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Spinal cord stimulation for the treatment of peripheral neuropathic pain

CLINICAL REVIEW

BÅRD LUNDELAND

E-mail: baalun@ous-hf.no
Norwegian National Advisory Unit on Neuropathic Pain and Department of Pain Management and Research
Oslo University Hospital
He has contributed to the concept and literature search, and to the drafting, revision and approval of the manuscript.
Bård Lundeland, senior consultant and specialist in anaesthesiology, and postdoctoral researcher.
The author has completed the ICMJE form and declares the following conflicts of interest: He received payment from Abbott for a lecture on radiofrequency ablation for neck and back pain in 2021.

MAREN TOENNIS

Department of Pain Management and Research
Oslo University Hospital
She has contributed to the concept and to the revision and approval of the manuscript.
Maren Toennis, senior consultant and specialist in anaesthesiology.
The author has completed the ICMJE form and declares no conflicts of interest.

MARK ZÜCHNER

Department of Neurosurgery
Oslo University Hospital
He has contributed to the concept and to the revision and approval of the manuscript.
Mark Züchner, senior consultant and specialist in neurosurgery.
The author has completed the ICMJE form and declares no conflicts of interest.

LARS JANERÅS

Department of Pain Management and Research
Oslo University Hospital
He has contributed to the concept and to the revision and approval of the manuscript.
Lars Janerås, senior consultant and specialist in anaesthesiology.
The author has completed the ICMJE form and declares no conflicts of interest.

AUDUN STUBHAUG

Norwegian National Advisory Unit on Neuropathic Pain and Department of Pain Management and Research
Oslo University Hospital
and
Institute of Clinical Medicine
University of Oslo
He has contributed to the concept and to the revision and approval of the manuscript.
Audun Stubhaug, specialist in anaesthesiology, head of department and professor.
The author has completed the ICMJE form and declares no conflicts of interest.

PER HANSSON

Norwegian National Advisory Unit on Neuropathic Pain and Department of Pain Management and Research
Oslo University Hospital
and
Department of Molecular Medicine and Surgery
Karolinska Institute
He has contributed to the concept and literature search, and to the drafting, revision and approval of the manuscript.
Per Hansson, senior consultant and specialist in neurology, and professor.
The author has completed the ICMJE form and declares the following conflicts of interest: He received payment for a lecture and for participation in a panel discussion at a symposium arranged by Abbott in 2018.

Spinal cord stimulation with weak electric current is a neuromodulatory treatment suitable for subgroups of patients with chronic neuropathic pain and certain other

pain conditions. Neuropathic pain can reduce quality of life, and the effectiveness of pharmacological treatment is often limited. Studies of spinal cord stimulation have shown significant pain relief and improved functioning at group level, and recent years have seen the development of new stimulation methods which are currently under evaluation.

Pain relief upon electrical stimulation of the spinal cord, first described in a case report in 1967 (1), can be achieved using a battery-powered pulse generator connected to an epidural electrode. The treatment is particularly appropriate for selected patients with peripheral neuropathic pain, but can also be effective in cases of complex regional pain syndrome, refractory angina pectoris and ischaemic pain resulting from peripheral vascular disease (2–4). In Norway, the treatment is mainly offered at university clinics, and in 2019 more than 300 test electrodes and permanent stimulation systems were implanted in total. Around 50 000 systems are implanted worldwide each year.

The aim of this article is to provide a brief overview of the use of spinal cord stimulation for its most common indication, peripheral neuropathic pain. The article is based on a discretionary selection of relevant literature identified through searches in PubMed, as well as several of the authors' 30-plus years of clinical experience with spinal cord stimulation.

Neuropathic pain

An estimated 7–10 % of the population suffers from neuropathic pain, which is defined as pain caused by a lesion or disease affecting the somatosensory system (5). The distribution of the pain corresponds neuroanatomically to the site of the injury or disease (6). A distinction is made between peripheral and central neuropathic pain according to which part of the nervous system is affected. Clinical examination reveals sensory changes corresponding to the innervation territory of the affected neural structure, with altered sensitivity of the skin to touch and/or temperature and/or pain. There may also be autonomic and motor signs, and imaging or neurophysiological testing may reveal concordant pathological findings.

The majority of patients with neuropathic pain do not receive treatment specific to their disorder. There is evidence that some antidepressants and gabapentinoids have an analgesic effect (7), but many patients experience an inadequate response or marked side effects. Spinal cord stimulation may be an option for selected patients with peripheral neuropathic pain that significantly affects functioning and quality of life (Box 1).

Box 1 Pain states for which spinal cord stimulation may be indicated, according to scientific research and the authors' clinical experience (2–4, 8).

