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DENTAL STATUS OF PATIENTS DURING THE SUPPORTIVE CARE AT ANTINEOPLASTIC CHEMOTHERAPY FOR BREAST CANCER

Abstract

Two groups were studied in a comparative aspect – 98 women with breast cancer during the courses of adjuvant chemotherapy: the first was comprised of 26 patients who used their conventional means for oral hygiene; the second included 72 patients, who received the complex of therapeutic and preventive measures of supportive care. Dental toxicity was observed in 84.6-96.2 %, and has grown with the increase of the cycles of chemotherapy, reaching a maximum value on the V cycle of treatment. It is shown that the application of the developed complex significantly reduces the manifestations of dental toxicity by 1.5 times on the I cycle and by 4.5 times on the VI cycle of chemotherapy.

Key words: dental toxicity, breast cancer, chemotherapy, supporting therapy.

Relevance

Cancer morbidity and mortality have been steadily increasing throughout the world, despite the introduction of new methods of diagnosis and treatment of this disease. According to the International Agency for Research on Cancer (IARC) the incidence of malignant tumors is prognosticated to grow – from 10 million per year at the present to 15 million by year 2020, the mortality rate is to increase from 6 to 9 million annually [1, 4, 7, 10].

Breast cancer is the leading disease in the structure of cancer incidence and mortality in women.

According to the National Cancer Registry of Ukraine, in 2012 there were identified newly diagnosed breast cancer patients: in the country – 16429 women, in Kyiv and its region – 1790, in Kharkiv and its region – 1133 women [10].

One of the main treatment methods for patients with malignancies is an antineoplastic chemotherapy (CTx), along with surgery and radiotherapy, which is able to inhibit the proliferation of tumor cells (cytostatic effect) or lead to their complete destruction [3, 4].

The conduction of systemic therapy, in addition to the expected therapeutic effect, is almost always accompanied by the development of adverse reactions from various organs and body systems, including oral cavity (oral mucositis – OM), the frequency of lesions of which in patients ranges from 30 to 90 % [8, 12].

It is still unclear why, under equal conditions, the complications of cancer treatment would develop only in some patients [9].

In domestic and foreign literature a lot of attention is paid to this issue during chemoradiotherapy of the oropharyngeal cancer and hemoblastosis [6, 11, 13], and only a few publications are devoted to malignant tumors at other sites [9, 12].

Scarce and conflicting information regarding the regularity of pathogenesis and clinical course of OM in various clinical situations is conditional on the peculiarities of oncology practice and the fragmentation of information.

In literature, there are separate works on forecasting and planning of prevention of these serious complications, often leading to a deterioration of cancer patients' condition which in turn requires a subsequent reduction of the chemotherapy dose and a change of the treatment terms. Unfortunately, clinicians – both dentists and oncologists – have paid insufficient attention to the issue of an adequate and differentiated approach to the prevention and treatment of this condition, what makes the need to develop a specific plan of a dental supportive care at all stages of antitumor treatment in breast cancer patients an urgent one.

The **aim** of this work was to develop the complex of a dental supportive care and to evaluate its effectiveness in breast cancer patients at the stages of adjuvant chemotherapy.

Materials and methods. Our own clinical observations of 98 breast cancer (BC) patients, who had received a comprehensive treatment of this disease in the clinic "Grigoriev Institute for Medical Radiology of National Academy of Medical Science of Ukraine" in Kharkiv during the period from 11.2010 to 12.2013, have become the basis for this study. For the accuracy of the results of the study a homogeneous group of patients was selected: only women with malignant breast disease who have received a combined treatment (modified radical mastectomy (Madden) + radiotherapy), and 6 cycles of adjuvant chemotherapy using the same scheme, in accordance with the international standards [7].

The diagnosis "breast cancer" was morphologically verified in all patients.

All participants of the clinical study were divided into two groups. Patients in Group 1 only brushed their teeth 1 time/day with any kind of toothpaste, or didn't use any hygiene products at all. Patients in Group 2 were given the detailed instructions on the application of the complex of therapeutic and preventive measures, developed by us (an application for an invention is filed), in the course of the whole chemotherapy treatment.

