

News from Good Life

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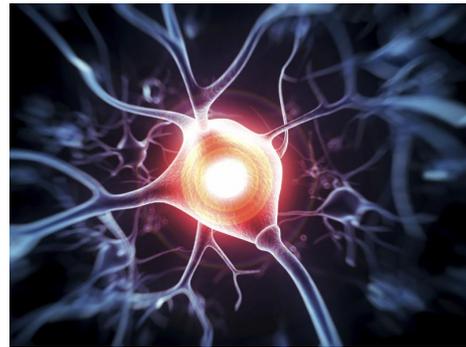


Sincerely,

Jim Andreesen, R.Ph., Angie Svoboda, Pharm.D. FIACP, and Ray Scott, R.Ph

Low Dose and Ultra Low Dose Naltrexone for Treatment of Pain and Autoimmune Diseases

"Naltrexone is an opioid receptor antagonist created by Endo Laboratories in 1963. In 1984, the FDA approved the use of naltrexone for treating opioid addiction. Intramuscular injection formulation of naltrexone was approved by the FDA in 2006 for alcohol dependence and in 2010 for opioid dependence. The typical dose for treating opioid addiction with naltrexone is between 50 mg to 150 mg. In contrast, low dose naltrexone (LDN) therapy utilizes much lower doses of naltrexone, usually ranging between 1.5 mg to 4.5 mg per day. Furthermore, microgram dosing of low dose naltrexone, referred to as ultra low dose naltrexone (ULDN), has been described in the literature.



"Naltrexone functions as a competitive antagonist for mu, kappa, and delta opioid receptors. Naltrexone selectively binds to the mu-opioid receptor as opposed to the kappa opioid (about 1:10) and to delta opioid receptors (about 1:100)

"Clinical use of low dose naltrexone was pioneered by Dr. Bernard Bihari in the 1980s who observed the regulation of immune function with use of low dose naltrexone in clinical practice. Bihari initially used LDN in those with human immunodeficiency virus (HIV) and later, in those with cancer. Today, LDN is most recognized for the management of autoimmune conditions. Accordingly, clinical trials are beginning to emerge. The effectiveness of LDN in the treatment of autoimmune conditions such as

Crohn's disease, multiple sclerosis, and systemic sclerosis [is] under active investigation."

Low dose naltrexone causes different pharmacological effects than higher doses of the drug. The theoretical basis of using ultra low dose naltrexone for pain is hormesis v. mu-opioid receptor-antagonist interaction. Hormesis is a phenomenon in which lower doses of a given antagonist may act, conversely, as a weak agonist. The action is biphasic; i.e., when an antagonist is given at a low dose, weak stimulation takes place whereas the same antagonist, given at a high dose, results in inhibition. The initial low dose of a drug may cause a temporary disruption in homeostasis. This is followed by an adaptive and compensatory stimulation. The naltrexone-mu receptor complex may provide another explanation as to how LDN may work.

The role of LDN and ultra low dose naltrexone (ULDN, microgram dosing of naltrexone) for chronic pain have been described recently in medical literature. A review from the University of Kansas Medical School evaluates the existing evidence for using LDN for treating pain and its microgram dosing in the potentiation of opioid medication while reducing side effects. "It has been proposed that LDN halts inflammatory cascades via glial cell inactivation. In addition, the role of microgram dosing of naltrexone has shown promise as a method to increase analgesia and decrease tolerance to opioid medications."

[J Pain Manage Ther. 2019; 3\(1\):1-5.](#)

LDN in Rheumatoid and Seropositive Arthritis

In recent years, low dose naltrexone (LDN) has been used as an off-label therapy for several chronic diseases. While studies indicate beneficial effects of LDN in autoimmune diseases, clinical research on LDN in rheumatic disease is limited. Using a pharmaco-epidemiological approach, Norwegian researchers tested the hypothesis that LDN use leads to reduced dispensing of other drugs (NSAIDs, opioids, TNF- α antagonists and DMARDs) used in the treatment of rheumatic disease. Patients (n = 360) were stratified into three groups based on LDN exposure. In persistent LDN users, there was a 13% relative reduction in cumulative defined daily doses (DDD) of all medicines examined and 23% reduction of analgesics. There was no significant DDD change in patients with less LDN exposure. There was a decrease in the number of NSAID users among patients with the least LDN exposure. The results support the hypothesis that persistent use of LDN reduces the need for other medications used in the treatment of rheumatic and seropositive arthritis. Randomized clinical trials of LDN in rheumatic disease are warranted.

[PLoS One. 2019 Feb 14;14\(2\):e0212460.](#)

The Use of Low Dose Naltrexone for Chronic Pain

The use of oral low dose naltrexone (1 mg to 4.5 mg) for the treatment of chronic pain is novel because it is a nonopioid alternative. Low dose naltrexone (LDN) use is "off label" and has been used successfully to manage chronic pain, autoimmune disorders, and dermatologic conditions. LDN could be a viable treatment option for chronic pain because other agents for chronic pain, such as nonsteroidal agents



(NSAIDs), have adverse effects of gastrointestinal bleeding, renal injury, and increase a patient's risk of myocardial infarction or stroke. Additionally, LDN has minimal adverse effects, no drug-drug interactions, and is relatively inexpensive compared with other options for chronic pain.

Sr Care Pharm. 2019 Jan 1;34(1):43-46.

Treatment of Autoimmune Disease with LDN

Zagon and McLaughlin of the Department of Neural and Behavioral Sciences, Penn State University College of Medicine, explained the intermittent blockade of the opioid growth factor (OGF) - OGF receptor (OGFr) axis by low dose naltrexone (LDN), and the role of enkephalin (i.e., OGF) in autoimmune disorders, specifically multiple sclerosis, Crohn's disease, and fibromyalgia. "Clinical reports on subjects taking LDN have documented reduced fatigue, few side-effects, and improved overall health... Intermittent OGFr blockade with LDN restores serum enkephalin levels... The interplay between LDN, and the onset and treatment of autoimmune diseases, chronic pain, and other addictive behaviors requires further investigation, but highlights a central role for enkephalins and intermittent blockade of the OGF-OGFr pathway in pathogenesis and treatment of these disorders."

Exp Biol Med (Maywood). 2018 Dec;243(17-18):1323-1330.

LDN for Chronic Inflammatory Dermatologic Conditions

Dermatology is encountering increasing rates of autoimmune disease manifesting in primary skin conditions that are difficult to treat without a risk of immunosuppression. The ability of low doses of naltrexone (LDN), 1.5 to 4.0 mg/day orally, to influence a variety of systemic pathways, including the immune system, has piqued the interest of researchers and practitioners, including Ekelem et al. of the Department of Dermatology, University of California, Irvine, and Juhasz of the Department of Dermatology, Howard University Hospital, Washington, DC.

A review of the literature from 1971 until April 2018 shows that LDN was effective in treating pruritus attributable to atopic dermatitis, prurigo nodularis, cholestasis, burn injury, systemic sclerosis, Hailey-Hailey disease, and lichen planopilaris. Serious side

effects were not reported. They concluded that LDN has the potential for the treatment of chronic inflammatory skin conditions; however, additional evidence is needed for dosing and long-term treatment guidelines.

JAMA Dermatol. 2018 Nov 28.

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