Spinal cord injury and chronic pain

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Key points
- Chronic pain is common in spinal cord injury (SCI) patients.
- An assessment of whether this pain is unrelated or related directly to the spinal injury or the compensatory mechanisms is important.
- A multidisciplinary approach to the management is recommended.
- Principles of treatment for neuropathic pain in SCI patients are similar to those in non-SCI patients.
- Treatment of pain and its impact on life should focus on improving the biological, cognitive, and social impacts of pain.

Pain is defined by the International Association for the Study of Pain (IASP) as "an unpleasant sensory or emotional experience associated with actual or potential tissue damage, or described in terms of such damage". Pain is classified as acute if it is <12 weeks, and chronic if it is >12 weeks and persists despite an apparent lack of ongoing injury.

In spinal cord injury (SCI) patients, chronic pain is common. It impacts about 70% of patients with one-third of these experiencing severely intense pain impacting on mood, functioning, and quality of life.¹ The pain can be nociceptive, neuropathic, or visceral. Nociceptive is the most common and can be due to the initial trauma, muscle and joint overuse, for example, upper limbs and wheelchair use, and injury-related muscle weakness, spasm, and contractures. Neuropathic pain can develop acutely or after 1 yr post-injury and can present at or below the level of injury. Visceral pain is thought to originate from the abdomen or thorax and may be related mainly to constipation.

We review here the classification, mechanisms, clinical diagnosis, and management of pain in SCI patients.

Definitions and classifications

Classification of the neurological deficits in SCI patients

The American Spinal Injury Association (ASIA) classifies SCI on the degree of sensory and motor loss. The level of injury is defined as the lowest spinal segment with intact sensation and antigravity muscle strength (MRC power >3) where there is normal sensorimotor function above. The type of injury is classified from complete injury (A), sensory incomplete (B), motor incomplete with more than half of the muscle groups below the injury involved (C), motor incomplete with less than half the muscle groups below the injury involved (D), and normal (E). The difference between complete and incomplete loss is sparing of sacral function. Understanding the sensory motor deficits of SCI patients is crucial to the examination of the nervous system when assessing neuropathic and nociceptive pain.

Classification of pain in SCI patients

Classification of chronic pain in SCI has three tiers² (Fig. 1) as defined by the 'International Spinal Cord Injury Pain' (ISCIP) group. Tier 1 describes pain by its pathological origin: nociceptive, neuropathic, other, and unknown. In tier 2, nociceptive pain is subcategorized into musculoskeletal, visceral, and other pain types, while neuropathic pain is classified into pain at the injury level or below and other pain type. Tier 3 describes the source of...
the pain, for example, osteoarthritis of the shoulder, bladder spasm.

**Pathophysiology of chronic pain in SCI**

We know far more about nociceptive pain mechanisms than neuropathic pain mechanisms. For this reason and because nociceptive pain transmission is the same in SCI and non-SCI patients, we focus on understanding how the injured spinal cord goes on to develop chronic neuropathic pain.

Our understanding of SCI neuropathic pain comes predominantly from animal research. After SCI, structural neuroplasticity and sprouting of new dendritic fibres is critical for recovery and it is these changes that may add to neuropathic pain, muscle spasticity, and autonomic dysreflexia.

At the level of injury, neuropathic pain is thought to result from hyper-excitatory neurones which have exaggerated responses to stimuli at or below the normal activation threshold. Hyper-excitability results from altered expression of N-methyl-D-aspartate and glutamate receptors, sodium and calcium channels, increased glial activation, and/or hypofunction of endogenous inhibitory neurones. The success of sodium and calcium channel blocking analgesics in providing neuropathic pain relief supports this hypothesis.

Below the level of injury, the mechanisms of perceived pain are less clear. In complete spinal cord transection, the origins theoretically must be in the intact portion of the central nervous system above the level of injury. In these patients, the source of the ‘pain generator’ is unknown and could arise from spontaneously active in disinhibited polysynaptic pathways, a sensitized spinthalamic tract, or from a more central origin such as the thalamus or cortex.

An alternative explanation is that below level, pain could be produced by a dysfunctional relationship between the fast lateral spinthalamic tract and the slow medially located polysynaptic pathway. It is possible that post-injury, the polysynaptic tract may dominate over the spinthalamic tract which explains the late onset and diffuse nature of pain with its associated after-sensations after a stimulus. Crucially, the polysynaptic pathway is also capable of transmitting to de-afferented pathways giving the sensation of pain below the level of injury.

