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OPTION THERAPEUTIC APPROACH FOR PRIMARY BREAST CANCER

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ВАРИАНТ ТЕРАПЕВТИЧЕСКОГО ПОДХОДА ДЛЯ ПЕРВИЧНОГО РАКА МОЛОЧНОЙ ЖЕЛЕЗЫ

Abstract.

The first place in the ranking of oncology and the most acute oncology problem is breast cancer (BC), in the vast majority of women [1,2,3,5,18]. The rate of abstinence is high, and the percentage of patients receiving special therapy is 80.4%. All this indicates a low level of qualified care (Kolesnik O.O., Fedorenko Z.P., 2017). The aim of the study was the desire to study the effectiveness of various schemes of preoperative chemo-radiation therapy with radioimodification in the scheme of complex treatment of primary localized BC.

Research results and their discussion. *Analyzing 1 year of supervision, it is evident that 35 (83.3%) patients died in the I group, 7 died (16.7%). Patients who did not have a recurrence of the process at 1 year of life 25 (59.92%). In the II group, they died at 1 year - 6 (12.76%). and patients without relapsing 36 (76.59%). Comparing the result clearly that the overall survival of a reliable result was not low, and the rate of recurrence is likely to speak for the benefit of Group II. During second year , another 14 patients died in Group I against 7 group II. In the I survived, 21 (50,0%) were left, of which 17 (40,47%) without relapse were against 34 (72,34%) of the live ones, of which 20 (42,55%) without relapse.*

Summing up our research, supervision over the results of treatment in two groups, we can say that the remote survival results show the following: For 36 months. The observation formed the number of patients who clearly showed the results of treatment in groups I and II. In group I, overall survival rate was 11 (26,19%), with relapse 4 (9,52%). In the II group, the total number of patients with 3 years of observation was 25 (53,19%), with relapse of 17 (36,17%).

Conclusions. *The study of the effectiveness of the scheme of neoadjuvant chemotherapy in combination with radiotherapy and radiomodification (group II) showed a positive trend in survival and relapse rates as well as a satisfactory state in the manifestations of toxicity of HT and radiation manifestations compared with the proposed scheme for group I.*

Реферат

Изучение эффективности схемы неоад`ювантной химиотерапии в сочетании с лучевой терапией и радиомодификацией (II группа) выявило положительную тенденцию по показателям выживаемости и рецидивирования, а также удовлетворительное состояние в проявлениях токсичности ХТ и проявлений лучевых реакций в сравнении со схемой предложенной I группе. По результатам лечения в обеих группах, можно сказать, что отдаленные результаты выживаемости показывают следующее: на 36 мес. наблюдения: в первой группе общая выживаемость 11 (26,19%), из них с рецидивом 4 (9,52%). Во II группе общее количество больных на 3 год наблюдения 25 (53,19%), с рецидивом 17 (36,17%).

Key words: *neoadjuvant chemotherapy, primary inoperable breast cancer, breast, multifraction, radiomodification.*

Ключевые слова: *неоадъювантная химиотерапия, первично-неоперабельный рак грудной железы, грудная железа, мультифракционирование, радиомодификация.*

