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Opinion Article

Breast Cancer 2018- The rationale for the effectiveness of systemic treatment of breast cancer depending on the body weight index

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DESCRIPTION

The prevalence of breast cancer (BMD) in the world in general and in Ukraine is steadily increasing. Epidemiological, experimental and clinical studies have shown that metabolic disturbances associated with body mass index (BMI)> 30 kg / m2 increase the risk of occurrence and worsen the clinical course of breast cancer. Thus, in patients with obesity, a decrease in the sensitivity of the tumor to systemic antitumor therapy, an increase in the frequency of postoperative complications and a decrease in the rates of general and non-recurrent survival.

The aim of the study was to improve the results of neoadjuvant systemic antitumor therapy in breast cancer patients with abdominal obesity (BMI greater than 30 kg / m2) by administering levocarnitine in combination with NSAT for the correction of metabolic disorders as the main pathogenetic part of obesity.

For the study used a retrospective study between 2010 and 2014 three hundred patients (prevalence of 12.4% which is 100 thousand. population in the Dnipropetrovsk region) with BMI> 30 kg / m2, morphologically verified diagnosis of different forms of breast cancer and all stages (I- IV). Subsequently, a group of comparisons with abdominal obesity BMI> 30kg / m2 with a definite molecular subtype of tumor, levels of expression of estrogen receptor ER, progesterone PgR, Her-2 / neu, Ki-67 proliferation index was formed. The observation group of patients with breast cancer and BMI> 30kg / m2 was formed in the period from 2014 to 2018 due to prospective observation of "case-control". Thus, the study involved 108 patients aged 32 to 76 years (mean age (58 ± 2). With nodal breast cancer II-III stage. As a result of randomization of all patients (n = 108) on breast cancer with BMI> 30 kg / m2, depending on the appointment of levocarnitine during NSAT, were divided into 2 groups: comparison and observation. In the comparison group, patients (n = 58) with BMI> 30 kg / m2 patients with breast cancer who did not receive levocarnitine during NSPT, and in the, observation group - patients (n = 50) on breast cancer with BMI> 30 kg / m2 who received levocarnitine during NIST. For the first time, on the basis of a comprehensive analysis of the results, it was established that the appointment of levocarnitine in patients with breast cancer with BMI> 30 kg / m2 contributes to increasing the clinical and morphological efficacy of neoadjuvant systemic antitumor therapy (NSAT). It was found that in patients with breast cancer with BMI> 30 kg / m2, who were prescribed levocarnitine, organosurgery surgical interventions were significantly more frequent. The algorithm of diagnosis and treatment of breast cancer in patients with obesity has been developed and scientifically substantiated. A theoretical generalization of modern scientific data on the influence of metabolic disorders that are characteristic of obesity, on carcinogenesis of breast cancer is carried out. A complex (integrated) scheme of mechanisms of influence of molecular disorders associated with obesity, on carcinogenesis of breast cancer is developed. It is determined that the leading role in carcinogenesis is played by: abdominal obesity, hyperglycemia, dyslipidemia and chronic subclinical inflammation. The carcinogenic effect of these factors is realized due to the ability of the adipose tissue of the mammary glands to increase the local concentration of estrogen by peripheral aromatization of androgens, the mitogenic effect of metabolic disorders on the epithelium of the mammary gland. It was established that in patients with breast cancer with BMI greater than 30 kg / m2 receiving levocarnitine, a statistically significant increase in the number of cases of clinically complete regression of tumors was observed at 12.8% (5.2% vs. 18.0%; p <0.05) and a partial regression of 13.1% (6.9% vs. 20.0%, p <0.05). Lowering the frequency of breast cancer progressing on the background neoadjuvant systemic anticancer therapy in patients with a group of observations by 44.3% compared with women with the comparison group (16.0 vs. 60.3%, p <0.05). According to the results of analysis of the parameters of cellular, humoral immunity (CD3, CD4, CD8, IgG, IgM, IgA) and proinflammatory cytokines (IL-6, TNF), there was a decrease in the number of patients with breast cancer with BMI greater than 30 kg / m2 in (NSAT) Levocarnitine with regression rates was used for juvenile systemic anticancer therapy, namely: for CD3, which was 41.4%; for CD4, which was 50.0%; for CD8, which was 23.5%; for IgG, which was 40.4%; for IgM, which equaled 48.7%; for IgA, which was 44.4%; for IL-6, which was 51.1%; for CD3, which was 50.0%, respectively. It was found that the appointment of levocarnitine in patients with breast cancer with BMI greater than 30 kg / m2 during preoperative systemic antitumor therapy increases its efficacy compared with patients who received neoadjuvant systemic antitumor therapy. Registered increase in the incidence of clinically significant responses (CR + PR) for the treatment in 63.2% of patients in the observation group who were administered in the treatment Levocarnitine (28.0% vs. 12.1%, p <0.05) compared with a comparison group. Based on the research, it was proved that in the group of patients with BMI greater than 30 kg / m2 receiving

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levocarnitine, there was a statistically significant increase in the frequency of performing functionally justified organoleptic operations by 53.8% compared with the comparison group (27.1% vs. 10.9%; p <0.05). Also, the administration of levocarnitine during neoadjuvant systemic antitumor therapy increases the number of cases of complete morphological regression (V degree of curative pathomorphosis) by 77.8% in the observation group compared to patients from the comparison group (18.8% vs. 3.6%; p <0.05).

Found that neoadjuvant systemic anticancer therapy in breast cancer patients with a BMI over 30 kg / m2 does not affect the degree of differentiation and histological type of tumor and the expression of Her2 / neu (p> 0.05). After neoadjuvant systemic anticancer therapy, regardless of the purpose levocarnitine in decreasing residual tumor cell proliferation index (Ki-67) and increased incidence of Luminal A molecular type of breast cancer.

CONCLUSION

This may indicate that neoadjuvant systemic antitumor therapy leads to the death of the most aggressive tumor clones. It was investigated that the appointment of levocarnitine in patients with breast cancer with BMI greater than 30 kg / m2 does not affect the indicators of general and non-recurrent survival, with observation (18,1 ± 1,5) months. These data are in the basis for integrated assessment and in-depth understanding of the negative impact of abdominal obesity associated with impaired carbohydrate and fat metabolism in carcinogenesis and criteria can be aggressive course of breast cancer and adverse prognostic factors.