

Alternative dose strategy

Original document by Steinar Hauge of the Norwegian LDN site www.ldn.no and the Facebook group "LDN Norge." Feb 13, 2014

This document describes how a larger dose of LDN possibly can be used to reduce or avoid aggravation of symptoms that can occur with the traditional dose strategy for LDN. It also suggests that this strategy is more suitable for patients who have constant inflammatory conditions in the body (eg. fibromyalgia, ME, progressive MS, arthritis, etc). This is a clinical **experimental approach** to another dosage strategy than that normally used, but it is grounded in scientific knowledge, research and experience that exists on LDN today. We consider this dose strategy to be safe and it only uses doses within therapeutic dose range (1.5 to 6 mg).

A reference for LDN as an anti-inflammatory agent:

<http://www.ncbi.nlm.nih.gov/pmc/articles/PMC3962576/>

A discussion of LDN in relation to the immune system:

http://www.lowdosenaltrexone.org/ldn_and_ai.htm

1. Background

There are now many reports from patients who have had good results from this strategy. Many patients with fibromyalgia (and possibly ME) in a Facebook group have started directly at a dose of 6 to 4.5 mg and report good, and for many, immediate effects. Those who started at this dose experienced little or no symptom exacerbation, which some patients can do when they start at a low dose (≤ 1.5 mg) and then increase the dose over time, which is the traditional way of dosing. 4.5 mg was the starting dose for clinical studies on fibromyalgia at Stanford University.

2. Medical information and explanation

Starting on a high dose is an exciting approach that we are now beginning to gain more experience with. This dosing level starts at 6 mg and then winds down to a normal dose of 4.5-3 mg over time, or possibly stays at the high dose if it proves to have good results. The medical explanation as to why this can have a positive effect makes sense. The explanation is in "everyday" language so that patients are able to understand it as well.

LDN has two mechanisms of action (See appendix A for additional medical explanation):

1.

LDN first stimulates and then stabilizes the immune system as a result of increased endorphin levels. Measurements made during the 80s showed that the number of T cells may rise significantly after LDN startup. It is this mechanism that can give some patients increased symptoms during initial use of LDN. This is usually followed by improvement when the immune system stabilizes with time. This mechanism generally provides beneficial effects over time once the standard dose is established.

2.

The effect of Immunosuppression on inflammation (Ref Stanford University) – A higher dose of Naltrexone will provide a more powerful immune suppression response. It is the incorrect activity of the immune system that is suppressed. This is why this dose strategy presumably can provide immediate effect on various inflammatory conditions.

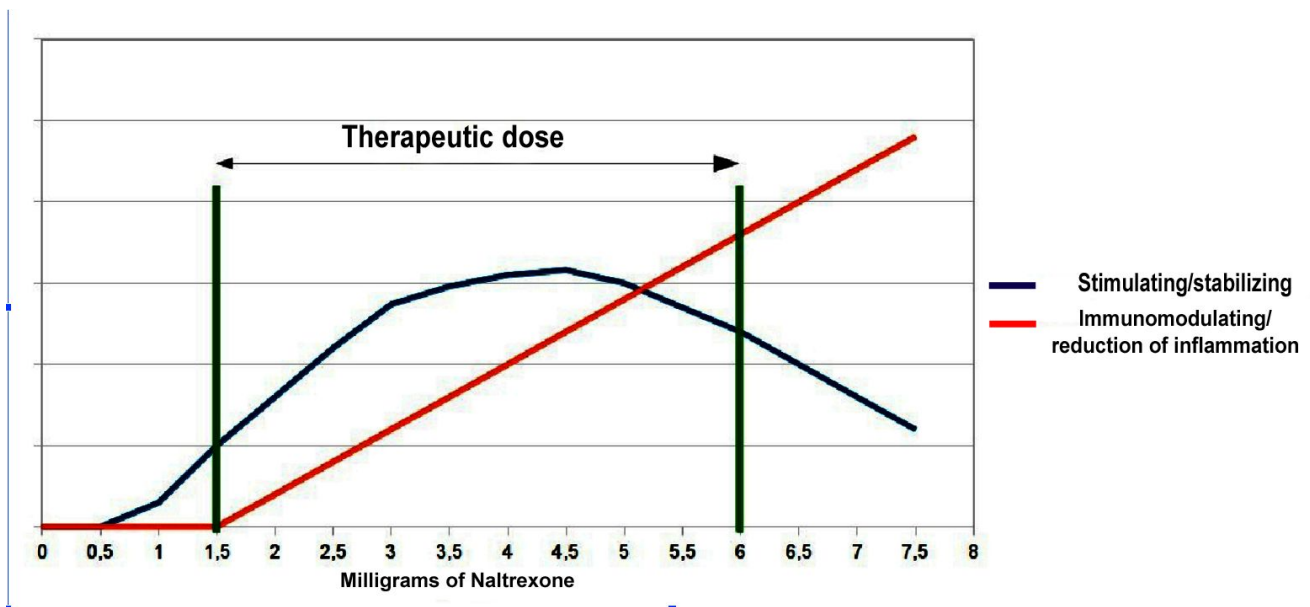
This strategy is actively using Naltrexone's mechanisms of action at different doses by way of the two mechanisms that are strong and weak in different dosing. We have the following **hypothesis** based on available research:

