INFORMATION BRIEF (RAPID REVIEW)

SPINAL CORD STIMULATOR IN THE TREATMENT OF CHRONIC NEUROPATHIC PAIN FOLLOWING TRANSVERSE MYELITIS

Malaysian Health Technology Assessment Section (MaHTAS)
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TITLE: SPINAL CORD STIMULATOR IN THE TREATMENT OF CHRONIC NEUROPATHIC PAIN FOLLOWING TRANSVERSE MYELITIS

PURPOSE

To provide evidence on the effectiveness and safety of spinal cord stimulator in treatment of chronic neuropathic pain secondary to transverse myelitis. This report has been made on request from the Director of Medical Practice Division, Ministry of Health as this procedure is not listed in the 13th Schedule of the Private Healthcare Facilities and Services (Private Hospital and Other Private Hospital Facilities) Regulation (2013).

BACKGROUND

Acute transverse myelitis (TM) is a rare, acquired neuro-immune mediated process that causing neural injury to the spinal cord resulting in varying degrees of sensory, motor and autonomic dysfunction. Patient usually present with rapid onset of weakness, sensory alterations and bowel or bladder dysfunction.[1] Symptoms exhibit by the patient correlate with segment of spinal cord that were affected. The diagnosis of TM is made from clinical signs and symptoms, cerebrospinal fluid (CSF) analysis and imaging. Cerebrospinal fluid may show pleocytosis with elevated immunoglobulin G, while imaging may show acute inflammation of spinal cord.[2]

Transverse myelitis may occur as part of multifocal central nervous system (CNS) disease, multisystemic inflammatory disease or as separate isolated entity.[1] Two-third of TM are idiopathic. In 30-60% of idiopathic TM cases, there are association with preceding illness or infection. Secondary TM can directly be associated with any infectious, autoimmune, systemic inflammatory, or multifocal central nervous system disease.[3] Thus, work up of a TM disease include identifying potential causes such as bacterial or viral infections, auto-immune diseases, cord infarction or history of radiation exposure.[2]

The incidence of transverse myelitis was 1 to 4.5 million per year globally with the highest incidence rate was between age of 10-19 and 30-39 years old. 60% of patient will experience complication of which 44% are mild to severe.[2] This complication might persist and causing disability or even death, however many patients recover fully. Among late complication of TM is chronic neuropathic pain below the level of spinal insult. The incidence of chronic neuropathic pain secondary to TM is unknown, but is considered rare.[4] Pathogenesis of chronic pain in TM is not well understood however it was thought to be due to inflammation of the spinal cord. Chronic pain in the background of spinal cord injury (SCI) has enormous crippling effect to quality of life and managing it is complex and challenging.[2] Such pain is hardly controlled by medications such as NSAIDs, opioids, or anticonvulsants.[5]

Technical Features

Spinal cord stimulator (SCS) was first reported in 1967 and since then, it has been used by physician in various pain syndromes.[5] Among population where SCS is widely and commonly been used are patient with failed back surgery syndrome (FBSS) and complex regional pain syndrome (CRPS). Other common indication includes neuropathic pain (e.g., diabetic neuropathy), and ischaemic pain syndromes (e.g. critical limb ischaemia, refractory angina pectoris, and pain secondary to peripheral vascular disease. Because of complexity and diversity of pain pathways in chronic pain, it is difficult to understand which patients' population would respond more favorably towards SCS.[6]

Spinal cord stimulator is thought to work by delivering electricity to the targeted spinal nerves to inhibit pain signals to the brain. It typically consists of several components: electrode leads, an implantable pulse generator, extension cables, and an external controller used to program the device. The pulse generator is implanted subcutaneously under the skin in the abdomen, buttock or flank. Some SCS come with a wireless external pulse generator where it does not require implantation. The electrode leads are inserted in the epidural space near the targeted spinal cord level. This insertion can be done either by percutaneously or by open surgery (laminectomy). The overall procedure is minimally invasive and most of the time, SCS are implanted under local anesthesia (LA).[6]

