Biomedical Data Mining

Extended Abstract

L-Carnitine in neoadjuvant systemic treatment in breast cancer patients with metabolic syndrome

Hojouj Mohammad I M, I N Bondarenko, V F Zavizion and Hojouj Tamara

Abstract

The frequency of breast cancer on the planet as a rule and in Ukraine in particular is developing. In 2017, in Ukraine the rate arrived at 16% of female population. As per the MOH (Ministry of Health) in Ukraine 26% of the female populace for 2017 were overweight or corpulent. There is a solid organic reason for a relationship of stoutness with helpless bosom malignancy results. Weight - an ongoing metabolic character, which is the aftereffect of the cooperation of the endogenous elements, natural conditions and way of life. Endogenous elements could be viewed as an infringement of the hereditary and hormonal balance. The outer conditions incorporate sporadic mood sustenance, utilization of inadequate items. Point: The point of this forthcoming randomized preliminary was to explore the impact of L-Carnitine on the viability of neoadjuvant fundamental anticancer treatment (NAST) in bosom disease patients with metabolic condition (MS). Approach: The examination included 64 patients (matured 44 to 78 years) who got neoadjuvant fundamental therapy for stage II-III bosom malignant growth, in Dnipropetrovsk Medical Academy at Municipal Institution "Dnipropetrovsk City Multi-field Clinical Hospital No 4", Dnepropetrovsk State Medical Academy from 2016-2017. All patients were assessed by the accompanying information: phase of the sickness, age and BMI at the hour of finding, the size, histological type and metastases, IHC (Immunohistochemistry) type, MRI (Magnetic Resonance Im-maturing) strategies, bioelectrical impedance investigation, Ultrasounds examination. All patients were diagnosed MS as indicated by the IDF rules and were analyzed by 2 gatherings; bunch 1 included 43 patients with MS and BC (Breast Cancer) who didn't take L-Carnitine during NAST, and gathering 2 - 21 metabolic condition patients with bosom malignancy taking L-Carnitine with NAST. Clinical and obsessive reaction rates were thought about between the two gatherings utilizing the fourfold table investigation strategy. Results: Clinical complete reaction (CR) was distinguished in 6% patients from bunch 1 and in 28% patients from bunch 2. Clinical advantage reaction of treatment (CR + PR) was accomplished in 68% of patients treated with L-Carnitine contrasted with 25% patients from bunch 1. In 53% of patients who were not taking metformin noticed stabile sickness (SD). The pace of pathological complete reaction (PCR) was 30% in the L-Carnitine gathering and 6% in the non metformin gathering. Ends: Thus utilization of L-Carnitine in neoadjuvant foundational anticancer treatment bosom cancer patients with metabolic disorder has a higher clinical and neurotic CR rate and clinical advantage reaction of therapy than BC understanding with MS not getting L-Carnitine. This examination showed the capability of L-Carnitine as an antitumor specialist in bosom malignancy patients with metabolic condition.

Introduction

The rate of cancer growth on the planet all in all and in Ukraine specifically is developing. In 2017, in Ukraine the rate arrived at 16% of female populace, for which, the bosom disease positioned first in construction of oncological occurrence among ladies. In breaking down the information of the National Cancer Registry of Ukraine, it ought to be noticed, that in examination with long term, the predominance pace of bosom malignant growth in 2016has expanded by 5, 1%, that shows significance of progress demonstrative methodology

Hojouj Mohammad I M
Dnipropetrovsk Medical Academy of Health Ministry of Ukraine, Ukraine, E-mail: Hojouj@yahoo.com

and strategies for therapy it. Contemplating the logical writing regarding this matter, we saw that there is a solid organic connection among heftiness and a helpless result of bosom malignant growth. Furthermore, having investigated the date of Ministry of Health in Ukraine it very well may be closed, that about 26% of ladies in long term had overweight or stoutness.

Heftiness has an ongoing metabolic character, which is the aftereffect of the association of the endogenous elements, ecological conditions and way of life. Endogenous elements could be viewed as an infringement of the hereditary and hormonal equilibrium. The outside conditions and kind of way of life incorporate unpredictable cadence nourishment, utilization of unsatisfactory items and inactive way of life. Heftiness is the principal hazard factor for metabolic condition, diabetes type II, cardiovascular infection and a few types of malignant growth, including bosom disease. Since overweight is a danger factor for bosom malignant growth, there is motivation to accept that among patients with bosom disease the level of large ladies is higher than in the populace. The danger of bosom disease in postmenopausal ladies by 30%, it is more than in premenopausal, ladies with stoutness half. Moreover it was demonstrated that stoutness is related with helpless visualization in patients with bosom disease, paying little mind to menopausal status, and viability of fundamental medicine bosom malignancy in patients that have over weight is lower than in patients with typical BMI.

In spite of the fact that stoutness is related with a helpless result in ladies with bosom malignant growth, it is hazy how weight reduction after analysis will change its course and results. As of late, correlative and elective medication (CAM) is broadly acknowledged among patients with bosom disease, which may give a few gainful impacts including decrease of treatment related harmfulness, improvement of malignancy related manifestations, encouraging of the safe framework, and even direct anticancer impacts. L-carnitine is a metabolite of C4 oil LC, which is associated with the exchange of palm-n-LC through the internal layer into the mitochondrial network and is a substrate for the arrangement of ATP atoms. Carnitine is a trim ethylated amino corrosive normally incorporated in the liver, mind and kidneys from protein lysine and methionine. A few variables, for example, sex chemicals and glucagon, can impact the conveyance and level of carnitine in tissues.