At a low dose (1.5 mg) "stimulation and stabilization" is strong and immune suppression is hardly present. When immune suppression is weak and the immune system is stimulated, the autoimmune reactions are enhanced and many are experiencing symptom aggravation until stabilization occurs.

At 3-4.5 mg the "stimulation and stabilization" action is at maximum strength and the immune suppression is weaker. This explains why starting at a 3 mg dose may give a tough startup sometimes.

At high doses (6 mg) the immune suppression action is strong and "stimulation and stabilization" is weaker. Therefore symptom aggravation will likely be less but your immune system will still be gently stimulated and the stabilization of the immune system will be in place gradually.

Schematically, the effects of LDN dosing look like this:



It should be noted that this is only an illustration to highlight the mechanisms of action and show the supposed effects at different doses. No scientific figures or evidence indicate that the curves are exactly so, but the effects that the curves illustrate is documented through research.

Attempts have been made by doctors in England to utilize these properties of Naltrexone, but they had other goals in mind than described in this document. We are aware that both doctors and specialists in Europe are using the alternative dose strategy with good results.

3. Start-up and reduction of alternative dose strategy

We are now beginning to get some experience with this dose strategy. In addition, we can use a bit of knowledge by "escalation" to do "de-escalation" of dosing as well, and we can use the knowledge of LDN's mechanisms of action to do this in the best possible way. Please note that all patients are different and react differently to medical treatment. There will therefore be individual differences in how patients react on this dose strategy.

The 6 mg starting dose of this strategy may be too high for some as an ongoing dose. If it is then it must be reduced to a normal dose of 3-4.5 mg. It is important to know that with a dose of 6 to 4.5 mg some may feel a bit miserable/uncomfortable in the period when LDN is active in the body (3-6 hr) because of the blockage of endorphins (applies mainly those taking LDN in the morning since bedtime dosers will be asleep).

3.1 Startup

We recommend starting with the normal startup strategy first. This will vary somewhat, but is usually as follows: Treatment should be stepped up with a starting dose of 1.5 mg and with an increase of 1.5 mg each 2 to 4 weeks up to 4.5 mg. If a dose is well tolerated then the increase can happen much faster. If the patient is experiencing that 4.5 mg is too high, **they should only return to 3 mg if it gives better effects**. The standard daily dose per day is usually between 3 and 4.5 mg. Generally speaking anyone's best dose will be the one that produces 4 hours of Endorphin blocking time but not more. This will optimize OGF production.

One factor that may sometimes call for lowering this dose is if herxing/retracing/detoxing effects from the healing factors are too much for the user to tolerate.

However if the patient is experiencing strong symptom exacerbation at the standard dose strategy or if the patient has a diagnosis characterized by constant inflammatory conditions in the body, then the alternative dose strategy can be tested. The startup dose is 6 mg. Because of the mechanism of action that is mobilized by this dose, it is recommended to take **3 mg in the morning and 3 mg on evening**.

3.2 Possible dose reduction

Dose reduction from 6 mg (2 * 3 mg) LDN:

1.

Try 6 mg for a few days but stop if experiencing severe discomfort. It may take a few days before any effect happens.

2.

