

# Low Dose Naltrexone and Chronic Pain

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*This article is not intended to provide advice on personal medical matters or to substitute for consultation with a physician. The material in this article is for informational purposes only and is not a substitute for medical advice, diagnosis or treatment provided by a qualified health care provider. The use of Low Dose Naltrexone is an off label use by the FDA.*



Opioids (narcotics) have been used for many years. It's counter-intuitive to think that a drug like naltrexone which blocks the effect of opioids to help manage chronic pain. We do have some understanding that LDN (Low Dose Naltrexone) helps with autoimmune conditions. Current literature in pain medicine supports the view that chronic pain, especially chronic nerve pain conditions such as Complex Regional Pain Syndrome, Reflex Sympathetic Dystrophy, Diabetic Peripheral Neuropathy are autoimmune based. A study done on treating Fibromyalgia pain with LDN showed a 30% reduction in symptoms. Below is a short description of the mechanism behind chronic nerve pain.

The Central Nervous system (CNS) is made up of nerves and cells called glia. The glia make up about 80% of the CNS while the nerves make up about 20%. The function of the glia is to provide immune protection and host defense to the CNS. Under normal conditions the glia remain in an inactivate state. They become activated readily in response to infection or injury. The most important change that happens during inflammation of the brain and spinal cord (Central Nervous System) is activation of glia cells.

When glia cells are activated they trigger the release of certain chemicals known as pro-inflammatory and neurotoxic factors. These factors include several cytokines such as tumor necrosis factor alpha (TNF- $\alpha$ ) and interleukin one beta (IL1- $\beta$ ), fatty acid metabolites and free radicals such as nitric oxide and superoxide. In painful conditions such as Complex regional pain) and neuropathic pain, damage to the peripheral nerves shifts the glia to an activated state within the spinal cord.

The family of glia cells are made up of microglia and astrocytes. Each of these family members have a specific role. The microglia guard and protect the immune system and the astrocytes help maintain cell fluid balance which is important for the action of chemicals in the cells called neurotransmitters (needed

to control nerve function). Glia are activated by trauma, injury, infection, opioids. When activated, glia release pro-inflammatory and neurotoxic factors (cytokines).

Drugs that block the effect of opioids (morphine) may help prevent activation of glia. Such drugs are naltrexone and naloxone. Low dose naltrexone (hence, LDN) may inhibit the activation of glia.

Cells use chemicals called neurotransmitters to communicate with each other. Like most drugs, neurotransmitters work by attaching to specific receptors on cells. When neurotransmitters attach to receptors on cells, it allows for the passage of other substances into the cell (such as sodium, calcium). When these substances enter the cells they trigger the cells to fire and transmit signals along the nerve fiber.

Glutamate is the most abundant neurotransmitter found in the central nervous system. It is an excitatory neurotransmitter. Glutamate binds to a receptor called NMDA (N-methyl D-aspartate).

The NMDA receptor is the most common receptor found in the Central Nervous System. When the NMDA receptor is activated by glutamate it opens up calcium channels which cause the nerves to fire.

To summarize, when glial cells are activated they release chemicals and neurotransmitters that cause NMDA receptors to be activated which cause nerves to fire.

LDN (Low Dose Naltrexone), by its ability to inhibit microglial activation, suppresses activation of NMDA receptors by decreasing the release of glutamate neurotransmitter.

Whether to try LDN for CRPS must be seriously considered, especially since it can have interactions with existing medical regimens, particularly if medications are opioids (morphine like drugs). It should not be taken by patients who are on opioids or tramadol. Often, the choice is easiest for patients who are not on opioids. Fortunately, LDN has a low risk of side effects, Before taking LDN, one must consider current research, clinical trials, strength of anecdotal reports, severity of CRPS, response to other therapies, drug interactions and any contraindications.

Most physicians are unfamiliar with LDN. Be prepared to discuss LDN with your physician and acquaint him or her. There are some resources at the end of this book to help you acquaint yourself and your physician.