Introduction. The first place in the ranking of oncological morbidity and the most severe three-fold oncology problem is breast cancer (BC), in the vast majority of women [1-4]. According to GLOBOCAN 2012, the world's BSE rate will increase by 25% from all new cases. Currently, there are three general directions in relation to the treatment of BC [5-6]. The first point is the reduction of the primary tumor in case of operable cases to increase the percentage of organ conservation and induction therapy for the purpose of obtaining the operative state of the tumor [7-8]. The second point is to obtain the sensitivity of the primary tumor to chemotherapy (CT) and, based on the results obtained, the possibility of planning further treatment [9-11]. The third is the way to improve the long-term results from the treatment [12,13]. Numerous randomized trials show that complete morphological logic regression improves overall survival [12,13]. The indication for conducting neoadjuvant chemotherapy (NCT) is a locally distributed BC. But there is no clear tactics in relation to operable cases of BC. Preoperative treatment in these forms of BC is dictated by the desire and ability to perform the operation that keeps the body, conducting the NCT, improving the quality of life of patients [13]. The development of technologicity of radiotherapeutic methods in oncology gives rise to the expansion of evidence of treatment by radioactive rays [14,15]. Also, chemo-therapeutic regimens, which are differently combined with radiotherapy, have a fairly progressive futurc[16,17]. That unanimous opinion, the only algorithms for the treatment of these or other localizations does not exist and therefore the constant search for efficiency and reduction of the toxicogenic influence on the limitations of the system of patients from conducting therapy is the task of scientists [17]. The aim of the study was the desire to study the effectiveness of various schemes of preoperative chemo-radiation therapy with radio-imodification in the scheme of complex treatment of primary localized BC.

The object and methods of research. For the period from 2011 to 2016, in the conditions of the Poltava Regional Clinical Oncology Center, 89 patients with primary inoperable locally advanced pulmonary tuberculosis in the third (T3-4N0-1M0) diseases, with obligatory verification of the process, received radiomodified chemo-rays treatment. Duration of patient supervision was 36 months.

Criteria for not inclusion in the study were: concomitant diseases in the stage of decompensation or are able to have a significant effect on the result of treatment; mental illness; Participate in another study in the last 30 days or at the moment. The age of the patients involved in the study varied from 20 to 80 years. The average age was 48.9 ± 1.9. By gender, women were 81 (91.01%), and men were 9 (10.11%).

Radiation therapy patients received on the apparatus of remote gamma radiation TERAGAM c01. Patients with primary and controversial examinations performed a CT scan of the thoracic cavity on a computer tomography CT / E Dual Hispeed of the firm GE (USA) by the usual mode according to the standard method. Ultrasound examination of the abdominal cavity, regional lymphatic collectors was performed on Sonolan G-50 and DP-9900. X-ray examination was carried out on the apparatus РУМ-20, РДК ВСМ. Cytological and Pathogistological studies were performed in the department of onco-morphology. The evaluation of toxic manifestations of chemotherapy was conducted in accordance with the recommendations of WHO and the International Cancer Alliance for the discovery of the degree of various types of toxicity after each course of polychemotherapy.

The efficacy of the treatment outcomes was evaluated after the disappearance of prominent reactions (2-3 weeks), the degree of regression of the tumor based on physical, ultrasound, CT scan, according to the criteria for the response of solid tumors (Response Evaluation Criteria In Solid Tumors - RECIST - 1994). For remote results, a 3-year overall survival rate and a non-recurring survival period were assessed, which were assessed at the level of clinical out-patient monitoring, analysis of statistical reports. Patients in both groups were recruited by blind randomization and divided into 2 groups. All patients were taken into work after signing, as a matter of compulsory, informed consent to the study.

I (n-42) group received 2 courses of chemotherapy (CT) at standard doses of the CMF scheme. After 2 weeks of rest, patients received a course of radiation therapy under the radical program: in the groin, lymph nodes, parastancal supraclavicular arcas, onc-timc ccn-ter-dose dose (RVD) of 2.2 Gr to a total focal dose (TFD) of 60-62 Gr.

II (n-47) group of patients received 2 courses of chemotherapy (CT) at standard doses of the CAF / FAC scheme. After 2 weeks of rest, patients received a course of radiation therapy under the radical program, but in multifractional mode: on the axillary lymph nodes, parastaneal supraclavicular areas, a single focal dose (SFD) of 1.1 Gr (morning) + 1.1 Gr (after 6 hours) = 2.2 Gr to the total focal dose (TFD) 60-62Gr with radiomodification Tegafur (800 mg in the morning and 400 mg in the evening), which was administered in accordance with the instructions.

