Dorsal root ganglion stimulation

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Dorsal root ganglion (DRG) stimulation is a neurostimulation technique that involves the implantation of a small electrical device, called a neurostimulator, near the dorsal root ganglion (DRG) of the spinal cord. The neurostimulator sends electrical impulses to the DRG, which can help to alleviate chronic pain caused by conditions such as peripheral neuropathy, complex regional pain syndrome, and certain types of chronic back and limb pain.

The procedure to implant a DRG stimulator involves a small surgical incision made near the spinal cord. Once the device is in place, the patient can control the electrical impulses using an external remote control. The device can be programmed to deliver different types of electrical pulses, such as constant or intermittent stimulation, to target different types of pain.

DRG stimulation is considered a safe and effective treatment option for chronic pain. It has been shown to provide significant pain relief and improve quality of life for patients who have not responded well to traditional treatments such as medications and physical therapy. It is still considered an emerging technology and the long term effectiveness and safety is still under study.

Stimulation of the dorsal root ganglion (DRG) in the treatment of chronic, intractable pain has shown excellent clinical results in multiple published studies, including a large prospective, randomized, controlled trial. Both safety and efficacy have been demonstrated utilizing this therapeutic approach for many chronic complaints. Continued assessment of neuromodulation therapies, such as DRG stimulation, is not only an important aspect of vigilant care but are also necessary for the evaluation of safety. Such technologies should be subject to rigorous evaluation as their mechanisms of action and long-term outcomes remain hitherto undefined [1) 2)].

Safety and complaint records for DRG and spinal cord stimulation (SCS) stimulation were obtained from the manufacturer, analyzed and compiled to further assess ongoing device safety. Complaint event data were stratified according to complain type as well as overall rates. Data from similar time periods were compared between epidural neurostimulation devices by the same manufacturer as well as rates reported in the literature.

Overall, DRG stimulation device event rates were lower or comparable to similar epidurally placed neurostimulation devices. Rates of events varied from 0 to 1.0% for DRG stimulation (n >500+ implants) which was similar to the event rate for SCS by the same manufacturer (n >2000+ implants). In comparison, complaints and adverse events ranged from 0 to 14% for SCS in the literature.

The current results from a large consecutive cohort obtained from manufacturer records indicates that DRG stimulation demonstrates an excellent safety profile. Reported event rates are similar to previously reported adverse event and complaint rates in the literature for this therapy. Similarly, safety events rates were lower or similar to previously reported rates for SCS, further demonstrating the comparative safety of this neuromodulation technique for chronic pain treatment [3)].

Indications

see Dorsal root ganglion stimulation for chronic neuropathic pain.

The Food and Drug Administration approved the use of DRG stimulation for refractory lower extremity pain related to complex regional pain syndrome (CRPS) in 2016. [4)].

Technique

Dorsal Root Ganglion Stimulation Technique.

Case series

A randomized double-blinded clinical trial with a crossover research design. Patients with an already implanted Dorsal Root Ganglion Stimulation Therapy DRG-S system was included and randomly tested with 4 Hz, 20 Hz, 60 Hz, and sham stimulation. Amplitude was adjusted to subthreshold values for each frequency. Each frequency was tested for 5 days, followed by a 2-day washout period. Patients

were assessed using VAS, McGill Pain Questionnaire, EQ-5D-5L, and Beck Depression Inventory.

Seventeen patients were included. The time between inclusion in this study and the primary implant was 32.8 months. The baseline stimulation frequency was 20 Hz in all patients. The mean baseline pain intensity was VAS 3.2 (SD 2.2). With 4-Hz stimulation, VAS was 3.8 (SD 1.9), with 20 Hz VAS 4.2 (SD 2.0), and with 60 Hz VAS 4.6 (SD 2.7). Worst pain control was seen with sham stimulation with a VAS of 5.3 (SD 3.0). Stimulation with 4 Hz achieved lower VAS scores, but this was only statistically significant when compared to sham ($p = 0.001$). A similar trend favoring 4-Hz stimulation was seen using the Beck Depression Inventory, but in this case, no statistical significance was found. Outcomes of McGill Pain Questionnaire and EQ-5D-5L favored 20 Hz stimulation, but again without statistical significance.

Low-frequency stimulation was not significantly better than classic 20-Hz stimulation in relieving pain intensity; the study might however be underpowered. Longer washout and observational periods might also be necessary to show clear differences in frequency response [5].

Smith et al. presented three patients, each with a different reason in which DRGS would not be accessible via the traditional anterograde approach, who all had successful DRGS transgrade placement.

The case series includes three patients with either CRPS or post-surgical neuropathic pain who had an anatomical or post-surgical condition that historically would have rendered DRGS contraindicated. Two patients had previously failed dorsal column stimulation. All three patients had successful placement with the transgrade approach-entry into the contralateral epidural space at the level of the targeted foramen from a cephalad angle. Each patient gave their verbal and written consent to be included in the case series.

Following treatment with a transgrade approach, all three patients had significant pain relief and improvement in function without complication.

