Committed to trials of LDN as a treatment for autoimmune diseases

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Low-dose Naltrexone (LDN) Fact Sheet 2014

Naltrexone is a class of drug known as an opiate antagonist. Its normal use is in treating addiction to opiate drugs such as heroin or morphine. The dose used for this purpose is usually between 50 and 300mg daily.

Low-dose Naltrexone (LDN) has been used in the treatment of autoimmune diseases in the USA since 1985, but is relatively new in the United Kingdom and Europe. Despite the fact that the drug is used at a very low dose, the occurrence of significant introductory or long term side effects cannot be excluded.

This method was devised and subsequently developed by the late Dr Bernard Bihari, a Neurophysician from New York, USA who passed away on May 16th 2010. Dr Bihari was qualified in Internal Medicine, Psychiatry and Neurology, and we hope to honour him by continuing with his pioneering work.
The main website is www.lowdosenaltrexone.org

Suggested Method of Therapy:

Your doctor will usually start treatment at an ultra-low dose and increase this gradually over a period of weeks – until you are stable and side effect free.

The starting dose can vary from 0.5mg to 1.5mg – and is usually increased over 4 - 8 weeks to 4.5mg or higher. Some doctors increase this to twice daily, for certain medical conditions.

For Autoimmune Diseases, patients normally start at 1mg or 1.5mg and increase to 4.5mg daily over a period of 4 - 8 weeks.

However, for Hashimotos, Chronic Fatigue Syndrome or Fibromyalgia, the suggested starting dose is usually 0.5mg - 1.0mg and it is increased by 0.5mg a week until 4.5mg is reached.

For Cancer, LDN can be taken at similar doses, but must be avoided the week before and the week after cancer chemotherapy. This does not include a drug called tamoxifen or daily medications for prostate cancer.

How Naltrexone Works

In Autoimmune disease:
The mechanism of action of naltrexone, in autoimmune diseases and cancer, is poorly understood.

The benefits of the drug are possibly due to the temporary inhibition of endorphins. This results in a reactive increase in the production of endorphins, which should result in a reduction of painful symptoms and an increased sense of wellbeing.

Increased levels of endorphins should be expected to stimulate the immune system, promoting an increase in the number of T lymphocytes. This effect was observed in Dr Bihari's research. This increase in T-cell numbers apparently restores a more normal balance of the T-cells such that the effects of the disease process are significantly reduced.

It may also act directly on these immune cells to stimulate or restore normal function.

There is research currently underway, to prove the hypothesis that naltrexone improves the immune system - by acting on a receptor called TLR4. Several published papers have shown that naltrexone binds to the TLR4 receptor, and has a clinically measurable effect. This is evident in Chron's disease and Ulcerative Colitis.

REF:
http://www.ncbi.nlm.nih.gov/pubmed/22850250
http://www.ncbi.nlm.nih.gov/pubmed/22826216
http://www.ncbi.nlm.nih.gov/pubmed/23188075
http://www.ncbi.nlm.nih.gov/pubmed/17222320

In Cancer:

Recent research by Dr Ian Zagon in multiple resistant breast cancer, has shown that it can stop breast cancer cells growing by acting on a new pathway “p21 cyclin-dependent inhibitory kinase pathway”.

REF:
http://www.sciencedaily.com/releases/2013/08/130810063639.htm

This is yet to be confirmed by a second study, but is likely to researched further in the future. This pathway is present in many solid tumors – as well as a large proportion of breast cancers. The article seems to offer some hope for people with multiple resistant breast cancer.

Multiple centers around the UK are quietly using LDN for all types of cancer. Prof. Angus George Dalgleish (Bsc, MD FRACPath FRACP FRCP FMedSci), professor of

oncology at University College London is extremely experienced is using LDN for cancer. Recent examples where it has been beneficial in anecdotal cases include lung, bowel and malignant melanoma. Dr Zagon's study points to a mechanism of action in these, and other solid tumor types.

There is also a combination therapy called the Berkson Method – using Alpha-Lipoic Acid and LDN. Dr Berkson talks about it here:
http://www.anticancer.org.uk/2011/10/q-with-dr-burt-berkson-low-dose.html

In Autism:

LDN has been used by many physicians, usually after expert assessment – in children with Autism.
This has been widely discussed and the mechanism is probably a mixture of inflammation and direct neurological effects.

More information can be found: http://www.autismtreatmenttrust.org/

Interestingly, dosage does not seem to be weight related – and the doses are the same as for adults when given orally, but often a cream of LDN is prescribed for ease of application.

