MANAGING PAIN AND SENSORY SYMPTOMS IN MS

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Objectives

- Differentiate neuropathic and nociceptive pain
- Identify types of pain and sensory symptoms typical to patients with MS
- Review pharmacological and non-pharmacological methods of managing pain
- Identify factors that contribute to pain response
Why does it matter?

- Pain prevalence reports vary from 29-86% of MS patients.
- More than 50% MS patients find pain to be a problem, and for 10-20% it is a significant problem.
- Pain is estimated to comprise nearly 30% of all symptomatic treatment.
- Pain can interfere substantially with the ability of patients with MS to work, sleep, maintain relationships and enjoy life.


Quality of Life

- Interdependent relationship between depression, fatigue, and pain.
- Influence of pain on psychological aspects of quality of life results in poorer mental health and increased social handicap.
- Comprehensive management recommended over single-system approach.

Patients more likely to experience pain:

- Older
- Longer disease duration
- Greater disease severity
- Men and women are equally likely to experience pain, but women tend to have greater severity of pain
- Progressive forms of MS
- Co-morbid depression and mental health impairment

Nociceptive Pain

- The result of stimulation of nociceptors that signal tissue irritation or injury to elicit an appropriate response
- Described as aching or throbbing
- Typically time limited
- Examples include sprains, burns, bone fractures, inflammation, myofascial pain
- Tends to respond to opioid treatment

Neuropathic Pain

- Result of an injury or malfunction of the peripheral or central nervous system
- Described as lancing, pins and needles, burning, electric shock
  - Commonly associated with allodynia (painful response to non-painful stimuli) and/or hyperalgesia (increased response to painful stimuli)
- Doesn’t typically respond to opioid treatment
- Responds to AED’s (anti-epileptic drugs) and certain antidepressants

Types of Pain in MS

Continuous Central Neuropathic Pain

- Correlates with a CNS lesion/ spinothalamic dysfunction
- Characterized by abnormal sensations including burning, tingling, aching, itching, band-like, throbbing
- Central neuropathic pain occurs in nearly 50% MS patients
- Most common type of pain associated with MS is dysesthetic extremity pain

Dysesthetic Extremity Pain

- Typically bilateral
  - Affects the legs and feet more often than upper extremities
  - Usually worse at night
  - Can be exacerbated by physical activity
- Symptoms may not be bothersome enough to merit medication
- Often managed with AEDs and/or certain antidepressants

Intermittent Central Neuropathic Pain

- Neuropathic pain that occurs spontaneously or paroxysmal
- Described as shooting, stabbing, shock-like, lancing, crushing or searing
- More intense than continuous central neuropathic pain
Trigeminal Neuralgia

- Incidence of TN in MS is roughly 20 times the prevalence of the general population
- Prevalence in patients with MS ranges 2-6%
- Described as a paroxysmal sharp, lancing pain lasting seconds to minutes affecting one or more branches of the trigeminal nerve
- Triggered by facial movement/stimulation talking, chewing, breeze


Trigeminal Neuralgia cont’d

- First line treatment consists of AEDs
- Poor tolerability of medications and/or severity of pain necessitates early consideration for neurosurgical consult
- Interventional treatment options:
  - Percutaneous retrogasserian glycerol rhizotomy
  - Radiofrequency rhizotomy
  - Microvascular decompression (reserved for non-responders)

**Painful Tonic Spasms**

- Paroxysmal abrupt onset attacks of abnormal posture of either arm or leg, typically lasting less than 2 minutes
- Estimated to occur in 11% MS patients
- Correlates with MRI lesions in the basal ganglia, internal capsule, cerebral peduncle, medulla, and spinal cord
- Anecdotal reports of benefit seen with AEDs, baclofen, benzodiazepines, Botox


**Lhermitte’s Sign**

- Transient, short-lasting sensation related to neck movement, felt in the back of the neck, lower back or in other parts of the body
- Associated with MRI lesions in the posterior columns of the cervical spine
- Tends to occur during exacerbations
- 25% patients never reported the symptom
- Symptomatic treatment is not necessary

**Musculoskeletal Pain**

- MS predisposes patients to secondary musculoskeletal pain by causing weakness, muscle spasms, spasticity and reduced mobility
- Prevalence ranges from 10-16%
- MS treatments can cause myalgias, osteoporosis resulting in compression fractures, AVN
- Low back pain can be associated with scoliosis, degenerative joint disease
- Back pain can be central in origin as well

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**Musculoskeletal Pain Cont’d**

- Management consists of identifying underlying issue
- Physical Therapy for assessment and management of safety, gait, positioning, seating and effective use of mobility aids
- Medication management to include NSAIDS, acetaminophen, muscle relaxers
Mixed Neuropathic and Non-neuropathic pain

- Headache
  - More common in patients with MS than in general population
- Muscle Spasms/Spasticity

Factors to consider….

