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Opinion

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Low dose naltrexone (LDN): the treatment you've never heard of…

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Opinion

Why haven't you heard about this amazing new breakthrough for conditions ranging from autoimmunity to cancer? Perhaps because as of yet no company has stepped forward with the billions of dollars needed to do a large-scale study on low-dose naltrexone (LDN). Unfortunately getting FDA-approval for use is not a straightforward process. With the patent expired, no drug company has been willing to pay such a large sum when they cannot sell the drug exclusively.

However, if you check PubMed, there are currently over 90 studies published on the various uses of LDN, from pain relief, fibromyalgia, Crohn's disease, multiple sclerosis, systemic sclerosis and even cancer. I have been using this drug in clinical practice with great results for the past several years and I want to tell you about it.

So how does ldn work?

Researchers at the Pennsylvania State University College of Medicine, Hershey, Pennsylvania have discovered the mechanism by which a low dose of the opioid antagonist naltrexone, an agent used clinically (off-label) to treat cancer and autoimmune diseases, exerts a profound inhibitory effect on cell proliferation. We believe that opioid receptor blockade by LDN provokes a compensatory elevation in endogenous opioids and opioid receptors that can function even after LDN is no longer available.

These papers revealed that a short-term opioid receptor blockade with naltrexone (LDN), a general opioid receptor antagonist devoid of intrinsic activity, results in an elevation in production of your own opioids and in response to the blockade. Interference of opioid peptide–opioid receptor interactions for a short time each day (from 4-6hours) with LDN provided a subsequent window of time (18–20hours) for the increased levels of endogenous opioids and opioid receptors to elicit a robust functional response: the inhibition of cell proliferation. In addition many patients report an improved sense of well-being and decrease in overall pain, as one might expect with higher levels of opioid production in the body.

Preliminary research abounds for cancer and autoimmune disease

Low dose of the opioid antagonist naltrexone (LDN) is being used clinically off-label to treat cancer and autoimmune diseases, by exerting a profound inhibitory effect on cell proliferation. LDN is an oral medication, generic, inexpensive, and non-toxic, and has been documented to alter the course of both neoplasias and autoimmune diseases such as Crohn's and multiple sclerosis, making this drug especially attractive as a therapeutic agent.

According to this study in Clinical Rheumatology, Low Dose Naltrexone (LDN) has been demonstrated to reduce symptom severity in conditions such as fibromyalgia, Crohn's disease, multiple sclerosis, and complex regional pain syndrome. They suggest that LDN may operate as a novel anti-inflammatory agent in the central nervous system, via action on microglial cells. These effects may be unique to low dosages of naltrexone and appear to be entirely independent from naltrexone's better-known activity on opioid receptors. As a daily oral therapy, LDN is inexpensive and well-tolerated.

A study published online in the Cochraine Library in February 2014 discusses using low-dose naltrexone to induce remission in Crohn's Disease. Although the authors conclude there is insufficient evidence to recommend and further research is needed, data from one small study suggests that LDN may provide a benefit in terms of clinical and endoscopic response in adult patients with active Crohn's disease. Data from two small studies suggest that LDN does not increase the rate of specific adverse events relative to placebo. In the Journal of Clinical Gastroenterology April 2013, Naltrexone therapy appears safe with limited toxicity when given to children with Crohn's disease and may even reduce disease activity.

Complex regional pain syndrome

(CRPS) is a neuropathic pain syndrome involves glial activation and central sensitization in the central nervous system. This can be a difficult disease to treat and patients suffer greatly with severe chronic pain. An article in the Journal of Neuroimmune Pharmacology showed positive outcomes of two CRPS patients, after they were treated with low-dose naltrexone, in combination with other CRPS therapies. Perhaps this is because Low Dose Naltrexone (LDN) is known to antagonize the Toll-like Receptor 4 (TLR4) pathway and attenuate activated microglia.

Link to fibromyalgia and autism

Another article posted online in Discovery Medicine came to the following conclusions:

a. Patients on chronic opioids relate autistically.

b. Autism is a hyperopioidergic disorder.

c. Fibromyalgia is a hypoopioidergic disorder.

d. Low opioid tone caused by opioid maintenance or fibromyalgia can usually is reversed with low-dose naltrexone.

e. The increase in the incidence of autism may have been caused by the increase in use of opioids for analgesia during childbirth.

The bottom line is that for disorders that involve low endogenous opioid production, like fibromyalgia and chronic fatigue syndrome, Low Dose Naltrexone may prove to be profoundly beneficial.

January 2013 article written in Arthritis and Rheumatology concluded that evidence continues to show that low dose naltrexone has a specific and clinically beneficial impact on fibromyalgia pain. The medication is widely available, inexpensive, safe, and well-tolerated.

Motility agent for small intestinal bacterial overgrowth (SIBO)

Another novel use of Low Dose Naltrexone has been for aiding motility in SIBO (small intestinal bacterial overgrowth). Ploesser et al described the use of LDN for aiding the migrating motor complex (MMC) in cleansing the small bowel. His small study use 2.5mg twice daily in patients with IBS and evidence of SIBO and 4.5mg daily in patients with inflammatory bowel disease. Approximately 68% of the study patients had improvement in symptoms taking LDN. According to other research, LDN may have effects on the gut to decrease inflammation, decrease intestinal permeability and stabilize toll like receptors, in addition to aiding motility.

Experimental and off-label but well tolerated and promising

The use of LDN for chronic disorders is still experimental and considered off-label. This doesn't stop progressive doctors from prescribing it due to its safety profile. The typical dose of LDN is a compounded immediate release tablet from 1.5 to 4.5mg taken at bedtime. The few reported side effects may be related to opioid blockade at night. Occasionally patients report anxiety, insomnia, vivid dreaming or nightmares. There are a portion of patients who already have elevated opioids that may not tolerate the drug. To avoid side effects, I generally start patients on half of intended dose and increase after 7-10days. If they still report symptoms, we move the dosing earlier in the day and May still get a beneficial effect. Low Dose Naltrexone is an oral medication, generic, inexpensive, and non-toxic, and has been documented to alter the course of both neoplasias and autoimmune diseases such as Crohn's and multiple sclerosis, making it an attractive and effective therapeutic agent.[1,2]

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Conflicts of interest

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References

1. Low Dose Naltrexone Research Trust.
2. LDN Clinical Trials.