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### What to expect from LDN

LDN does not work immediately. It may take anywhere from a few weeks to many months. Users have reported to notice a difference after 9 to 12 months. After the initial response, it continues to show a benefit. The main goal of LDN is to slow or halt the progression of disease. In addition, symptoms may improve. Improvements seen in pain include decreases in exacerbation of pain, symptom improvement, improved functioning and better tolerance to pain.

LDN may increase endorphins (morphine like substances produced by the body) which may result in a feeling of well being. Human trials have demonstrated improvement in mood and in quality-of-life scores. This feeling helps lower stress, reduce depression, and increase healing. This is especially true for conditions like CRPS where stress can lead to exacerbations.

### Safety

Naltrexone was initially tested in humans for safety at the 50 to 100 mg dose level. There have been a number of studies such as a Crohn's disease study. Studies have assessed naltrexone administered at low-dose for safety and found no major issues to date.

Physicians who prescribe LDN feel that at such a low dose, it is unlikely to cause any harm. At high doses (50mg to 300mg of naltrexone) it may affect the liver. Patients with pre-existing liver and kidney conditions using LDN should have their metabolic functions monitored by their doctors.

No studies have been done to see the long term effects of LDN and its intermittent opioid blocking effect. Naltrexone has different effects when used in high doses and it is unknown whether the long-term use of LDN could have effects similar to those of high dose naltrexone. Patients who are considering taking LDN long term should approach with caution if they do not have a serious condition.

LDN does not stay in the body very long, hence if an emergency arises and a patient has to be administered an opioid for managing severe pain, they are unlikely to see any withdrawal effects.

### Contraindications

LDN can be taken with other medications or supplements as long as they do not contain opiates or synthetic narcotics, examples of which include fentanyl, meperidine (Demerol, Pethidine), tramadol, morphine, oxycodone and hydrocodone. Naltrexone



blocks the opioid receptors. Therefore pain medications will be blocked from working and could lead to withdrawal problems. Check with your doctor and pharmacist to make sure that none of your medications are contraindicated. They can also advise you on stopping pain medications that might interfere with LDN and offer advice and amount of time to allow between stopping opiates and starting LDN.

After starting LDN, if you have surgery scheduled or a procedure that may require pain medications, consult with your doctor to determine the amount of time needed to clear again from your system so that it does not interfere with anesthesia or pain medications. LDN must also be stopped if your doctor plans to prescribe opiate-based medications for postoperative use. The time required to clear naltrexone for the body may vary, based on dosage and body weight. After a procedure under anesthesia or requiring pain medications allow adequate time for the opiates to clear from your system before restarting LDN.

### Side effects

Considering that the naltrexone is such a low dose, it is uncommon to cause any side effects; potential side effects diminish as the body adjusts to LDN and increased endorphin levels. Side effects are less likely to occur when a small starting dose is used and gradually increased over time. It is better to start LDN at the lowest dose possible and increase slowly to allow for any side effects that may occur. If side effects occur, the dose can be reduced. Some of the more common side effects are: sleep disturbance, insomnia, vivid dreams.

If sleep disturbances do occur, LDN can be taken in the morning. Sleep disturbances diminish after taking LDN for some time.

### Compounding Low-Dose Naltrexone (LDN)

Naltrexone is manufactured as 50mg pills. Compounding pharmacies can prepare Low Dose Naltrexone to any dose specified. Because of differences in compounding pharmacies and the fillers, it's suggested that patients use a compounding pharmacy that has experience with LDN. The pharmacy must produce LDN in an instant release formulation and not as timed release or slow release. The LDN must not be released in to the body slowly. Compounding pharmacies can prepare the drug as capsules, tablets, liquid or topical cream. In preparing LDN, pharmacies can change the inactive ingredients (fillers) especially if a reaction is suspected. They can also make it in a gluten-free filler. For ultra low doses of naltrexone, it is prepared as a liquid suspension.

### Dose

The dose recommended by Dr. Bihari was 1.5mg to 4.5 mg taken at bedtime. However studies show that taking LDN at night is not necessary. If side effects occur then lowering the dose is recommended, or taking it in the morning in case of insomnia.