

Mellen Center Approaches: Pain in Multiple Sclerosis

Q: How often do MS patients have pain?

A: Pooled overall pain prevalence in a systematic review of 17 studies with 5319 subjects was 63% (95% CI 55-70%). The quantified prevalence of specific pain in this studies was as follows: headache 43%(95% CI 33–52%), neuropathic extremity pain 26% (95% CI 7–53%), back pain 20% (95% CI 13–28%), painful spasms 15% (95% CI 8.5–23%), Lhermitte sign 16% (95% CI 10–25%), and trigeminal neuralgia 3.8% (95% CI 2–6%) in included studies. Compared to controls, MS patients were more likely to have moderate to severe pain, use analgesics and describe interference with daily activities. Pain has been associated with poor quality of life measures. Risk factors associated with increase pain in MS patients include: older age, longer disease duration and greater EDSS scores. In a systematic review of 8 studies with 1864 MS patients and 261563 controls, there was a significant association between migraine and MS (odds ratio 2.60, 95% CI 1.12-6.04) with significant heterogeneity.

REFERENCES

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Foley P et al. Prevalence and natural history of pain in adults with multiple sclerosis: systematic review and meta-analysis. *Pain* 2013;154:632-642

Pakpoor J, et al. Meta-analysis of the relationship between multiple sclerosis and migraine. *PLoS One* 2013;8(4):10.1371

Q: Are there different types of MS pain?

A: Pain can be described on the basis of different factors: location, etiology and duration or time course: acute or chronic.

Common acute pain syndromes include: Paroxysmal pain, Trigeminal neuralgia, Lhermitte's phenomenon and dystonic (or tonic) spasms.

The common chronic pains are: low back pain, dysesthetic extremity pain, spasms, cramps, complex regional pain syndrome (CRPS).

Table 1. Pain Syndromes according to lesion location

Demyelinating Lesions in the Nerve entry Zone	Trigeminal Neuralgia Glossopharyngeal Spinal roots-Pseudoradicular syndrome
Demyelination in the Sensory Pathways	Chronic Paresthesia Lhermitte's Dysesthesia Pain Syndromes (includes spinal cord lesions)
Secondary Complications of MS	Optic Neuritis (eye pain) Partial Myelitis Severe spasticity Musculoskeletal – related to disability Headaches (Migraine, other)

This information is not intended to replace the medical advice of your health care provider. Please consult your health care provider for advice about a specific medical condition.

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Q: Do MS patients get headaches?

A: Headaches, particularly migraine, appear to be reported more commonly in the MS population. Headaches can sometimes be associated with a relapse, but at the Mellen center we do not consider isolated new headache to be a definite marker of a relapse of MS. Interferon Beta and fingolimod can increase the risk of headaches, especially in the first few months of therapy. Cervicogenic headaches are common and can be helped by physical therapy focused on the neck.

Other than altering medicines which may induce headache, we treat headaches in MS the same way they are treated in the general public. There is nothing specific about the MS treatment. MS medications do not reduce headache in the MS population, and some may be associated with increased headache frequency (for example interferon betas and fingolimod). We often work with local neurologists or a headache center in the ongoing care of such headaches.

REFERENCES

LaMantia IFN treatment may trigger primary Ha in MS patients. *MS* 2006;12;476-80.

Rolak LA, Headaches and MS, *J Neurol*: 1990;237:300-2.

Pakpoor J, et al. Meta-analysis of the relationship between multiple sclerosis and migraine. *PLoS One*. 2013;8(4):10.1371

Q: What is neuropathic pain?

A: "Pain arising as a direct consequence of a lesion of disease affecting the somatosensory system."

Geber C, Neuropathic Pain Special Interest Group of the International Association for the Study of Pain. *Am J of Med* 2009;122(10 Suppl):S3-S12

In MS patients commonly have neuropathic pain. It often affects a limb or limbs, and sometimes involved the trunk. It is described in a various ways but often the following descriptions are used: "burning, tingling, jabbing, electrical, itching". Sensory exam is often abnormal at the site of the pain, but may be minimally abnormal. Neuropathic pain is commonly worse at night and may be associated with allodynic pain (painful sensation to a touch stimulus). Neuropathic

pain may be intermittent or continuous.

Q: What is Lhermitte's phenomenon?

