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Thank you for entrusting in the compounding services at Madison Medical Compounding Pharmacy to help meet the unique medication needs of your patients. We are excited to share our monthly newsletter with you and look forward to working with you. Please don't hesitate to let us know how we can assist you and your practice.

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Low Dose Naltrexone: Potential Benefits in Patients with Cancer

Naltrexone is an opioid antagonist that inhibits cell proliferation in vivo when administered in low doses, i.e., as Low Dose Naltrexone (LDN). LDN can reduce tumor growth by interfering with cell signaling and by modifying the immune system. LDN in oral dosages from 1.5-4.5mg/day has immunomodulatory and antitumor effects. Tumorigenic events appear to be dictated by the duration of opioid receptor blockade. McLaughlin and Zagon[1] observed through preclinical studies that the duration of opioid receptor blockade is responsible for LDN's effect. The intermittent blocking (i.e., 4–6 hours/day) of opioid growth factor receptor (OGFr) by LDN results in an upregulation of endogenous opioid growth factor (OGF), chemically called [Met5]-enkephalin. This produces an antitumor effect by impairing cancer cell proliferation, blocking tumor mitosis, and preventing uncontrolled proliferation. NOTE: At standard doses of naltrexone such as 50-100mg used to treat addiction, naltrexone has produced the opposite effect: it invokes a continuous receptor blockade of the OGF-OGFr axis that results in enhanced cell proliferation and cancer progression.

LDN's effect on the OGF-OGFr axis has been shown to slow cell proliferation in multiple human cancer lines, including breast, soft tissue, gastrointestinal, brain, and liver cell cultures, without interfering with apoptosis. LDN alters the growth of pancreatic, colorectal, and squamous cells by blocking OGFr, reduces tumor growth, interferes with cell signaling, and regulates the immune system function. LDN shows promising results for people with primary cancer of the bladder, liver, lung, and lymph nodes.

Several studies, investigating additive effects of OGF and standard chemotherapy, have demonstrated enhanced efficacy, as well as decreased toxicity, when OGF is combined with paclitaxel (taxol), cisplatin, or gemcitabine. In this sense, LDN shows promising results for people with primary cancer of the bladder, breast, liver, lung, lymph nodes, colon, and rectum. LDN has an antitumor effect. Lissoni et al.[2] reported the LDN and radiotherapy treatments of patients with malignant astrocytomas. The study demonstrates significant survival when compared to radiotherapy alone. Through treatment based on LDN and α-lipoic acid (ALA/NTX), patients with metastatic or non-metastatic pancreatic cancer showed prolonged survival, without adverse effects. LDN was also effective in inhibiting tumor growth when combined with D vitamin and panobinostat. Berkson et al. reported that the signs and symptoms of a B-cell lymphoma patient have been attenuated after using LDN solely. Individuals with pancreatic cancer treated with OGF had a longer survival time and no pronounced toxicity in other organs, when compared to those treated with chemotherapy.

The incidence of colorectal and cervical cancer is increasing annually worldwide. LDN has been reported to increase M1-type macrophages and activate the Bax/Bcl-2/caspase-3/PARP pathway, which may promote apoptosis and indicates the potential to inhibit colorectal cancer progression.[3] LDN has been shown to inhibit cervical cancer progression in mice models, and therefore LDN may be considered a potential treatment option for cervical cancer.[4]

Ovarian cancer is the leading cause of death from gynecological malignancies. Although initial therapeutic modalities are successful, 65% of these women relapse with only palliative treatments available thereafter. Many “studies have investigated the use of LDN alone or in combination with standard therapies in ovarian cancer and renal carcinomas with promising results. Donahue, McLaughlin, and Zagon[5] [of the Pennsylvania State University College of Medicine] observed that the combination of LDN and cisplatin in ovarian tumors enhanced the inhibition of tumorigenesis, depressed DNA synthesis, and reduced angiogenesis. Additionally, LDN seemed to reduce adverse events [e.g. weight loss] associated with cisplatin therapy. Another study confirmed that LDN upregulates OGF and OGFr, inhibiting tumorigenesis and cancer proliferation[6]… Evidence seems to support LDN as an adjunct to current anticancer regimens, both by enhancing the drugs' anti-tumorigenesis effects and by decreasing the severity of side effects related to chemotherapy regimens.”[7]

“A case study by Miskoff and Chaudhr[8] [of Jersey Shore University Medical Center] evaluated LDN in a 50-year-old male with prolonged survival and a history of prostate and lung cancer after a resection of adenocarcinoma in the right upper lobe of the lung. The patient began chemo-radiotherapy with cisplatin and pemetrexed post-surgery. Chemotherapy was stopped after the second treatment session due to intolerable side effects. After numerous additional health challenges, the patient was started on LDN 4.5 mg nightly. Imaging performed following the initiation of LDN has been unremarkable. At the time of publication by study authors, this patient had been on LDN for almost 4 years. More research is needed to assess the clinical efficacy of the use of LDN in these patients.”[7]

LDN is not commercially available but can be compounded as a prescription medication by our pharmacy.

We are not suggesting that Low Dose Naltrexone (LDN) be used to replace current standards of treatment for cancer, but rather, that LDN may be considered as adjuvant therapy due to its low cost and minimal adverse effects.

References:
1 Biochem Pharmacol 2015; 97(3): 236-46.
2 Curr Drug Res Rev. 2021 Jan 26.
3 Int Immunopharmacol. 2020 Jun; 83:106388.
4 Transl Oncol. 2021 Apr; 14(4):101028.
5 Exp Biol Med (Maywood) 2011; 236(7):883-895.
6 Exp Biol Med (Maywood) 2013; 238(5):579-587.
7 Advanced Therapeutics in Pain Medicine. Sahar Swidan and Matthew Bennett. First edition published 2021: 282-283.
8 Cureus. 2018 Jul 5; 10(7):e2924.

Our compounding pharmacy can customize medications to help solve many problems experienced by patients with cancer or chronic illness.

- Customized doses for patients with renal or hepatic failure.
- Change in route of administration, such as to transdermal or rectal preparations, for patients who are unable to swallow or take oral medications, and who don't want to have regular injections.
- Topical medications to promote wound healing.
- Medications to help with symptoms such as shortness of breath, excessive salivation, dry mouth, and nausea and vomiting
- Customized therapy to treat the causes of chronic pain.

We work together with patients and their health care providers to meet specific needs that have not responded to commercially available drugs. Compounded medications are often used to treat common conditions such as ulcers/wounds, pain and dyspnea, intractable cough, nausea and vomiting, and depression.

Your questions are welcome.