The Role of Low Dose Naltrexone (LDN) in Cancer Treatment

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Despite the advances in management of many serious diseases over the last decade, the main modality of cancer treatment is still chemotherapy. Chemo is often a harsh treatment associated with poor quality of life. Non-toxic "targeted" therapies are emerging (drugs like Tarceva for lung cancer or Herceptin for breast cancer), but are not yet available or approved for most types of cancer. It's not surprising to note that an increasing number of patients are looking for alternative gentler treatment regimens.

Although it is not a replacement for proven cancer therapies, one of the drugs that may be considered is naltrexone. Naltrexone is a synthetic drug which blocks the effects of medications like morphine, codeine, heroin, methadone, fentanyl and oxycodone (the class of drugs called *opiates*[1]). It also blocks the effects of natural opiates called *endorphins* which are made within the body. One of the functions of endorphins is generating pleasure sensations in the brain. For that reason, naltrexone is approved for treatment of alcoholism – it reduces the pleasure resulting from endorphin release after drinking alcohol.

Dr. Bernard Bihari is an American neurologist who discovered that naltrexone may have a role in cancer treatment if used in low doses[2]. Instead of completely blocking the effects of opiates in the body, low doses of naltrexone provide a partial block for a short time. This fools the body into increasing endorphin production, which can have an anti-cancer effect and an immune modulating effect. One of the endorphins shown to have significant anti-cancer activity is Opioid Growth Factor (OGF) or met-enkephalin. Extensively research by Zagon and his group has shown OGF can improve survival in pancreatic cancer[3] and can enhance the effects of chemo in squamous cell carcinoma of the head and neck[4].

Existing research on LDN use in cancer is very limited. LDN is currently being used mainly as a result of findings reported by Dr. Bihari from his own practice and indirect scientific evidence. A detailed review of the extensive literature on the subject of opiates and cell growth / immune modulation was conducted by Tegeder and Geisslinger (2004)[5]. They found that the scientific evidence supports the theory that endorphin release inhibits exaggerated inflammation and boosts immune defense (by natural killer cells) against cancer and invading microorganisms. There is also new evidence that LDN can significantly improve quality of life in blood cancers[6]. Because of the reduction of inflammation by LDN, it is being used increasingly for "off-label" treatment of immune diseases like MS and inflammatory bowel disease.

Based on the supporting scientific literature and the work of Dr. Bihari, we began using LDN at Medicor Cancer Centres in 2007 for patients who had exhausted standard proven treatment options. To date we have treated about 50 cancer patients with LDN by itself and in combination with other drugs. Our experience indicates that LDN can be a useful part of a cancer treatment program in properly selected patients. Due to the small number of patients treated, we have not yet observed results comparable to Dr. Bihari's (he has treated over 450 cancer patients).

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Continued

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One of the issues with LDN is that cancer patients frequently require opiate medication for pain control, and LDN will interfere with these medications resulting in uncontrolled pain. LDN may be considered for patients who do not use opiates or who infrequently use shot-acting opiates. For patients taking any form of controlled-release opiate, opiate patch, pain pump or methadone, LDN should not be used. We are using direct treatment with OGF in this group of patients. The down side is that OGF requires daily subcutaneous injection, and is also significantly more expensive than LDN.

Our clinic is also using LDN in combination with chemotherapy in selected patients. Due to the benefits of LDN mentioned above, it is possible that LDN can enhance the effects of chemotherapy, and improve immune system function during this immune-suppressing treatment. This may translate into reduced infection risk and improved survival. In the near future, we are planning to offer combination therapy with LDN or OGF and an immune modulating drug called [1] miquimod which has now been shown to increase OGF receptors, potentially boosting the anti-cancer effect of LDN[7]. These ideas have yet to be proven by clinical trials, and in fact may never be proven since naltrexone is now off patent and therefore a financially unattractive target for research funding.

Since LDN is cost effective and safe[8], we feel its use as a cancer treatment and as a supplement to conventional cancer treatment warrants careful consideration. Patients interested in using LDN should consult their own physician and provide references, since most physicians are unfamiliar with LDN. Patients may also consult with one of our physicians. LDN requires a doctor's prescription, and is not routinely available at most pharmacies[9] since it requires specialized preparation by a qualified compounding pharmacist.

For further information : www.medicorcancer.com/promisingtherapies.html and www.ldninfo.org.

1 Opiates are chemicals that are derived from, or related to the natural substance opium which is found in Papaver somniferum (the poppy plant). The main active ingredient in opium is morphine.
2 See www.ldninfo.org
3 Anti-Cancer Drugs15:203-209 Lippincott Williams & Wilkins
4 International journal of oncology 2005;26(3):809-16 "Enhanced growth inhibition of squamous cell carcinoma of the head and neck by combination therapy of paclitaxel and opioid growth factor.
5 Pharmacol Rev 56:351–369, 2004 "Opioids As Modulators of Cell Death and Survival Unraveling Mechanisms and Revealing New Indications"
6 American Journal of Applied Sciences 5 (7): 872-875, 2008 "Quality of Life in Hematologic Cancer Patients: A Randomized Clinical Trial of Low Dose Naltrexone Versus Placebo"
7 Exp Biol Med (Maywood), 2008 Aug;233(8):968-79. **"**Imiquimod upregulates the opioid growth factor receptor to inhibit cell proliferation independent of immune function."
8 LDN side effects are essentially limited to insomnia and vivid dreams; liver toxicity with doses < 5mg per day is highly unlikely; low potential for allergic reaction exists
9 Standard dose naltrexone is readily available as a 50mg tablet; low dose naltrexone generally ranges from 3 - 4.5mg per day; Medicor has arrangements with a compounding pharmacy in Toronto to produce high quality LDN and www.ldninfo.org has compiled a list pharmacies in USA where high quality LDN capsules are available.

Conflict of Interest Declaration: Medicor Cancer Centres profits from the provision of cancer medications and treatments, and is owned by a family member of Dr. Khan.