Top Five Challenges In Osteoporosis Tx

BY BRUCE JANCIN

ESTES PARK, COLO. — Poor adherence accounts for more than 90% of all cases of failure to respond to osteoporosis therapy as evidenced by declining bone density or a fracture.

Lack of medication efficacy, on the other hand, is the least likely of the common causes for failure to respond. It ranks behind calcium/vitamin D deficiency, hyperthyroidism and other comorbid conditions, and the use of corticosteroids or other osteoporosis-inducing medications to treat comorbid conditions, Dr. Michael T. McDermott said at a conference on internal medicine sponsored by the University of Colorado.

He singled out failure to respond to treatment as one of the five top challenges in osteoporosis management today. Here are the other challenges highlighted by Dr. McDermott, professor of medicine and director of endocrinology and diabetes practice at University of Colorado Hospital, Denver:

► **Osteoporosis-inducing drugs.** Glucocorticoids top the list. They simultaneously reduce bone formation and increase bone resorption, resulting in quick bone loss in patients taking steroids. Serious consideration should be given to prescribing osteoporosis therapy in any patient who has ever been on 5 mg/day or more of prednisone for at least 3 months, Dr. McDermott said.

Compelling 18-month data from a randomized trial of teriparatide (Forteo) versus alendronate (Fosamax) for the treatment of glucocorticoid-induced osteoporosis showed teriparatide to be the clear winner, both in terms of increased bone density and fewer vertebral fractures (N. Engl. J. Med. 2007;357:2028-39). The soon-to-be-published 3-year follow-up data confirm this.

"Teriparatide may be one of our go-to medications for our more severe cases of glucocorticoid-induced osteoporosis," Dr. McDermott said.

He added that the No. 2 class of medications causing osteoporosis may come as a surprise to many physicians: anticonvulsants. "Anticonvulsant-induced osteoporosis hasn't been recognized as much, but it's emerging as quite important. It's a much bigger problem with phenobarbital, Dilantin, and Tegretol than with the newer anticonvulsants," he said.

"If you have a person on chronic anticonvulsant therapy, monitor their bone density, monitor their calcium, and rather than having a goal of 1,000 IU/day of vitamin D, they should be on 2,000-4,000 IU/day. I think that's reasonable. There's no data on bisphosphonate use in patients on anticonvulsants, so I'd just have a high index of suspicion," he continued.

► **Atypical fractures of the femoral diaphysis.** These fractures are the most recent and worrisome development in the osteoporosis field. Many experts now informally advocate a bisphosphonate therapy holiday after 5 years of use in an effort to avoid these fractures.

► **Osteonecrosis of the jaw.** This condition is marked by nonhealing exposed bone for at least 8 weeks following an invasive dental procedure such as tooth extraction. Dr. McDermott said that he doesn't see it often, but he fields many phone calls about it from physicians and dentists.

The great majority of cases have occurred in patients on high-dose intravenous bisphosphonate therapy for underlying bone cancer; oral bisphosphonates have not been shown to cause the disorder. Nevertheless, when Dr. McDermott is ready to start a patient on a bisphosphonate, he asks if a tooth extraction or dental implant is planned; if so, he'll wait to start the drug until after the procedure.

"If a person is on a bisphosphonate and a dentist calls me and says, 'I will not do this dental work while your patient is on that medication,' I'll stop it for 3 months," he said. "There's no data to support what I've just said. However, we know that the resolution of effect for these medications is 6-12 months. People will not lose bone density by stopping their medicine for only 3 months, and it gets the dentist to do the surgery."

► **Osteoporosis medications and renal disease.** Citing a lack of safety data, the Food and Drug Administration recommends against using bisphosphonates in patients with an estimated glomerular filtration rate (eGFR) below 30 mL/min per 1.73 m^2. However, limited experience indicates that treatment is reassuringly safe and effective in patients with an eGFR of 15-30 mL/min per 1.73 m^2, Dr. McDermott said.

"I do caution against antiresorptive therapy in patients with an eGFR below 15 mL/min—stage 5 chronic kidney disease—because it may predispose to adynamic bone disease," he added.

Dr. McDermott disclosed serving on the speakers bureaus of several pharmaceutical companies. ■

MINDFUL PRACTICE

Does Vertebroplasty Stand Up?

BY JON O. EBBERT, M.D., AND ERIC G. TANGALOS, M.D.