- Disease activity
- Infection
- Weakness/deconditioning
- Altered gait/posture
- Inappropriate mobility aids
- Falls
Assessing Pain

Visual Analog Scale

Simple Descriptive Pain Intensity Scale

0–10 Numeric Pain Intensity Scale

Visual Analog Scale (VAS)

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1 If used as a graphic rating scale, a 10 cm baseline is recommended.
2 A 10-cm baseline is recommended for VAS scales.
The 4 A’s of Analgesia

- Analgesia (pain-relief)
- Activities of daily living (psychosocial functioning)
- Adverse effects (side effects)
- Aberrant drug-taking behaviors (addiction-related outcomes)
Pharmacological Management

Guiding Principles

- Educate patients regarding off label uses of medications
- Start low, go slow
- Lower doses of a combination of medications may result in better toleration than high dose of a single agent
- All AEDs and antidepressants increase the risk of suicidal thoughts and behaviors for patients taking them for any reason
- Consistently assess for benefit and wean appropriately
Antidepressants

Tricyclic Antidepressants

- Indications: Depression
- Common side effects include weight gain, sedation, dry mouth, constipation, urinary retention
- Contraindications: heart block, BPH, use of MAOIs
  - Amitriptyline
    - Initial 10-25 mg q hs, may increase up to 150 mg/d
    - Typically most effective, but also has most side effects. Carries potential for cardiac conduction changes, especially with higher doses
    - Nortriptyline
    - Desipramine
### SNRI
(Serotonin Norepinephrine Reuptake Inhibitor)

- **Venlafaxine**
  - Indications: MDD (major depressive disorder)
  - CI: use of MAOi
  - Side effects: nausea, agitation, dry mouth, sweating, may increase blood pressure
  - Start 37.5 mg each morning. Increase by 37.5-75 mg per week. Max dosage 450 mg/d
  - Inhibits NE reuptake at dosages >150 mg/d. Weakly blocks dopamine reuptake at very high doses (above 350 mg/d)

### SNRI cont’d

- **Duloxetine**
  - Indications: MDD, GAD (generalized anxiety disorder), PDPN (painful diabetic peripheral neuropathy), fibromyalgia, chronic OA pain, chronic low back pain
  - Balanced inhibitor of NE and 5-HT reuptake
  - Common side effects: nausea, dry mouth, somnolence, decreased appetite
  - Start 30 mg daily x 7 days then increase to 60 mg daily. Max dosage of 120 mg/day
  - Isolated cases of liver failure have been reported, most cases in patients with history of liver injury, including alcohol abuse
SNRI cont’d

- **Milnacipran**
  - Indications: management of fibromyalgia
  - MOA: NE and 5-HT reuptake inhibition (3:1 NE to 5-HT)
  - Side effects: nausea, headache, constipation, dizziness, insomnia, increased heart rate and blood pressure
  - Dosing: Day 1: 12.5 MG. Day 2-3: 12.5 mg bid. Day 4-7: 25 mg bid. After day 7: 50 mg bid

Anticonvulsants
Anticonvulsants

- **Gabapentin (Neurontin)**
  - Indications: AED and post herpetic neuralgia (PHN)
  - Side Effects: somnolence, weight gain, dizziness, ataxia, peripheral edema
  - Caution in renal impairment
  - ~30% prescriptions for fibromyalgia or chronic neuropathic pain
  - Initial: 100-300 mg tid, max dosage 3600 mg/day

- **Pregabalin (Lyrica)**
  - FDA indications: AED, neuropathic pain associated with diabetes, fibromyalgia, PHN, and GAD
  - Similar SE profile to gabapentin
  - Initial: 50 mg bid, max dosage 600 mg/d

*Moore, RA; Wiffin, PJ; Derry, S; McQuay, JH (2011-03-16). "Gabapentin for chronic neuropathic pain and fibromyalgia in adults." Cochrane database of systematic reviews (Online) (3): CD007938.