In Hayfever / Severe Allergy:

Many patients who experience severe hayfever have noticed that their hayfever symptoms resolve after LDN treatment for another autoimmune disease. This has led to many patient with severe allergies trying LDN as an adjunct to their existing treatments, like anti-histamines.

The mechanism of action is probably via TLR-4 – but no research has specifically been done on this yet.

In Thyroid Disease:

Patients with thyroid disease often have a strong auto-immune component.
Using LDN to dampen down the immune system often leads to a reduction in hypothyroidism and an improvement in symptoms. Patients with Thyroid disease must always be very careful when starting LDN as the results can be very fast – and rapidly cause hyperthyroidism if they do not reduce their Thyroid medication intake.

The mechanism is also quite vague – but is most likely central, via modification of OGF / Endorphin pathways.

Ref:
http://www.stopthethyroidmadness.com/ldn/

Overview:

In layman's terms, no one is really sure how LDN works – there are multiple pathways being investigated. Due to the number of biological systems affected by inhibition of receptors that LDN binds to, this is not surprising and research is ongoing in many areas. The most exciting being its apparent ability to block many auto-immune diseases, and even more excitingly being able to stop the growth or spread of some tumor types in animals.

The Use of Low-dose Naltrexone, and the Occurrence of Side Effects

Many patients who start LDN do not experience any severe side effects.

Initially, your symptoms may become worse – in MS, this can be characterised by increased fatigue, or increased spasticity. In CFS/ME, this can be the onset of apparent 'flu like symptoms.

LDN can cause sleep disturbances if taken at nighttime – this is most likely because of the increase in endorphin release. These disturbances can take the form of vivid dreams, or insomnia.

Taking LDN at night is often recommended by patients on the internet, but there are many patients who take it in the morning and still get excellent benefits. This is a discussion you should have with your doctor.

In various studies (and anecdotal accounts), the number of T-Lymphocytes has been shown to dramatically increase when a patient starts on LDN. This may account for some of the benefits patients feel when they are being treated for an autoimmune disease, or cancer.

In less than ten percent of cases treated, increased introductory symptoms may be more severe or more prolonged than usual, lasting sometimes for several weeks. Rarely, symptoms may persist for two or three months before the appropriate beneficial response is achieved.

If side effects are troublesome, then reducing your dose by 0.5mg for 7 days, before increasing it again, is a good idea.

Some patients, very rarely, experience gastro-intestinal side effects. Nausea and or constipation/diarrhea. The reason for this is currently unknown, but may be due to the presence of large numbers of TLR4 receptors in intestines.

Patients experiencing this side effect can request LDN Sublingual Drops, which transfer the LDN directly into the bloodstream – avoiding the stomach area.

Patients who do have these side effects should increase their dose by no more than 0.5mg per week – and should consult with their GP or pharmacist for appropriate treatment for the stomach upset, if necessary. (Omeprazole, Ranitidine, Gaviscon, Fybogel, Mucogel and Pepto Bismol are ok – but not Kaolin & Morphine or Loperamide/Imodium.)

Types of LDN:

Liquid

Oral Liquid Formulation at 1mg/1ml is the most commonly used type of LDN in the UK. It is taken daily, and dosed using a baby oral syringe. It does not contain very high amounts of lactose or any other excipient known to cause hypersensitivity. The base is similar to children's cough syrup – so is quite palatable. Because there are so few preservatives, it should be stored in the fridge. It can last for 3 months if stored in the fridge.

Capsules

For patients who the liquid would be impractical or undesirable, there are capsules available in 1.5mg, 3mg and 4.5mg strengths as well as other specific doses.

IMPORTANT: Make sure to specify that you do NOT want LDN in a slow-release form.
Pharmacies should be instructed NOT to provide LDN in an "SR" or slow-release or timed-release form. Unless the low dose of naltrexone is in an unaltered form, which permits it to reach a prompt "spike" in the blood stream, its therapeutic effects may be inhibited.
Fillers. Capsules of LDN necessarily contain a substantial percentage of neutral inactive filler. Experiments by the compounding pharmacist, Dr. Skip Lenz, have demonstrated that the use of calcium carbonate as a filler will interfere with absorption of the LDN capsule. Therefore, it is suggested that calcium carbonate filler NOT be employed in compounding LDN capsules. He recommends either Avicel, lactose (if lactose intolerance is not a problem), or sucrose fillers as useful fast-release fillers.
> **IMPORTANT: Make sure to fill your Rx at a compounding pharmacy that has a reputation for consistent reliability in the quality of the LDN it delivers.**

Sublingual Drops

Sublingual drops are designed for patients who are having problems taking the medication orally, or for people who want to guarantee the fastest delivery of the drug into their bloodstream. A number of drops are placed under the tongue from a dropper bottle and dose is increased and decreased by the number of drops taken. There are basically no excipients in this product, trace lactose and a small amount of glycerol.

