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[1]
- Some subjective symptoms of MS include fatigue, depression, and neuropathic pain[1]
- The prevalence of concurrent **depression and anxiety** with MS is 35-50% (over twice the general prevalence)[2]
- **Pain** is prevalent in 50% of MS patients[3]
  - Associated with overall decreased mental health, including reduction of social coping[4]
- Depression with concurrent pain negatively impacts functionality and quality of life[5]
- **Duloxetine** is a balanced, dual-acting selective serotonin and norepinephrine reuptake inhibitor (SNRI) with affinities for both neurotransmitters at low doses[6]
  - Approved for treatment of depression, anxiety, and pain associated with diabetic peripheral neuropathy, fibromyalgia, and chronic musculoskeletal pain[6]
  - Could potentially address multiple MS-related symptoms in a multi-axial fashion

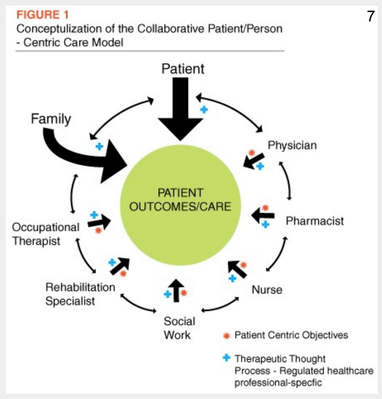
Case Description

- 36-year old female diagnosed with MS in 2008
- **Primary Complaints:** Anxiety, depression, and neuropathic pain
- **Other Presenting Symptoms:** Neck and bilateral upper extremity pain, right-sided hemiparesis, L'Hermitte sign, anhedonia, anorgasmia and sexual dysfunction
- **History of Presenting Illness:**
  - Panic attacks and generalized anxiety disorder exacerbated since MS diagnosis
  - Upper extremity pain described as "stabbing" and "radiating"
  - Global Assessment of Functioning (GAF) Score in April of 2010 = 35 (range 0-100)
- **Social History**:
  - Off work due to disability associated with MS
  - Self-reported alcohol dependence in past
- **Past Medical History**: major depressive disorder, generalized anxiety disorder, rosacea
- **Medication Trials for Depression and Anxiety:**

Date	Drug	Outcome
March 2010	Venlafaxine	Intolerance → Discontinued
April 2010	Citalopram	Intolerance → Discontinued
May 2010	Paroxetine	Experienced worsening anhedonia, pain and ↓libido → Discontinued

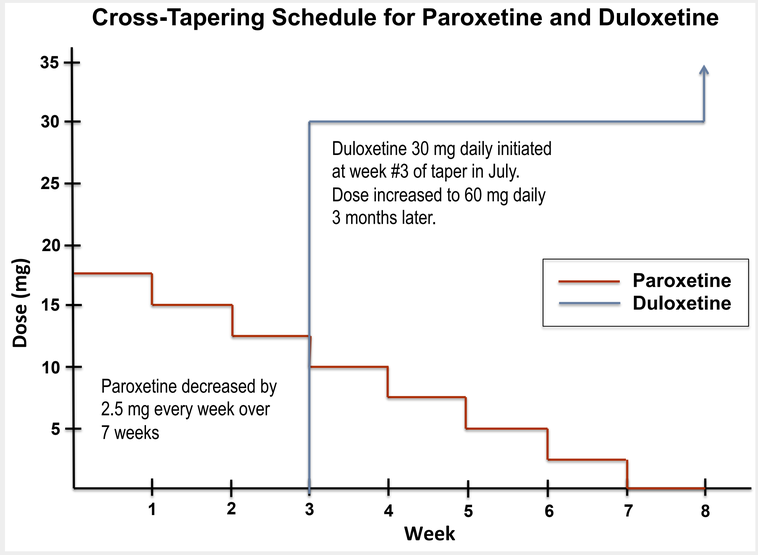
- **Medications at presentation:**
  - Paroxetine 17.5 mg daily (patient had slowly titrated the dose upwards in 2.5 mg increments)
  - Clonazepam 0.25 mg BID and 0.5 mg HS
  - Vitamin B12 injection monthly
  - Ibuprofen as needed
  - Vitamin D 2000 IU daily
  - Fish oil 2 teaspoons daily
  - Probiotic daily

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 co-morbidity
- **Rationale for the Gradual Tapering Schedule:**
  - MS patients are observed to be more sensitive to serotonergic agents
  - Paroxetine discontinuation syndrome has been well-documented with quick tapers[8]
- **Intervention:** Paroxetine cross-tapered with duloxetine over several weeks. This avoided a discontinuation syndrome secondary to serotonergic withdrawal-related adverse effects[8]

Cross-Tapering Schedule for Paroxetine and Duloxetine



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[9-11]
  - Published reports of efficacy and safety using other antidepressants in MS patients is limited to case reports
- **Neuropathic Pain & MS:** Traditional guidelines include use of tricyclic antidepressants and/or anticonvulsants[3,4]
  - Recent placebo-controlled trials have demonstrated efficacy for the cannabinoids in neuropathic pain in MS[3,12]
- **Duloxetine & MS:** Official indications of duloxetine include the treatment of major depression, generalized anxiety disorder, fibromyalgia, and neuropathic pain[13,14]
  - Experimental Autoimmune Encephalomyelitis in rats, which mimics MS symptomatology, has demonstrated a partial reduction by duloxetine in sensory and serotonin abnormalities[15]
  - A recent Phase III randomized, placebo-controlled trial has positively addressed duloxetine's safety and efficacy for reducing central neuropathic pain due to MS[16]
  - Published literature specifically examining the use of duloxetine to treat a combination of central neuropathic pain, depression, and anxiety in MS patients is lacking

Patient Outcomes

7 Weeks after Duloxetine Initiation	
Anxiety	No panic attacks Reduced clonazepam from 1 mg/day to 0.75 mg/day
Mood	Self-reported improvements in coping and stress levels
Pain	Radiating pain began to subside over 4-5 weeks Rated upper extremity pain decreased from 6/10 to "0/10" on pain scale
Functionality	Reports fully functional in cognitive and mobility aspects Returned to work full-time Axis V – GAF scores: April 2010 = 35 July 2010 = 45 November 2010 = 60 December 2010 = 70

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

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