

## **Low Dose Naltrexone**

**Ashton Embry**

Hardly a week goes by without someone asking my opinion on the use of the drug low dose naltrexone (LDN) for MS. Thus I thought I'd discuss my current views on the use of LDN.

Naltrexone blocks opioid receptors which occur on many tissues in the body, mostly notably in the brain. The drug was developed to fight heroin addiction. By blocking the opioid receptors in the brain, naltrexone negates the positive effects of heroin. In this capacity, naltrexone is given in doses of 50 -300 mg to ensure a widespread and long lasting blockade.

In the late 80s and 90s, low dose naltrexone, which means dosages of 1 -5 mg, was used by a few physicians, led by Dr Bernard Bihari, to treat a variety of diseases from cancer to autoimmune diseases to chronic degenerative diseases such as Parkinson's and ALS. The doctors reported a lot of success with LDN and its potential value for autoimmune diseases such as MS has become quite well known to many persons with MS.

Currently we have mainly anecdotal data to support the use of LDN for MS. On one hand this is a little worrisome because most MS therapies, no matter how scientifically improbable (e.g. "homeopathic neuropeptide spray"), usually are supported by abundant anecdotal claims for a period of time until they fade into obscurity and are replaced by the next off the wall therapy. However, one wants a lot of positive anecdotal data for any proposed therapy and the key is to have some good science to go along with the anecdotes.

I would certainly not classify LDN as a bizarre, flash-in-the-pan therapy and I think it is important to emphasize the scientific data and rationale we do have to support the use of LDN.

Currently we have two hypotheses concerning why LDN might be helpful for MS. Dr Bihari postulates that the low dose only blocks some opioid receptors for a relatively short time and that this causes an over production of beta-endorphins. There is some evidence suggesting that beta-endorphins modulate the immune system and it is important to realize that immune cells

have opioid receptors on them. Thus LDN has the potential to dampen the autoimmune reactions which drive MS and other autoimmune diseases such as Crohn's and rheumatoid arthritis.

Dr Agrawal provides a different hypothesis and postulates that by blocking the opioid receptors can, though a complex pathway, protect the cells which produce myelin from damage and destruction. I find this hypothesis less appealing than that of Bihari simply because it then becomes difficult to explain why LDN would be of value for other autoimmune diseases such as Crohn's. However, LDN may have a number of effects and the protection of myelin-making cells may be an added bonus for helping to control the MS disease process.

To me the strongest scientific evidence for LDN for MS is the outcome of a small, open-label pilot study of LDN for Crohn's disease (Smith et al, 2007). Crohn's and MS have a lot in common being characterized by a T cell-led autoimmune attack on specific proteins in the CNS in the case of MS and in the gut for Crohn's.

In the small, 3 month trial, 12 of 17 subjects went into remission and another 4 experienced some improvement. Only one person had an attack and withdrew from the trial in order to resume her medication. The authors report that impressive healing was also experienced by some subjects and that most had improved quality of life. It is also worth noting that one person in the trial had MS as well as Crohn's and the authors comment that this person "also had improvement of her neurological symptoms". Such results are very hopeful and a larger trial for Crohn's is currently in the planning stage.

In the Crohn's paper the authors speculate on the possible mechanisms through which LDN might have effected the reported improvements. They discuss various ways that LDN may have an anti-inflammatory effect and they also emphasize how LDN can promote DNA synthesis and healing. There is no doubt that much more research is necessary before we understand how LDN has a positive effect on autoimmune diseases such as MS and Crohn's but there is no need to wait for such understanding before using LDN.

A few small trials to test the efficacy of LDN for MS are currently being carried out in the USA and in Italy and these are small but are controlled.

They are of short duration (6 months or less) and they will not be using changes in MRI parameters as outcomes. To me we will need a much longer controlled trial (2 years) with serial MRI scans in order to be able to properly assess the value of LDN for MS.

With the above information, and the facts that LDN is low cost (a daily dose costs much less than a cup of coffee) and is safe (as demonstrated by the Crohn's trial not to mention countless anecdotal reports), it seems to me anyone who has not been able to keep MS well controlled with their therapy choice might be wise to add LDN to their therapeutic package. I expect it will be many years, if ever, before a multi-million dollar, phase III clinical trial will be done to establish beyond a reasonable doubt if LDN has significant value for MS. Persons with active MS do not have the luxury of waiting for such a final decision. One has very little to lose and much to potentially gain from the use of LDN given the current scientific data.

It is most important that persons with MS do not look to their national MS societies or their neurologists for advice or information regarding LDN. The societies and neurologists mainly ignore it or provide little and somewhat patronizing information on it. A recent check of the MS Society of Canada website revealed only one reference for LDN and it was in an article which warned people about the use of alternative and complementary therapies. The NMSS website was a little better in that it provided some factual information on LDN but certainly did not encourage their members to give such a therapy a try or even to investigate it further.

It would be interesting to hear how the societies would rationalize their position that a person with MS who is experiencing progression should not give LDN a try. I expect they would say there has been no clinical trial which proves it is of value so they can't recommend it. Of course the only source of funding for such a trial is the MS societies so they can play this game *ad finitum*. The lack of a patient-centred approach by the MS societies and most neurologists has always been a major problem for the MS community.

In summary, LDN has good potential to be of benefit for persons with MS. Given that it is safe and very low cost, anyone experiencing progression might want to seriously contemplate giving it a try in spite of discouragement from their neurologist and MS society.