The Problem

A 76-year-old woman with a history of hypertension, coronary artery disease, and osteoporosis presents with subacute onset of lumbar back pain. She describes the pain as sharp, 10 out of 10 in severity, with some radiation around to her right side. She says she obtains little relief with over-the-counter analgesics. She denies fevers and chills, recent trauma, or bowel or bladder changes, and has no history of cancer. She is on aspirin, metoprolol, simvastatin, hydrochlorothiazide, alendronate, and acetaminophen. On exam, she is afebrile with sharp pain over the midline lumbar region. Neurologic examination is normal. Radiography shows anterior wedging of the L3 vertebra clinically suspicious for a new compression fracture. The patient lives at home alone and, up until this point, she has been able to care for herself. However, because of the back pain, she is having increasing difficulty standing for prolonged periods of time to prepare her meals. You diagnose the patient with a vertebral compression fracture at L3 and consider vertebroplasty due to her pain and impaired functional status. Before referring her for evaluation for vertebroplasty, you decide to review the evidence.

The Question

In patients with acute vertebral compression fracture, does vertebroplasty decrease pain and disability, compared with a control condition?

The Search

You log on to PubMed (www.pubmed.gov) and enter "vertebroplasty," limiting the search to "randomized controlled trials." You find a relevant study. (See box at right.)

Our Critique

This was a well-conceived and well-conducted clinical trial performed to answer an important clinical question. We were impressed that a sham procedure was included to evaluate the treatment modality. Some uncertainty exists relating to the type of subject complaints that triggered a crossover to the alternative procedure; however, this is less of a concern because primary outcomes were assessed before crossover.

Clinical Decision

You prescribe calcitonin, acetaminophen, oxycodone, and polyethylene glycol or Milk of Magnesia as needed to produce a bowel movement every day. She wants to continue living independently at home, so she arranges to have a family member check on her twice per day. You arrange a follow-up visit with you 1 week later to assess her pain and make medication adjustments as necessary.

DR. EBBERT *and* DR. TANGALOS *are with the Mayo Clinic in Rochester, Minn. They report having no conflicts of interest. To respond to this column or suggest topics for consideration, write to Dr. Ebbert and Dr. Tangalos at our editorial offices or e-mail them at imnews@elsevier.com.*

D.F. Kallmes, et al.

A randomized trial of vertebroplasty for osteoporotic spinal fractures. N. Engl. J. Med. 2009;361:569-79. PubMed PMID: 19657122.

► **Design and Setting:** Multicenter randomized, controlled clinical trial of interventional radiology patients.

► **Subjects:** To be enrolled, potential subjects had to be at least 50 years of age and have one to three recent, painful vertebral compression fracture at levels T4 to L5 occurring within the previous 12 months and confirmed with a physical examination and radiographic imaging, tried medical therapy for pain, current subjective pain rating of at least 3 on a 0-10 scale (10 being highest), and a confirmed diagnosis of osteoporosis or osteopenia.

► **Intervention:** Subjects were randomly assigned to receive either a full vertebroplasty procedure or the control intervention. For the control arm, verbal and physical cues were given such as pressure on the patient's back and the smell of polymethylmethacrylate (PMMA), but the needle was not placed and PMMA was not infused. Patients were allowed to cross over after 1 month if adequate pain relief was not achieved.

► **Outcomes:** The primary outcome measures were scores on the modified Roland-Morris Disability Questionnaire (RDQ) (on a scale of 0-23, with higher scores meaning more disability) and patients' ratings of average back-pain intensity during the preceding 24 hours (0-10 scale, with higher scores indicating more severe pain). The primary outcome timepoint was 1 month. Treatment effects and confidence intervals were adjusted for baseline values of the outcome measure, recruitment site, and an indicator of study group as the predictor of interest. Secondary outcomes included pain and quality of life measures.

► **Results:** A total of 131 patients were randomized (68 vertebroplasty and 63 control). Subjects were similar at baseline. At 1 month, mean (±SD) RDQ score in the vertebroplasty group was 12.0 ± 6.3, compared with 13.0 ± 6.4 in the control group (adjusted treatment effect, 0.7; 95% confidence interval [CI], –1.3 to 2.8; $P = .49$). At 1 month, mean pain-intensity rating was 3.9 ± 2.9 in the vertebroplasty group and 4.6 ± 3.0 in controls (adjusted treatment effect, 0.7; 95% CI, –0.3 to 1.7; $P = .19$). Both groups had significant improvement in back-related disability and pain within 3 days of the procedure, and the improvement was maintained at 3 months. No differences were observed between groups in pain or quality of life. Notably, 8 subjects (12%) in the vertebroplasty group and 27 (43%) of control subjects crossed over.