UPDATES ON LOW DOSE NALTREXONE (LDN)

BRYAN ZIEGLER, PHARMD, MBA
MOSS COMPOUNDING PHARMACY
SEPTEMBER 28, 2021

INTRODUCTION

- Bryan Ziegler, PharmD/MBA
  - President/Clinical Compounding Pharmacist @ Moss Compounding
  - Clinical Adjunct Associate Professor – Univ. of S. Carolina Coll. Of Pharmacy

- Moss Compounding Pharmacy
  - Full scale compounding pharmacy
    - Human and Veterinary compounding
    - Sterile and Non-sterile
    - Hazardous (Non-sterile only)

TONIGHT'S TOPIC

- We are discussing NAL**TREX**ONE

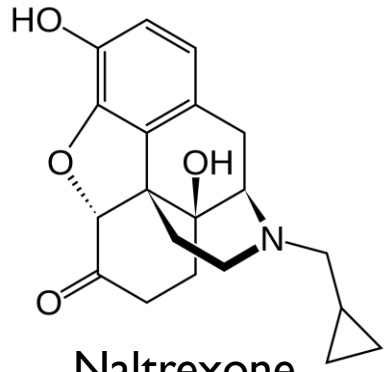
Not Naloxone (for opioid reversal)

WHAT IS LDN?

- LDN is a competitive opioid receptor antagonist.
- At the standard “full strength” dose (50-100mg), naltrexone blocks the effects of both the endogenous opioids, which are in endorphins and pharmaceutical opioids.
- But tonight we are talking about **LOW DOSE** Naltrexone

WHAT IS LDN?

- LDN is a pure antagonist, therefore it is NOT a controlled substance, narcotic, or opioid.
- It is a pure antagonist at various opioid receptors, Delta Kappa, Mu, and Opioid Growth Factor (OGF) receptors.
- The chemical structure is almost identical to endorphins that we make naturally called met-enkephalin, also known as OGF or Opioid Growth Factor.



Naltrexone

https://ldnresearchtrust.org/what-is-low-dose-naltrexone-ldn

WHAT IS LDN?

- LDN is an antagonist at the OGF receptors and there are OGF receptors on a wide range of cells in the body.
- When we talk about low dose naltrexone (LDN) we mean doses that are a 10th or less of the standard dose of Naltrexone.
- Most of the research studies have used 4.5mg per day.
- Doses range from 0.001mg – 16mg in clinical practice.

https://ldnresearchtrust.org/what-is-low-dose-naltrexone-ldn

WHAT IS LDN?

- “It reduces pain, and fights inflammation. It is used to treat cancers, autoimmune diseases, chronic pain and mental health issues, to name a few. Treatment is constantly evolving, with new conditions and methods of treatment being shared regularly.”

  - LDN Research Trust

https://ldnresearchtrust.org/what-is-low-dose-naltrexone-ldn

HISTORY OF NALTREXONE & LDN

- Naltrexone was synthesized in 1963 as an orally active competitive opioid receptor antagonist.
- Naltrexone is structurally and functionally similar to the opioid antagonist naloxone, but it has greater oral bioavailability and a longer biologic half-life.
- Naltrexone HCl was approved by FDA in 1984 for the treatment of opioid addiction. The typical daily dosage for opioid addiction is 50–100 mg daily, and 50-mg tablets are available commercially.
- The effects of LDN were first discovered in the late 1980s

https://ldnresearchtrust.org/what-is-low-dose-naltrexone-ldn

PHARMACOLOGIC EFFECTS

- Low Dose Naltrexone binds to the endorphin receptors for about 1 – 1/2 hours, and the blockade lasts about 4 - 6 hours.
- The effects of LDN are analgesia and anti-inflammatory.
- One of the other effects is that it increases the production of endogenous endorphins.

https://ldnresearchtrust.org/what-is-low-dose-naltrexone-ldn

PHARMACOLOGIC EFFECTS

- Naltrexone exists in a racemic mixture of isomers ("left-handedness and right-handedness")
- Dextro-naltrexone binds toll-like receptors (TLR)
- Levo-naltrexone binds opioid receptors