If one feels worse after directly starting at 6 mg (2 * 3 mg) LDN or if one feels worse after a period of 6 mg LDN then the dose is probably too high and should be lowered down to 4.5 mg. Reassess at this dose and read paragraph 4 below.

3.

If one has dosed at 6 mg (2 * 3 mg) LDN for 2 to 3 weeks with good effect, try to decrease to 4.5 mg. If results are not as good at 4.5 mg, then go back to 6 mg and stay at this dose even longer before again trying to reduce to 4.5 mg. Attempting to move periodically to 4.5 mg may provide better results. **N.B.** If reduction does not give better results, you can continue to use 6mg (2 * 3mg) as standard dose.

4.

Whether to take 3 mg, 4.5 mg or 3mg * 2 as standard dose is individual and will vary from person to person. If one has reduced the dose to 4.5 mg and has had good effects then stay at this dose. If the effects are still poor, but better than the 6 mg, one can try to vary

between 3 and 4.5 mg to see what dose works best. When you have found the dose that seems to work best (eg. 1 * 3mg, 1 * 4,5mg or 2 * 3mg), then stay at this dose.

I repeat that we have no easy answer as to how to do this reduction strategy, but this is a decent start on a method for reduction of 6 mg that takes into account the knowledge we have now. Our experience indicates that 2 * 3mg 12 hours apart is best for some patients.

4. Tryout

We do not give any general recommendations that people should do it this way, there is too little empirical basis, but we note that several now have had good experience with this dosing and we think it has a plausible medical explanation.

If anyone wants to try this dosing, it's a decision one takes on their own initiative or in consultation with their doctor.

5. Caution

Cancer patients should NOT try the alternative dose strategy. There are different mechanism applicable to cancer patients. According to Dr. Zagon the optimal dose for cancer patients is likely to be 3mg and should not exceed 4 mg. This is because Endorphin blocking time is not as important as maximizing OGF healing time. Excessive blocking time could possibly lead to undesirable cancer cell growth . No clinical trials have been conducted with LDN and cancer although many doctors and patients use LDN as an effective way for controlling cancer cell proliferation. It is the upregulated levels of the body's OGF that suppresses cell proliferation, inhibits inflammation and promotes healing/homeostasis during the rebound effect. (In Norway the LDN tablets in the pharmacies are 3 mg and can be divided in halves. This mean that 3.75 mg is the highest practical dose based on the tablet size for cancer patients.) People with metabolic problems also discouraged from trying this at present.

Appendix A: About Naltrexone

Naltrexone molecules are both right and left rotated, a so-called racemic mixture:

- The right-turned portion of the molecule blocks the opiate receptors a short time and causes an increase in endorphin production and a "rebound" of endorphin when blocking ceases. This increase in the specific endorphin known as metenkephalin has been shown to have immunomodulatory effects. In a study by Professor Dr Zagon, the effect of the hormone, also known as opioid growth factor (OGF), was found to be an important factor in controlling tumor growth.

- The left turned portion of the molecule reduces cell inflammation by reducing the production of signal molecule NF Kappa B cells. This reduction of the signal molecule results in a regulation of production of inflammatory proteins called cytokines. Reduction in inflammation because regulation of cytokines is believed to be the dominant effect of LDN.

Reference: <http://www.ldnresearchtrust.org/content/ldn-and-cancer-dr-tom-gilhooly>

Related talk by Dr. Tom Gilhooly at the 2013 LDN Conference:

Video: <https://www.youtube.com/watch?v=G6SWv7HEj8M>

PDF of the Power Point slides:

<http://www.ldnresearchtrust.org/sites/default/files/Dr%20Tom%20Gilhooly%20LDN%202013%20Conference.pdf>

Until more research and documentation is available on the mechanism of action of LDN, it is assumed that these two anti-inflammatory mechanisms are creating the benefits for the diagnoses for which LDN is used.

Changes in document:

Document established	30/5 - 2013	
Document updated	31/5 - 2013	Changes in "Startup" in order to improve tolerability.
Document updated	13/1 - 2014	Updated and edited regarding wider experience with this dose strategy
Document updated	13/2 - 2016	Editor: Original Norwegian document translated to English by Brian Haviland and Steinar Hauge for Facebook group GotEndorphins LDN