Peripheral neuropathic pain

Radiculopathy

Polyneuropathy

Peripheral nerve injury

Stump pain after amputation

Phantom limb pain

Complex regional pain syndrome

Type 1: without significant nerve injury Type 2: with significant nerve injury

Cardiovascular disorders

Refractory angina pectoris

Certain peripheral vascular diseases

Patient selection and contraindications

Box 1 shows pain states that may be indications for spinal cord stimulation. The pain must cause substantial distress and have been present for at least 3–6 months (8). The most frequent indication among patients in our department is painful radiculopathy. Transcutaneous electrical nerve stimulation cannot be used to predict the effectiveness of spinal cord stimulation for neuropathic pain (9). There are often biopsychosocial components to chronic pain, and in the Department of Pain Management and Research at Oslo University Hospital, neurostimulation is considered only after a patient's pain state has been thoroughly characterised. This interdisciplinary assessment may involve various healthcare professionals, including specialist physicians, a physiotherapist, a nurse and a psychologist.

Coagulation disorders, pregnancy and local infections are absolute contraindications to spinal cord stimulation (8). Relative contraindications include cognitive impairment, mental/psychiatric disorders and substance abuse that may disrupt treatment.

Testing, evaluation and permanent implantation

Figure 1 shows a permanent spinal cord stimulation system. In most cases the electrode is implanted percutaneously through an epidural needle, and is tested for a week using an external pulse generator. Throughout this period, patients repeatedly record their pain intensity and their ability to perform personally selected activities using a patient-specific functional scale (10). In our department, approximately 70 % of patients with peripheral neuropathic pain who meet the criteria for testing, report good enough outcomes to be offered implantation of a permanent system.

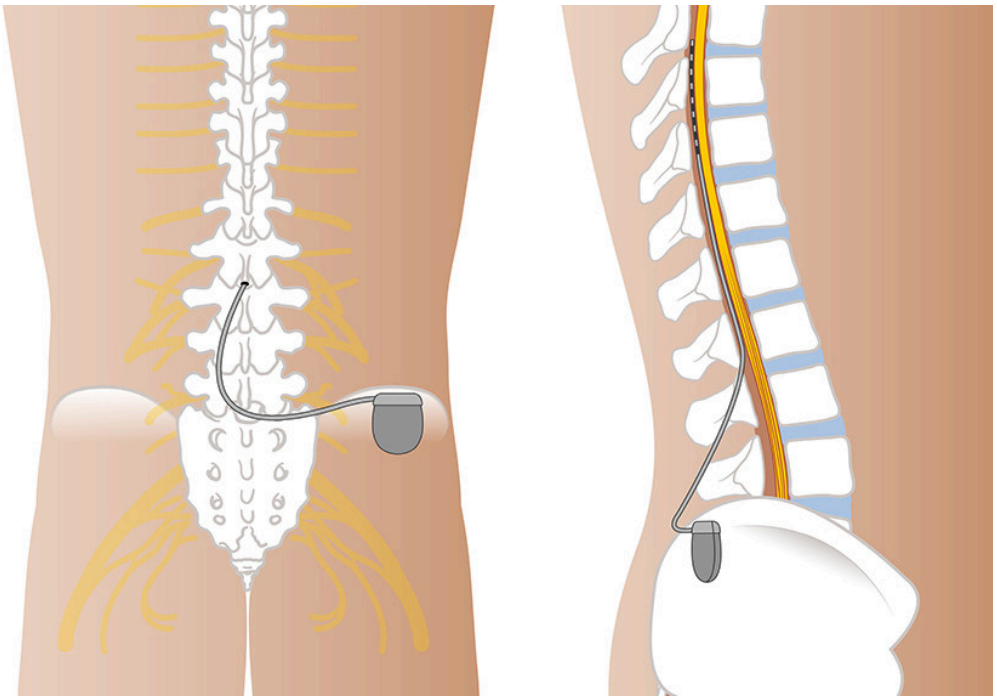

Figure 1 Spinal cord stimulator system with epidural electrode and subcutaneous pulse generator. Illustration: Øystein Horgmo, University of Oslo

The electrode may also be implanted by a neurosurgeon using microsurgical technique; for example if degenerative changes preclude placement of the electrode through an epidural needle. Collaboration with the neurosurgical department is also important for managing any serious complications, although such events are very rare (11).

The patient can use a handheld device to choose between different stimulation programmes. It will usually be several years before the pulse generator needs replacing, but implantation of a rechargeable pulse generator can be considered in the event of particularly high power consumption.

Programmes for intermittent stimulation can increase the longevity of the pulse generator. Most newer stimulation systems are compatible with MRI, but may require specific scanner types and protocols.

Conventional spinal cord stimulation

Conventional tonic spinal cord stimulation involves continuous electrical stimulation at 40–100 Hz, which elicits projected paraesthesias corresponding to the stimulated region of the dorsal columns in the spinal cord. The mechanisms underlying the relief of neuropathic pain have yet to be determined, but experimental studies suggest that neurochemical changes in the dorsal horn of the spinal cord may have an inhibitory effect on hyperactivity of the nociceptive system (12).

Although spinal cord stimulation has been used clinically for decades, a systematic review from 2016 described only four randomised controlled trials of conventional spinal cord stimulation for the treatment of neuropathic pain (2). Three of the studies found that, compared to conservative treatment, six months of spinal cord stimulation produced significant pain relief in cases of

diabetic polyneuropathy and of leg pain following lumbar spinal surgery, while the fourth study concluded that spinal cord stimulation produced better pain relief than reoperation in patients with leg pain after previous lumbar spinal surgery.

