21st Annual Meeting of the American Academy of Pain Medicine.

Interventional Approaches to Pain Management CME/CE

Disclosures

Daniel S. Bennett, MD, DABPM

The treatment of pain encompasses the use of both drug and nondrug therapies. At the 21 st Annual Meeting of the of the American Academy of Pain Medicine (AAPM), both topics were given free reign. Because the efficacy of pharmacologic therapies is estimated to be less than 40%, neuromodulation in both chemical and electrical modes is emerging as a leading technology in the treatment of neuropathic pain. Numerous exceptional sessions at this year's meeting addressed both chemical and electrical approaches to pain management.

This discussion focuses on the various symposia, clinical and scientific presentations, and research poster submissions related to the use of nonopioid therapies for the management of pain.

The Cutting Edge

Dr. Robert Levy discussed the use of supraorbital stimulation for neuropathic facial pain, in an Update Session on innovative surgical strategies for pain management.[1] This type of pain has been recalcitrant to pharmacotherapeutics, and outcomes following ablative and decompressive surgery have been suboptimal. Levy demonstrated the percutaneous surgical implantation techniques of positioning linear electrode "strings," which have shown high success rates (> 75%) in treating pain syndromes involving the peripheral distributions of V ı· The small energy requirements inherent in the electrode configurations allow the use of an implanted pulse generator that will have a life expectancy for many years.

Next, Dr. Oren Sag her then discussed the physiological effects of spinal neuromodulation and the implications for treatment. He reminded the audience of the animal work showing a spinal cord/brainstem loop through the thalamic structures, and later work that found the loop extending to structures as deep as the prefrontal cortexlcingulate gyrus and somatosensory cortex. He compared these humble beginnings of the studies of the electric organ fish to the state of electrotherapy for the treatment of the vascular and sensory systems in the United States. Our colleagues in Europe are using spinal cord stimulation to treat angina and promote ulcer healing/limb salvage (via increasing transcutaneous pressure of CO_2 [$TpC0_2$D to a great degree. In the United States, we are limited with regard to these approaches because of US Food and Drug Administration (FDA) constraints and insurance reimbursement issues. Dr. Sag her presented compelling data showing the cerebrovascular effects of spinal cord stimulation and the use of this modality for treating spasticity via corticomotor pathways.

Occipital neuralgia, hyperextension cervicogenic headaches, and transformed migraine have been extremely difficult to treat. In the same session, Richard Weiner, MD, described a highly effective technique of occipital nerve stimulation. This form of peripheral nerve stimulation is thought to work through a "backdoor approach" -- retrograde conduction via C1, C2, and C3 interneuronal connections to the cell body of cranial nerve V, which lies in the tissues near the fourth ventricle. This path forms the "migraine" circuit, and its electrical neuromodulation can quiet the phenomena of migraine common in these conditions. Although this method of neural stimulator placement is "off-label" (as is peripheral nerve stimulation, in general), its outcome has been consistently excellent. Dr. Weiner advocates this in patients who have failed traditional medication regimens

Peripheral Nerve Stimulation for Facial Neuralgias

Hayek and colleagues[2] reported 3 cases of refractory chronic postsurgical trigeminal neuropathic pain successfully treated with peripheral *neNe* stimulation with percutaneously implanted leads. One patient suffered from supraorbital neuralgia and 2 had infraorbital neuralgia that were refractory to pharmacologic therapies. All 3 patients experienced more than 50% reduction in visual analog scale (VAS) scores after stimulation; all 3 had responded to diagnostic nerve blockade prior to implantation.

Spinal Cord Stimulation for Visceral Pelvic Pain

Kapural and Mekhail[3] presented the results of spinal cord stimulation for 5 women with visceral pelvic pain that had been poorly responsive to pharmacotherapeutics, therapeutic injections, and other conservative therapies. Diagnoses included endometriosus, multiple surgical explorations with adhesions, and dyspareunia. All 5 patients had received hypogastic blocks with 1-4 weeks of complete relief. A trial of stimulation preceded implantation. Average follow-up was 33.6 months. The mean VAS score dropped from 8 to 3. The pain disability index changed from an average of 58 to 19.7. Opioid use decreased from an average of 26 mg to 5 mg morphine sulfate equivalent per day.

Spinal Injections

At another Update Session, Or. Aaron Calodney and Dr. Curtis Shipman,[4] brought an evidencebased focus to the rationale for interventional techniques in the diagnosis and treatment of lumbar radicular pain. Dr. Calodney began by discussing the anatomy of the lumbar space and the anterior/posterior compartments, stressing that an inflammatory cascade begins when disc herniation occurs: These effects can be mitigated by steroids. Because studies strongly support inflammation as the cause of radicular pain in the absence of spinal nerve compression, early application of steroids is advocated; no evidence exists, however, supporting an alteration in the rate of disc resorption. In general, nerve pain, not somatic-referred pain, is the indication for lumbar injections.