Group 1 (the control group) consisted of 26 breast cancer patients with $T_1N_0M_0$ – $T_2N_1M_0$ stages. The age of BC patients in Group 1 varied in the range of 35 to 72 years. The mean age was (54.1 ± 9.2) years. The median age equaled to 55.5 years.

Group 2 (the study group) included 72 breast cancer patients with $T_1N_0M_0$ – $T_2N_1M_0$ stages. The age of BC patients in Group 2 ranged between 28 to 73 years. The mean age was (56.0 ± 1.1) years. The median age equaled to 58.0 years.

Patients' examination was performed before the start and at the end of each cycle of CTx by the common pattern: a survey, inspection, percussion, palpation and thermodiagnostics. The oral mucosal condition was assessed relying on the inspection, noting the degree of its hydration, the presence of congestion, fur, and other elements of lesions.

The manifestation of the side effects of cytostatic treatment in the oral cavity was also assessed based on the patients' survey data. A questionnaire was developed, in which all patients denoted their complaints during the

course of the whole chemotherapy treatment.

The obtained data were put in a specifically designed unified card and consequently used for statistical analysis. Statistical analysis of the obtained material was carried out using the software package STATISTICA.

Results

The application of the developed complex of supportive care in BC patients during adjuvant CTx reduced the incidence of side effects of cytostatic therapy in the oral cavity as compared to the control group (Fig. 1).

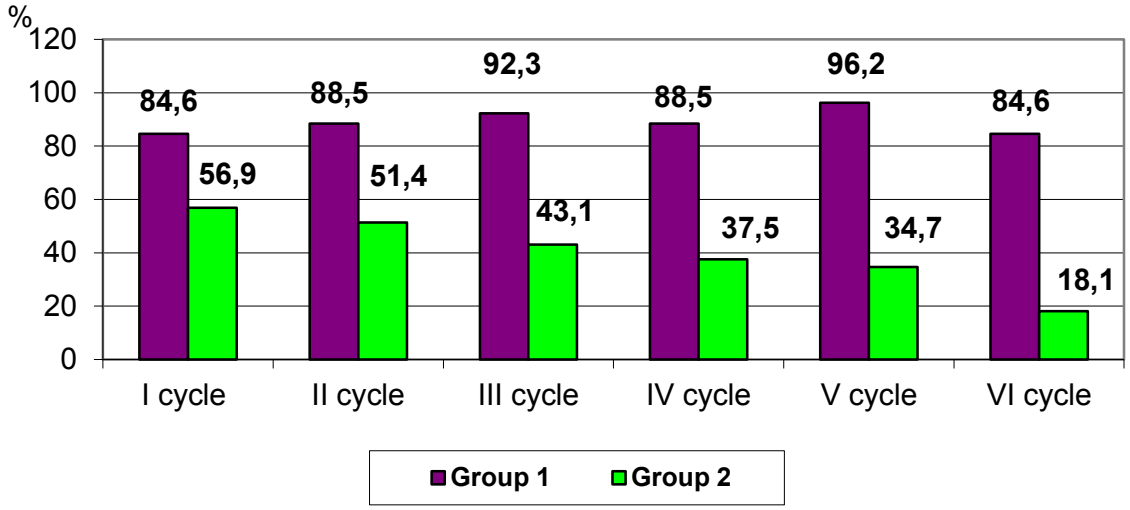

Figure 1. – The frequency of CTx-related complications in the oral cavity of breast cancer patients in Groups 1 and 2 during CTx

Thus, the frequency of dental toxicity during the I cycle in the study group (Group 2) has decreased to (56.9 ± 5.9) versus (84.6 ± 7.2) % in the control group (Group 1). If in Group 1 the maximum manifestation of toxicity was observed during the III and V cycles of CTx – (92.3 ± 5.3) and (96.2 ± 3.8) %, in Group 2 this indicator was observed only during the I cycle of CTx. The minimal manifestation of toxicity was marked during the VI cycle of CTx: (84.6 ± 7.2) and (18.1 ± 4.6) %, Groups 1 and 2 respectively.

