Low Dose Naltrexone

Naltrexone is more commonly known for its indication in addiction medicine, given at 50 – 100 mg per dose. When naltrexone is dosed between 0.5 mg and 6 mg it is termed low dose naltrexone or LDN. LDN is used for ME/CFS and post-COVID condition (more severe cases of post-COVID condition are also classified as ME/CFS). At these doses, there is reduction in glial inflammatory response and upregulation of endogenous opioid signaling by transient opioid receptor blockage. The blockade lasts for about 4 hours after LDN is dosed, after which opioid receptor signaling is upregulated. Ultra-low dose naltrexone is dosed from 0.1 mg and lower and works to potentiate opioid analgesia by acting on filamin A which is involved in opioid signaling (1).

Some have recommended LDN be started at 0.5mg and titrated up to the most effective dose with the least side effects. Titration varies between providers, but a conservative approach would be to start at 0.5 mg daily and increase by 0.5 mg every 5 days. In more sensitive patients, a slower titration may be preferred, while other patients may tolerate a quicker titration. Many providers aim for a target dose of 4.5 mg daily. In some patients with side effects, lowering the dose for a month or so and then again trying to titrate upward can be an effective method of achieving this dose.

LDN is traditionally dosed once daily by mouth and can be given in the morning before breakfast to avoid nausea. If given in the morning, the side effects of intense dreaming may be lessened. Some people prefer to take it in the evening because it makes them sleepy. Other side effects include insomnia, bone pain, fatigue, and GI symptoms. Caution is advised if using LDN with opioids as it can cause the opioids to be less effective or potentially cause withdrawal symptoms. Some recommend that LDN be stopped 3 days prior to surgery to avoid interference with opioids that may be given for pain control.

LDN may improve brain fog, fatigue, and pain. It is also prescribed to decrease the incidence and severity of post-exertional malaise (PEM) episodes.

Time to improvement can vary from a few days to 8 weeks before patients notice a significant improvement. Unless there are sustained and/or significant side effects a trial of at least 8 weeks should be given. It may take several months for the full benefit of LDN to manifest (2).

References

1. Toljan K, Vrooman B. Low-Dose Naltrexone (LDN)-Review of Therapeutic Utilization. Med Sci (Basel). 2018 Sep 21;6(4):82. doi: 10.3390/medsci6040082. PMID: 30248938; PMCID: PMC6313374.
2. McKenzie-Brown AM, Boorman DW, Ibanez KR, Agwu E, Singh V. Low-Dose Naltrexone (LDN) for Chronic Pain at a Single Institution: A Case Series. J Pain Res. 2023 Jun 14; 16:1993-1998. doi: 10.2147/JPR.S389957. PMID: 37337611; PMCID: PMC10276990.

Resources

https://ldnresearchtrust.org/

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