

Multiple Sclerosis and Pain

A Medical Focus

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ABSTRACT

About 65% of multiple sclerosis (MS) patients experience a broad range of both acute and subacute painful syndromes. Acute conditions (eg, trigeminal neuralgia and Lhermitte's syndrome) cause intense, unrelenting pain that may worsen with age and disease progression. Chronic pain (eg, joint pain) is also a component of MS. Pain syndromes, including optic neuritis, complex regional pain syndrome [CRPS], and other less well-known syndromes, may respond to a variety of pharmacologic, surgical, or alternative interventions. MS patients may also experience iatrogenic pain. Some successful drug treatments for pain that are used in combination or alone include anticonvulsants, tricyclics, antidepressants, methylprednisolone, and narcotics. Surgical interventions, percutaneous compression-balloons, and radiofrequency ablation are other viable options for some pain syndromes. (Int J MS Care. 2000;2(3):30-34.)

The medical community has often underestimated both the extent of pain experienced by people with multiple sclerosis (MS) and the pain's impact on their lives. While physical disability resulting from the disease is usually the primary concern in treatment, pain causes serious disability in its own right.

MS patients experience a broad range of painful syndromes—from acute conditions, such as trigeminal neuralgia and Lhermitte's syndrome, to chronic symptoms that may arise secondarily, such as from spasticity.¹ Pain syndromes may last more than a month at a time, and some may increase with the age of the patient and progression of the MS.^{2,3} Certain common painful syndromes are the result of the MS disease process itself (eg, optic neuritis, cramps, and neuralgias). Other syndromes, such as complex regional pain syndrome (CRPS), occur less frequently. Secondary pain may result from pressure sores, from stiffened joints, muscle contractures, and other causes. MS patients may also experience iatrogenic pain.

Pain is also more prevalent among MS patients than might otherwise be assumed. In 1991, Warnell⁴ found that 233 (64%) of the 364 patients with MS in his descriptive study had experienced pain at some time during their disease, and 40% of those patients

reported that they were never pain-free. Forty-nine percent of respondents with pain experienced difficulty in working, and 44% had difficulty sleeping because of pain. Approximately 34% of the MS patients who were experiencing pain reported that they were having troubled relationships.

Stenager and colleagues² came to similar conclusions—only 35% of patients with MS in their study were pain-free. Of patients reporting pain, 45% were experiencing pain at the time of examination. Perhaps more important, 32% of these patients reported pain as among the most severe symptoms of their disease. Given the number of patients suffering from either constant pain or pain as a severe symptom of MS, development of effective treatment strategies for the many different pain syndromes is a vital concern for patients and physicians.

ACUTE PAIN SYNDROMES

Trigeminal Neuralgia

Trigeminal neuralgia (tic douloureux) affects the first, second, or third distribution of the fifth cranial nerve and is usually unilateral. It is more common in the second or third distribution (the maxillary and mandibular divisions) and may be triggered by a sen-

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sory stimulus, such as brushing the teeth or even a breeze touching the face. It is more common in women than in men: 56 is the average age of onset, but it may occur earlier in MS patients, of whom 1.9% develop trigeminal neuralgia.⁵ In MS, trigeminal neuralgia may be caused by a demyelinating plaque at the root entry zone or in the pontine tegmental pathways.⁶ In a small percentage of patients, trigeminal neuralgia is the first sign of MS.⁵

Trigeminal pain is excruciating. It is often described as stabbing; it may last for only a few seconds or go on

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for a minute. It may be unrelenting, with up to 100 attacks a day. As the disease progresses, the frequency of attacks may increase without a remission.⁷

Because trigger points may be anywhere on the face or head, including the scalp, they may inhibit the patient's normal functioning and interfere with hygiene. Patients with trigger points on their scalp may not want to wash their hair; those with dental triggers may avoid brushing their teeth and may thus develop dental caries. If the pain is triggered by chewing, patients can become malnourished.⁷

In the early stages of trigeminal neuralgia, the mainstay of treatment is carbamazepine, which often works quite well initially.⁵ However, as the attacks of neuralgia increase, this agent may become less effective and an alternative drug may be added, such as baclofen, gabapentin,⁸ lamotrigine,⁹ or misoprostol.¹⁰

Solaro and colleagues found that a combination of low-dose gabapentin (300 to 1,200 mg daily) with either lamotrigine or carbamazepine controlled the pain of trigeminal neuralgia in 10 out of 11 patients with MS.¹¹ Mean dosages were carbamazepine 400 mg and gabapentin 850 mg daily in one group, and lamotrigine 150 mg and gabapentin 780 mg daily in the oth-

er. Currently, reports of use of gabapentin have been from uncontrolled trials. Two other traditional treatment options are injections of alcohol or glycerin.¹²