**Clinical assessment**

A careful pain history and a neurological and clinical examination are needed to make a diagnosis and guide treatment. Patients might have a range of symptoms including allodynia, hyperaesthesia, dysesthesia, and paraesthesia and asking only for pain descriptors in the history might not reveal the problem. Patients often describe their symptoms as ‘I don’t have sensation below my level of injury, but I do get pain’.

The approach to assessing pain requires an appreciation of biological, psychological, and social elements. Information about the site, onset, character, radiation, alleviating factors, temporal pain profile, exacerbating factors, and severity of pain is a reasonable start. Diagrams of the body where people can shade in areas of felt pain are useful where the pain location is not discrete. Understanding the characteristics of the pain is important to differentiate nociceptive from neuropathic pain. Nociceptive pain is dull, aching, stabbing, heavy, movement sensitive, and non-spontaneous. Neuropathic pain can be spontaneous or stimulus-provoked. Its characteristics are burning, shooting, electric shock, loss or gain of odd somatosensations, allodynia, and hyperaesthesia. Criteria used for diagnosis of SCI-related neuropathic pain would include:

(i) A history of a relevant lesion or disease affecting the spinal cord, cauda equine, or both.

(ii) The pain is located at or below the neurological level of the SCI and there is either:

(a) at least one diagnostic test confirming a lesion or disease of the spinal cord, cauda equine, or both and/or;

(b) a negative or positive sensory signs in the area of pain compatible with the spinal cord or root lesion.

(iii) Other causes of pain, such as nociceptive or peripheral neuropathic pain, are excluded or considered highly unlikely.

Without meeting these criteria, the pain may otherwise be regarded as nociceptive with either a sensory, mechanical, or visceral origin.

When taking a pain history, it is also important to elicit factors the patient has recognized may predispose to pain, why they think they are in pain, and what has caused them to address their pain now. This information addresses the patient’s ideas, concerns, and expectations of how their pain can be managed and allows the clinician to start understanding what may be done to help.

A drug history will reveal what medications they may have tried and failed to control the pain, along with their other medications which could contribute to pain or mood. A previous medical history may reveal medical conditions that are the cause of the patient’s pain which have been missed because of the focus on the SCI itself. A family, social, psychological, and smoking/alcohol history may reveal elements of how the psychology and social elements are influencing pain perception. One of the many anxiety and depression scales may be used to this end. Psychosocial factors have been found to strongly influence perceived pain severity and coping mechanisms.

The examination for pain involves assessing the various areas where the pain is reported. This includes a neurological examination of the area and testing the different sensory modalities looking for normal or abnormal sensory or motor conduction. Joint, skin, and other examinations where indicated should also be undertaken when required.
When the above information has been collated, formulation of a diagnosis, required investigations, and management plan will follow and should be done in conjunction with the patient. The management plan will usually have three aspects: pain control, treat psychological factors, and aid the return of function. The success of the plan depends heavily on patient involvement in the management of their pain, as it is a pain they will likely have for life.

Managing pain in SCI

General approach

The general approach to managing pain acute or chronic is the multidisciplinary team. This team involves pain specialists, clinical psychologists, psychiatrists, physiotherapists, a spinal cord injury specialist/rehabilitation specialist, and social and occupational therapy services. The entire team is necessary to treat the biology of pain, address psychological factors, and reduce obstacles to a normal life.

The psychosocial impact of the injury on the patient is huge and is a variable factor in successful management. Depression is common and patients might benefit from a multidisciplinary CBT-based approach to managing their pain. This may involve referral to a clinical psychologist, psychiatrist, or both. CBT in non-SCI chronic pain has been shown to significantly change pain experience, cognitive coping, and positive coping measures and reduce behavioural expression of pain. The psychological therapy may also be delivered as formal pain management programmes, psychological counselling, physiotherapy, occupational therapy, and self-help strategies. A psychiatrist may be needed if depression, anxiety, or another new or pre-existing psychiatric condition is affecting their pain or vice versa. A close working relationship is essential in these cases to manage the psychiatric components of the pain management, and ensure that pain medications do not upset any psychiatric disease.

When social factors play a large role, referral to the social services may be needed. The SCI population receive heavy social and occupational therapy input to help them return to work and life after their injury. Involving these teams in pain management may be required to aid this process and manage pain, particularly when concerns over housing, finances, having the correct wheelchair, etc. are causing them to focus negatively on their pain.

