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THE QUALITY OF LIFE ROLE IN PATIENTS WITH LOCALLY ADVANCED BREAST CANCER IN THE COMPREHENSIVE EVALUATION OF THE COMPLEX NEOADJUVANT TREATMENT EFFICACY

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Abstract

In recent years, breast cancer has been the most common cancer and the most common cause of disability among women in developed countries.

Determining the role of the quality of life parameter of patients during complex neoadjuvant treatment with the use of polychemotherapy in systemic (SPCT), endolymphatic (ELPCT) and selective intraarterial (SIAPCT) variants in patients with locally advanced breast cancer M.

The study was conducted on the basis of materials from 526 cases of MR RMZ T4A-DN0-2M0. The total sample was divided into three subgroups by parameter of route of neoadjuvant polychemotherapy (PCT): first control group (22 patients) - SPCT; the second control group (27 patients) - ELPCT; study group (41 patients) - SIAPCT.

Clinical effect with qualitative changes of local status and transfer of patients to the category of those with resectable tumors appeared in 46% of women of the first control group after 6 courses of SPCT, in 59% of the second control group after 4 courses of ELPHT and in 90% of the studied group after 3 courses SIAPCT.

After 3 courses of PCT, statistically better results of the experimental group were obtained in the positive dynamics of quality of life index in the amplitude and chronometric complex logran study as a result of neoadjuvant SIAPCT compared with the first ($p<0.001$) and second ($p<0.05$) control groups.

On the social well-being scale, the control group showed the best dynamics ($p> 0.05$ in both comparisons) with a high evaluation of restitution of work and social status.

On the symptom scales in the third group, after each course of polychemotherapy, symptoms of nausea and loss of appetite were observed at a significantly lower intensity compared to both control groups within 15 - 25 points of the group ($p<0.05$ in both comparisons) and lasted 1 - 2 days less ($p<0.05$ in both comparisons).

Quality of life (QOL) research is a reliable, informative, and cost-effective method for assessing a patient's state of health at both group and individual levels. In cancer studies, QOL assessment is an important criterion for evaluating treatment effectiveness and is of prognostic value.

Key words: locally advanced breast cancer; systemic polychemotherapy; endolymphatic polychemotherapy; selective intra-arterial polychemotherapy; quality of life.

Introduction. Breast cancer (BC) is the most common cancer among women worldwide [1]. This is partly due to the increase in the number of breast cancer patients [2]. Statistics show that every year more than one million women worldwide find out about their diagnosis for the first time and more than half a million die from the disease [3]. On the other hand, individualized and specialized programs for complex treatment of breast cancer have led to an increase in the survival rate of these patients [4].

Diagnosis and living with BC is a very stressful experience that can adversely affect many aspects of human life and health and can have a long-term effect after treatment [5]. Along with an increase in the number of patients with breast cancer and an increase in survival due to advances in medical technology, accurate assessment of their quality of life (QOL) is crucial [6].

In addition to health, breast cancer affects the identity of women, and therefore the study of the quality of life of women with the disease is fundamentally important in the context of comprehensive examination to reproduce the full understanding of the problem on behalf of the patient, as well as to formulate tactics for complex treatment of physical, mental, social and cognitive disorders caused by disease and therapy [7, 8]. For this reason, quality of

life has become a common criterion for evaluating outcomes for cancer patients and an integral part of their management. By far, one of the most popular QOL oncology tools is the EORTC-C30-QLQ-C30 European Quality of Life Questionnaire [9, 10].

To answer the question to what extent the study of the quality of life of patients with breast cancer has altered our understanding or contributed to the improvement of the results of breast cancer treatment - it is necessary to study the relationship of subjective and objective treatment indices in dynamics in each specific research.

The aim of our study. Determination of the role of the quality of life parameter of patients during complex neoadjuvant treatment using polychemotherapy in systemic (SPCT), endolymphatic (ELPCT) and selective intraarterial (SIAPCT) variants in patients with locally advanced breast canceer (LABC).

Materials and methods

After standardization by target age and clinical parameters, the total sample was divided into three subgroups by the parameter of polychemotherapy (PCT) administration, which was used in the complex neoadjuvant treatment: first control group (89 patients) - systemic PCT; second control group (75 patients) - endolymphatic PCT; study group (362 patients) - selective intra-arterial PCT.