Cream

LDN Cream in 0.5mg/ml (or higher) is available for application to the skin. This is helpful for children, or for patients allergic to colorants – flavorings or any excipients in all other forms of LDN. It is generally the most expensive.

Intrinsic Toxicity of the Drug:

Naltrexone, in full doses of 50-300mg, have been shown to transiently increase liver enzymes. Patients being prescribed Naltrexone for addictions must have liver function tests performed before initiating therapy.

This is not necessary with LDN – as the dose is much smaller, however, patients with advanced liver failure should consult their GP before considering treatment.

Patients with renal or liver failure should only start treatment after a consultation with their own GP or specialist, and should be monitored during the treatment initiation period. It is normal for people with poor renal or liver function to experience a transient elevation – but this usually resolves after a few weeks.

Contraindications and Special Precautions:

LDN is compatible with most other therapies. It does not directly interact with steroids, however, can negate the effect of opiate based painkillers. Patients should give their doctor a full drug history before starting therapy.

Patients who are taking multiple medications and/or herbal medicines – especially those with cancer or advanced disease, should take careful advice from a qualified doctor or pharmacist before initiating LDN.

http://www.ldnresearchtrust.org/node/148
www.ldn-international.com

This is beneficial if you are taking many medications and need a thorough check as to whether LDN will be suitable for you – before going to the expense of getting a private GP consultation. This is very valuable in cancer where complex regimens are used, or where you are already taking herbal medicines.

Obtaining a prescription for LDN:

********WARNING*** DO NOT buy LDN on the internet. There is no guarantee that the drug is genuine or safe. On multiple occasions LDN purchased from the internet or from overseas has been proven to be of low quality, completely fake or otherwise dangerous.**

The only way to legally and safely obtain LDN, is via a doctor's prescription.

Should you need help finding an LDN prescribing doctor in the US please email mailto:linda@ldnrt.org

Low Dose Naltrexone - Key clinical studies
Complied by Dr Tom Gilhooly

Low Dose Naltrexone has been the subject of much debate but actually very few clinical trials. Ian Zagon from Penn State University has been studying LDN for over 20 years and conducted many pre clinical studies investigating LDN in cancer and in the animal model of MS (1,2). He has also been involved in two clinical studies into Crohn's disease with his colleague Prof Jill Smith from Penn State. These demonstrated a significant improvement in symptoms and in bowel mucosal appearance with LDN treatment (3,4). In the RCT, LDN patients were twice as likely to have a 70 point decline in the Crohn's Disease Activity Index. 78% of the LDN group achieved an endoscopic response compared to 28% with placebo.

Jarred Younger from Stanford University has studied LDN in Fibromyalgia, firstly in a small pilot study and more recently in a yet to be published randomized controlled trial. The pilot study showed significant improvement in symptoms of pain in these patients(5).

Multiple Sclerosis in one of the areas where LDN has been used the most frequently. There are three published studies, one in primary progressive MS(6) and two on quality of life (7,8). The results of two studies was positive with improved quality of life in one and reduced spasm in the PPMS study. The third (allowing patients to continue on DMDs) showed no significant difference between the treatment and placebo groups but found the treatment to be safe. A review of the available studies into LDN and MS was published in 2009 (9). All studies have confirmed the safety of the drug and there is enough positive evidence to merit greater investigation.

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Conditions where LDN could be of benefit.

Acute disseminated encephalomyelitis
Acute hemorrhagic leukoencephalitis
Addison's Disease
Agammaglobulinemia
Alopecia areata
Amyotrophic Lateral Sclerosis
Ankylosing Spondylitis
Anti-GBM/TBM Nephritis
Antiphospholipid syndrome
Antisynthetase syndrome
Asthma
Atopic allergy
Atopic dermatitis
Autoimmune aplastic anemia
Autoimmune cardiomyopathy
Autoimmune enteropathy
Autoimmune hemolytic anemia
Autoimmune hepatitis
Autoimmune inner ear disease
Autoimmune lymphoproliferative syndrome
Autoimmune pancreatitis
Autoimmune peripheral neuropathy
Autoimmune polyendocrine syndrome
Autoimmune progesterone dermatitis
Autoimmune thrombocytopenic purpura
Autoimmune urticaria
Autoimmune uveitis
Balo disease/Balo concentric sclerosis
Bechets Syndrome
Berger's disease
Bickerstaff's encephalitis
Blau syndrome
Bullous pemphigoid
Cancers