Barriers to anterograde foraminal access including previous implantation, previous instrumentation, and epidural adhesions may prevent DRGS placement in certain indicated patients. This can be especially challenging in patients who have failed other neuromodulation options like dorsal column stimulation. This case series demonstrated that the transgrade technique can be successfully used in these cases to increase access to DRGS [6].

Piedade et al., from University Hospital of Düsseldorf, reported a consecutive series of 20 patients treated with DRG stimulation in the upper thoracic and cervical region. All patients suffered from chronic neuropathic pain unresponsive to best medical treatment. Main pain etiologies were trauma, spine surgery, postherpetic neuralgia, and peripheral nerve surgery. All patients were trialed with externalized electrodes prior to permanent pulse generator implantation. Routine clinical follow-up was performed during reprogramming sessions.

Out of all 20 patients trialed, 18 were successfully trialed and implanted with a permanent stimulation system. The average pain relief after three months compared to the baseline was of 60.9% (mean VAS 8.5 to VAS 3.2). 77.8% of the patients reported a pain relief of at least 50% after three months. One patient developed a transient paresis of the arm caused by the procedure. She completely recovered within three months.

Cervical and upper thoracic DRG stimulation resulted in good overall response rates to trialing and similar pain relief when compared to DRG stimulation for groin and lower limb pain. A modified surgical approach has to be used when compared with lumbar DRG electrode placement. Surgery itself in this region is more complication prone and challenging [7].

Morgalla et al., prospectively enrolled 12 adult patients with unilateral localized neuropathic pain in the lower limbs or inguinal region and followed them up for six months Laser evoked potentials (LEP) were assessed at baseline, after one month of DRGS, and after six months of DRGS. Clinical assessment included the Numerical Rating Scale (NRS), Brief Pain Inventory (BPI), SF-36, and Beck Depression Inventory (BDI). For each patient, LEP amplitudes and latencies of the N2 and P2 components on the deafferented side were measured and compared to those of the healthy side and correlated with pain intensity, as measured with the NRS.

At the one- and six-month follow-ups, N2-P2 amplitudes were significantly greater and NRS scores were significantly lower compared with baseline (all p's < 0.01). There was a negative correlation between LEP amplitudes and NRS scores ($rs = -0.31$, $p < 0.10$).

DRGS is able to restore LEPs to normal values in patients with localized neuropathic pain, and LEP alterations are correlated with clinical response in terms of pain intensity [8].

Case reports

van Velsen et al. used a single-incision approach to tunnel and implant the leads and pulse generator for DRG stimulation treatment in a patient suffering from intractable foot pain. At long-term follow-up, the patient experienced a decrease in pain intensity and improvement in function, without any complications. A single-incision implantation technique for DRG stimulator implantation may simplify implantation and decrease the risk of complications [9].

References

[1], [3]
Deer T, Pope J, Hunter C, Falowski S, Kapural L, Kramer J, Levy R. Safety Analysis of Dorsal Root Ganglion Stimulation in the Treatment of Chronic Pain. Neuromodulation. 2019 Mar 12. doi: 10.1111/ner.12941. [Epub ahead of print] PubMed PMID: 30861617.

[2]
Shamji MF, De Vos C, Sharan A. The Advancing Role of Neuromodulation for the Management of Chronic Treatment-Refractory Pain. Neurosurgery. 2017 Mar 1;80(3S):S108-S113. doi: 10.1093/neuros/nyw047. PubMed PMID: 28350939.

[4]
https://www.asra.com/news/237/dorsal-root-ganglion-stimulation-the-lat

[5]
Piedade GS, Gillner S, McPhillips PS, Vesper J, Slotty PJ. Effect of low-frequency dorsal root ganglion stimulation in the treatment of chronic pain. Acta Neurochir (Wien). 2023 Jan 27. doi: 10.1007/s00701-023-05500-1. Epub ahead of print. PMID: 36705762.

[6]
Smith GL, Petersen EA, Paul C, Goree JH. Transgrade Dorsal Root Ganglion Stimulation as a Salvage Technique for Three Different Anatomical Barriers: A Case Series [published online ahead of print,

2020 Sep 9]. Neuromodulation. 2020;10.1111/ner.13276. doi:10.1111/ner.13276
7)

Piedade GS, Vesper J, Chatzikalfas A, Slotty PJ. Cervical and High-Thoracic Dorsal Root Ganglion Stimulation in Chronic Neuropathic Pain. Neuromodulation. 2019 Jan 8. doi: 10.1111/ner.12916. [Epub ahead of print] PubMed PMID: 30620789.
8)

Morgalla MH, de Barros Filho MF, Chander BS, Soekadar SR, Tatagiba M, Lepski G. Neurophysiological Effects of Dorsal Root Ganglion Stimulation (DRGS) in Pain Processing at the Cortical Level. Neuromodulation. 2018 Dec 18. doi: 10.1111/ner.12900. [Epub ahead of print] PubMed PMID: 30561852.
9)

van Velsen V, van Helmond N, Levine ME, Chapman KB. Single-Incision Approach to Implantation of the Pulse Generator and Leads for Dorsal Root Ganglion Stimulation: A Case Report. A A Case Rep. 2017 Aug 14. doi: 10.1213/XAA.0000000000000625. [Epub ahead of print] PubMed PMID: 28816708.