If medical therapy fails, then surgical treatment may be necessary. Microvascular decompression (MVD) is one of the two surgical procedures for the treatment of this syndrome.¹³ However, Resnick et al found that on its own, MVD failed to provide adequate relief of pain.¹⁴ They suggested that exploration of the cerebellopontine angle and partial sectioning of the nerve might prove more beneficial. Another surgical technique employs a percutaneous compression-balloon,¹⁵ which may reduce the ephapsis (the "cross-talk" between nerves) that can induce this pain. Radiofrequency ablation (or denervation, as it may be referred to) is sometimes used in patients unable to tolerate medication.¹⁶

Lhermitte's Sign

Another cause of severe pain is Lhermitte's sign, which is a well-known phenomenon in multiple sclerosis and is usually caused by a cervical cord lesion. It is a sudden, severe sensation like a strong electric shock that spreads through the body when the patient's head is tilted forward; it appears to be associated with active lesions.¹⁷ At least 25% of MS patients suffer from Lhermitte's sign.¹⁸ Sandyk and Dann reported that treatment with weak electromagnetic fields can relieve the intense pain caused by Lhermitte's sign.¹⁸

NONACUTE PAIN CAUSED BY THE DISEASE PROCESS

Optic Neuritis

Optic neuritis, an inflammation of the optic nerve, is often an early sign of MS. At least 42% of people who have an initial attack of optic neuritis develop MS within 10 years.¹⁹ Optic neuritis usually has a subacute onset (within several hours), and its hallmarks are pain and some loss of vision. In patients with MS and optic neuritis, visual loss is unilateral, although vision is usually restored. The physical appearance of the eye is normal, but it exhibits what is known as Marcus Gunn pupil (ie, a light shone directly into the eye will cause the pupil to dilate rather than contract).

As several other conditions can mimic optic neuritis, including neuroretinitis (papillophlebitis), accurate diagnosis is important.²⁰ If the optic disk is not painful and swollen and there are no abnormal magnetic resonance imaging findings, however, MS is less likely to develop. An examination of the spinal fluid for oligoclonal bands also may help to predict which patients are most likely to develop MS within five years.²¹

There are controversies surrounding the treatment of optic neuritis, with differences surfacing between ophthalmologists and neurologists.²² Oral methylprednisolone has been used in some cases,²³ while in others intravenous (IV) methylprednisolone has been recommended.²⁴

The large Optic Neuritis Treatment Trial (389 patients with optic neuritis, without known MS) clearly demonstrated that oral prednisone doubled the risk of recurrent optic neuritis over the following two years.²⁵ On the other hand, IV methylprednisolone (1 g/d for three days) halved the risk of developing MS in the next two years. The IV methylprednisolone did not affect recurrence rate. At the trial's five-year follow-up point, the investigators reiterated their earlier management recommendations.²⁶

Despite the side effects associated with glucocorticoids, a recent Japanese study has shown that IV methylprednisolone provides faster recovery of visual acuity within a week.²⁷ The American Academy of Neurology practice parameters published in 2000 do not address the effect of higher-dose oral or parenteral methylprednisolone or adrenocorticotropic hormone (ACTH) on pain, but they suggest that use of these agents may aid in faster recovery. Patients on either drug regimen had similar results in visual acuity.²⁸

Another suggested treatment for optic neuritis is IV immunoglobulin (IVIg). However, current studies have not demonstrated efficacy and have shown worsened visual function during active disease.²⁹

Spasticity

Approximately 40% to 50% of MS patients have some degree of spasticity, which can be very painful. Spasticity is a motor disorder with some or all of the following symptoms: exaggerated tendon reflexes, stiffness, contractures, and violent muscle spasms. Spasticity may possibly be severe enough to cause fractures or dislocations. In some rare cases, the muscle spasms are severe enough to dislocate joints or sprain muscles. Pain and nocturnal spasms may cause loss of sleep, and the strong contractures may lead to

permanent deformations.³⁰

The new pharmacologic agents that have improved the treatment of spasticity in recent years present a dilemma. Many disabled patients come to rely on their stiffness to make standing transfers. Short-acting agents provide a partial solution. They can be used to treat painful nocturnal spasms that interfere with sleep and to relieve morning stiffness,³⁰ while still leaving the patient with some stiffness during the day for making transfers.

Oral baclofen has been used effectively for years to treat spasticity (typically in nonambulatory patients). More recently, tizanidine has shown efficacy in this condition. Both agents are considered to be first-line treatment.

