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A scoping review of low dose naltrexone's utility in inflammatory and centralized pain conditions

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Introduction

Low dose naltrexone (LDN) is a novel compounded medication that was originally used to treat opioid or alcohol abuse due to its opioid antagonistic properties [1]. However, at low doses naltrexone has been shown to modulate inflammation through the interruption of microglial cells within the central nervous system as well as peripheral modulation of CD4 and CD8 cells through the Mu opioid receptor [2,3]. Subsequently, LDN has been proposed for the management of pain stemming from both central sensitization as well as peripheral immune system dysregulation pain [4]. Several case reports and small trials have been completed to support this hypothesis. Large scale trials are limited. This narrative review aims to review low dose naltrexone and its off-label utility for various inflammatory and centralized pain conditions.

Materials and Methods

A comprehensive literature search was conducted with the aid of a research librarian and included PubMed, Embase and Google Scholar. Search terms included low dose naltrexone, pain, low back pain, chronic pain, Crohns, fibromyalgia, complex regional pain syndrome, inflammatory bowel and neuropathy. All results were screened for eligibility and records not meeting inclusion criteria were excluded. Inclusion criteria represented all articles utilizing LDN for pain in human subjects. Exclusion criteria included studies focusing on the use of full dose naltrexone, naltrexone for alcohol and opioid abuse, obesity, dermatological conditions and other non-painful disease processes (amyotrophic lateral sclerosis, primary sclerosing cholangitis, Haily-Haily, opioid induced constipation and chronic fatigue). Studies involving cancer or chemotherapy induced neuropathy pain were also excluded. Relevant articles were included, and study data tabulated. As this review is devoid of patient identifiable information, it is exempt from IRB review requirements as per University of Kansas guidelines.

Results/Case Report

47 studies related to the off-label use of LDN and complex regional pain syndrome (CRPS), Crohn's, fibromyalgia, diabetic neuropathy, rheumatoid arthritis and low back pain were retrieved. The majority of

studies were case reports and reviews however some randomized control trials (RCTs) and prospective studies have been conducted, specifically for Crohn's and fibromyalgia. The outcome measures, follow up times and doses utilized throughout the studies varied considerably and thus statistical analysis was not employed. Despite this, however, there does appear to be possible trends across studies and throughout the various conditions. The majority of the evidence shows improvements in not only VAS, NRS and hyperalgesia but also function (ODI, MODQ), quality of life and symptom severity. In addition to the aforementioned, patients with Crohns also had improvements in the endoscopic appearance of their intestinal mucosa. Across the various pathologies, typical adverse effects associated with LDN use were vivid dreams, insomnia, diarrhea and headaches though these usually resolved after extended use of the medication. There were some infrequent cases of patients not tolerating LDN or having no improvement in symptoms and these patients discontinued usage.

Discussion

The evidence in this review provides support for the off-label use of LDN for various chronic inflammatory or centralized pain conditions. However, it is apparent that high-quality controlled studies focusing on administration, dosing and follow up time are needed before formal recommendations can be made. In addition, investigation into the synergistic effects of LDN with other medications, e.g. improved tolerance to opiates and enhanced anti-allodynic effects of anti-seizure medications, would be beneficial in expanding LDNs utility [5]. Despite the current paucity of high-quality evidence in the literature, LDN continues to offer promising results in the management of symptoms in patients with chronic inflammatory or centralized pain conditions.

References

1. Younger J, Parkitny L, McLain D. The use of low-dose naltrexone (LDN) as a novel anti-inflammatory treatment for chronic pain. *Clin Rheumatol*. 2014 Apr;33(4):451-9. doi: 10.1007/s10067-014-2517-2. Epub 2014 Feb 15. PMID: 24526250; PMCID: PMC3962576.
2. Patten DK, Schultz BG, Berlau DJ. The Safety and Efficacy of Low-Dose Naltrexone in the Management of Chronic Pain and Inflammation in Multiple Sclerosis, Fibromyalgia, Crohn's Disease, and Other Chronic Pain Disorders. *Pharmacotherapy*. 2018 Mar;38(3):382-389. doi: 10.1002/phar.2086. Epub 2018 Feb 23. PMID: 29377216.
3. Segal D, Macdonald JK, Chande N. Low dose naltrexone for induction of remission in Crohn's disease. *Cochrane Database Syst Rev*. 2014 Feb 21;(2):CD010410. doi: 10.1002/14651858.CD010410.pub2. Update in: *Cochrane Database Syst Rev*. 2018 Apr 01;4:CD010410. PMID: 24558033.
4. Smith JP, Bingaman SI, Ruggiero F, Mauger DT, Mukherjee A, McGovern CO, Zagon IS. Therapy with the opioid antagonist naltrexone promotes mucosal healing in active Crohn's disease: a randomized placebo-controlled trial. *Dig Dis Sci*. 2011 Jul;56(7):2088-97. doi: 10.1007/s10620-011-1653-7. Epub 2011 Mar 8. PMID: 21380937; PMCID: PMC3381945.
5. Holman CM, Minssen T, Solovy EM. Patentability standards for follow on pharmaceutical innovation. *Biotechnology Law Report* 2018; 37:131-161.

Disclosures

No

Tables / Images