A: Lhermitte's phenomenon is a sudden sensation of electrical shock that spreads through the body on flexion of the neck, occurs in 25-33% of patients with MS. The sensation usually lasts for less than 2 seconds. Pharmacotherapy is not usually necessary. A cervical intramedullary lesion is often found in these patients, most typically at C4 level.

REFERENCES

A multimodal approach to managing symptoms of MS. Crayton H. *Neurology* 2004;63(Suppl 5):S12-S18.

Gutrecht JA, Zamani AA, Salgado ED. Anatomic-Radiologic Basis of Lhermitte's Sign in Multiple Sclerosis *Arch Neurol* 1993;50:849-851

Q: How often does back pain occur in MS?

A: The prevalence of back pain in MS can range from 10-16%. In many MS patients the pain is musculoskeletal in origin and therefore aggravated by prolonged sitting or standing. Less commonly back pain is associated with Scoliosis or Degenerative disease of the spine. It is rare that back pain is central in origin. Treatment of MS back pain is similar to back pain protocol in non MS patients: PT, NSAIDS, heat, cold packs and if needed consultation with Pain Management.

Q: Are Spasms painful?

A: Spasms are not always painful. Please refer to the Mellen Center document on treating Spasticity in MS. Tonic Spasms or Dystonic spasms can sometimes be painful uncontrolled spasms precipitated by voluntary movement, sensory stimulation or hyperventilation. They are rarely seen outside MS patients or neuromyelitis optica, and they are seen in 10-24% of MS patients. Treatment with anticonvulsants can lessen the spasms and pain and be efficacious in low doses.

REFERENCE

A multimodal approach to managing symptoms of MS. Crayton H. *Neurology* 2004;63(Suppl 5):S12-S18.

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Q: What is Trigeminal Neuralgia (TN)?

A: TN is the sudden, usually unilateral, severe, stabbing recurrent episodic pain in the distribution of one or more branches of the Trigeminal nerve. At the Mellen Center we evaluate young patients with new onset of TN as this may be a first symptom of MS. The prevalence of TN in MS patients is thought to be 1-2%, 20x the prevalence of the general population. The prevalence of bilateral TN in MS patients is 11-31% more common than in non MS patients.

REFERENCE

Hooge JP. Trigeminal neuralgia in MS. *Neurology* 1995;45:1294-6.

Q: Which drugs are effective in TN pain?

A: Clinical trials have demonstrated various levels of pain control; carbamazepine (200-1200mg/d) is established as effective, oxcarbazepine (600-1200mg/d) is probably effective and lioresal, lamotrigine and pimozide are possibly effective for controlling pain in patients with TN. There is insufficient evidence to support the use of clonazepam, gabapentin, phenytoin, tizandine, topical capsaicin and VPA for controlling pain in TN. There are no published studies comparing polypharmacy to monotherapy although it is our experience that polypharmacy with various drug classes can result in improved TN pain control. Patients with MS may have difficulty tolerating medicines such as carbamazepine due to fatigue and ataxia. Occasionally IV or po steroids have temporarily helped TN pain.

Our current approach is to start with oxcarbazepine, once this dose is maximized and is ineffective we will add another antiepileptic medication to improve pain control. If the TN pain flares and the patient is having trouble eating, a short course of po or IV steroids is indicated. Topical therapies also can help pain control, such as Capsaicin, Lidocaine or Gabapentin cream.

REFERENCES

A multimodal approach to managing symptoms of MS. Crayton H. *Neurology* 2004;63(Suppl 5):S12-S18.

Gronseth G et al. Practice Parameter: The diagnostic evaluation and treatment of trigeminal neuralgia. *Neurology* 2008;71:1183-1190

Q: When should other interventions for TN in MS patients be considered?

A: At the Mellen Center we usually try one or two first line medicines for the Trigeminal neuralgia in a reasonable dose escalation. If efficacy is not sufficient or if side effects are prohibitive we recommend that an interventional approach be considered to improve quality of life.

For patients with TN refractory to medical therapy, Gasserian ganglion percutaneous techniques, gamma knife, and microvascular decompression (MVD) may be considered (Level C AAN GDDI methodology). However, there is limited data on any of these techniques in the MS population, and MVD mechanistically may not make sense in the MS population.

Percutaneous procedures on the Gasserian ganglion, gamma knife and microvascular decompression are possibly effective in the treatment of TN(multiple Class III studies).