The incidence of CTx-associated mucositis in the group of patients who didn't receive the supportive care, correlates with the literature data, where the presented rate is 70-100 %, especially in patients treated with 5-fluorouracil [3, 4, 5, 9].

The use of preventive therapy has led to a significant decrease in the frequency of complaints about the fur, the presence of oral ulcers, the cracks in the corners of the mouth, the dry lips, the inflamed and bleeding gums, and the presence of foamy saliva, the changes in taste sensation and the decreased appetite (Tab. 1).

The frequency of complaints received by us in the control group is slightly lower compared to the data presented by several authors, who note that 100 % of patients complain of the dry mouth and thirst during the course of CTx for breast cancer [2].

Comparing the dynamics of complaints throughout the course of CTx in patients in the study group, it should be emphasized that the I cycle was marked by the maximum percentage of complaints of dry lips – 12.2 ± 5.2 %, the swelling of the oral mucosa – 9.8 ± 4.7 %, the decreased appetite – 39.0 ± 7.7 %.

Maximum percentage of complaints during the II cycle of CTx was formed by such figures: thirst – 51.4 ± 8.3 %, rash on the lips – 5.4 ± 3.8 %, cracks in the corners of the mouth – 5.4 ± 3.8 %, fur – 5.4 ± 3.8 %, changes in taste sensation – 43.2 ± 8.3 %.

The III cycle of CTx was accompanied by the greatest manifestation of the inflammation of the oral mucosa – 6.5 ± 4.5 %, the presence of oral ulcers – 9.7 ± 5.4 %, the swelling of the tongue – 9.7 ± 5.4 %, and the inflamed and bleeding gums – 9.7 ± 5.4 %.

It should be mentioned that such complaints as pain of the mucous membrane of the cheeks, burning tongue, burning gingival papillae were absent during all 6 cycles of chemotherapy treatment; complaints of foamy saliva were absent, starting from the II cycle of CTx, of oral ulcers and the cracks in the corners of the mouth – from the IV cycle of CTx. There were practically no changes in the frequency of complaints of burning tongue tip and the inflammation of the oral mucosa.

The complaints, described above, are a manifestation of cheilitis, mucositis and salivary gland dysfunction (Tab. 2).

As we can see from the offered data, in the control group cheilitis is the most common pathology with a peak on the III cycle of CTx – 69.2 ± 9.2 %, which is then gradually reduced to 34.6 ± 9.5 % on the VI cycle. The frequency of salivary gland dysfunction is maximal during the II cycle of CTx – 61.5 ± 9.7 %, with a following reduction in the frequency of its manifestations to 26.9 ± 8.9 % by the VI cycle. The frequency of mucositis increases by the III cycle to 73.1 ± 8.9 %, subsequently declining to 34.6 ± 9.5 % on the VI cycle of chemotherapy.

The application of the complex of therapeutic and preventive measures in these patients has significantly reduced the incidence of cheilitis to 12.5 ± 3.9 % on the I cycle in comparison to the control group. During the VI cycle of CTx this figure was 1.4 ± 1.4 %. The frequency of mucositis was also significantly lower compared to the control group, with a peak on the II cycle – 27.8 ± 5.3 % and a gradual decrease by the VI cycle of chemotherapy – 4.2 ± 2.4 %. Salivary gland dysfunction is the second most common disease with a peak on the I-II cycles of CTx, reaching 33.3 ± 5.6 %, and then declining to 11.1 ± 3.6 % on the VI cycle. The significance of differences is noted during the I-V cycles of CTx.

Table 1

The frequency and type of dental toxicity in breast cancer patients, depending on the cycle of chemotherapy