Without L-carnitine, the internal layer of the mitochondria gets impermeable to unsaturated fats, which involves a chain of different metabolic problems in the human body. Carnitine has a regulating impact on the capacity of acetylcholine excitatory synapse, glutamate excitatory amino corrosive, insulin development factor-1 (IGF-1) and nitric oxide (NO). Additionally demonstrated, that L-carnitine may have a double defensive impact by improving the energy elements of the cell and hindering cell film hyper sensitivity, which make it an ideal supplement for malignancy avoidance and treatment. Considering the prior, the investigation of the impact of the weight list on the adequacy of fundamental therapy of bosom disease is an earnest logical issue and a promising field of examination. This article presents the data of epidemiological and clinical investigations of the impact of the weight file on the adequacy of bosom malignancy treatment by individualizing remedial estimates considering the attributes of patient's digestion.

Epidemiological and Clinical Studies

DSM Chan and co-authors reported that women who have BMI> 30 course and outcomes of breast cancer are significantly worse than women with BMI <30. They proved, that women with BMI> 30 have the overall relative risk of total mortality 1.41, women with BMI of 25> 30 - 1.07. At the same time, for every 5 kg / m2 of the increase BMI, the risk of both total mortality and mortality from breast cancer increased, namely by 18% and 14%, respectively M. Protani and co-authors have shown that women with breast cancer, who are

suffering in obesity, have lower survival rate than women with breast cancer without obesity. Recently published data of randomized clinical researches by ML Neuhouser and coauthors demonstrated, that for women> 50 years old, with 2 and 3 stages of obesity (BMI> 35) is typically the development of GR+ breast cancer.

Similarly, B. Pajares et al. who found significantly worse results for patients with BMI >35 compared with patients with BMI <25, stated that the magnitude of the effect depended on the cancer subtype (estrogen receptor (ER) / progesterone (PR) positive and HER2 negative, HER2 positive, triple negative). An analysis of the pooled data of the three adjuvant studies of the Eastern Cooperative Cancer Group showed significantly worse results for patients with obesity (BMI > 30) than for patients with normal BMI with a hormonal receptor-positive disease. And it was noted absence of negative effect of obesity on survival in patients with other breast cancer subtypes. C Fontanella et al. studied the effect of BMI on different molecular subtypes of breast cancer and concluded that in women with ER / PR-positive and HER2-negative breast cancer, as well as with TNBC, the risk of death is significantly higher than in other subtypes of cancer.

It is proved that even the highest BMI figures are not a risk factor for death for patients with luminal A-like subtype of breast cancer. The reason for this is that fatty tissue produces an excessive amount of estrogen, a high level of which is associated with an increased risk of developing breast, endometrial, ovarian and some other cancers. It has also been proven that the level of adipokine, that promotes cell proliferation, increases in the blood with increasing of level of fat in organism. And adiponectin, which people with obesity have less than people with normal BMI, can have anti proliferative effects. Such data can serve as evidence of the effect of BMI on the course and outcome of breast cancer. Yet another proof of influence developing metabolic syndrome on the course and outcome of breast cancer was proposed by R. Bhandari et al. They proved that that the presence of metabolic disorders (that is, the metabolic syndrome) is associated with an increased risk of breast cancer in adult women.

The above data led to the need to investigate medicines that contribute to fat burning, such as L-carnitine. Based on the data provided by Rania M. Khalil and co-authors, 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).

Using of L-carnitine in patients with breast cancer and obesity improves the metabolism of fatty acids in mitochondria, restores normal mitochondrial function and, thus, improves the general condition and quality of patients' life. Carnitine may alsomimic some of the biological activities of glucocorticoids, particularly immunomodulation, via suppressing TNF-a 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 EGFbinding. 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.

Experimental evidence is available showing that ROS may induce the light and independent phosphorylation of the EGFR activating Her-2/neu. Moreover, the expression of the receptor is induced in conditions of oxidative stress. 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. Although the tumor markers and IGF-1 showed no significant difference in TAM-treated patients before and after administration of L-CAR, there was a tendency to decline after L-CAR supplementation. The results of the above studies became a prerequisite for

Hojouj Mohammad I M
Dnipropetrovsk Medical Academy of Health Ministry of Ukraine, Ukraine, E-mail: Hojouj@yahoo.com

conducting clinical studies aimed at establishing the role of L-carnitine in the treatment of breast cancer.
To date, the search in the online clinical research registration system ClinicalTrials.gov using key words L-carnitine + breast cancer has revealed several studies evaluating the efficacy and safety of L-carnitine in the treatment of breast cancer patients. Analyzing the obtained results, we can conclude that L-carnitine was the drug of choice for neuropathies, as a consequence of chemotherapy, in patients with breast cancer.

Conclusion

L-carnitine is widely used in clinical practice. However, recently this medicine causes growing interest among oncologists. In a number of studies, L-carnitine has proven itself as a medicine that capable, during the preoperative systemic antitumor therapy, to increase its effectiveness compared with standard neoadjuvant systemic antitumor therapy. And also, taking L-carnitine with neoadjuvant systemic antitumor therapy helps to increase the number of cases of complete morphological regression (V degree of therapeutic pathomorphosis). To date, there are several clinical studies that are researching using L-carnitine in various malignant tumors, the results of which are the basis for further in-depth study of the effect of the medicine in the treatment of malignant neoplasms.

This work is partly presented at 11th European Biosimilars Congress, April 26-27, 2018 Rome, Italy