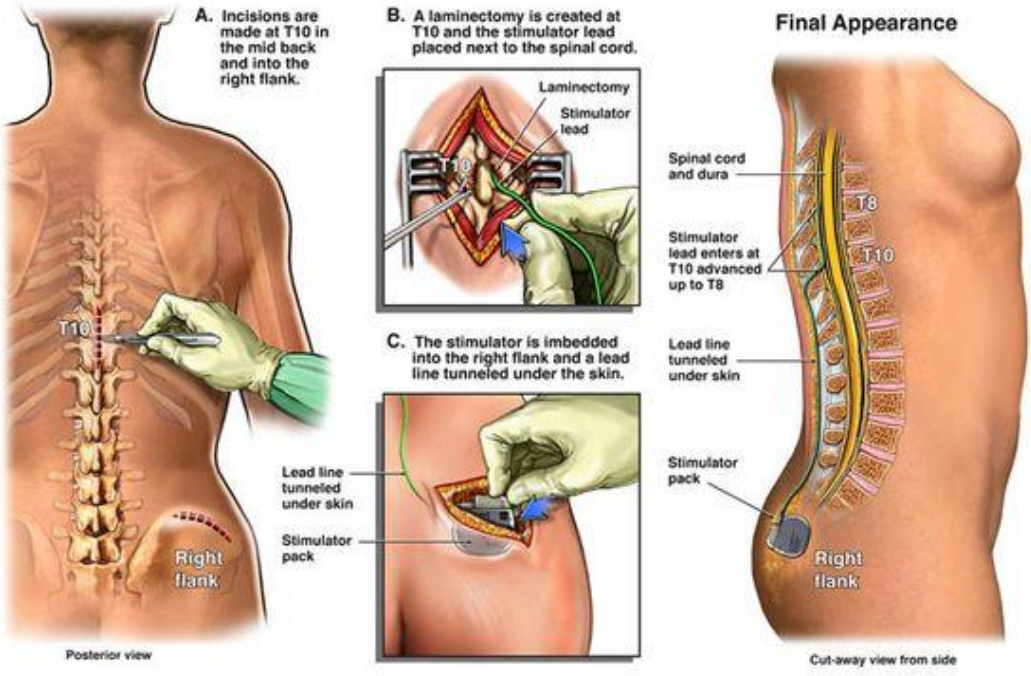

Figure 1: Spinal Cord Stimulator

Once SCS has been placed, electrical setting can be adjusted through control system. The basic unit of electrical stimulation which is pulse will deliver specific amount of current. This current will stimulate dorsal fibers, interfering with the transmission of pain signals to the brain. Physician or patient can adjust the amplitude, pulse width and frequency of the pulse delivered to optimise pain management.[6]

Treatment of SCS will begin with trial period, typically one to two weeks, during this period, leads are placed and programming protocols are tested on temporary pulse generator. Once desired outcome achieved – usually defined as 50% or greater reduction in a patient's pain intensity over baseline – then only the pulse generator is implanted permanently.[6]

EVIDENCE SUMMARY

A total of 25 titles were retrieved from the scientific databases such as Medline, EBM Reviews, EMBASE via OVID, and PubMed, using the search term; *neuralgia*, *chronic pain*, *transverse myelitis*, *myelopathy* and *spinal cord stimulation*. No limits were applied to the search. The last search was run on 14 November 2023. After reading full articles, four studies that were found to be relevant and included in this review, of which were case reports.

EFFECTIVENESS

Reddy et al. (2019) reported a case of 37-years-old male with one year history of idiopathic transverse myelitis in San Diego, California. He presented with complaints of circumferential allodynia over the mid-thorax, affecting the T5-T7 dermatomes. He reported difficulty wearing clothes over the area and often used a compressive garment across the waist and chest to prevent tactile stimulation. He scored his pain as 8/10 on the numeric rating scale. His pain was persistent despite on treatment with neuropathic medications, including duloxetine 60mg daily, pregabalin 150mg three times daily, and gabapentin 600mg four times daily. Because of his extensive medication, he noted side effects of word-finding and short-term memory issues even when he was not on opioids. On examination, there was consistent area of patchy sensory deficit and allodynia over the mid thorax, without any associated motor deficits. Lead placement was done spanning T3 to T5. Lead placement was achieved without complications. They found, in seven-day trial period there was 70% improvement in thoracic neuropathic pain, pain score reduced from 8/10 on NRS to 2/10. There was functional improvement in ability to tolerate clothing, improved quality of sleep, mood, and overall quality of life. Given the successful of trial period, permanent SCS were implanted with the top of the leads placed at the bottom of T2 and T3. There were no intra- or post procedural complications. At nine months follow up, there was reduction in his medication doses to duloxetine 60mg daily, pregabalin 150mg twice daily and gabapentin 300mg four times daily. He reported less difficulty with word finding and short-term memory. He described being able to sleep through the night, resume light exercises and no longer uses a compressive garment underneath his clothes. Overall satisfaction was reported at >80% following procedure given his pain reduction and functional improvements.[2]