LEVO-NALTREXONE

- Antagonist effect at opioid receptors
- Small temporary opioid blockade
- Upregulates endogenous opioid production
- Upregulates opioid receptors
- Increased endorphins favorable to the immune system

Modulate Immune response via Increase Endorphins

DEXTRO-NALTREXONE

- Antagonist effect at Toll-like receptors (TLR)
- TLR-4 receptors exist on microglial cells, other macrophages, mast cells
- Activated microglial cells produce proinflammatory cytokines, substance P, nitric oxide
- Inhibition leads to a decreased proinflammatory cascade

Anti-inflammatory & Suppressed Cytokine modulated immune response (modulation)

https://ldnresearchtrust.org/what-is-low-dose-naltrexone-ldn

PHARMACOLOGIC EFFECTS

- Endorphins are your natural peptides produced in many cells which regulate cell growth, including your immune cells. **Many patients who have autoimmune disease tend to have low levels of endorphins, Met-enkephalin**, aka opioid growth factor (OGF), an important immunomodulator.
- Opioid receptors are in the central and the peripheral nervous system, the GI tract, and on lymphocytes.
- By using **LDN you receive a brief blockade, creating a rebound effect giving you more endorphins, including OGF, and increased production of the OGF receptors**.

https://ldnresearchtrust.org/what-is-low-dose-naltrexone-ldn

IMPORTANT NOTE

- Taking Naltrexone in larger doses of 50-300mg seems to **negate the immunomodulatory effect by overwhelming the receptors**, so **for the effect to work, the dose must be in the range of 0.5-10mg, usually maxing at 4.5mg in clinical experience**.

https://ldnresearchtrust.org/what-is-low-dose-naltrexone-ldn

SIDE EFFECTS

- Many patients who start LDN do not experience any severe side effects.
- Most common SE:
  - Vivid Dreams/Sleep disturbances (likely due to increase in endorphin release)
  - Headache
  - Anxiety
- In <10% of cases treated, increased introductory symptoms may be more severe or more prolonged than usual, lasting sometimes for several weeks. Rarely, symptoms may persist for two or three months before the appropriate beneficial response is achieved.

- Some patients very rarely experience gastrointestinal side effects, such as nausea and or constipation/diarrhea.
  - Reason for this is currently unknown, but may be due to the presence of large numbers of delta-opiate receptors in the intestines.

https://ldnresearchtrust.org/what-is-low-dose-naltrexone-ldn

MANAGING SIDE EFFECTS

- Start low, go slow with titration = minimizing SE
- If side effects are troublesome, try reducing your dose by 50% for 7 days, before increasing it again.
- If sleep disturbed, change dose time away from bedtime
- If GI related SE, consider Sublingual drops as an option in order to avoid the GI tract.
- If GI related SE, increase dose by no more than 0.5mg per week
  - Can use appropriate treatment for the stomach upset, if necessary. (eg Omeprazole, Famotidine, Gaviscon, and Pepto Bismol are ok – but not Kaolin or Loperamide/Imodium.)

https://ldnresearchtrust.org/what-is-low-dose-naltrexone-ldn

OUR CURRENT EXPERIENCE

- Have been treating patients for over 4 years with LDN
- Currently have an active treatment population of 127 patients (June ‘21 – present)
    - Most common diagnoses treating:
        - Fibromyalgia
        - Rheumatoid Arthritis
        - Chronic pain
        - IBS/Crohn’s/Colitis
        - Lupus
        - MS

    - 76% currently on therapy and reporting symptom improvement
    - 24% discontinue or loss to follow up
        - Limited response during titration phase/unrealistic expectations
        - Side effects

CASE REPORTS

- ER is a 75 yo female who presented with chronic pain and fibromyalgia
- Previous meds
  - Opiate (Oxycodone/APAP) PRN (wanted to d/c)
  - Lyrica
  - Savella (tried and d/c)
- Started on LDN
  - D/c opiate, Lyrica
  - Within 4 weeks reported tremendous pain improvement and improved QOL
  - Current dose = 6mg po QD (target was 4.5mg)