There are many other medications for spasticity, including diazepam, clonazepam, dantrolene, and botulinum toxin A (Botox®). For nonambulatory patients, refractory spasticity may call for intrathecal baclofen,³⁰ which necessitates surgical installation of a pump. Only 1/100th of the oral dose of baclofen is needed for intrathecal administration to achieve a therapeutic effect.

Low-frequency transcutaneous electrical nerve stimulation (TENS) has also been used, although a recent article on spasticity in stroke patients found no efficacy. Physical therapy is another important management tool for spasticity. While it cannot eliminate spasticity, active and passive stretching may help prevent contractures.²⁸

Spasms, Cramps, and Other Causes of Pain

Patients with MS suffer from a number of other painful symptoms, including spasms, cramps, and sensory symptoms, as well as significant joint trauma and pain resulting from weakness. Painful tonic spasms or cramps are sudden, unpredictable, and powerful enough to eject a patient from a wheelchair. These spasms are usually unilateral and thought to be the result of lesions of the posterior limb of the internal capsule.³¹ Temporary treatment includes epidural or intrathecal opioids, but anticonvulsants are often a good first-line therapy. Phenytoin has proved very effective in many of these patients, although carbamazepine and gabapentin,³² as well as baclofen, have all been used. Before subjecting patients to surgery, the clinician should consider prescribing acetazolamide³³ (a carbonic anhydrase inhibitor used to treat a number of conditions, including epilepsy). It works

well in some patients.

The neuropathic pain that afflicts many MS patients—burning, itching, and electric pain—can be quite severe, and it often increases as the disease progresses.³⁴ More unusual pain syndromes of MS include glossopharyngeal neuralgia, which is marked by severe paroxysmal pain in the throat, posterior pharynx, base of the tongue, and tonsillar area. It may even spread to the ear. This type of neuralgia may be provoked by a yawn, by chewing, or by a tongue depressor. Although it is relatively rare—only four out of 8,000 patients experience it—the pain is extreme and causes the patients suffering from it to become tremendously anxious.³⁵

Effective treatment of glossopharyngeal neuralgia has been achieved with carbamazepine. Some practitioners use ACTH and cyclophosphamide; but because the patient population is so small, definitive studies have yet to be done with these therapies.

Complex Regional Pain Syndrome

Although it is rare in MS patients, CRPS causes the most excruciating pain. It can go on indefinitely, with the lightest touch perceived as pain. The pain can be shooting, stabbing, lancinating, or burning; it tends to become much worse at night. As a result, many of these patients cannot sleep. CRPS is found in MS patients of Southeast Asian origin who have tissue destruction in the spinal cord and who develop syringomyelia in the area of active demyelination.³⁶

Of all the pain syndromes, CRPS is perhaps one of the most difficult to treat. Consequently, many therapeutic measures have been tried, including physical therapy, exercise, nonsteroidal anti-inflammatory drugs, narcotic medications, and epidural blocks. Although they are of help to some patients, these therapies do not work for many others. Tricyclics, antidepressants, and anticonvulsants have also been used.³⁷

IATROGENIC PAIN

Many MS therapies can exacerbate the patients' pain. Long-term steroid treatment can induce osteoporosis, which can lead to vertebral fractures. In patients undergoing steroid therapy, bone density should be measured and deficiencies treated with calcium, benzothiadiazides, calcitonin, or bisphosphonates.³⁸ An injection of polymethylmethacrylate³⁹ will alleviate the pain almost immediately. The most important

measure that can be taken in this situation, however, is prevention.

Other drugs, such as beta interferons, which are commonly used to treat MS, can cause considerable pain. Patients who are taking beta interferons may experience migraine or local injection site reactions. Migraine has also been reported by many patients receiving IVIg. Prophylactic treatment for migraine is now recommended for these patients.

ALTERNATIVE INTERVENTIONS

Although this paper focuses on pharmacologic treatments for pain, some nonpharmacologic treatment options are available. MS patients may benefit from education and counseling provided by physical therapists, social workers, or occupational therapists to help manage their pain. Anecdotal patient reports include positive effects from acupuncture and TENS.

CONCLUSIONS

Although pain syndromes accompanying MS are very common, various pharmacologic, surgical, and other traditional and alternative therapies can provide relief. The first choice of treatment is pharmacotherapy. Treatment may not be successful with the first selected drug, but combinations of drugs or alternative monotherapies may relieve pain. Secondary treatment is surgical intervention, which has been successful for treating some of the pain syndromes of MS.

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