Kim et al. (2010) evaluated effectiveness of SCS in another case report at Asan Medical Center, Seoul, Korea. They reported a case of 53-year-old male who contracted intractable neuropathic pain below the T3 level as a result of spinal cord injury suffered after TM caused by schistosomiasis. He has developed hypesthesia in his lower limb with motor weakness and voiding difficulty. Subsequently he had underwent resection of schistosomiasis-related granulomas on the cerebella and at T3-T4 level of spinal cord. Post surgery he developed neuropathic pain below level T3 for 15 years. The pain was pricking, throbbing and shooting in nature and can be intermittent or continuous. His pain was unable to be controlled by NSAIDs, opioids, and anticonvulsants. A nerve block has also been performed several times with negligible result. The pain was scored 9-10 on VAS score. On the Korean McGill Pain Questionnaire, the pain rating index (PRI) was 57/75 and the present pain intensity score (PPI) was 5/5. Functional disability was 62/70 on the Korean Brief Pain Inventory. A SCS was implanted at the midline between C1 and C3 through surgical laminotomy. They found, during trial period, pain score was reduced by more than 50%. After successful trial phase, permanent implantable pulse generated were implanted. Nine months after, the PRI on Korean McGill Pain Questionnaire was reduced to 21/75 and the PPI 3/5. Functional disability score was improved to 43/70 according to Korean Brief Pain Inventory. They concluded high level cervical stimulation can provide effective pain relief in patient with chronic neuropathic pain caused by transverse myelitis resulting from schistosomiasis. However more studies on long-term efficacy of such treatment are warranted.[5]

Hamid et al. (2007) reported a case of 54-year-old gentleman with non-small cell lung carcinoma in Michigan, United States, who contracted radiation-induced transverse myelitis with intractable neuropathic pain. He developed gradual onset of severe dysesthesia in the left leg with burning, pins and needle sensation, accompanied by severe tactile hypersensitivity after two-month completion of radiation therapy. The pain aggravated by physical activity and impacting his ability to ambulate. The pain also prevented him from getting adequate sleep. The reported verbal pain scored at first interview was 10/10. Patient was subsequently on gabapentin which was escalated to 900mg three times a day, Nortriptyline titrated up to 100mg at bedtime. In view of no improvement in pain, transdermal fentanyl was also started and gradually increased to 75mcg/hours every 72hours. Morphine IR 15mg every 4hours PRN were also added for any breakthrough pain. Patient were also continued on acetaminophen 500mg and ibuprofen 400mg every 6hours. He persistently complained of pain rated at 9-10/10 despite on medication; accompanied with fatigue, drowsiness and dizziness. He also complained of depression, function and quality of life were worsen. Spinal cord stimulator was introduced after eight months of conservative treatment. Spinal cord stimulator was planted at the level T10 through thoracic laminotomy. They found, post SCS implantation, patient had huge reduction in pain relief. His medications were able to be discontinued except from methadone and paroxetine. 18months post implantation, he continues to rate his pain at 0-1/10 with stimulator on. They concluded that in this case, spinal cord stimulation has shown potential beneficial effect in treatment of neuropathic pain that were resistant to conventional treatment resulting from radiation-induced transverse myelitis.[7]

Laffey J et al. (1998) described a case of 43-year-old lady in Dublin, Ireland, who had chronic neuropathic pain in both lower limbs, presented secondary to idiopathic acute transverse myelitis (IATM) at the level of T5. She was initially presented with symptoms of back pain, spinal shock and loss of sphincter control and sensorimotor function below the level of lesion. Diagnosis was made after careful CSF analysis and MRI imaging. She was treated with high

dose methyl-prednisolone and pulse dose cyclophosphamide for 3 months, followed by tapered dose of prednisone. Motor and sensory function were gradually returned in period of one year. However, severe constant pain began in her left foot as power returned to that limb. The pain described as sharp, progressively became more severe and spread to her right lower limb, from ankle to knee. Multiple therapeutic interventions including transcutaneous electrical nerve stimulation (TENS), diagnostic selective nerve blocks and trials of several medications proved unsuccessful in controlling her pain. A Quad plus electrode lead was inserted under local anaesthesia into epidural space at level of L1-L2 and guided to T11 under fluoroscopic guidance. The electrode was connected to external patient-controlled stimulator for a five-day trial period. They found, during trial period, complete cessation of pain was achieved, thus permanent implantation of pulse generator was inserted into subcutaneous pocket over right chest wall. At 12months post-implantation, she has experienced a vast improvement in her quality of life. Pain severity has decreased from a median Visual Analogue Scale (VAS) score of 8.1 (range 7-10) to 0.8 (range 0-2). There was significant decrease in her analgesic consumption, at which post- implantation limited to simple analgesics. Activity of daily living scores reveal a marked improvement in independent function, and from having been dependent on assistance to perform several activities (Class F) she is now almost fully independent (Class B). However, SCS does not improve her other neurological signs such residual spastic paraparesis with no change in her sensory abnormalities. They concluded that in their case, there was improvement in pain control and quality of life that can be achieved with SCS in a patient with neuropathic pain post idiopathic acute transverse myelitis.[4]