The analysis of qualitative comparisons between groups was performed using conjugate tables and applied the Fisher and Pearson $\chi 2$ criteria. The adequacy of the differences between the groups was estimated by the t-criterion of the Students. Resilience in the groups was estimated by the Kaplan-Meier method. The sufficiency of the distribution of variables was obtained by the Kolmogorov-Smirnov, Mann-Whitrashkel-Wallace and W-Wilcoxon criteria. Meaning-my difference was considered $p = 0,05$.

Research results and their discussion. The results of treatment of patients with locally advanced BC were evaluated for regression of tumor, survival, which was determined by comparing clinical manifestations and indices, visualization information. The method of evaluation was the analysis of the radiation reactions, as well as the degree of toxicity after the spent CT, which is shown in Table 1.

Table 1.

Aggressiveness of treatment depending on the proposed CRT regimens in I - II groups

Complications	Groups of patients, n (абс. %)	
	I (n=42)	II (n=47)
nausea and vomiting	2 (4,76)	2 (4,25)
leukopenia	2 (4,76)	7 (14,89)
increase in body temperature	3 (7,14)	15 (31,91)
diarrhea	5 (11,90)	9 (19,15)
dry cough	29 (69,05)	14 (29,79)
epidermis in the irradiation zone	1 st. – 26 (61,9) 2 st. – 5(11,90) 3 st. – 2(4,76) 4 st. – 0	1 st. – 30 (63,83) 2 st. – 10 (21,28) 3 st. – 3 (6,38) 4 st. – 0
no manifestations at all	0	0
no skin manifestations	9 (21,43)	4 (8,51)
no manifestations of the internal state of the organism were observed	1 (2,38)	0

Analyzing the results of the data on the manifestations of toxicity in both group, one can see that the results are more positive in the I group of patients. Except of dry cough: 29 (69,05%) patients of I group had such manifestation against 14 (29,79%) patients of II group, which is 2.1 times better. But we explain this by the effect of manifestation of multi-fractionation of the dose. And even radiomodification, in which the manifestation of toxicity is brighter, did not give the picture an extremely bad one. Such an indicator as the temperature increase had a 5-time divergence not in favor of Group II. 3 (7,14%) and groups against 15 (31,91%) of group II. But the anticipated activation of the process, thanks to Tegafur, has in its arsenal moderate temperature attacks that are sufficiently controlled. Terrible enemy of chemo-radiotherapy - leukopenia. In the I group of such patients, who needed a pause in treatment due to leukopenia, 2 (4.76%). After symptomatic therapy, treatment is continued. In the II group of such patients was 7 (14,89%). It is 3.5 times worse, but all patients received treatment in full and increased toxicity in Group II was justified by radioimodification.

Analyzing the manifestations of the gastrointestinal tract, there was such a manifestation as diarrhea. In group I, group 5 (11.90%) against II group 9 (19.15%), which is 1.8 times worse. There were positions that did not produce fruitful differences, such as nausea and vomiting.

The monitoring of the condition of the skin covering in the irradiation zone, namely, the radiation reactions, was continuously monitored. In the 4 stage of patients was not at all. 1 and 3 stage did not give differences. But here 2 was not in favor of Group II. 2 items - 5 (11.90%) and group 2 in comparison with 10 (21.28%) of the II group gave a worse result. The following indicator was observed as the absence of manifestations from the side of the skin. Here in 2,5 times the state is the best in group I. Evaluation of treatment outcomes for the regression of the tumor of the weight monitoring component, summarized in Table 2.

Table 2.

