The Mortar & Pestle:

MD Custom Rx's monthly e-newsletter

September 2018

MD Custom Rx — Quality Matters

PCAB ACCREDITED Compounding Pharmacy

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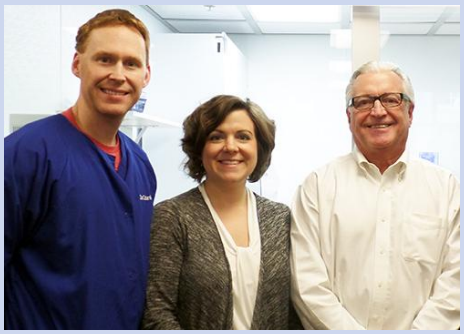
MDCustomRx.com

Greetings!



Thank you for entrusting in the compounding services at MD Custom Rx to help meet the unique medication needs of your patients. We are excited to share our monthly newsletter with you and look forward to continuing to be your medication problem solvers. Please don't ever hesitate to let us know how we can be of further assistance to you and your practice.

Sincerely,

Dan, Monica and John

Low Dose Naltrexone - The Paradox

Within a specific dosage window, opioid antagonists such as naltrexone can exert a “paradoxical” analgesic effect. Low Dose Naltrexone (LDN) is a primary example of a relatively new class of therapeutic agents called glial cell modulators. Harvard-educated Bernard Bihari, MD, (1931-2010) discovered the beneficial effects of LDN (naltrexone at less than 1/10th the dose used to treat addiction) in 1985 while working in New York clinics treating drug addiction, alcoholism and HIV-AIDS.

LDN has been used to treat many problems including:

- Pain and Inflammation
- Hashimoto’s Thyroiditis
- Autism Spectrum Disorder
- Allergies & Asthma
- Chronic Pruritus
- Mood Disorders
- Lyme Disease
- Multiple Sclerosis
- Crohn’s and Ulcerative Colitis
- Complex Regional Pain Syndrome
- Chronic Fatigue & Fibromyalgia

The Science Behind LDN

“In describing LDN’s clinical utility, it is important to understand the dual physiologic mechanisms of naltrexone and other opioid antagonists. Naltrexone, at typical doses [50

mg], significantly blocks activity at mu- and delta-opioid receptors as well as (to a lesser extent) kappa-opioid receptors. Because beta-endorphin activity at mu-opioid receptors is associated with endogenous analgesic processes, it may seem counterintuitive to administer naltrexone to individuals with chronic pain, as we might expect the medication to reduce analgesia produced by beneficial endogenous opioid activity. Naltrexone, however, exerts its effects on humans via at least two distinct receptor mechanisms. In addition to the antagonist effect on mu-opioid and other opioid receptors, naltrexone simultaneously has an antagonist effect on non-opioid receptors (Toll-Like Receptor 4 or TLR4) that are found on macrophages such as microglia. It is via the non-opioid antagonist path that LDN is thought to exert its anti-inflammatory effects. Microglia are central nervous system immune cells that are activated by a wide range of triggers. Once activated, microglia produce inflammatory and excitatory factors that can cause sickness behaviors such as pain sensitivity, fatigue, cognitive disruption, sleep disorders, mood disorders, and general malaise... Conditions such as fibromyalgia may involve chronic glial cell activation and subsequent production of proinflammatory factors." Naltrexone has been demonstrated to exert neuroprotective and analgesic effects. "The neuroprotective action appears to result when microglia activation in the brain and spinal cord is inhibited [by LDN]."

Clin Rheumatol. 2014; 33(4): 451–459.

Naltrexone is a chiral molecule of the stereoisomers L-Naltrexone & D-Naltrexone. Following transient blockade of opioid receptors by LDN which lasts approximately 4 – 6 hours (as opposed to higher doses that block receptors for 24 hours), the receptor sites rebound with increased and persistent production of:

- Endorphins (endogenous opioids) associated with L-Naltrexone. Increased endorphin release causes a significant full body anti-inflammatory effect which:
    - May attenuate pain
    - Down regulates inflammatory cytokines, while increasing T cells and Natural Killer cells.
    - Stimulates mucosal and tissue healing.
    - Directly inhibits tumor growth
    - Reduces death of neurons (oligodendrocytes) that produce myelin in the brain.
- Opioid Growth Factor (OGF), also known as met (5) enkephalin and associated with D-Naltrexone. OGF and the OGF receptor axis regulate cell growth in normal and abnormal cells.

Toll Like Receptors (TLR) are implicated in almost all causes of inflammation. When activated, TLR trigger an immune response and signal for increased release of:

- Inflammatory cytokines
- Various macrophages
- The oncogene NF-KappaB

Blocking TLR with LDN:

- Suppresses the immune response and inflammation.
- Reduces inflammatory cytokines
- Suppresses NF-kappaB to block tumor growth

Cancer and LDN:

- Intermittent Dosing with LDN causes increased cell death and has been reported to increase cell sensitivity to chemotherapeutic agents.
- LDN should not be taken during treatment with PD-1 inhibitors.

Clinical use has shown that patients usually begin to see benefits within the first 60 days of LDN therapy but several months of continuous therapy is a thorough trial.

LDN side effects are usually transient. LDN is well tolerated in most patients. However, care should be taken to slowly titrate the dose up to avoid side effects.

Common Side Effects:

- Sleep disturbances/Vivid dreams
- Gastrointestinal upset, nausea

- Mild headache
- Mild agitation

Uncommon Side Effects:
- Flu-like symptoms
- Rash
- High temperature
- Dizziness
- Increased fatigue or spasticity

The following may require dosage adjustments:
- Thyroid sensitivity in Hashimoto's patients may require decrease in dose of thyroid medication.
- Agitation/extrapyramidal symptoms in patients with Parkinson's disease may require adjustment of dopamine dose.
- Liver enzyme elevation may respond to dosage reductions.
- Decline in renal function - monitor patients with kidney disease.

Caution: Do not use LDN to treat patients who are taking opioids. It is possible that even a low dosage of naltrexone could cause a sufficient blockade of opioid receptors to reduce the effectiveness of opioid analgesics.

Forms of LDN
LDN can be compounded in various dosage forms per prescription:
- Liquid - allows for slow titration to optimal dose.
- Sublingual drops - for patients with swallowing difficulties or GI side effects from the liquid. SL drops facilitate more rapid absorption through the oral mucosa.
- Capsules – compounded in appropriate dose.
- Topical Cream – can be helpful when administering to children.

In summary, the research involving LDN and proposed uses are expanding. LDN is low cost, has low side effects, and no known abuse potential. Many peer-reviewed articles about the benefits of LDN can be found on PubMed, and references are available upon request. Visit https://www.ldnresearchtrust.org and click on "Medical Professional Pathway" for more information.

MD Custom Rx Educational Events

We regularly offer educational events at the pharmacy. Be sure to share our events with your patients. **VISIT OUR WEBSITE** to see our schedule and to register. If you are interested in speaking on a topic, please contact the pharmacy.

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Please take a moment to review us.