Complaint	The cycle of chemotherapy. The number of patients.											
	I		II		III		IV		V		VI	
	Group 1 (n=22)	Group 2 (n=41)	Group 1 (n=23)	Group 2 (n=37)	Group 1 (n=24)	Group 2 (n=31)	Group 1 (n=23)	Group 2 (n=27)	Group 1 (n=25)	Group 2 (n=25)	Group 1 (n=22)	Group 2 (n=13)
Dry mouth	45.5±10.9	56.1±7.8	52.2±10.7	56.8±8.3	37.5±10.1	51.6±9.1	30.4±9.8	48.1±9.8	40.0±10.0	44.0±10.1	18.2±8.4	53.8±14.4*
Fur	36.4±10.5	–	39.1±10.4	5.4±3.8*	45.8±10.4	3.2±3.2*	34.8±10.2	3.7±3.7*	32.0±9.5	–	27.3±9.7	–
Thirst	50.0±10.9	46.3±7.8	52.2±10.7	51.4±8.3	45.8±10.4	41.9±9.0	39.1±10.4	37.0±9.5	36.0±9,8	36.0±9.8	13.6±7.5	46.2±14.3*
Oral ulcers	27.3±9.7	2.4±2.4*	26.1±9.4	2.7±2.7*	33.3±9.8	9.7±5.4*	26.1±9.4	–	28.0±9.2	–	36.4±10.5	–
Pain of the mucous membrane of the cheeks	22.7±9.1	–	26.1±9.4	–	25.0±9.0	–	21.7±8.8	–	16.0±7.5	–	45.5±10.9	–
Burning tongue tip	13.6±7.5	2.4±2.4	13.0±7.2	2.7±2.7	12.5±6.9	–	13.0±7.2	–	16.0±7.5	–	13.6±7.5	–
Burning tongue	9.1±6.3	–	13.0±7.2	–	12.5±6.9	–	13.0±7.2	–	12.0±6.6	–	27.3±9.7	–
Burning gingival papillae	13.6±7.5	–	13.0±7.2	–	12.5±6.9	–	17.4±8.1	–	8.0±5.5	–	22.7±9.1	–
Cracks in the corners of the mouth	40.9±10.7	4.9±3.4*	30.4±9.8	5.4±3.8*	37.5±10.1	3.2±3.2*	30.4±9.8	–	32.0±9.5	–	27.3±9.7	–
Dry lips	59.1±10.7	12.2±5.2*	52.2±10.7	8.1±4.5*	54.2±10.4	9.7±5.4*	47.8±10.7	7.4±5.1*	40.0±10.0	4.0±4.0*	36.4±10.5	7.7±7.7*
Inflammation of the oral mucosa	13.6±7.5	4.9±3.4	17.4±8.1	5.4±3.8	16.7±7.8	6.5±4.5	17.4±8.1	3.7±3.7	16.0±7.5	4.0±4.0	27.3±9.7	–
Rash on the lips	18.2±8.4	2.4±2.4*	17.4±8.1	5.4±3.8	20.8±8.5	–	17.4±8.1	3.7±3.7	16.0±7.5	4.0±4.0	18.2±8.4	–
Inflamed and bleeding gums	18.2±8.4	2.4±2.4*	30.4±9.8	5.4±3.8*	29.2±9.5	9.7±5.4*	30.4±9.8	7.4±5.1*	16.0±7.5	4.0±4.0	9.1±6.3	–
Swelling of the tongue	9.1±6.3	4.9±3.4	21.7±8.8	5.4±3.8*	20.8±8.5	9.7±5.4	8.7±6.0	3.7±3.7	12.0±6.6	–	22.7±9.1	7.7±7.7
Swelling of the oral mucosa	27.3±9.7	9.8±4.7	21.7±8.8	8.1±4.5	25.0±9.0	9.7±5.4	17.4±8.1	7.4±5.1	8.0±5.5	4.0±4.0	18.2±8.4	–
Foamy saliva	27.3±9.7	2.4±2.4*	26.1±9.4	–	29.2±9.5	–	26.1±9.4	–	12.0±6.6	–	27.3±9.7	–
Changes in taste sensation	68.2±10.2	34.1±7.5*	69.6±9.8	43.2±8.3*	79.2±8.5	29.0±8.3*	69.6±9.8	25.9±8.6*	56.0±10.1	24.0±8.7*	63.6±10.5	15.4±10.4*
Decreased appetite	72.7±9.7	39.0±7.7*	82.6±8.1	37.8±8.1*	70.8±9.5	25.8±8.0*	69.6±9.8	29.6±8.9*	60.0±10.0	28.0±9.2*	63.6±10.5	7.7±7.7*
Increased tooth sensitivity	–	4.9±3.4	–	5.4±3.8	–	6.5±4.5	–	7.4±5.1	–	4.0±4.0	–	–

* – the statistical significance of differences in indices for Groups 1 and 2

Table 2.