Indirect comparison suggests microvascular decompression has longer duration of pain control than other surgical interventions. There are studies showing lesser efficacy of these procedures in MS patients yet overall insufficient evidence to support or refute use of these procedures in MS. In our experience Gamma Knife procedure is the least invasive and most efficacious (anecdotal data) procedure. Balloon ablation can also be effective in MS patients. We send the patients for surgical evaluation for further advice on the most efficacious procedure for the TN pain.

REFERENCE

Gronseth G et al. Practice Parameter: The diagnostic evaluation and treatment of trigeminal neuralgia. *Neurology* 2008;71:1183-1190

Practice Parameter: the diagnostic evaluation and treatment of trigeminal neuralgia *Neurology* 2008; 71:1183-1190.

Q: Can Optic Neuritis be painful?

A: Optic Neuritis is common in MS patients and pain is a diagnostic feature of Optic Neuritis. Pain is usually characterized as retroorbital and worse with movement, present first few days of optic neuritis event. Treating the ON as needed with IV steroids can reduce the

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associated pain. Most patients do not require specific pain management for this symptom as it is self limited. Chronic photophobia can occur in MS and this can be uncomfortable.

REFERENCE

Chronic and Acute pain syndromes in MS. *Acta Neurol (Napoli)*1994;45:1294-6.

Q. Can MS patients have Fibromyalgia as well as MS?

A: MS patients can have fibromyalgia as well as MS. Fibromyalgia patients may also have symptoms similar to MS, and often seek information on whether they have MS causing their symptoms. Medications, graded exercise, aquatic exercise, improved sleep efficacy, and physical therapy can help manage fibromyalgia symptoms. We recommend using international criteria for the diagnosis of fibromyalgia to aide in identification of such patients.

REFERENCES

Wolfe F, et al. The ACR 1990 criteria for the classification of fibromyalgia. *Arthritis Rheumatism* 1990;33:160-172

Wolfe F et al. The ACR preliminary diagnostic criteria for fibromyalgia and measurement of symptom severity. *Arthritis Care Res* 2010;62:600-610

Q: Do Psychosocial factors play a role in pain?

A: Psychosocial factors, including pain related catastrophizing and pain coping, were not only strongly associated with pain interference but were more strongly associated with pain intensity. Therefore adding Psychology and nonpharmacologic means of helping pain (exercise, meditation, deep breathing, healthy diet) may improve pain coping. It is not clear if depression in and of itself is a risk factor for pain in MS.

REFERENCE

Pain Associated with MS: Systemic review and proposed classification. O'Connor P, *Pain* 137(2008) 96-111.

Q: Does MRI help to localize the pain syndromes of MS?

A: Central MS pain patients have been found to have between 5-16 focal brain lesions mainly in the

periventricular white matter. One third of these cases had lesions in the lateral or medial thalamus and most patients have cervical or thoracic spine lesions. Tonic spasm patients were found to have lesions at the level of the internal capsule posterior limb or in the cerebral peduncle. Patients with Lhermitte's phenomenon were found to have lesions of the cervical spinal cord. Further evaluation is needed if the pain syndrome is atypical for MS or difficult to control to rule out alternative etiology of the pain syndrome.

Patients with spinal cord lesions (Both MS and Devic's disease) may be more likely to have neuropathic pain, likely due to altered afferent traffic to the thalamus.

Clinically we note that in patients with MS pain we cannot specifically identify a generator for pain, as there may be multiple different demyelinating plaques or areas of demyelination not visualized on MRI imaging.

In 15 % of the TN cases routine neuroimaging may identify the cause of the TN. There are currently inconsistent results regarding sensitivity of MRI to identify vascular contact in CTN. MS patients may have lesions at the Trigeminal nerve root entry zone as well as pontine lesions at the intramedullary portion of the trigeminal root.

REFERENCE

Gass A. TN in patients with MS:lesion localization with MRI. *Neurology* 1997;49;1142-4.

Reference:Ostenberg A. Central pain in MS : prevalence and clinical characteristics. *Eur J Pain* 2005;9;531-42.

Q: How do we best help MS patients with neuropathic pain?

