is a two-way street, and psychiatrists are uniquely qualified to deal with that complexity."

Questions about pain should be standard in the initial psychiatric evaluation. When patients under treatment for chronic pain are referred for management of emotional issues, "psychiatrists need to provide empathy and an understanding of their suffering, and help with healthy adaptation to the sick role," said Dr. John R. Sharp of Beth Israel Deaconess Medical Center and Harvard Medical School, Boston.

Clinicians should communicate with the patient's other health care providers and be familiar with comprehensive pain centers and other community resources.

The bidirectional relationship between pain and depression is well recognized. Nearly half of depressed individuals in one survey reported at least one painful physical condition of at least 6 months' duration (low back pain and headache were most common), a rate four times as high as that reported by a nondepressed population (Arch. Gen. Psychiatry 2003;60:39-47).

"Pain can cause depression. It can make depression worse, more difficult to treat, and less likely to go into remission," said Dr. David A. Fishbain, professor of psychiatry at the University of Miami and a staff member at the university's comprehensive pain center.

Noradrenergic and serotonergic systems are implicated in pain transmission, and antidepressants that affect both are the drugs of choice for chronic pain.

"Tricyclics probably have the highest efficacy for the treatment of pain, and serotonin norepinephrine reuptake inhibitors [SNRIs] the next greatest efficacy," Dr. Fishbain said. "Selective serotonin reuptake inhibitors have [the] least."

Because tricyclics at antidepressant dosages might be difficult to tolerate, the SNRIs venlafaxine (Effexor) and duloxetine (Cymbalta) have become first-line treatment for most psychiatrists.

Dr. Fishbain observed that duloxetine is the only antidepressant with Food and Drug Administration approval for pain, and he said that his experience with this drug has in general been "slightly better" than it has been with venlafaxine.

Robert L. Barkin, Pharm.D., prefers venlafaxine. He noted that the older agent poses little risk of drug-drug interactions, whereas duloxetine inhibits cytochrome P450 2D6, a liver enzyme system involved in the metabolism of other drugs, including opiates.

Hepatotoxicity concerns make alcohol use problematic for patients taking duloxetine, said Dr. Barkin, clinical pharmacologist at the Rush Pain Center in Chicago and the North Shore Pain Center in Skokie, Ill.

The dual-action antidepressants also have a role in treating chronic pain without depression. Here, too, venlafaxine is his drug of choice.

The rationale for this drug should be explained carefully to patients who are sensitive to implications about the psychogenic origins of their persistent pain. "I say that venlafaxine, although an antidepressant, isn't being used because they're depressed but because it affects the same spinal pain pathways as opiates," he said.

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To minimize side effects, Dr. Barkin titrates very slowly: 37.5 mg/day for 15 days, 37.5 mg b.i.d. for another 2 weeks, then 75 mg b.i.d. Most patients respond at 150-225 mg/day.

A low-dose tricyclic is another option. Dr. Sharp said that he might consider this first, most often nortriptyline (10-25 mg/day) or an equivalent dosage of amitriptyline (25-50 mg). At these levels, which are well below those needed for antidepressant efficacy, the drugs are usually well tolerated. Serum levels can be monitored, he said.

For older patients and others in whom even low-dose tricyclics are contraindicated, poorly tolerated, or ineffective, he would probably opt for duloxetine, Dr. Sharp said.

Anticonvulsants have an important role for pain that is neuropathic in origin: diabetic peripheral neuropathy, postherpetic neuralgia, or trigeminal neuralgia.

According to Dr. Gallagher, this neuropathic category also includes low back pain with radiculopathy (sciatica), persistent pain that follows brachial plexus injury in a motor vehicle accident, repetitive motion injury like carpal tunnel syndrome, and the consequences of cancer chemotherapy, surgery, and radiation therapy.

Although various forms of neuropathic pain may involve different mechanisms and respond to different drugs, his first choice is frequently gabapentin (Neurontin), which is FDA approved for postherpetic neuralgia. "It's completely safe and doesn't react with anything else"—a particularly important consideration because many patients are taking anti-inflammatories and other drugs.

When prescribing gabapentin, "the big mistake is undertreatment," he said. In high-dose clinical trials, patients have received 3,600 mg/day, and he has prescribed doses as high as 5,000 mg. "Side effects tend to be minimal if you go up slowly," Dr. Gallagher said.