Dental pathology during the adjuvant treatment of breast cancer patients.

Pathology	The cycle of chemotherapy. The number of patients.											
	I		II		III		IV		V		VI	
	Group 1 (n=26)	Group 2 (n=72)	Group 1 (n=26)	Group 2 (n=72)	Group 1 (n=26)	Group 2 (n=72)	Group 1 (n=26)	Group 2 (n=72)	Group 1 (n=26)	Group 2 (n=72)	Group 1 (n=26)	Group 2 (n=72)
Cheilitis	65.4±9.5	12.5±3.9*	57.7±9.9	9.7±3.5*	69.2±9.2	4.2±2.4*	57.7±9.9	4.2±2.4*	50.0±10.0	2.8±2.0*	34.6±9.5	1.4±1.4*
Mucositis	53.8±10.0	22.2±4.9*	53.8±10.0	27.8±5.3*	73.1±8.9	16.7±4.4*	50.0±10.0	12.5±3.9*	42.3±9.9	9.7±3.5*	34.6±9.5	4.2±2.4*
Salivary gland dysfunction	57.7±9.9	33.3±5.6*	61.5±9.7	33.3±5.6*	53.8±10.0	23.6±5.0*	42.3±9.9	18.1±4.6*	42.3±9.9	16.7±4.4*	26.9±8.9	11.1±3.7

Conclusion

Suchwise, the research data indicate the substantial effect of adjuvant chemotherapy on the state of the organs of oral cavity in breast cancer patients.

The dental toxicity is observed in 84.6-96.2 % of patients, and increases with the number of cycles of chemotherapy conducted, reaching a maximum on the V cycle of treatment. The main manifestations of the side effects of cytostatic therapy are cheilitis and mucositis, the incidence of which is maximal on the III cycle of chemotherapy, and salivary gland dysfunction, which peaks during the II cycle.

The use of the complex of therapeutic and preventive measures, developed by us, as a support therapy in this contingent of patients has contributed to a significant reduction of dental toxicity compared to the control group by 1.5 times on the I cycle (56.9 %), and by 4.5 times on the VI cycle of CTx (18,1 %).

The result is a reduction of major toxicity levels of cheilitis by 5.2 times on the I cycle in comparison to the control group, to the practical absence during the VI cycle (1.4 %); mucositis – by 2.4 times on the I cycle to 8.2 times on the VI cycle; salivary gland dysfunction – significantly lower by 1.7 times than on the I cycle of chemotherapy to 2.5 times during the V cycle compared to the control group.

This demonstrates the effectiveness of the applied complex of therapeutic and preventive measures in breast cancer patients in the course of adjuvant chemotherapy.

The above-stated data dictates the necessity for monitoring the condition of the organs of oral cavity of breast cancer patients during the treatment.

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Резюме

СТОМАТОЛОГИЧЕСКИЙ СТАТУС ПАЦИЕНТОК НА ФОНЕ ПРИМЕНЕНИЯ СОПРОВОДИТЕЛЬНОЙ ТЕРАПИИ ПРИ ПРОВЕДЕНИИ ПРОТИВООПУХОЛЕВОЙ ХИМИОТЕРАПИИ РАКА МОЛОЧНОЙ ЖЕЛЕЗЫ

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В сравнительном аспекте изучены две группы обследованных – 98 женщин, больных раком молочной железы на этапах адъювантной полихимиотерапии: первую составили 26 пациенток, которые использовали обычные для себя средства гигиены для полости рта; во вторую включены 72 пациентки, получавшие лечебно-профилактический комплекс сопроводительной терапии. Стоматотоксичность наблюдается в 84,6 – 96,2% и нарастает с увеличением про-

веденнях циклов полихимиотерапии, достигая максимального значения на V цикле лечения. Показано, что применение разработанного комплекса достоверно снижает проявления стоматотоксичности в 1,5 раза на I цикле и в 4,5 раза на VI цикле полихимиотерапии.