Medical management (drugs, psychology, and physiotherapy)

Treatment of chronic non-neuropathic/nociceptive pain should follow an escalation ladder. Initially, regular simple analgesics such as paracetamol used in conjunction with non-steroidal anti-inflammatory drugs are appropriate, but must be used with caution due to the risk of stress ulcers and impairing kidney function. Escalating to tramadol or mild opioids such as codeine and then stronger opioids such as morphine may be justified. Treatment of pain contributors such as muscular spasm is equally important as treating the pain. Muscular spasm is treated with spasmolytics, such as baclofen or methocarbamol.

Treatment of neuropathic pain is similar to that of non-SCI patients. In our unit at Stoke Mandeville Hospital, we provide treatment in accordance with the NICE guidelines. First-line drugs are the tricyclic antidepressants. Second-line drugs are the anti-convulsants. Treating neuropathic pain with medication requires starting a medication, and observing for a benefit after 6 weeks. If there is no benefit at 6 weeks, the dose may be increased or the drug can be stopped. Neuropathic analgesics should not be stopped suddenly but reduced gradually as they affect multiple organ systems.

First-line drugs commonly used are amitriptyline and dosulepin. Starting doses of amitriptyline 10–25 mg at night increased to a maximum of 75 mg daily are used. Higher doses require specialist supervision. Increases should be made in 10–25 mg increments per week. Amitriptyline should be avoided in severe liver disease, recent myocardial infarction, and cardiac arrhythmias. Tricyclic agent side-effects include dry mouth, blurred vision, constipation, difficulty with micturition, and cardiovascular side-effects. Dosulepin should be started at 25 mg at night for 3 days and then escalated to 25 mg increments 3 daily to 75 mg. A dose of 150 mg may be required. Its contraindications are identical to amitriptyline. If the sedation produced by amitriptyline and dosulepin is not tolerated, alternative non-sedating tricyclic antidepressants such as nortriptyline, imipramine, or lofepramine may be better alternatives.

The second-line anticonvulsant neuroromodulatory analgesics are the gabapentinoids. Pregabalin is effective and well tolerated by patients with neuropathic pain after SCI. The use of gabapentin and its effectiveness has been debated. Gabapentin should be started at 300 mg on day 1, 300 mg twice a day on day 2, and 300 mg three times a day on day 3. Based on individual patient response and tolerance of side-effects, the dose can be escalated to a maximum of 1200 mg three times a day in increments of 300 mg day−1 every 2–3 days. Slower increments may be required where side-effects are an issue, but a faster titration is strongly advised against. Withdrawing gabapentin likewise requires a slow decrement of the dose as abrupt cessation can cause anxiety, insomnia, nausea, pain, and sweating. Common gabapentin side-effects include dizziness, diarrhoea, dry mouth, dyspepsia, nausea and vomiting, abdominal pain, weight gain, and memory loss. Rarely, gabapentin may be the cause of acute pancreatitis.

Tramadol has shown to be effective, as a third-line treatment after gabapentinoids in some studies. Duloxetine may have some beneficial effect in central pain, and in those who have neuropathic pain and diabetes. It seems to work by preventing the re-uptake of norepinephrine, serotonin, and dopamine. Lamotrigine reduces spontaneous pain in patients with incomplete SCI. Sodium channel blockers such as lidocaine can produce analgesia both by a central and peripheral action. An i.v. lidocaine test is occasionally used in patients with a view to trying oral mexiletine. In refractory pain and spasm, intrathecal morphine, alone or in combination with baclofen and clonidine, has been used. Visceral pain requires regular gastroenterology and urology reviews for treatment of underlying causes such as constipation and urinary tract problems.

Specialist physiotherapy for preventing and treating overuse of muscles and joints is as important as is treating the pain itself. For individuals with SCI and neuropathic pain, regular exercise training leads to significant improvements in pain, stress, and reduces depression. The mechanism by which exercise does this is poorly understood, but it does change perceived pain and therefore reduces stress related to pain. Moreover, exercise exerts its influence on depression through reducing stress. Furthermore, exercise may help to improve chronic musculoskeletal pain and may indirectly influence neuropathic SCI pain. Abnormal posture, gait, and overuse all contribute to pain and may be addressed by physiotherapy, exercise, retraining, and environmental modifications. One of the most disabling and frequent causes of mechanical pain in the SCI population is shoulder pain. Shoulder range of motion exercise started as early as possible after injury is important to minimize shoulder pain. The overall aim of a rehabilitative physiotherapy programme is...
to increase self-efficacy and promote greater activity and normal participation.