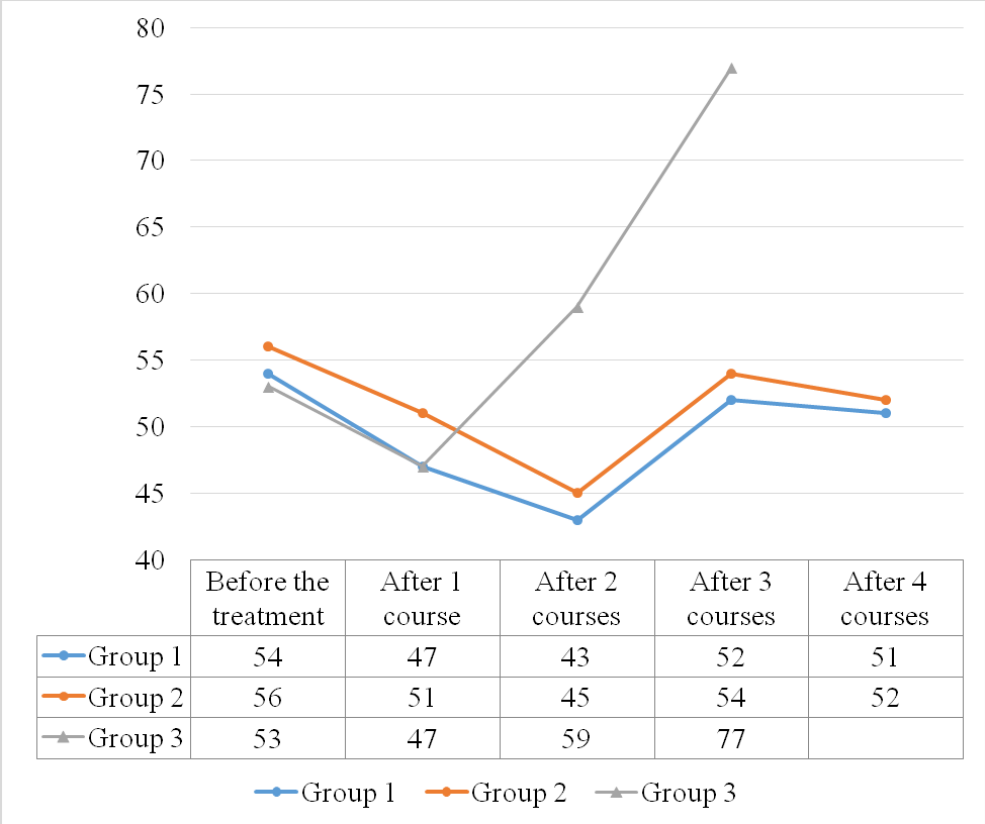
The study of patients' quality of life was conducted within the framework of the International Protocol of the European Organization for Research and Treatment of Cancer using the European Organization for the Research and Treatment of Cancer (EORTC QLQ-C30) questionnaire. Patients were interviewed within 1 week before PCT onset and 10-14 days after PCT.

At all stages of the statistical analysis, standard features of MS Excel were used to prepare the primary spreadsheets and group the features. The mean, (M), standard error (m), and median were calculated to to evaluate the quantitative indicators. Pearson's $\chi 2$ criterion was used to compare non-parametric indicators, and Mann-Whitney test was used for parametric values. To estimate the incremental changes in nonparametric indices within one group, the Mc-Nemar $\chi 2$ criterion was used, and the Wilcoxon test was used for parametric values. In all cases, the differences were considered statistically significant at a significance level of $p<0.05$.

Results

The general condition of patients at all stages is formed mainly due to the objective (presence of tumor neoplasm; intoxication syndrome; asthenic syndrome; local and systemic manifestations of tumor lysis; attachment of secondary infection of compromised tissues) and

subjective (psychological and emotional state, social maladaptation through cancer stigma and disability) factors. After QOL index analysis (Fig. 1) there were no statistically significant differences found according to Kolmogorov-Smirnov estimation: in the experimental group the average value was 53.0±7.4 points, in the first control – 54.0±8.2 points, in the second control – 56.0±4.1 points.



