DRUGMonitor

Brief summaries of recent drug approvals, interactions, and adverse events

Gel Implant Relieves Sciatica

As many as 40% of people experience ≥ 1 episode of sciatica in their lifetime due to spinal disk herniation and nerve root irritation. Treatment may not help—research has shown that pain associated with sciatica often remains the same over the long-term. For that reason, most treatment is aimed at relieving short- to mid-term pain and reducing functional mid- to long-term disability.

Treatment for sciatica ranges from oral treatments to spinal corticoids to surgery. Discectomy is avoided when possible, because the outcomes are often compromised by chronic pain and postoperative complications. However, there may be some hope for individuals with sciatica whose only recourse might be aggressive surgery: a percutaneously implanted medical device that injects into the spine a viscous gel containing ethylcellulose and tungsten radiopaque suspended in 95% ethanol.

Researchers from Hôpital Tastet-Girard in Bordeaux and Hôpital Haut-Lévêque in Pessac, both in France, conducted a study of 79 patients who had experienced lumbar sciatica for an average of 14 months. The patients were injected (under neurosedation) with 0.7 mL gel at the recommended rate of 0.1 mL every 30 seconds. Once the injection was complete, the needle was left in position for 2 minutes to minimize the risk of leakage when it was removed. To increase the procedure's safety and efficacy, filtered air discography was performed with a 10-mL syringe and a bacterial filter.

After the operation, 3 patients reported an increase in pain by 1 to 4 points. When evaluated 1 week after the procedure, mean pain levels had significantly declined ($P < .0001$), although 4 patients reported pain increases by 1 to 4 points.

Two months after treatment, the mean reduction in the initial pain level was 74%. Those results remained relatively stable during the 8 months of follow-up. The researchers say they observed a tendency for initially unsatisfactory outcomes to worsen, but they also saw further improvement in patients who reported a > 50% reduction in pain during the first 2 months. No one reported sensory or motor impairments.

Only 3 patients with extreme initial pain reported that pain recurred during the long-term follow-up. By the end of the 8 months, 61% of patients no longer experienced any pain, and 76% of patients considered the treatment outcome good or very good. Moreover, 74% had returned to work.

Source: de Sèze M, Saliba L, Mazaux JM. *Ann Phys Rehabil Med.* 2013;56(2):143-154. doi: 10.1016/j.rehab.2013.01.006.

Antidepressants for Heart Failure Patients—Are There Benefits?

Heart failure (HF) patients with symptoms of depression have triple the risk of hospitalization and double the risk of death at 1 year vs patients without depression. But the research on whether antidepressants raise or reduce risks of rehospitalization and death for HF patients has produced conflicting findings.

To help settle the question, researchers from the University of Kentucky in Lexington conducted a secondary analysis of data from a multicenter registry of HF patients. They found that depression, not antidepressant use, independently predicted death and cardiac hospitalization. Depressed patients had 4 times the risk of cardiac events compared with nondepressed patients on antidepressants. In fact, antidepressant use not only did not improve outcomes, but also was associated with worse outcomes in outpatients who still reported depressive symptoms.

The "most compelling finding" in their study, the researchers say, was that patients who were prescribed antidepressants but still reported high levels of depressive symptoms had the highest risk of hospitalization or death compared with other groups.

Of 209 patients studied, 48 patients (23%) were on antidepressants at baseline, including patients who did not have symptoms of depression. During the 1-year follow-up period, 68 patients were hospitalized and 6 died. More than half the hospitalizations were related to worsening HF symptoms or another cardiovascular diagnosis. However, patients with depressive symptoms had more than double the risk of cardiac hospitalization or death compared with those patients without depression.

