Enhancing Functionality with Duloxetine Monotherapy in Multiple Sclerosis

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Rationale

- **Multiple sclerosis (MS)** is a chronic, relapsing disease characterized by areas of demyelination and inflammatory lesions in the brain and spinal cord.
- Some subjective symptoms of MS include fatigue, depression, and neuropathic pain.
- The prevalence of concurrent depression and anxiety with MS is 35-50% (over twice the general prevalence).
- Pain is prevalent in 50% of MS patients.
- Associated with overall decremented mental health, including reduction of social coping.
- Depression with concurrent pain negatively impacts functionality and quality of life.

- **Duloxetine** is a balanced, dual-acting selective serotonin and noradrenaline reuptake inhibitor (SNRI) with affinities for both neurotransmitters at low doses.
- Approved for treatment of depression, anxiety, and pain associated with diabetic peripheral neuropathy, fibromyalgia, and chronic musculoskeletal pain.
- Could potentially address multiple MS-related symptoms in a multi-axial fashion.

Case Description

- 36-year-old female diagnosed with MS in 2008.
- **Primary Complaints:** Anxiety, depression, and neuropathic pain.
- **Past Medical History:** Neck and bilateral upper extremity pain, right-sided hemiparesis.
- **Social History:** Off work due to disability associated with MS.
- **Medication Trials for Depression and Anxiety:**
  - Paroxetine 17.5 mg daily (patient had slowly titrated the dose over 4-5 months).
  - Venlafaxine 75 mg BID introduced via cross-titration once the patient had completed week 3 of taper in July.
  - Duloxetine 30 mg daily initiated at week #3 of taper in July. Dose increased to 60 mg daily in 4 months.

Clinical Interventions

- **Therapeutic Challenge:** Increased neuropathic pain, marked sexual dysfunction, anhedonia, and worsening anxiety/depression despite trials of customary antidepressants.
  - Duloxetine 30 mg BID introduced via cross-titration.
  - Choice of antidepressant based on neurotransmitter and receptor affinities coupled with medical MS comorbidity.
- **Rationale for the Gradual Tapering Schedule:**
  - MS patients observed to be more sensitive to serotoninergic agents.
  - Paroxetine discontinuation syndrome has been well-documented with quick tapers.
- **Intervention:** Paroxetine cross-tapered with duloxetine over several weeks. This avoided a discontinuation syndrome secondary to serotoninergic withdrawal-related adverse effects.

References

12. Thibault K, Calvino B, Pezet S, 2010 Characterization of sensory abnormalities which mimic MS symptomatology, has demonstrated a partial reduction by duloxetine in sensory and serotonin abnormalities.
13. A recent Phase III randomized, placebo-controlled trial published literature specifically examining the use of duloxetine to treat a combination of central neuropathic pain, depression, and anxiety in MS patients is lacking.
14. A recent Phase III randomized, placebo-controlled trial of duloxetine in patients with central neuropathic pain due to MS.
15. Published reports of efficacy and safety using other antidepressants and/or anticonvulsants in patients with MS experiencing neuropathic pain with psychiatric co-morbidities.
16. Duloxetine decreased anxiety and pain, elevated mood, and improved functionality in this case report.
17. Further studies are warranted in MS patients with pain and psychiatric co-morbidities.

Patient Outcomes

- **Anxiety:** No panic attacks.
- **Mood:** Reduced clonazepam from 1 mg/day to 0.75 mg/day.
- **Pain:** Radiating pain began to subside over 4-5 weeks.
- **Functionality:** Reports fully functional in cognitive and mobility aspects.

Relevance for Clinicians

- Identification of patient-specific goals is essential prior to introduction of clinical interventions.
- Appreciate the bi-directional interface between neuropsychiatric and physical manifestations of MS.
- Patient- and medication-specific outcomes must be considered in the cross-titration of medications to prevent adverse effects.
- Duloxetine, through balanced impact on neurotransmitters, may be a viable option for patients with MS experiencing neuropathic pain with psychiatric co-morbidities.
- Duloxetine decreased anxiety and pain, elevated mood, and improved functionality in this case report.
- Further studies are warranted in MS patients with pain and psychiatric co-morbidities.

Evaluation of the Literature

- **Depression & MS:** Controlled studies examined the use of a selective serotonin reuptake inhibitor (sertraline) and a tricyclic antidepressant (desipramine) in MS patients.
  - Published reports of efficacy and safety using other antidepressants and/or anticonvulsants in MS patients.
  - Recent placebo-controlled trials have demonstrated efficacy for the cannabinoids in neuropathic pain in MS.
- **Duloxetine & MS:** Official indications of duloxetine include the treatment of major depression, generalized anxiety disorder, fibromyalgia, and neuropathic pain.
  - Experimental Autoimmune Encephalomyelitis in rats, which mimics MS symptomatology, has demonstrated a partial reduction by duloxetine in sensory and serotonin abnormalities.
  - A recent Phase III randomized, placebo-controlled trial has positively addressed duloxetine’s safety and efficacy for reducing central neuropathic pain due to MS.
- Published literature specifically examining the use of duloxetine to treat a combination of central neuropathic pain, depression, and anxiety in MS patients is lacking.

Date | Drug | Outcome
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March 2010 | Venlafaxine, Intolerance | Discontinued
April 2010 | Citralex, Intolerance | Discontinued
May 2010 | Paroxetine, Experienced worsening anhedonia | Discontinued

**Medications at presentation:**
- Paroxetine 17.5 mg daily (patient had slowly titrated the dose over 4-5 months).
- Clonazepam 0.25 mg BID and 0.5 mg HS.
- Vitamin B12 injection monthly.
- Bupropion as needed.
- Vitamin D 2000 IU daily.
- Fish oil 2 teaspoons daily.
- Probiotic daily.

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