Pregabalin (Lyrica), recently approved for the pain of diabetic neuropathy as well as postherpetic neuralgia, is another option. Typical dosages are 150 mg b.i.d., he said.

The anticonvulsant that Dr. Barkin prefers is topiramate (Topamax), which he prescribes for neuropathic pain if venlafaxine fails. Topiramate affects neurotransmitters more broadly than other drugs, he pointed out, and causes weight loss.

For Dr. Fishbain, carbamazepine, an older anticonvulsant approved for one neuropathic pain indication—trigeminal neuralgia—has been effective for other indications as well.

"Some patients with complex regional pain syndrome have responded" to duloxetine, as have "some with fibromyalgia syndrome, which is now thought by many to be a neuropathic pain condition," he said.

Dr. Gallagher observed that polypharmacy is the rule when treating neuropathic pain. "You can't change the disease process itself. What you can do with each drug is incrementally turn the pain down," he said.

Anxiety frequently exacerbates chronic pain conditions: The association, notably in posttraumatic stress disorder and panic disorder, is in fact stronger than the one between pain and depression (Curr. Psychiatry Rep. 2005;7:213-9). A dual-action antidepressant such as venlafaxine, may be effective for these patients.

Low-dose benzodiazepines can have a role as well, Dr. Sharp said. When other central nervous system depressants, such as opioids, are prescribed, benzodiazepines must be used with particular caution and at the lowest practicable dose, he said. ■

By Carl Sherman, contributing writer

Trial Data Awaited on PFO Closure for Migraine Relief

BY DAMIAN McNAMARA
Miami Bureau

SCOTTSDALE, ARIZ. — Existing data suggest that a subset of migraine patients may benefit from closure of their patent foramen ovale, Dr. David W. Dodick said during a symposium sponsored by the American Headache Society.

However, any clinical decision of the merits of surgical closure of a patent foramen ovale for patients with migraine should await the results of a number of ongoing safety and efficacy trials, he stressed.

Closures are being done with regularity as a treatment for migraines in the United States and Europe despite the lack of safety and efficacy data. "This [procedure] is gathering momentum, to say the least. We have a responsibility to know the data and give patients proper and appropriate advice," said Dr. Dodick, professor of neurology at Mayo Clinic Arizona. "This is something patients will come into your office wanting to talk about, if they haven't already."

Physicians are in a tough spot between patient demand and a dearth of data to support patent foramen ovale (PFO) closure for migraine relief, he acknowledged.

Some research indicates an association between a PFO and migraines with aura, particularly in patients with a large left-to-right shunt. In one study, patients with migraine with aura were three times more likely to have a PFO than those who experienced migraines without aura (Neurology 1999;53:2213-4).

The main take-home message for now remains that PFO appears to be more prevalent in patients whose migraines involve aura, Dr. Dodick said.

A left-to-right shunt is also more common among migraine-with-aura patients. In addition, both large atrial shunts and large PFOs are dominantly inherited and might therefore share a genetic origin (Heart 2004;90:1315-20).

One of the large, prospective trials underway is the Migraine Intervention with STARFlex Technology (MIST) study. Patients with migraine with aura will be assessed by a cardiologist and then randomized to closure or no closure.

Although results are not finalized, enrollment data show 60% of 370 participants having a right-to-left shunt (versus 27% of the general population) and 38% having a large PFO (versus 7% of the general population).

Updates and an animation that shows a possible role of PFO in migraine can be viewed on www.migraine-mist.org.

PFO closure might effectively treat migraine in a subgroup of patients, Dr. Dodick proposed. A number of studies suggest that closure eliminates migraines in about one-third of migraineurs, reduces frequency in another third, and does not alter attacks in another third of patients.

"Are there factors that will reliably predict which patients will benefit? If these studies are positive, how will we know that a patient in front of us in the future will benefit significantly from this invasive procedure?" he asked.

Many headache specialists are taking a conservative stance. "While many patients have disabling migraines, many people think migraines are not life threatening. They are life altering but not life threatening," Dr. Dodick. "And the surgery is invasive."

There is an overall peri-interventional adverse-event rate of about 6% (Catheter Cardiovasc. Interv. 2004;62:512-6). ■