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Brief Overview of Low Dose Naltrexone (LDN)

Low-Dose Naltrexone

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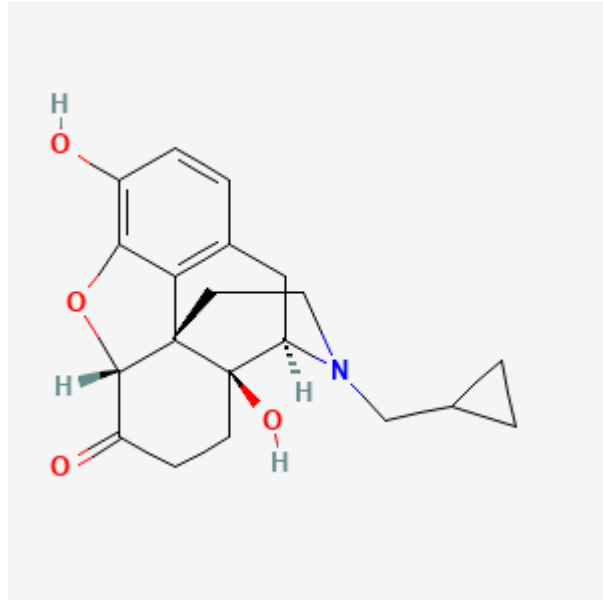
Disclosures

- I am a pharmacist working for Dinno Health, LLC – Acton Pharmacy, Inc.

Objectives

- To understand what LDN is
- To understand how LDN is prescribed

What is Naltrexone?



- Naltrexone is a competitive μ -opioid receptor antagonist
 - Commonly prescribed at 50mg (or higher) doses for substance abuse
 - Also seen in other dependence situations (food, sex)
 - Blocks effect of endorphins and opioids which limits “high” feeling

Hormesis

- “Hormesis is a term used by toxicologists to refer to a biphasic dose response to an environmental agent characterized by a low dose stimulation or beneficial effect and a high dose inhibitory or toxic effect...Recent findings have elucidated the cellular signaling pathways and molecular mechanisms that mediate hormetic responses which typically involve enzymes such as kinases and deacetylases, and transcription factors such as Nrf-2 and NF-κB. As a result, cells increase their production of cytoprotective and restorative proteins including growth factors, phase 2 and antioxidant enzymes, and protein chaperones.”

Low-Dose Naltrexone (LDN)

- Range defined as 0.25-10mg
 - Can be QD or multiple times a day
- Started in the 1980's by Dr. Bihari and his research into HIV/AIDS patients' immune modulation
 - Showed an increase in endorphin levels when administered at bedtime as well as an improved immune response/immune system
- Mechanism now shown to be a modification/downregulation of the Opioid Growth Factor Receptor (OGFR), reduction in Heat-Shock Protein (HSP), and reduction of Interleukin-6 (IL-6) via Toll-Like Receptors (TLR) have been seen

LDN

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RESULTS BY YEAR

TEXT AVAILABILITY

- Abstract
- Free full text
- Full text

ARTICLE ATTRIBUTE

- Associated data

ARTICLE TYPE

- Books and Documents
- Clinical Trial
- Meta-Analysis
- Randomized Controlled Trial

1 **Low-Dose Naltrexone for Chronic Pain: Update and Systemic Review.**
Kim PS, Fishman MA.
Curr Pain Headache Rep. 2020 Aug 26;24(10):64. doi: 10.1007/s11916-020-00898-0. PMID: 32845365
PURPOSE OF REVIEW: The purpose of this review is to evaluate and explain our current understanding of the clinical use of **low-dose naltrexone** in the treatment of chronic pain. RECENT FINDINGS: Recent pre-clinical uses and clinical studies further elucidate th ...

2 **Low Dose Naltrexone in the Treatment of Fibromyalgia.**
Metyas S, Chen CL, Yeter K, Solyman J, Arkfeld DG.
Curr Rheumatol Rev. 2018;14(2):177-180. doi: 10.2174/1573397113666170321120329. PMID: 28325149 Clinical Trial.
It is hypothesized that **low dose naltrexone** causes transient blockade of opioid receptors centrally resulting in a rebound of endorphin function which may attenuate pain in fibromyalgia. RESULTS: Two small prospective pilot studies have previously shown that ...