	Before the treatment	After 1 course	After 2 courses	After 3 courses	After 4 courses
Group 1	54	47	43	52	51
Group 2	56	51	45	54	52
Group 3	53	47	59	77	

Fig. 1. Quality of life (QOL) of patients before and after neoadjuvant polychemotherapy

After completion of the 1st course of chemotherapy, the QOL indicator had a negative trend in the first (decrease by 7% with a final result of 47±4.3 points), in the second (decrease by 5% with a final result of 51±3.1 points) and the third (decrease by 6% with a final result of 47±5.6 points) groups, maintaining proportional statistical discrepancy in results. Such dynamics of indicators are connected, first of all, with the advent of toxic effects of chemotherapy treatment, of which most patients were negatively informed by the media. On the other hand, there was also an insufficient level of compliance with patients and an insufficient explanation of the essence of treatment: persistence of intoxication syndrome,

dissonance of expected and actual changes in tumor dimensions, panic fear of failure of treatment and lack of well-being improvement was interpreted by some patients as a negative result.

In 32 patients of group 1, 22 - of the second and 94 - of the third there were signs of negative dynamics according to RECIST criteria, as a result of which they were transferred to systemic polychemotherapy with the use of drugs 2 and 3 lines.

At the same time, patients of group 3 had the greatest discrepancy between the evaluation of QOL and the real dynamics of the local tumor status: in 268 persons there was a complete reduction of the signs of tissue disintegration and secondary infection in all persons with ulcerative-destructive forms of LABC; there was no re-regression of the wound after debridement. In the majority of patients of groups 1 (57 persons) and 2 (53 persons) with superficial destructive forms of LABC similar effect had temporary character (on average, within 2 weeks) - with the phenomena of partial recurrence of ulceration on the surface of the affected skin, although of much less intensity. However, the stabilization of the process was not perceived by the patients as a positive result, and systemic manifestations of intoxication were prevalent.

After the second course of PCT, there was a further decrease of the index in the first (by 4% to 43±4.3 points) and the second (by 6% to 45±3.1 points) control groups, with an acute increase in the parameter value in the experimental group (increase by 12% with a final result of 59±4.9 points). The difference between the results was statistically significant in the comparison between the experimental and the two control groups ($p<0.05$ for the pair [groups 1 and 3], and $p<0.05$ for the pair [groups 2 and 3]).

After the completion of the third course of chemotherapy, the reference values of QOL parameter were positive in all groups: QOL increase was noted in patients of group 1 (7% to 52±2.3 points) and 2 groups (9% to 54±6.8 points) as a result of improvement of the general condition, addiction to systematic wave-like dynamics of PCT intoxication symptoms, positive dynamics of local tumor status. Three courses of PCT were sufficient for 261 patients in the study group, after which they completed a non-adjuvant chemotherapy course and began receiving further treatment. This is reflected in the QOL score of this cohort: further significant improvement in quality of life by 18 points with a final result of 77±6.3 points. The statistical advantage remained significant with $p<0.001$.

A further study of quality of life was conducted in degenerative form, given the lack of data from group 3; at this stage, 261 patients had positive clinical dynamics followed by radiotherapy and operative steps, and 101 patients had to change their neoadjuvant PCT

regimen due to negative dynamics or no effect of therapy. Fifty patients on systemic PCT and 48 patients on endolymphatic showed moderate positive dynamics of RECIST regression with better results in the second group ($p<0.05$).

After completing 4 courses of PCT, the scores decreased by one or two points in both control groups (51±4.4 and 52±2.3 points, respectively) and remained at the same level in patients of group 1 during subsequent cycles of NPCT, which was interpreted as a result of physical and moral exhaustion of patients. , absence of the same dynamics of clinical symptoms as in other patients, lack of positive results and dissatisfaction with the symptoms of iatrogenic intoxication.

Clinical effect with qualitative changes of local status and transfer of patients to the category of resectable tumors appeared in 50 women of the first control group after 6 courses of SPCT, in 48 - the second control group after 4 courses of ELPCT and 261 patients of the experimental group.