Furthermore, these authorities emphasized that there is no role for a "series" of injections without regard to the response to a previous injection (provided the injection was performed properly and the injectate went into the right space). Thus, the old adage of "a series of 3 injections" is simply an "old wives' tale." The use of fluoroscopy is the standard of care, and Calodney and Shipman stressed the importance of fluoroscopically guided injections.

They also differentiated *translaminar* injections from *transforaminal* injections. A translaminar injection is not selective or specific and is typically used when multiple nerve rootlets are being targeted. Studies by Stanley and colleagues[5] and Van Akkerveeken[6] showed that selective nerve root injections (transforaminal epidural injections) correlated with positive surgical outcomes as high as 95%. Thus, in patients with radicular pain patterns, Calodney and Shipman[4] recommend transforaminal injections for both diagnostic and therapeutic benefit because these correlate with optimal surgical outcomes, should the patient eventually undergo surgical therapy. (The surgeon can correlate the nerve rootlet to the images, thereby honing in on the level in question.)

Intrathecal Therapies

Although further along the continuum of care, intrathecal therapies offer a method of treatment for complex conditions that are unresponsive to other neuromodulation techniques or in situations in which technically electrical means are riskier or impossible. As expressed by Dr. Krames during the introductory comments for a session devoted to this topic,!?] intrathecal therapy is "the end of the pain treatment continuum" and is an expensive delivery system for analgesic medications and an alternative to systemic means, to be used after more conservative approaches have failed.

Next, Peter Staats reviewed common agents and newer agents with a special emphasis on ziconotide, an agent that was recently approved for marketing by the FDA. Ziconotide is an omegaconopeptide, which is a synthetic pharmaceutical version of a substance derived from the conus magus (a piscivorous marine snail discovered off the coast of the Philippines). It is an N-type voltage-sensitive calcium channel modulator (NVSCaM). In the human, the predominance of the NVSCaM is found on the dorsal horn where it blocks Ca^{H} channels, leading to diminution in excitatory neurotransmitter release associated with A-delta and C-nociceptors. Unfortunately, side effects, such as psychosis, can be seen in susceptible individuals, likely because of crossover to hippocampus receptors for the drug.

Samuel Hassenbusch, MD, then reviewed the polyanalgesic guidelines (similar to those covered at the 20th Annual Meeting of the AAPM held in Orlando, Florida, in 2004). Finally, Alexander Krakovsky, MD, closed the session by reviewing the complications associated with intrathecal therapies. Although precise numbers are lacking, the incidence of inflammatory masses involving the implanted catheter tips is estimated to be as high as 2% to 3%. Dr. Krakovsky stated that opioids, predominately morphine, are a leading factor in causing inflammatory masses. Left untreated, these masses grow exponentially and can cause spinal cord compromise leading to neurologic deficits and eventually paralysis. MRI with gadolinium must be performed with careful imaging at the known area of the catheter tip; suspicion should be raised if the patient reports an increase in pain unresponsive to typical dosing, a change in the neurologic baseline, muscle weakness, or bowel/bladder changes. (He recommends neurologic examination each time the medication reservoir is filled.) Aside from technical complications surrounding implantation and perioperative factors, medication errors (compounding) and dosing errors (programming) are the next highest area for concern, and constant vigilance in computation checking is crucial to avoid potentially fatal errors. Last, using manufacturer specified refill kits minimizes the chances of inadvertent filling of side ports (which provide a direct entry into the cerebrospinal fluid) rather than the intended reservoir and should be used where possible.

Studies of Intrathecal Ziconotide and Chronic Pain

Fisher and Lokey[8] presented a case of a 16-year-old boy with reflex sympathetic dystrophy in the bilateral lower extremities with chronic burning pain, partial loss of proprioception in the feet, photophobia, sensitivity to touch/temperature changes, and antalgic gait. He was prescribed intrathecal ziconotide 5 mcg daily. Titration schedules fluctuated with stabilization at 4.5 mcg daily at year 2. The patient established normal activities, graduated from high school, is employed full time, and has discontinued all oral medications. His VAS range has dropped from 70-100 mm, before intrathecal therapy, to 0-10 mm.

Dr. Lynn Webster[9] presented a study that followed 220 patients who were weaned from all intrathecal medications, stabilized on intrathecal saline for 1 week, and then randomized to either receive intrathecal ziconotide (112 patients) or saline (108 patients). In all, 92% of participants completed the study. Mean baseline VAS of pain intensity was 80.7 mm for both groups. After 3 weeks, patients who received ziconotide achieved a mean 14.7% reduction in VAS pain intensity score compared with a 7.2% reduction for patients who received saline *(P* = .036). On the Clinical Global Impressions scales, a significantly higher percentage of ziconotide (28.4%) than placebo patients (12.1%) reported "a lot" or "complete" satisfaction with treatment *(P* = .0027) and "very good" or "excellent" pain control (11.9% and 0.9%, respectively; *P* = .0004). The majority (84%) of adverse events were mild to moderate in severity;

5.4% of the ziconotide group withdrew because of adverse events, as compared with 4.6% of placebo patients. The most frequently reported ziconotide-related adverse effects were dizziness (34.8%), nausea (19.6%), and confusion (14.3%).