Ключевые слова: стоматотоксичность, рак молочной железы, полихимиотерапия, сопроводительная терапия.

Тұжырым
СҮТ БЕЗІ ОБЫРЫ ІСІККЕ ҚАРСЫ ХИМИОТЕРАПИЯ ӨТКІЗУ КЕЗІНДЕГІ ІЛЕСПЕ ТЕРАПИЯНЫ ҚОЛДАНУ АЯСЫНДА ПАЦИАНТТЕРДІҢ СТОМАТОЛОГИЯЛЫҚ МӘРТЕБЕСІ
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Салыстырмалы аспектіде тексерілген екі топ зерттелді - адъювантты полихимиотерапия кезеңдеріндегі сүт безі обырымен ауыратын 98 әйел: біріншісін 26 пациенткалар құрады, олар өздері үшін ауыз қуысы үшін қарапайым гигиена құралдарын қолданды; екіншісін 72 пациентка құрады, олар ілеспе терапияның емдеу – алдын алу кешенін қабылдады. 84,6 – 96,2% стоматотоксикалық байқалады және емдеудің V циклында максималды мәнге жетумен, полихимиотерапия циклдарының өтіуін көбейтумен артады.көрсетілгені, әдістелген кешенді қолдану полихимиотерапиныңI циклында 1,05 есеге және VI циклында стоматотоксикалықтың айқындалуын нақты төмендетеді

Негізгі сөздер: стоматотоксикалық, сүт бездері обыры, полихимиотерапия, ілеспе терапия.

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СРАВНИТЕЛЬНОЕ ИССЛЕДОВАНИЕ ПРОЧНОСТИ КОРНЕЙ ЗУБОВ ПОСЛЕ ПЛОМБИРОВАНИЯ КАНАЛОВ МЕТОДОМ ТЕРМОПЛАСТИФИЦИРОВАННОЙ И ХОЛОДНОЙ ГУТТАПЕРЧИ

Аннотация

Диагностика вертикальных переломов корня зуба крайне сложна, а современное широкое распространение технологии применения термопластической гуттаперчи указывает на актуальность данной темы. Для проведения исследования были отобраны 20 премоляров, механическую обработку корневых каналов которых проводили с помощью системы ProTaper, а обтурацию осуществляли методом холодной и термапластифицированной гуттаперчи, после чего подвергали измерению сопротивления образца давлению на корень зуба. Полученные статистически достоверные результаты свидетельствуют о том, что корни зубов, обтурированные термопластифицированной гуттаперчей обладали большей устойчивостью к вертикальным нагрузкам, чем образцы с пломбированием корневых каналов холодной гуттаперчей.

Ключевые слова: вертикальный перелом корня зуба, ProTaper, термопластифицированная гуттаперча.

Актуальность.

Одной из актуальных проблем современной эндодонтии является вертикальный перелом корня зуба (полный или неполный линейный дефект, направленный вдоль оси корня в сторону апекса) [3]. Эндодонтические факторы, которые могу оказывать влияние на появление переломов зубов нетравматического происхождения (Gutmann, 2008): чрезмерное препарирование корневого канала; использование избыточных сил при конденсации пломбировочного материала, возникновение расклинивающих сил при введении в канал инструментов, слишком агрессивное использование прямых ротационных инструментов, чрезмерное использование ультразвуковых инструментов в процессе очистки и формирования корневых каналов [2].

Диагностика вертикальных фрактур корня крайне сложна, дополнительные методы обследования не всегда информативны, что приводит к потере времени и, как следствие, к значительной потере костной ткани, вызывая сложности при дентальной имплантации [1]. Недиагностированные трещины ведут со временем к тому, что эндодонтическое лечение становится бесполезным, прибегая по необходимости к хирургических методикам (удаления, гемисекции) [6]. По данным Temse (2006) вертикальные трещины явились причиной удаления зубов в 11-20%, а среднее время между обтурацией корневого канала и моментом возникновения трещины составляет от 3-х дней до 14 лет, что не благополучно влияет на стратегическую ценность зуба в процессе оказания стоматологической помощи [4,5].