The presented data demonstrate statistically better results of the experimental group on the positive dynamics of the quality of life index in the amplitude and chronometric complex logran study as a result of neoadjuvant SIAPCT compared to the first ($p<0.001$) and second ($p<0.05$) control groups. According to the results of the general state scale, the following dynamics were observed: statistically unreliable difference when compared to the beginning of chemotherapy (63±6.4 points in the first group, 65±4.3 points in the second group, 59±3.8 points in the third group; $p> 0.05$ in both pairs of comparisons) with a linear deterioration of 5-10 points after the first 2 courses of PCT and a further improvement in the range of 10 points in the third group without dynamics in the control groups. The following dynamics were observed in the evaluation of the physical health scale: statistically unreliable difference when compared to the beginning of chemotherapy (83±5.4 points in the first group 81±9.6 points in the second group, 85±9.6 points in the third group, $\chi 2>0.05$ in both comparison groups) with statistically acceptable fluctuations in the range of 10 points in all groups during the period of neoadjuvant treatment.

The cognitive status was the least responsive to chemotherapy: the intergroup and intragroup incomplete differentials were within the range of 10 points and had no statistical differences in all three groups. Indicators of emotional state and social well-being revealed the most variable pattern. And if, on the scale of the emotional state, changes occurred haphazardly ($p>0.05$ in both comparisons), which certainly makes this parameter the most subjective and the least reliable for a separate assessment, but, as already mentioned, necessary for a comprehensive approach; then the social adaptation scale reflects a bright

positive dynamic for the third group and more moderate for the first and second and is, in the authors' opinion, the most important parameter in the quality of life indicator.

As already stated, improving social adaptation (both physically, through the ability to eliminate the potential source of tissue destruction, and morally - by eliminating the patient's stigmatization and giving them the opportunity to return to normal life) and restoring the health is the ultimate goal of comprehensive treatment and interim treatment. for each of the steps.

Prior to chemotherapy, patients rated their social status equally low (47±3.7 points in the 1st group, 49±3.9 points in the 2nd group and 51±5.7 points in the 3rd). After the first two courses of PCT in both groups, the scores improved: 12 points in patients of the first control group, making 59±7.2 points, 14 points in patients of the second control group, making 64±7.2 points, and 22 points in the experimental cohort of 69±8.9 points.

In the future, positive dynamics persisted: in the first group, an increase of 19 points (68±7.1 points) after the third course and another 6 points (74±4.6 points) after the fourth; in the second - by 16 points (65±4.9 points) in the third stage of the study and by 6 points (72±6.3 points) in the fourth; in the third - by 16 points (80±5.3 points) in the third stage of the study. At the same time, objective reduction of local symptoms in all categories was really observed in patients with significant temporal and amplitude predominance of the third group.

This dynamic of assessing one's social status is crucial in treating advanced forms of cancer, especially breast cancer, as a result of a positive change in a woman's perception of herself as a full member of society and her illness - not as a stigma that condemns death and deprives the struggle for survival of meaning, but as a condition in which there is medical care that allows to increase the length and quality of later life and to restore social and employment status ($p>0.05$ in both comparisons in favor of the control group).

Finally, the symptomatic panel selected only those that had high reference values, statistical significance, and pathogenetic association with the intervention: pain, nausea, and loss of appetite - as parameters that characterize local and general changes in the body.

Intoxication syndrome is a serious and major side effect of chemotherapy treatment. It should be noted that objectively, the symptoms of intoxication persisted for an average of 5-7 days after systemic and endolymphatic administration of the drugs and 3-5 days after regional perfusion.

Due to the rational selection of drugs for chemotherapy, intoxication did not reach a pronounced scale, so the parameters of insomnia, apathy, depression and general fatigue did not change significantly.

Symptoms of nausea and loss of appetite were noted in several patients with first-stage tumor lysis syndrome, which averages low (13±1.4 and 11±0.9, respectively, in the 1st group, 13±1.2, and 11±0.7, respectively, in the 2nd group, 10±0.9 and 10±1.1 - in the 3rd group). In subsequent stages, loss of appetite and nausea was noted by almost all patients in both control groups as a response to iatrogenic chemotherapy aggression over typical time intervals and evaluated as severe. In the third group, after each course of polychemotherapy, symptoms of nausea and loss of appetite were markedly less intense compared to both control groups within 15-25 points of the group ($p<0.05$ in both comparisons) and lasted 1-2 days less ($p<0.05$ in both comparisons), which characterizes the better tolerability of selective intra-arterial PCT due to a rational dosing system (⅓ the course dose of each drug per day) while maintaining efficacy due to the "shock effect" of regional perfusion.

