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The Role of L-Carnitine in the Treatment of Malignant Neoplasms

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Introduction: L-carnitine is a metabolite of C_4 oil LC, which is involved in the transfer of palm-n-LC through the inner membrane into the mitochondrial matrix and is a substrate for the formation of ATP molecules. Carnitine is a trimethylated amino acid naturally synthesized in the liver, brain and kidneys from protein lysine and methionine. Several factors, such as sex hormones and glucagon, can influence the distribution and level of carnitine in tissues. It is generally believed that carnitine transports long-chain acyl groups from fatty acids into the mitochondrial matrix, where they can be broken down through β-oxidation to acetyl-CoA to obtain usable energy via the citric acid cycle. Therefore LC is required for the generation of metabolic energy in living cells.

As we know, malignant neoplasms have specific influence on the organism in general and on DNA in particular. So, in vitro studies in human tumor cell lines have shown a positive effect of L-Carnitine regarding the inhibition of apoptosis and DNA-damage. Using of L-carnitine in patients with cancer improves the metabolism of fatty acids in mitochondria, restores normal mitochondrial function and, thus, improves the general condition and quality of patients' life. On the other hand, L-Carnitine is well known for its potential to modulate the inflammatory response mechanisms, which is known to play the predominant role in the generation of cancer cachexia. Increasing the effectiveness of antitumor therapy who received L-carnitine compared with patients who don't take it, served as a prerequisite for studying possible antitumor mechanisms of L-carnitine's action.

In this article presents epidemiological, preclinical and clinical studies information of the antitumor efficacy of L-carnitine.

The mechanism of L-carnitine's action:

Carnitine is synthesized from the amino acids lysine and methionine. The rate limiting step in carnitine biosynthesis is the availability of trimethyllysine at the intramitochondrial site of trimethyllysine hydroxylase activity. L-carnitine is absorbed in the intestine by a combination of active transport and passive diffusion. In the absence of L-carnitine, the inner membrane of the mitochondria becomes impermeable to fatty acids, which entails a chain of various metabolic disorders in the human body.

This medicine has many effects on the organism. One of them is a modulating effect on the function of acetylcholine excitatory neurotransmitter, glutamate excitatory amino acid, insulin growth factor-1 (IGF-1) and nitric oxide (NO). Also proved, that L-carnitine may have a dual protective effect by enhancing the energy dynamics of the cell and inhibiting cell membrane hyper excitability, which make it an ideal nutrient for cancer prevention and treatment. Carnitine may also mimic some of the biological activities of glucocorticoids, particularly immunomodulation, via suppressing TNF-α and IL-12 release from monocytes. L-carnitine as adjuvant therapy in cisplatin-treated cancer patients proved a beneficial effect in reducing the cisplatin-induced organ toxicity.

It is possible that, the extremely lipophilic nature of carnitine may be responsible for the decrease in EGF binding. Carnitine may insert in the cell membrane and/or interact with one of the many cellular enzymes having lipid substrates or cofactors. In addition, carnitine may interact directly with the EGFR. L-carnitine, via its free radical scavenging and antioxidant properties, may inhibit ROS-mediated EGFR phosphorylation. It has been found that palmitoyl-carnitine can inhibit the activity of heart and brain protein kinase C in a competitive manner and subsequent phosphorylation of the EGFR.

Studies on the role of L-carnitine for the prevention and treatment of cancer:

The efficacy of using L-carnitine for the prevention and treatment of malignant neoplasms has been proven in epidemiological, experimental and clinical studies.

Based on the data provided by Rania M. Khalil and co-authors (2013), we can prove the positive effect of this medicine on the course and outcome of breast cancer. The study showed that patients who received Tamoxifen with L-carnitine had significant decrease of Her-2 / neu and IGF-1 level ($P < 0.05$) in the serum compared with patients who received only Tamoxifen. Using of L-carnitine led to significant decrease Her-2 / neu level in the serum ($P < 0.05$) compared to each of the control patients namely, 59.5%. The effect of tamoxifen on IGF-1 ($P < 0.05$) -decrease its level by 5.4%.

However, it has been proved that using of L-carnitine in the treatment of ER+ breast cancer does not significantly reduce the level of estradiol, but leads to decrease both tumor markers CEA and CA15.3 ($P < 0.05$,% decrease by 80.9% and 67, 8%, respectively).

Matthias Kraft and co-authors (2012) have shown that using L-carnitine reduces chemotherapy related side effects of treatment of advanced pancreatic cancer.

Waldner et al. (2006) examined the effects of L-carnitine with a view to reducing cardiotoxicity of DOX-containing chemotherapy in 20 patients with Non-Hodgkin lymphoma. Patients were scheduled to receive 3g L-carnitine before each chemotherapy cycle, followed by 1g L-carnitine/day during the following 21 days. Carnitine-treated patients showed a rise in plasma carnitine which led to an increase of relative mRNA levels from CPT 1 and OCTN2. They concluded that biochemical and molecular analyses indicated a stimulation of oxidative metabolism in white blood cells through carnitine uptake.

Hongbiao Huang and co-authors (2012) compared the effects of LC on normal tissue and cancer growth in vivo. Normal Balb/c mice or Balb/c nude mice inoculated with HepG2 cancer cells were i.p. injected with a tolerated dose of the medicine. It was found that LC treatment inhibited more than 70% of cancer growth, while the same treatment decreased less than 20% of the normal organ development and body weight. Also they proved that LC treatment increased protein (histone) acetylation in cultured cells.

Biography:

Dr. Mohammad Hojouj presently is an Assistant Professor, Oncologist, research scientist, sub-investigator in clinical trials, Associate professor at the Oncology and Medical Radiology Department, (More than 340 trials & Principal Investigator Bondarenko Igor) from the Municipal Institution “Dnipropetrovsk City Multi-field Clinical Hospital #4”, Chemotherapy Department, State Institution “Dnipropetrovsk Medical Academy at the Ministry of Health of Ukraine”, Ukraine. He was a speaker at German Pharmaceutical Phytoneering Company “Bionorica”/Ukrainian representative office. In 2014 was a Specialist-oncologist from Territorial oncological hospital/Dnepropetrovsk, Ukraine.

He obtained his Doctor Philosophy, Ph.D. from Special Academic Council of Dnepropetrovsk state Medical Academy, Master of Medicine (oncology) degree, Medical Specialist of Oncology and Medical Doctor from Dnepropetrovsk State Medical Academy/Dnepropetrovsk, Ukraine

He is in association & a member in various organizations - ASCO; ESMO; ESGO; NCCN, EDS, certificate NCCN (September, 2015); AAPU; The Arab Medical Union in Europe (ARABMED) (Certificate ARAB MED, November, 2015); The Arab Medical Union in UKRAINE (AMUU), “Association of Arabic doctors in Ukraine”. He is a certified doctor-oncologist. And participated at many regional research and practical conferences, obtained maximum CME credits, 12 certificates from NCCN-national comprehensive cancer network to confirm the results of professional skills improvement. He is a Medical license holder.

He delivered some lectures about the prevention of breast and skin cancer on Ukrainian television and holds some publications. As a doctor-oncologist he took part in organization of cancer care to the population, made diagnosis and treatment of main localization tumors such as: Breast cancer (I, II, III, IV), Lung cancer, Ovarian cancer, Bone cancer, Lymphoma cancer, Kidneys cancer, Colorectal cancer, Skin cancer and minimally invasive skin operations, Malignant acrospiroma, Head and neck cancer, Hematology. He worked as assistant at tumour’s surgical operations & performed minor surgeries.