Spinal cord stimulator has been mentioned in a few guidelines in treating chronic neuropathic pain due to various causes. In 2005, a health technology appraisal from Ontario Ministry of Health and Long-term Care has concluded that there was weak-to moderate-quality evidence available supporting the use of SCS to decrease pain in neuropathic conditions.[8] In the UK, the National Institute for Health and Care Excellence (NICE) recommended SCS for people with chronic pain of neuropathic origin for at least six months who had not been responded to conventional medical management, and who had successful trial of stimulation as part of assessment.[9] In 2016, the European Academy of Neurology (EAN) guideline on central neurostimulation therapy in chronic pain conditions, made a weak recommendation to add SCS to medical management in painful diabetic neuropathy, chronic post-surgical back and leg pain, and complex regional pain syndrome (CRPS) type 1, and recommended offering SCS instead of re-operation in chronic low back pain.[10]

However, these guidelines only mentioned effectiveness of SCS in treating neuropathic pain in specific neuro related condition and not specified to transverse myelitis. To date, there is no guideline or algorithm specifically outlining the management of transverse myelitis sequalae. Relatively low incidence of transverse myelitis might be one of the challenge poses in demonstrating evidences.[2]

SAFETY

There was no evidence retrieved on safety of SCS in chronic neuropathic pain following transverse myelitis. However, recent systemic review published by Cochrane Library; assessed effectiveness and safety of SCS in chronic pain done by O'Connell et al (2022). The systemic review included 15 published randomized control trial (RCT) enrolling 908 patients with chronic pain due to a variety of causes including nerve disease. They found at medium follow up (reported between three to six months), the incidence of lead failure/displacement ranged from 0.9 to 14% (RD 0.04, 95% CI -0.04 to 0.11), the incidence of infection ranged from 3% to 7% (RD 0.04, 95%CI 0.01, 0.07), the incidence of reoperation/reimplantation ranged from 2% to 31% (RD 0.11, 95% CI 0.02 to 0.21). At five-year follow up, one study has reported a 55% incidence of lead failure/displacement (RD 0.55, 95% CI 0.35, 0 to 75) and a 94% incidence of reoperation/reimplantation (RD 0.94, 95% CI 0.80 to 1.07). They also found reports of some serious adverse events related to SCS such autonomic neuropathy, prolonged hospitalization, prolonged monoparesis, pulmonary oedema, wound infection, device extrusion and one death resulting from subdural haematoma.[11]

The US Food and Drug Administration (USFDA) has cleared a spinal cord stimulator for indications as an aid to manage chronic pain in the trunk or limbs associated with failed back surgery syndrome (FBSS), intractable low back pain and diabetic neuropathy.[12 13]

COST-EFFECTIVENESS (If any)

There was no evidence retrieved on cost-effectiveness of spinal cord stimulator in treatment of transverse myelitis. However, Rod et al (2004) in his systematic review on evaluation of the cost and cost effectiveness of SCS for the treatment of chronic pain, described that the healthcare cost associated with SCS in general can be classified into two categories: costs associated with the initial implantation (i.e., screening device / leads, physician / surgeon time, hospitalization), and costs associated with the post implantation period (i.e., concomitant therapy such as analgesic medication and physical therapy, follow-up visits and implant revision. Several studies have reported cost of SCS in US$; the cost of implant varied from US$8,796 to US$19,500; cost of inpatient hospitalisation ranged from US$1000 to US$14,000 and cost of revision varied from US$4,500 to US$13,100.[14]

CONCLUSION

There was very limited evidence retrieved on effectiveness of spinal cord stimulator for chronic neuropathic pain in transverse myelitis. The evidence was only from case reports.

There was no evidence retrieved on safety of spinal cord stimulator for chronic neuropathic pain following transverse myelitis. However, there were complications related to SCS reported in chronic neuropathic pain due to variety of causes. Among associated

complications reported include infection, electrode lead failure/migration and a need for re-operation/re-implantation.

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