The researchers offer several potential reasons for why a significant portion of the patients in the study had high levels of depressive symptoms even though they were taking antidepressants ($P < .001$). One reason is that the patients could have treatment-resistant depression, which is clinically significant, because it can lead to a higher risk of death. A second reason is nonadherence, a problem among depressed patients with HF who often do not follow treatment regimens for medications, diet, and exercise. A third reason could be inadequate dosage or follow-up; the researchers say clinicians need to continually reevaluate depressive symptoms to ensure adequate treatment once patients are started on antidepressants.

Many patients with advanced HF

had depressive symptoms regardless of antidepressant use: 75% of those taking antidepressants and 81% of those who were not. That high rate of untreated or undetected depression may represent the symptom overlap—for example, fatigue, loss of appetite, sleep disturbance—between depression and advanced HF, the researchers say.

Another important reason why the study found so many patients with untreated depression may be that health care providers are "uncomfortable" or "reluctant" to prescribe antidepressants because of potential adverse effects, such as hypotension and drug interactions, the researchers say. For the patients who simply do not want to take antidepressants, nonpharmacologic strategies (eg, cognitive behavioral therapy, exercise, and psychosocial interventions) may help.

Source: Chung ML, Dekker RL, Lennie TA, Moser DK. *Heart Lung.* 2013;42(2):85-91. doi: 10.1016/j.hrtlng.2012.12.003.

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Chelation: Long Established, but Is It Safe?

Chelation with disodium ethylenediaminetetraacetic acid (EDTA) has been used since the 1950s to treat angina, atherosclerosis, and other coronary and peripheral artery diseases. However, although anecdotal and case reports were favorable, no clinical studies had found any treatment efficacy. Mainstream medical organizations consider chelation potentially dangerous, because it can lead to hypocalcemia and even death, say researchers from the Trial to Assess Chelation Therapy (TACT) sponsored by Mount Sinai Medical Center in Miami, Florida, the first randomized trial designed to evaluate the effects of an EDTA-based chelation regimen in patients with coronary disease.

In response to the "public health problem…[of] large numbers of patients being exposed to undefined risks for unproven benefits," the researchers recruited 1,708 patients at 134 sites in the U.S. and Canada. The participants were aged ≥ 50 years, had experienced a myocardial infarction (MI) at least 6 weeks prior, and had serum creatinine levels of ≤ 2 mg/dL. Patients were randomly assigned to receive 40 infusions of a 500-mL chelation solution or placebo and, additionally, to an oral high-dose vitamin-and-mineral regimen or placebo. This report describes the results of the chelation-vs-placebo protocol.

The primary endpoint was a composite of death from any cause, reinfarction, stroke, coronary revascularization, or hospitalization for angina. Data from 115 chelation patients and 174 placebo patients who withdrew consent for continued follow-up were included in the analysis.

In stable patients with MI, chelation resulted in a "modest" reduction (18%) of a composite of cardiovascular events, an effect that persisted over 5 years without evident attenuation. Two groups in particular seemed to benefit from the chelation regimen: Patients with diabetes and patients with anterior MI both saw reduced risk of cardiovascular events. The researchers note that, "an 18% relative treatment effect is within the range of effects that have been considered clinically important in prior trials, such as the use of clopidogrel for patients with acute coronary syndromes."

Revascularization accounted for 45% of primary endpoint events. The composite of cardiovascular death, nonfatal MI, or nonfatal stroke occurred in 96 chelation patients (11%) and 113 placebo patients (13%) (P = .22).

Four patients suffered unexpected severe adverse events possibly or definitely attributed to the study therapy; 1 patient in each group died. In addition, 52 chelation patients and 30 placebo patients developed hypocalcemia. In each group, 7% to 8% of patients had heart failure. The study was underpowered to detect a difference between groups for cardiovascular death, MI, or stroke.

Their results provide evidence to guide further research, the TACT investigators say, but are not sufficient to support the routine use of chelation for patients who have experienced MI.

Source: Lamas GA, Goertz C, Boineau R, et al; TACT Investigators. *JAMA.* 2013;309(12):1241-1250. doi: 10.1001/jama.2013.2107.

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