Interventional Controversies

A rousing, well-attended session on interventional pain management[10] brought together 10 experts to present evidence on controversial topics in interventional pain medicine. An expert was asked to take either a pro or contra position and then make his/her case regarding the proposed technology; this was followed by an audience computerized question and answer session. The use of this interactive session with computerized audience feedback was excellent. The lecturers and audience were able to view the predebate opinion vote compared with the percentage change following the debate. The topics that were debated included the following.

The use of non-FDA-approved drugs in the intrathecal space: The audience was quite interested in this topic and was of the opinion that it is the physicians' decision as to what to use to alleviate pain for any given patient. Off-label use is accepted and was of little issue in this discussion.

Permanent implantation of surgical leads in the spine -- surgical or percutaneous: Although each presenter made excellent points, Jaime Henderson, MD, from Stanford University, Stanford, California, swayed the audience by a slight margin to the side of paddle electrodes in the final vote. (These are inserted via laminectomy.) In the final discussion, however, he did admit that the percutaneous lead(s) caused less trauma.

The use of high-frequency (spinal cord) stimulation when treating complex regional pain syndrome: The pro speaker Claudio Feler, MD, overwhelmed the audience with his vast experience in this area. David Caraway, MD, PhD, the contra speaker, admitted during the discussion that he too would utilize this modality when treating complex regional pain syndrome because it is a highly effective method.

,Highce--rvical **spinal cord stimulation leads for 4-extremity neuropathic pain vs intrathecal pump:** This debate leaned in favor of an intrathecal pump primarily because this kind of electrical neuromodulation requires 2 implants -- 1 in the cervical region for the arms and 1 in the thoracic region for the legs. Nonetheless, this outcome is puzzling because high cervical spinal cord stimulation is less invasive than a spinal catheter with medications.

Percutaneous disc treatment vs surgical treatment for lumbar radiculopathy: Surgical disc treatment won overwhelmingly when it was shown how simply this modality is performed. The audience expressed a misconception regarding the simple discectomy vs a more radical approach. Dr. Levy did an outstanding job of explaining both approaches.

This program was supported by an independent educational grant from Cepha/on.

References

1. Levy R, Sag her 0, Weiner R, et al. On the cutting edge: innovative surgical treatment for central and neuropathic pain (204). Program and abstracts of the 21 st Annual Meeting of the American Academy of Pain Medicine; February 23-27, 2005: Palm Springs, California.
2. Hayek S, Henderson J, Soul is N, Kapural L, Stanton-Hicks M, Nagy M. Peripheral nerve stimulation for post surgical facial neuralgias. Program and abstracts of the 21 st Annual Meeting of the American Academy of Pain Medicine; February 23-27, 2005; Palm Springs, California. Abstract 105.
3. Kapural L, Mekhail N. Spinal cord stimulation may be an effective treatment for severe visceral pelvic pain. Program and abstracts of the 21 st Annual Meeting of the American Academy of Pain Medicine; February 23-27,2005; Palm Springs, California. Abstract 114.
4. Calodney A, Shipman C. Spinal injections for lumbar radicular pain. Update session 207. Program and abstracts of the 21 st Annual Meeting of the American Academy of Pain Medicine; February 23-27,2005; Palm Springs, California.
5. Stanley D, McLaren MI, Euinton HA, Getty CJ. A prospective study of nerve root infiltration in the diagnosis of sciatica. A comparison with radiculography, computed tomography, and operative findings. Spine. 1990;15:540-543.
6. Van Akkerveeken PF. The diagnostic value of nerve root sheath infiltration. Acta Orthop Scand Suppl. 1993;251 :61-63.
7. Krames E, Staats P, Hassenbusch SJ, Krakovsky AA. Intrathecal therapies. Update session 301. Program and abstracts of the 21 st Annual Meeting of the American Academy of Pain Medicine; February 23-27, 2005; Palm Springs, California.
8. Fisher R, Lokey K. Intrathecal ziconotide for chronic, severe pain: a case study. Program and abstracts of the 21 st Annual Meeting of the American Academy of Pain Medicine; February 23-27, 2005; Palm Springs, California. Abstract 111.
9. Webster L. Efficacy of intrathecal ziconotide for the treatment of severe chronic pain in adults. Program and abstracts of the 21 st Annual Meeting of the American Academy of Pain Medicine; February 23-27,2005; Palm Springs, California. Abstract 160.
10. Follett K, Hassenbusch SJ, Henderson J, et al. Controversies in interventional pain medicine. Update session 401. Program and abstracts of the 21 st Annual Meeting of the American Academy of Pain Medicine; February 23-27,2005; Palm Springs, California.