Castleman's disease
Celiac disease
Chronic Fatigue Syndrome (CFS)
Chronic inflammatory demyelinating polyneuropathy
Chronic recurrent multifocal osteomyelitis
Chrons disease (CD / IBD)
Churg-Strauss syndrome
Cicatricial pemphigoid
Cogan syndrome
Cold agglutinin disease
Complement component 2 deficiency
Cranial arteritis
CREST syndrome
Crohns Disease (one of two types of idiopathic inflammatory bowel disease "IBD")
Cushing's Syndrome
Cutaneous leukocytoclastic angiitis
Dego's disease
Depression
Dercum's disease
Dermatitis herpetiformis
Dermatomyositis
Diabetes mellitus type 1
Diffuse cutaneous systemic sclerosis
Discoid lupus erythematosus
Dressler's syndrome
Eczema
Enthesitis-related arthritis
Eosinophilic fasciitis
Eosinophilic gastroenteritis
Epidermolysis bullosa acquisita
Erythema nodosum
Essential mixed cryoglobulinemia
Evan's syndrome
Fibrodysplasia ossificans progressiva
Fibromyalgia (FB)
Fibrosing aveolitis
Gastritis
Gastrointestinal pemphigoid
Giant cell arteritis
Glomerulonephritis
Goodpasture's syndrome
Graves' disease
Guillain-Barré syndrome (GBS)
Haemolytic anaemia
Hailey – Hailey Disease
Hashimoto's encephalitis
Hashimoto's thyroiditis
Henoch-Schonlein purpura

Herpes gestationis
HIV
Hypogammaglobulinemia
Idiopathic Inflammatory Demyelinating Diseases
Idiopathic pulmonary fibrosis
Idiopathic thrombocytopenic purpura (See Autoimmune thrombocytopenic purpura)
IgA nephropathy
Inclusion body myositis
Inflammatory demyelinating polyneuopathy
Interstitial cystitis
Juvenile idiopathic arthritis
Juvenile rheumatoid arthritis
Kawasaki's Disease
Lambert-Eaton myasthenic syndrome
Leukocytoclastic vasculitis
Lichen planus
Lichen sclerosus
Linear IgA disease (LAD)
Lou Gehrig's disease (Also Amyotrophic lateral sclerosis)
Lupoid hepatitis
Lupus erythematosus
Majeed syndrome
Ménière's disease
Microscopic polyangiitis
Miller-Fisher syndrome
Mixed Connective Tissue Disease
Morphea
Mucha-Habermann disease
Multiple Sclerosis (MS)
Myalgic Encephalomyelitis (ME)
Myasthenia gravis
Myositis
Neuromyelitis optica (Also Devic's Disease)
Neuromyotonia
Occular cicatricial pemphigoid
Opsoclonus myoclonus syndrome
Ord thyroiditis
Parkinson’s Disease
Palindromic rheumatism
PANDAS (pediatric autoimmune neuropsychiatric disorders associated with streptococcus)
Paraneoplastic cerebellar degeneration
Parkinson’s Disease
Paroxysmal nocturnal hemoglobinuria (PNH)
Parry Romberg syndrome
Pars planitis
Parsonnage-Turner syndrome
Pemphigus

Pemphigus vulgaris
Perivenous encephalomyelitis
Pernicious anaemia
POEMS syndrome
Polyarteritis nodosa
Polymyalgia rheumatica
Polymyositis
Primary biliary cirrhosis
Primary sclerosing cholangitis
Progressive inflammatory neuropathy
Psoriasis
Psoriatic arthritis
Pure red cell aplasia
Pyoderma gangrenosum
Rasmussen's encephalitis
Raynaud phenomenon
Reiter's syndrome
Relapsing polychondritis
Restless leg syndrome
Retroperitoneal fibrosis
Rheumatoid arthritis
Rheumatoid fever
Sarcoidosis
Schmidt syndrome
Schnitzler syndrome
Scleritis
Scleroderma
Sjögren's syndrome
Spondyloarthropathy
Stiff person syndrome
Still's disease
Subacute bacterial endocarditis (SBE)
Susac's syndrome
Sweet's syndrome
Sydenham chorea
Sympathetic ophthalmia
Takayasu's arteritis
Temporal arteritis (also known as ""giant cell arteritis"")
Tolosa-Hunt syndrome
Transverse myelitis
Ulcerative colitis (one of two types of idiopathic inflammatory bowel disease "IBD")
Undifferentiated connective tissue disease
Undifferentiated spondyloarthropathy
Vasculitis
Vitiligo