CASE REPORTS

- JA is 51 yo male who presented with severe colitis
- Patient reported at LDN therapy initiation that:
  - Condition was chronic
  - Had tried all the standards of therapy with limited results
  - Was afraid to go too far away from home/restroom
  - High level of gastrointestinal discomfort
- Started LDN (target dose was 3mg – 4.5mg)
  - Started low, increased dose slowly
  - Patient reported some initial loose stool which subsided. Also reported this when attempting to increase dose above 2mg.
  - Patient currently at 2mg po QHS
  - Reports tremendous improvement in symptoms and glowing feedback on therapy. "Wish I started this med sooner"

CASE REPORTS

- GB is 63 yo male patient with MS
- Started therapy 2016
- Current dose = 3mg po QD
- Prior to LDN
  - Severe progressing disease
  - Experiencing 4-5 exacerbations per year (avg per patient report)
  - Utilized every disease modifying therapy available with little improvement
  - Drug spend $$$$
- Post LDN
  - Improved quality of life
  - Able to drive
  - 1 exacerbation per year
  - D/c all other disease modifying therapy
  - Drug spend ~$500/yr

Prescribers Learning Center

Low Dose Naltrexone (LDN)

- What is LDN?
- Mechanism of Action
  - Presentation
  - Slides

Pain Management

- Dr. John Kim (Presentation)
- Dr. John Kim (Ultra-Low Dose Naltrexone Presentation)
- Dr. Pradeep Chopra (LDN Pain Seminar)
- Dr. Phil Boyle (LDN Use in

Recommended Reading

- LDN Book (Request a copy)
- LDN Dosing Guide (MOSS)
- LDN Research Trust Dosing Guide

MOSS COMPOUNDING PHARMACY

Low Dose Naltrexone Dosing Guide Sheet

Key Definitions:[1,2]

- **Ultra Low Dose Naltrexone (ULDN)** = 1mcg – 20mcg
- **Very Low Dose Naltrexone (VLDN)** = 50mcg – 500mcg (0.5mg)
- **Low Dose Naltrexone (LDN)** = typically 0.5mg – 4.5mg daily dose (up to 16mg)

Key Points to Keep in Mind:

- Onset of Pain relief varies from 1 week – 6 months. Set patient expectations realistically.
- Dosing rule of thumb…..Start Low and Go Slow…..then listen to the patient and adjust titration schedule as needed. We start with target goals, but adjust as patient tolerates the medication and achieves response.
- Mood/Depression improvement seen with low dose in AM (typically 0.5mg – 1mg) with remainder of pain relief/immune enhancement dose given HS

3. **LDN For Pain Management/Autoimmune (without opiates)**
    a. See LDN 2020 Dosing Information for Prescribers for various conditions and additional information
    b. Dosing Guidance provided for:
        i. Autoimmune
        ii. Chronic Pain
    c. Typical dosing regimen is starting with 1mg QHS then increase by 0.5mg-1mg q2 weeks with target goal dose of 4.5mg (or highest dose tolerated above 3mg)
        i. Start low, go slow…..monitor patient response and adjust schedule as necessary
        ii. NOTE: may need to start patients even lower (0.5mg)
    d. Have patient keep a pain journal to help identify “sweet spot” dose.

4. **LDN for Additional conditions**
    a. See LDN 2020 Dosing Information for Prescribers for various conditions and additional information
    b. Dosing Guidance provided for:
        i. Cancer
        ii. Fertility
        iii. Anxiety/Depression/PTSD

UPCOMING EVENTS

Join us the 4th Tuesday of every month for new presentations

COMPOUNDING FOR DENTAL/ORAL HEALTH NEEDS

TUESDAY, OCTOBER 26 @ 6:30 – 7 PM

COMPOUNDING IDEAS FOR MEN'S HEALTH

TUESDAY, NOVEMBER 23 @ 6:30 – 7 PM

FOR DETAILS - VISIT THE **PRESCRIBER LEARNING CENTER @**
www.mosscompounding.com

QUESTIONS?

Bryan Ziegler, PharmD, MBA
843.665.0289
bziegler@mosscompounding.com


MOSS
COMPOUNDING
PHARMACY