The pain syndrome and its dynamics during the period of neoadjuvant treatment require special characteristics. In general, it reflects the dynamics of the local process, and therefore correlates with the system of clinical effect (tumor resectability) and is almost indistinguishable between groups.

Complaints and discomfort in the affected breast or in the tumor itself were noted by all patients of the first group in varying degrees of intensity in the form of actually pain syndrome in - the first (a) 65 (73%), the second (b) 56 (75%), the third (c) 235 (65%) groups of patients – or its equivalents: feeling of heaviness, compression, itching, paresthesia - a) 34 (27%), b) 19 (25%), c) 127 (35%) of clinical cases. Prior to the onset of chemotherapy treatment, high intensity pain syndrome (requiring injection of non-steroidal analgesics for 24 hours without complete reduction of discomfort) was characteristic of a) 4 (4%), b) 1 (1%), c) 29 (8%) cases of coccross mastitis by type of inflammatory pain syndrome, medium intensity (satisfactory control of pain syndrome by oral NSAIDs with non-permanent use of injection forms - for a) 34 (38%), b) 29 (39%), c) 116 (32%) cases of invasion into the elements of the chest wall by type are not and (a) 27 (30%), b) 16 (21%), c) 90 (25%) cases of breast cancer with mixed type of pain syndrome.

According to the linear visual-analogue scale (VAS), the mean pain intensity M±m was a) 17.5±8.8, b) 16.2±5.7, c) 18.0±6.3. In general, during the neoadjuvant PCT, the proportions and distribution of pain syndrome incidents and its equivalents were maintained, while their intensity varied widely, which had the following tendency: during the first course of PCT and during the first days after its completion, there was an increase in the intensity of existing symptoms (a) +22, b) +16, c) +9 points) by increasing the cytotoxic effect of the synthesis of inflammatory mediators in damaged tissues with increased edema and hyperemia,

an increase in intra-tissue pressure, blood circulation and cell metabolism. Subsequent reduction to a) 14.2, b) 9.1, c) 1.9 points after the second PCT cycle and a) 2.2, b) 2.0, c) 1 points after the third (when paired comparison of the study group with both control groups $p>0.05$) is explained by the effectiveness of the first effective PCT courses in reducing the tumor cell volume and reducing perifocal infiltration with a decrease in mediator synthesis activity and inhibition of the local inflammation process.

The described dynamics indicate a higher efficiency of selective intra-arterial chemotherapy and antibiotic therapy in relation to the reduction of intensity ($p<0.05$) and duration ($p>0.05$) of the inflammation and pain syndrome during neoadjuvant treatment.

The general condition of patients at all stages is formed mainly due to the objective (presence of tumor neoplasm; intoxication syndrome; asthenic syndrome; local and systemic manifestations of tumor lysis; attachment of secondary infection of compromised tissues) and subjective (psychological and emotional state). , social maladaptation through cancer stigma and disability) factors.

After 3 courses of PCT, statistically better results of the experimental group were obtained by positive dynamics of the quality of life index in the amplitude and chronometric complex logran study as a result of neoadjuvant SIAPCT compared to the first ($p<0.001$) and second ($p<0.05$) control groups.

The physical scale was strongly and directly correlated with objective changes in the breast after neoadjuvant treatment with significantly better results in group 3 ($p<0.05$).

The lowest cognitive response rate ($p>0.05$ for all groups) responded to chemotherapy. The most variable pattern was found by indicators of emotional state ($p> 0.05$ for all groups). On the social well-being scale, the control group showed the best dynamics ($p> 0.05$ in both comparisons) with a high evaluation of restitution of work and social status.

On the symptom scales in the third group, after each course of polychemotherapy, symptoms of nausea and loss of appetite were observed at a significantly lower intensity compared to both control groups within 15-25 points of the group ($p<0.05$ in both comparisons) and lasted 1-2 days less ($p<0.05$ in both comparisons).

Conclusions

1. The scheme of complex neoadjuvant treatment based on SIAPCT allowed to improve the overall tolerability and psycho-emotional background of patients during the period of polychemotherapy and to increase the overall quality of their life in the fields of mental and physical condition ($p<0.05$) compared to those receiving standard treatment.

2. The investigation of QOL is a reliable, informative, and cost-effective method of assessing a patient's health at both group and individual levels. In cancer studies, QOL assessment is an important criterion for evaluating treatment effectiveness and is of prognostic value.

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