**Surgical pain interventions**

Surgical interventions can be classified by what they are intending to treat: nociceptive pain, neuropathic pain, visceral pain, or other pain. Typically, surgical intervention for pain is used in compression neuropathies, syringomyelia drainage, and treatment of segmental pain at the level of injury with dorsal root entry zone (DREZ) lesioning.

- Chronic wheelchair use can cause carpal tunnel syndrome, ulnar nerve entrapment, thoracic outlet syndrome, and pudendal neuropathy. Carpal tunnel syndrome is treated with surgical decompression or injections, and ulnar entrapment with nerve trunk transposition surgery. Thoracic outlet syndrome is treated by minimizing physical activities that potentiate nerve irritation. Surgical decompression is a last resort and involves nerve decompression by removal of the first rib, release of the scalenes, or both. Thoracic outlet syndrome must not be confused with syringomyelia whose presentation is similar but whose treatment is very different. Pudendal neuropathy occurs when the pudendal nerve is compressed by thickened sacrotuberous, sacrospinous ligaments, or both from prolonged sitting. It can be the cause of perineal pain when lying down. Its treatment includes alterations to wheelchair ergonomics, physical therapy, analgesia, steroid injections around the ligaments and nerve canal, pulsed radiofrequency ablation of pudendal nerve, and surgical decompression as a last resort.

- Early-onset radicular pain after any spine surgery may result from malposition of the implanted screws or clips. For late onset radicular pain, dislocated material, worsening kyphosis, or both can be the cause. Correction of any of these causes requires further surgery.

- Syringomyelia may present initially with pain at the level of injury and new neurological deficit. Diagnosed with MRI, it results from blockade of cerebrospinal fluid (CSF) flow at the level of the injury caused by vertebral disc compression, arachnoiditis, or both. The treatment includes CSF bypass shunting, arachnoid grafting, and duraplasty. However, pain is rarely the indication for surgery as it remains unclear whether the pain originates at or above the level of the injury.

- DREZ ablation is effective on segmental pain at the level of injury. The DREZ is the section of small pain fibres that enter the spinal cord at the dorsal horn tip. It is mainly used for pain at lower injury levels, incomplete SCI, and for unilateral pain.

**Specialist therapies for pain in SCI: neurostimulation**

A large portion of patients’ SCI pain is refractory to pharmacological treatment and so alternative interventions are being explored. Categorized as non-invasive and invasive, they are all essentially a form of neurostimulation. Non-invasive neurostimulation techniques are transcutaneous electrical nerve stimulation, repetitive transcranial magnetic stimulation, and transcranial direct current stimulation. Invasive neurostimulation techniques are peripheral nerve stimulation, nerve root stimulation, spinal cord stimulation (SCS), deep brain stimulation (DBS), and motor cortex stimulation (MCS).

Invasive neurostimulation of the spinal cord or brain should only be considered when there is severe debilitating chronic pain and all other therapies have failed. SCS possibly works by: decreasing spinothalamic tract activity, reestablishing sensory afferents, interrupting pain processing due to maladaptive plasticity, and stimulating spinal cord–brainstem loops. DBS is more effective on nociceptive pain than deafferentation pain. MCS-induced pain relief may relate to activation of descending pain control systems. MCS has a better clinical potential as it has fewer complications than DBS, and is better supported by evidence for its use in central pain in SCI patients.

**Summary**

Pain in SCI patients is complex. The mechanism is poorly understood and it is further complicated by the psychosocial impact of the nature of injury. Treatment and management modalities do not work in isolation and need to be combined with pharmacological methods, physical therapy, and psychological input in specialist centres. More research needs to be conducted in novel experimental therapies with emphasis on improving patients’ quality of life after SCI.

**Declaration of interest**

None declared.

**MCQs**

The associated MCQs (to support CME/CPD activity) can be accessed at https://access.oxfordjournals.org by subscribers to BJA Education.

**References**

11. Rintala DH, Holmes SA, Courtade D, Fiess RN, Tastard LV, Loubser PG. Comparison of the effectiveness of amitriptyline...