Vertebral endplates are a significant source of chronic low back pain

The evidence behind the Intrapept Procedure

Thirty million people in the U.S. suffer from debilitating chronic low back pain, resulting in direct costs of over $90 billion annually. Individuals with chronic low back pain (CLBP) have few good treatment options, leading to compromised quality of life.

Eighty-five percent of LBP patients are diagnosed with non-specific low back pain leading to non-specific conservative care. When lesser treatments fail, many patients are prescribed opioid analgesics or are recommended for spinal fusion, despite its invasiveness, high costs and high complication rate. Once started, opioid use is difficult to discontinue even though the magnitude of pain relief afforded by opioids for chronic, non-cancer pain is only about 30 percent. Thus, individuals may end up with opioid use disorder and complications even though their pain relief is modest. All of these options leave CLBP patients in a never-ending cycle of suffering and disability.

“Historically, the disc has been the presumed source of most CLBP, but discogenic pain treatments did not produce the desired success rates and did not correlate with disc degeneration on MR imaging or on discography results. This led some to question about the origin of pain previously ascribed to the intervertebral disc,” said Ray Baker, MD, Chief Medical Officer at Relievant Medsystems. Evidence behind vertebral endplate pain

In 1991, Stephen Kuslich, MD, published an article detailing how he pinpointed the exact source of chronic low back pain in his patients. He found that “pressure or curettement of the vertebral endplate frequently resulted in a deep, rather severe low back pain. It was usually more severe and sharper in quality than the preoperative discomfort.”

In the late 1990s, a team of researchers led by Michael Heggeness, MD, PhD found that the vertebral endplates were richly innervated by nerves that traced back to a single source, the basivertebral nerve (BVN) located within the vertebral body. They postulated that these nerves played a role in low back pain, leading them to perform immunohistochemical assays documenting the presence of Substance-P and proving the BVN was in fact a pain transmitting nerve. While nerves had previously been documented in long bones, they had not been documented within the vertebral body itself.

Jeffrey Lotz, PhD, extended the research into sources of CLBP. He noted the disc and adjacent endplates acted as one functional unit, and the endplates’ dual roles of nutritional support for the disc and structural support for the spine were at odds, making the endplates the weak link and most vulnerable to damage.

“Many conditions lead to endplate failure, including the nature of mechanical loading, local morphology of the endplate structure, tissue material properties and condition of intervertebral disc,” noted Dr. Lotz. “Endplates that are not thick or dense enough can become damaged, leading to cellular communication between the disc nucleus and vertebral bone marrow. The resulting pathologic cross talk between factors that are secreted from the disc and the bone marrow triggers an inflammatory response leading to endplate nerve proliferation as well as chemical sensitization and mechanical stimulation that can cause low back pain. Targeting the disc early on continues to be strategic, but for patients who are already symptomatic, targeting the endplate is the more logical approach.”

In 2013, Lotz published these findings in Global Spine Journal. “The challenge is the vertebral endplate is not well imaged or seen with routine clinical imaging,” Dr. Lotz said. “However, the edema in the vertebral body, known as Modic change, are qualitative assessments now being linked to clinical outcomes and pain conditions.”

Connecting this research with the basic science on Modic changes and endplate degeneration, a link between Modic changes and painful endplate degeneration was discovered. It gave spine physicians the opportunity to identify and put forward a treatment plan for their most difficult patients. “Modic endplate changes were initially described in 1988 but fell into disuse due to a lack of successful treatments associated with the changes. With the evidence endplates are a significant source of pain, Modic type 1 and type 2 changes are once again in the clinical limelight,” said Dr. Baker.

“There have been so many clinical therapies targeting the disc that have been unsuccessful,” said Dr. Lotz. “It is clear we were continuing down the wrong path. The clinical and basic scientific evidence, along with failures of disc-focused therapies, reinforce that vertebral endplate changes are the root cause of pain in many patients.”

Evidence behind the Intrapept Procedure

Based upon 20 years of scientific research on endplates and the BVN, Relievant Medsystems developed a minimally invasive, outpatient procedure designed to effectively address patients’ chronic low back pain. The Intrapept Procedure targets the BVN while preserving the structure of the spine and without the use of an implant. Focused on providing clinically convincing evidence, Relievant Medsystems then set about testing the effectiveness of the Intrapept Procedure in clinical trials.
They began with a pilot study in patients with CLBP pain and Modic type 1 or 2 changes. Patients in the 17-person study had chronic back pain for more than six months and had received at least three months of consecutive care without success. At three months postoperatively, the mean baseline Oswestry Disability Index (ODI) score was 23±21, a significant decrease from 52±13 preoperatively. The improvements persisted at one-year follow-up, leading researchers to conclude the treatment method was valid.

Following the successful pilot study, Jeffrey Fischgrund, MD, spearheaded the pivotal SMART trial, a level I, randomized, double-blind, sham-controlled clinical trial to test the safety and effectiveness of the Intracept Procedure to treat CLBP.

“I was approached with the hypothesis that if you ablated the BVN in the bone, you could help relieve CLBP,” Dr. Fischgrund said. “I had a healthy amount of skepticism because it was a new theory for low back pain. As a spine surgeon, we know fusions for low back pain don’t always have the best outcomes. Classically, we have been taught that the source of low back pain is a disc. So, while the anatomy supported basivertebral nerve ablation, there was not a significant amount of clinical data.”

Publishing the findings in the European Spine Journal, Dr. Fischgrund evaluated the outcomes and progression of 225 patients diagnosed with CLBP. The patients were randomized 2:1 to treatment or a sham procedure, with 147 patients receiving the Intracept Procedure and 78 patients randomized to the sham treatment. Patients included in the study had a mean ODI score of 42.4 preoperatively and all had type 1 or type 2 Modic changes. To maintain blinding, treating clinicians differed from providers that evaluated patients postoperatively. After the procedure, investigators followed up with the patients at two weeks, six weeks, three months, six months, 12 months and 24 months.

The SMART trial demonstrated statistical significance in the primary endpoint at three months; subjects in the per protocol (PP) population randomized to BVN ablation reported a mean ODI improvement of 48 percent. Based on observed data, 75.6 percent of these subjects reached the minimal clinically important difference (MCID) of a 10-point improvement in ODI, and 48.0 percent achieved a 20-point improvement.

Long-term results demonstrated durable improvements in ODI and Visual Analogue Scale (VAS) scores. Subjects in the per protocol (PP) population reported a 54 percent decrease in ODI and 53 percent decrease in VAS at 24-month follow up. Responder rates for ODI and VAS were also maintained through two years, with patients showing clinically meaningful improvements in both: ODI ≥ 10-point improvement in 76.4 percent of patients and ODI ≥ 20-point improvement in 57.5 percent; VAS ≥ 1.5 cm improvement in 70.2 percent of patients. Patients that received the Intracept Procedure also decreased utilization of opioids and spinal injections as compared to utilization prior to treatment.

“The SMART clinical trial conclusively shows that BVN ablation is a durable, effective treatment for LBP,” Dr. Fischgrund noted. “We also found the procedure to be safe, with minimal short-term adverse events and no difference in serious adverse events between arms. In select patients, Intracept can be an alternative to more invasive procedures, such as fusion or disc replacement.”

The Intracept System received 510(k) clearance based, in part, upon the outcomes of the SMART Trial. The procedure is now commercially available in the US.

The Intracept System is intended to be used in conjunction with radiofrequency (RF) generators for the ablation of BVNs of the L3 through S1 vertebrae for the relief of CLBP of at least six months duration that has not responded to at least six months of conservative care and is also accompanied by either type 1 or type 2 Modic changes on an MRI.

References