Naltrexone Therapy for Irritable Bowel Syndrome and Small Intestinal Bacterial Overgrowth

The body has narcotic (opioid) nerves in the brain and the gastrointestinal tract – the nerve endings have receptors for opioids that are prescribed and those that occur naturally (endorphins). Naltrexone is an “anti-narcotic” medication. At high doses (50 – 100 mg) this medication is prescribed to prevent narcotic addiction. When prescribed at low doses (2.5 – 4.5 mg) it is called low dose naltrexone (LDN) and has different effects and uses. At the low dose it decreases inflammation by increasing the body’s production of endorphins.

Irritable bowel syndrome may have components of inflammation in the lining of the intestine. This has been shown after various infections (post-infectious irritable bowel syndrome) and in irritable bowel syndrome associated with small intestinal bacterial overgrowth (SIBO). The main reason to use it in SIBO is to reduce the damage from the bacteria but there may be an effect on the small intestinal motility.

Neuropeptides may play a role in irritable bowel syndrome and these molecules (e.g., enkephalins and endorphins) are present in the gastrointestinal tract and these modulate immune responses. Up-regulation of met-enkephelin (opioid growth factor - OGF) and opioid receptors can be induced by a rebound effect from administration of the short-acting, low dose naltrexone. Naltrexone displaces endogenous endorphins bound to the OGF receptor. Affected cells become deficient in OGF which results in a rebound in receptor production. Receptor sensitivity is increased to capture more OGF and production of OGF is also increased to compensate for the perceived shortage of this molecule. Higher levels of endogenous opioids and receptors inhibit cell proliferation which suppresses B and T lymphocyte responses. Naltrexone acts to reverse a mouse colitis model by decreasing the pro-inflammatory interleukins 6 and 12.

Our practice has prescribed LDN since 2005 and found many patients who have seen clinical benefit. There are potential side effects from taking the medication – mostly insomnia and vivid dreams.

Clinical studies:

Irritable bowel syndrome:


Preclinical studies have shown that a very low dose of naltrexone hydrochloride (NTX), an opiate antagonist, can block excitatory opioid receptors without affecting inhibitory opioid receptors, resulting in analgesic potency without side
effects. The present study assessed the efficacy and safety of PTI-901 (low-dose NTX) treatment in Irritable bowel syndrome (IBS) patients. Forty-two IBS patients participated in an open-label study. Participants received 0.5 mg PTI-901/day for 4 weeks and were evaluated during baseline, during treatment, and at 4-week follow-up. Patients recorded degree of abdominal pain, stool urgency, consistency, and frequency. Primary outcomes were number of pain-free days and overall symptom relief, evaluated by a global assessment score. Data were analyzed per protocol. Global assessment improved in 76% of 42 patients. During treatment, the mean weekly number of pain-free days increased from 0.5+/−1 to 1.25+/−2.14 (P=0.011). There were no significant adverse reactions. PTI-901 improves pain and overall feeling, and is well tolerated by IBS patients. A large, randomized, double-blind, placebo-controlled study is justified.

Motility effects:


The gut is a neurological organ, which implies that many neuroactive drugs such as opioid analgesics can seriously disturb gastrointestinal function, because many of the transmitters and transmitter receptors present in the brain are also found in the enteric nervous system. One of the most common manifestations of opioid-induced bowel dysfunction is constipation which results from blockade of peristalsis and intestinal fluid secretion. The discovery of opioid receptor antagonists with a peripherally restricted site of action, such as N-methylnaltrexone and alvimopan, makes it possible to normalize bowel function in opiate-treated patients without compromising central opioid analgesia. There is emerging evidence that opioid receptor antagonists may also have prokinetic actions, reversing pathological states of gastrointestinal hypomotility that are due to overactivity of the enteric opioid system.

Cautionary warnings

1. Because LDN blocks opioid receptors throughout the body for three or four hours, people using medicine that is an opioid agonist, i.e. narcotic medication — such as Ultram (tramadol), morphine, Percocet, Duragesic patch or codeine-containing medication — should not take LDN until such medicine is completely out of one’s system. Patients who have become dependant on daily use of narcotic-containing pain medication may require 10 days to 2 weeks of slowly weaning off of such drugs entirely (while first substituting full doses of non-narcotic pain medications) before being able to begin LDN safely.

2. LDN should not be taken during pregnancy until research into that question is completed.
3. Those patients who are taking thyroid hormone replacement for a diagnosis of Hashimoto’s thyroiditis with hypothyroidism ought to begin LDN at the lowest range (1.5mg for an adult). Be aware that LDN may lead to a prompt decrease in the autoimmune disorder, which then may require a rapid reduction in the dose of thyroid hormone replacement in order to avoid symptoms of hyperthyroidism.

4. Full-dose naltrexone (50mg) carries a cautionary warning against its use in those with liver disease. This warning was placed because of adverse liver effects that were found in experiments involving 300mg daily. The 50mg dose does not apparently produce impairment of liver function nor, of course, do the much smaller 3mg and 4.5mg doses.

5. People who have received organ transplants and who therefore are taking immunosuppressive medication on a permanent basis are cautioned against the use of LDN because it may act to counter the effect of those medications.

FDA approval status

Naltrexone itself is an FDA-approved drug, but the varied uses of LDN still await application to the FDA.

The FDA approved naltrexone at the 50mg dosage in 1984. LDN (in the 3mg or 4.5mg dosage) has not yet been submitted for approval because the prospective clinical trials that are required for FDA approval need to be funded at the cost of many millions of dollars. Physicians understand that appropriate off-label use of an already FDA-approved medication such as naltrexone is ethical and legal. Because naltrexone itself has already passed animal toxicity studies, one could expect that once testing is able to begin, LDN could complete additional clinical trials in humans and receive FDA approval for one or more uses within two to four years.

More information about naltrexone: www.LDNscience.org