3 **Low-dose naltrexone (LDN): A promising treatment in immune-related diseases and cancer therapy.**
Li Z, You Y, Griffin N, Feng J, Shan F.
Int Immunopharmacol. 2018 Aug;61:178-184. doi: 10.1016/j.intimp.2018.05.020. Epub 2018 Jun 7. PMID: 29885638 Review.
Naltrexone, a non-selective antagonist of opioid receptors, is mainly used as rehabilitation therapy for discharged opiate addicts to eliminate addiction in order to maintain a normal life and prevent or reduce relapse. In recent years, there have been some novel and signi ...

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1 **Low-Dose Naltrexone for Chronic Pain: Update and Systemic Review.**
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2 **The Safety and Efficacy of Low-Dose Naltrexone in the Management of Chronic Pain and Inflammation in Multiple Sclerosis, Fibromyalgia, Crohn's Disease, and Other Chronic Pain Disorders.**
Patten DK, Schultz BG, Berlau DJ.
Pharmacotherapy. 2018 Mar;38(3):382-389. doi: 10.1002/phar.2086. Epub 2018 Feb 23. PMID: 29377216 Review.
It is the purpose of this review to examine the evidence of the safety, tolerability, and efficacy of **low-dose naltrexone** for use in chronic **pain** and inflammatory conditions. ...Fewer studies support the efficacy of **low-dose naltrexone** ...

3 **Low-dose naltrexone's utility for non-cancer centralized pain conditions: a scoping review.**
Rupp A, Young E, Chadwick AL.
Pain Med. 2023 Nov 2;24(11):1270-1281. doi: 10.1093/pm/pnad074. PMID: 37302106 Free PMC article. Review.
BACKGROUND: At **low** doses, **naltrexone** (LDN) has been shown to modulate inflammation through the interruption of microglial cell activation within the central nervous system. ...In summary, LDN continues to offer promising results in the management of **pain** and ...

“LDN” Search yields >1200 results

LDN

- Browsing through search results, LDN has been studied for:
 - Autoimmune disorders
 - RA, Crohn's, UC, SLE, MS
 - Pain
 - Fibromyalgia, Chronic Pain, Neuropathy, Cancer Pain
 - Neurological Conditions
 - Autism, Depression, Dissociation, OCD
 - Cancer
- Most trials are small group studies
 - Some are patient cases
 - Some are animal or cell models

LDN – Dosing

- Variable from patient to patient, their disease state, their response
 - General starting dose 0.5mg-1.5mg QD
 - Depends on patient and their general sensitivity to medications
 - Titrate up every 1-4 weeks by adding on another starting dose daily
 - Stop at dose that patient sees less benefit from the increase and back down to last dose that they were doing well
 - When side effects become prevalent
- Takes about 3-6 months before full benefit of medication is seen
 - Some patients see relief in a week, but that is rare

LDN – Dosing

- Can be taken any time of day
 - QHS has been the norm for many years because of Dr. Bihari's protocols
- No administration concerns with food
 - Patients who enjoyed a glass of wine with dinner or in the evening have reported to not enjoy it as much
- Minimal drug interactions
 - Has been used in patients who take opioids currently and has shown to decrease opioid doses over time, published in clinical articles
- Drug holiday?

LDN – Side effects

- Most reported:
 - Dizziness/Drowsiness
 - Insomnia
 - Vivid dreams/nightmares
- Headache
- Fatigue
- Unwell feeling
- **Use side effects as a dosing tool!

Questions?

Additional Citations

- Tolijan A, and Vrooman B. *Low-Dose Naltrexone (LDN) – Review of Therapeutic Utilization. Medical Sciences*. 2018; 6(82): 1-18.
- Younger J, Noor N, McCue R, et al. *Low-Dose Naltrexone For the Treatment of Fibromyalgia. American College of Rheumatology*. 2013; 65(2): 529-538.
- McNaull B, Trang T, Sutak M, Jhamandas K. *Inhibition of tolerance to spinal morphine antinociception by low doses of opioid receptor antagonists. Eur J Pharmacol*. 2007 Apr 10;560(2-3):132-41. doi: 10.1016/j.ejphar.2006.12.013. Epub 2007 Jan 17. PMID: 17307158.
- Patten DK, Schultz BG, Berlau DJ. *The Safety and Efficacy of Low-Dose Naltrexone in the Management of Chronic Pain and Inflammation in Multiple Sclerosis, Fibromyalgia, Crohn's Disease, and Other Chronic Pain Disorders. Pharmacotherapy*. 2018 Mar;38(3):382-389. doi: 10.1002/phar.2086. Epub 2018 Feb 23. PMID: 29377216.
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