A: We first diagnose the pain syndrome and educate the patient. We try to follow a multidisciplinary process, involving health psychology, physical and occupational therapy, and other health care practitioners as needed. Anticonvulsants have been the first line therapy for MS related neuropathic pain. We generally start treatment with Gabapentin or Pre-Gabalin. These medications can make patients sleepy or dizzy, so starting in low doses or at bed time can help the patient better tolerate the medications. Neuropathic pain may need higher doses of these

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medications for full efficacy, ie. 1800 mg of Gabapentin a day is a common dose to help neuropathic pain. The FDA has approved Pregabalin and Cymbalta for treatment of diabetic related peripheral neuropathic pain and fibromyalgia, but we also use these medications for MS neuropathic pain in an off label fashion. Oxcarbazepine (and other related compounds), lamotrigine and tricyclic antidepressants have also been found to be helpful for treatment of central neuropathic pain. It may also be reasonable to consider using medications that have helped peripheral neuropathic pain: tramadol, selective serotonin reuptake inhibitors (SSRIs) and selective norepinephrine reuptake inhibitors (SNRIs). There are times when combination therapy of various drug classes also may help lessen MS patient's pain. Disease modifying therapies for MS have not been shown to be helpful in treating MS pain. Baclofen may help painful spasms and has been found to also help TN pain.

REFERENCE

Dworkin RH. *Arch Neurol* 2003;60;1524-34.

Q: What about chronic opioids for this population?

A: There is limited data on the use of chronic opioids in the MS population. However our experience is that this is a common practice. For some patients with chronic neuropathic pain this may be an important option when other avenues for treatment have been exhausted. However, central sensitization appears to worsen with the use of narcotics and may be counterproductive. Physicians prescribing such medications such be adept at the use and prevention of side effects of such medicine, and should have a narcotic agreement for care with the patient understanding the limits and restrictions on the use of such medicine.

NOTE: At the Mellen Center we do not participate in pain management with long acting opioids. We prefer to work with pain management physicians or neurologists in the local area. Chronic opioid therapy is best managed in the context of an overall pain management program.

Q: Is there presently a role for Cannabinoids in MS pain management?

A: There are at least 5 randomized control trials looking at the use of Cannabinoids for MS pain. The oral synthetic tetrahydrocannabinol (THC) in a crossover

design, reduced pain and improved certain QOL measures but had a high frequency of side effects. In other studies the results showed no statistically significant benefit. The results are mixed and further research is required. A recent AAN systematic review on cannabinoids found that for patients with MS with central pain or painful spasms, oral cannabinoid extract is effective for reduction of central pain (2 Class I studies), that THC or nabiximols are probably effective for treating MS related pain or painful spasms (one class I study each), and that there was insufficient evidence for efficacy for smoked marijuana in reducing pain (2 class III studies examining different issues). At the Mellen Center we do not generally utilize Cannabinoids for MS related pain at this time.

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Wade DT. *MS* 2004;10;434-41.

Svendsen KB *BMJ* 2004;329;253-60.

Koppel BS et. Al. Systematic review: efficacy and safety of medical marijuana in selected neurological disorders. *Neurology* 2014;82:1556-1563

The National MS Society has an Expert Opinion paper on this topic, please see for further recommendations.

<http://www.nationalmssociety.org/about-multiple-sclerosis/treatments/complementary--alternative-medicine/marijuana/download.aspx?id=1023>

Q: When should Pain management or Chronic Pain Programs be involved?

A: These services should be considered when the patient has inadequate pain control after working with RN/MD teams with various trials of pharmacologic and alternative health measures. Pain Management programs may recommend procedures such as epidural injections, an Intrathecal pump and or a Spinal cord stimulator for pain control. Spinal cord stimulators, at this time, interfere with the use of further MRI imaging for MS management.

Q: What is the role of exercise and wellness interventions on pain in MS?

A: There is evidence that exercise and wellness interventions can affect pain.

In one study wellness interventions in MS affected

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women resulted in fewer reports of bodily pain. Exercise is also associated with lower rates of complaints of pain.

The practice of meditation over two months resulted in significant pain reduction and improved physical health measures in MS patients compared to controls.

Therefore helping MS patients engage in regular exercise and nonpharmacologic measures may help with pain control. We offer our patients with pain a consultation with PT for conditioning and to help them establish a regular exercise routine.

We encourage people with multiple sclerosis to use non-medicinal approaches to pain and wellness that can include:

1. Meditation
2. Exercise
3. Consultation with Integrative medicine
4. Nutrition therapy
5. Smoking
6. Sleep Hygiene
7. Aquatic therapy
8. Yoga or chair yoga
9. Behavioral medicine approaches

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