Evaluation of the results of treatment of patients with locally advanced BC for the degree of regression of the tumor

Results of treatment	Groups of patients, n (абс. %)	
	I (n=42)	II (n=47)
Complete regression	0	2 (4,26)
Partial regression	14 (33,33) *	22 (46,81)*
Stabilization	10 (23,81) *	20 (42,55) *
Progression	18 (42,86) *	3 (6,38) *

*Note. * - the difference is probable (p = 0.05)*

Analyzing the results of the treatment by the proposed methods, it was noted that in the I group no complete regression occurred to anyone. However, in the 2nd group complete regression was traced in 2 (4.26%) patients. The difference is unlikely and we did not consider the difference. The analysis of partial regression showed a significant difference: in group I in 14 (33.33%) patients versus 22 (46.81%) patients in group II, which 1.6 times said in favor of treatment tactics of the proposed group II (p = 0, 05). Regarding stabilization, the difference between the groups is significant: in the I group, 10 (23.81%), and in the second group, 20 (42.55%) and this is 50%, namely in the 2nd time the result of treatment is the best. Partial regression and stabilization, as indicators worse than complete regression, but for prolonging the patient's life and preparing him for further surgical intervention, the results obtained in Group II are quite comforting. Regarding the number of progressions, in group I, 18 (42.86%) patients, in II group 3 (6.38%). This is 6 times worse than in the 2nd group, and therefore the methods of treatment speak for themselves.

Summing up above, it seems that the treatment regimen in the second group of patients is quite aggressive. But given the results of regression of down-line and survival, as well as taking into account that toxicity

was not given grounds for complete cessation of treatment and were managed by symptomatic therapy, it is possible to recommend such a scheme for the treatment of patients with BC.

An analysis of the survival rate of patients and the frequency of recurrences of the disease is an important indicator of oncology. At the beginning of the analysis, I would like to note the figures indicating the number of patients who were operated after the treatment received within the period of our monitoring. Survival results are presented in Table 3.

Table 3.

Analysis of survival and recurrence of patients with BC I and II groups

Observation time (years)	I group (n = 42) абс./(%)		II group (n = 47) абс./(%)	
	survival without recurrence	General survival	survival without recurrence	General survival
1 year	25 (59,92)	35 (83,33)	36 (76,59)	41 (87,23)
2 year	17 (40,47)	21 (50,0)	20 (42,55)	34 (72,34)
3 year	4 (9,52)	11 (26,19)	17 (36,17)	25 (53,19)
Patients are operated after treatment	8 (19,05)*		27 (57,45)*	

*Note. * - the difference is probable (p = 0.05)*

In the I group of such patients, 8 (19.05%) were counted. practically 1/5 of the patients in the group. In the II group - 27 (57.45%), more than half of the declared patients. Also, comparing between groups, in 3 times the number of patients in Group II exaggerates the number of group I. These figures speak for the quality of the proposed scheme II scheme. Analyzing 1 year of supervision, it is evident that 35 (83.3%) patients died in the I group, 7 died (16.7%). Patients who did not have a recurrence of the process at 1 year of life 25 (59.92%).

In the II group, they died at 1 year - 6 (12.76%), and patients without relapsing 36 (76.59%). Comparing the result clearly that the overall survival of the reliable result was not low, and the rate of recurrence is likely to speak for the benefit of Group II. At year 2, another 14 patients died in Group I against 7th group II. There were 21 (50,0%) , of which 17 (40,47%) without relapse were against 34 (72,34%) of the live ones, of which 20 (42,55%) without recurrence.

Summing up our research, supervision over the results of treatment in two groups, we can say that the remote survival results show the following: For 36 months. The observation was made of the number of patients who clearly showed the results of treatment in groups I and II. In group I, overall survival rate was 11 (26,19%), with relapse 4 (9,52%). In the II group, the total number of patients with 3 years of observation was 25 (53,19%), with relapse of 17 (36,17%).

Conclusions. The study of the efficacy of a neoadjuvant chemotherapy regimen in combination with radiation therapy and radiomodification (Group II) showed a positive tendency for survival and relapse rates as well as a satisfactory state in the manifestations of CT toxicity and manifestations of radiation in comparison with the proposed scheme for group I. Prospects for further research: the lack of a single point of view for the implementation of the NCT and the criteria for the designation of this or that scheme leads to the prospect of further development of this problem and conducting research in this direction. Therefore, further elongation of this study is planned with the inclusion of patients with BC and other schemes of CT.

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