Medical Cannabis in the Treatment of Multiple Sclerosis

A Review of the Literature

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Multiple Sclerosis (MS): An Autoimmune Central Nervous System (CNS) Disease

- Chronic inflammatory CNS disease
  - Incurable
  - Affects > 400,000 people in the US
- Innate and acquired humoral and cellular immune destruction of CNS myelin
  - Produces axonal degeneration and neurological deficits
  - Relapsing and remitting course
• CB1 and CB2 mRNA, Anandamide in lymphocytes

• Elevated in patients with MS

• Decreases with Interferon Rx
Endocannabinoid System in MS

- **CSF anandamide**
  - Increased in MS
  - Concentration correlates with number active lesions
- **Lymphocytic endocannabinoids**
  - Increased AEA
  - Increased NAPE-PLD
  - Decreased FAAH

*Brain (2007), 130, 2543-2553*
Animal Models of MS

- Experimental Autoimmune Encephalomyelitis (EAE) is most common animal model
- Differences between EAE and MS are myriad and have a variety of causes
- EAS does not recapitulate the spectrum of pathologic features of MS
- Genetic ablation effects on endocannabinoid system components are
  - Species and strain specific
  - Have off-target effects
- Relevance of animal studies to MS in humans is not clear
- Beware of conflicts of interest
Medical Cannabis in the Treatment of MS

- Oral cannabis extract recognized as effective as add-on therapy for
  - MS-patient reported spasticity
  - Central pain
  - Painful muscle spasms
  - 40% of patients are resistant to anti-spasticity effects
  - Not effective for bladder symptoms
  - Not effective for MS-related tremor
- Pure cannabinoids / terpenes
  - There are no data on CBD single-agent efficacy in MS
  - THC and nabiximols are effective in MS-spasticity and pain
  - PEA (found in many plants in addition to Cannabis)
    - Decreases proinflammatory cytokines
    - Blunts the side-effects of interferon-b
- “Patients with MS who are frequent long-term cannabis users can show improvements in memory, processing speed, and executive function after 28 days of drug abstinence.” BRAIN 2019: 142; 2800–2812
15 agents for modifying the course of MS

- 5 preparations of interferon-β
  - 2 preparations of glatiramer acetate
  - Interferon beta
  - Mitoxantrone
  - Ocrelizumab
  - Teriflunomide
- Monoclonal antibodies
  - Natalizumab
  - Alemtuzumab
  - Daclizumab
  - Diethyl fumarate
  - Fingolimod
- Chemotherapeutic agents
  - Mitoxanthrone
- Small molecule oral agents
  - Fingolimod
  - Dimethyl fumarate
  - Teriflunomide
  - Dilfampridine

Does Medical Cannabis Have a Role in MS as a Disease Modifying Agent?

- No solid data to suggest that doses of medical cannabis cause significant immunosuppressive effects in MS.
- Alterations in endocannabinoids in MS patients may reflect activation of nonspecific inflammatory pathways.
- Animal models of MS (e.g. EAE) are not equivalent to clinical MS.
- Natural products with anti-inflammatory properties found in Cannabis are also found in many other plants.