Anticonvulsants

- **Carbamazepine (Tegretol)**
  - Indications: AED, TN
  - Side Effects: drowsiness, dizziness, nausea, unsteadiness
  - Black Box Warning: SJS, TEN, Aplastic Anemia, SI
  - Monitoring: CBC and CMP at baseline and periodically
  - Start 100 mg bid. Max dosage 1200 mg/day
  - Reduces plasma concentrations of oral contraceptives

- **Oxcarbazepine (Trileptal)**
  - Indications: AED
  - Side Effects: drowsiness, dizziness, nausea, unsteadiness
  - Monitoring: hyponatremia
    - Caution with concurrent meds known to decrease Na levels
  - Start 150 mg bid, increase every 3-7 days. Max dosage 2400 mg/d
  - Reduces plasma concentrations of oral contraceptives
Anticonvulsants

- Topiramate (Topamax)
  - Indications: Migraine Prophylaxis, AED
  - Side Effects: weight loss, somnolence, psychomotor slowing, paresthesias
    - Rare: acute myopia and secondary angle closure glaucoma
  - Caution: history of renal calculi, renal or hepatic impairment
  - Monitoring: metabolic acidosis
  - Start 25 mg q hs, can increase by 25 mg weekly. Max dosage 400 mg daily

Opioid Therapy
**Opioid Therapy**

- Opiates have minimal effect in central MS pain and are not recommended
- In 2007, opioids were associated with more deaths than heroin and cocaine combined
- Approximately 1/3 of chronic pain patients may not use prescribed opioids as prescribed or may abuse them
- Opioids have become the most commonly prescribed drug category in the US


**Opioid Prescribing...**

- Understand the expectations of regulatory authorities
- Medication agreement
- Regular urine drug screening
- Use prescription drug monitoring program
- 4 A’s

Short Acting Opioids
- Hydrocodone
- Oxycodone
- Meperidine
- Morphine
- Fentanyl
- Tapentadol
- Codeine
- Propoxyphene (no longer available)

Long Acting Opiates
- Oxycodone (OxyContin)
- Morphine (Kadian, Avinza, MS Contin)
- Oxymorphone (Opana ER)
- Methadone
- Fentanyl patches (Duragesic)
- Meperidine (Exalgo)
- Tapentadol (Nucynta ER)
REMS

- Risk Evaluation and Mitigation Strategy
- In 2012, The US Food and Drug Administration (FDA) directed makers of all ER/LA opioids to provide CME grants to educate prescribers and patients.
  - Ensure that benefits outweigh risks
  - Help reduce risk for ER/LA opioid use in chronic pain management.

Cannabanoids
Cannabanoids

- Nabiximols and nabilone use in MS pain treatment have been supported by trials outside the US.
- Inhaled cannabis is implicated in oncogenesis by several molecular pathways and has an effect on cognition.
- Medical marijuana use is legal in Alaska, Arizona, California, Colorado, DC, Delaware, Hawaii, Maine, Massachusetts, Michigan, Montana, Nevada, New Jersey, New Mexico, Oregon, Rhode Island, Vermont, Washington.


Other Treatment Considerations

- Diclofenac topical options
  - available as a lotion, patch and gel
- Lidocaine 5% patches (Lidoderm)
  - FDA indication for post-herpetic neuralgia
  - Apply 12 hours on/Max 3 patches in 24 hours
- TENS (transcutaneous electrical nerve stimulation)
Non-pharmacologic Management

Correlates of reduced functioning

- Catastrophizing cognitions
- Guarding and resting as coping techniques
- Belief that one is disabled by pain, that others should be solicitous when one experiences pain, and that pain is an indication of physical damage
- Solicitous environmental responses to pain behaviors

Measures to address reduced functionality

- Increase the use of coping strategies such as task persistence, acceptance of disability, behavioral activities, exercise, ignoring pain, and coping self-statements
- Increase the belief that the patient can control pain and its effects
- Help the patient seek and obtain more general (non-pain contingent) social support


Exercise...

Chronic pain >>>> kinesiophobia >>>> deconditioning>>>>>pain when attempt activity>>>>>more rest

Breaking this cycle is critical for rehabilitation to take place

Exercise is another way for patients to be active participants in their own care

Other Measures

- Chronic Pain Rehabilitation Program
  - Stretching for spasticity
  - Massage
  - Distraction
  - Acupressure and Acupuncture
  - Cooling
  - Guided imagery

Conclusion

- Pain and sensory symptoms comprise significant amount of symptomatic treatment
- Multiple modalities exist to assist in the management of pain
- A comprehensive approach is recommended over single-system approach
Case Study

Thank you!

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