Leg pain in patients who have undergone lumbar spinal surgery (failed back surgery syndrome) can consist of several components (13). Radiculopathy is a neurological condition in which the transmission of nerve impulses is reduced or blocked at the nerve root, which can lead to pain distributed in the corresponding dermatome. Clinical examination reveals changes in sensitivity in the affected dermatome, possibly in combination with corresponding motor and autonomic deficits. Radicular pain stems from ectopic activity in a dorsal root or its ganglion as a result of compression and inflammation, and typically manifests as a narrow band of pain radiating down the thigh and calf. Referred pain from structures in the back, e.g. facet joints, can also spread diffusely down the legs without following the dermatomes. Such pain is usually described proximal to the knee joint and varies with the intensity of the back pain. In contrast to radiculopathy, no consistent changes in skin sensitivity are seen confined to dermatomes in cases of radicular or referred pain. Of these various forms of leg pain, in our experience it is mainly radiculopathy which responds positively to spinal cord stimulation.

New stimulation methods

In recent years, higher frequency stimulation patterns have increasingly been used for spinal cord stimulation, including burst (500 Hz intermittent) and 10 K (10 000 Hz continuous). Both result in greater energy transfer to the spinal cord without the patient experiencing paraesthesias, thereby enabling double-blind, placebo-controlled studies to be performed.

These types of stimulation exceed the neurons' maximum firing frequency of around 250 Hz (14), and knowledge of the associated physiological effects is limited, especially in light of the absence of paraesthesias. Burst stimulation may also result in supraspinal effects, including changes in the emotional components of pain and a reduction in patients' attention to pain (15).

In randomised controlled trials including mostly patients with leg and back pain following lumbar spinal surgery, both burst and 10 K stimulation showed superior efficacy to conventional spinal cord stimulation (16, 17). One of the trials was a crossover study in which patients were randomised to receive three months of burst followed by three months of conventional stimulation, or vice versa (16). With burst stimulation, 60 % of patients reported a reduction in pain intensity of at least 30 % compared to baseline, a reduction that is considered clinically significant. With conventional tonic stimulation, 51 % of patients reported a similar effect. In total, 69 % of patients described a clinically significant reduction in pain with one or both of the stimulation methods. After the study period, most patients opted to continue with burst stimulation, either because it provided better pain relief or because it did not

induce paraesthesias. The Oswestry Disability Index revealed a statistically significant improvement in functioning with both burst and conventional stimulation, with no difference between the two.

Although the scientific justification for using spinal cord stimulation to treat neuropathic pain is based largely on studies of patients with either leg/back pain after lumbar spinal surgery or with painful diabetic polyneuropathy, it is standard practice to offer the treatment to patients with peripheral neuropathic pain of other origins as well (8).

Stimulation of the dorsal root ganglion (DRG stimulation) can also be an option in some cases, e.g. for patients with neuropathic pain in the groin (18), where it can be difficult to achieve an effect with spinal cord stimulation.

Because the new stimulation methods are often simply compared directly to conventional spinal cord stimulation in head-to-head studies, the scientific justification for the new protocols remains limited. Patients may also have high expectations of technologically advanced treatments, leading to placebo effects (19). A systematic review from 2020 examined eight randomised studies in which paraesthesia-free spinal cord stimulation was compared to placebo/sham treatment (20). A meta-analysis found that active treatment led to a statistically significant reduction in pain intensity of 1.15 points on a 10-point scale.

Complications

Spinal cord stimulation following percutaneous electrode implantation is a non-destructive treatment with a low risk of serious complications. The most frequent complications are electrode migration and electrode breakage. Superficial infection has occurred in less than 3 % of patients treated at our practice over the past five years. Serious complications such as epidural infection or haematoma have been described, but are very rare (11).

Cost-benefit analysis

The equipment that we use as standard for the testing and permanent implantation of a spinal cord stimulator, including the electrodes, pulse generator and handheld device, costs approximately 17 000 USD. International studies have shown the treatment to be cost-effective in terms of the reductions in pain and improvements in quality of life that are achieved (21, 22), with costs that are below the willingness-to-pay threshold per quality-adjusted life year. In the UK, for example, spinal cord stimulation was found to be cost-effective for patients with leg/back pain after lumbar spinal surgery, both as an adjunct to conservative measures and as an alternative to reoperation (21).

Summary

Selected patients with peripheral neuropathic pain may achieve clinically significant pain relief and improved functioning as a result of spinal cord stimulation. The development of new stimulation methods and pulse generators that can deliver different types of stimulation allows increasingly personalised treatment.

The scientific knowledge base for use of spinal cord stimulation remains limited. There is a need for greater understanding of the mechanisms of action and of factors that predict therapeutic efficacy of spinal cord stimulation. The relatively few randomised controlled trials that are performed are mostly supported by the industry, and compare conventional spinal cord stimulation with conventional medical management. The efficacy of the newer stimulation methods has mainly been examined in head-to-head studies versus conventional stimulation. Placebo effects can be revealed via sham-controlled studies using paraesthesia-free stimulation methods.

This article has been peer-reviewed.

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