South Russian Journal of Cancer 2020, v.1, №3, p. 6-17
https://doi.org/10.37748/2687-0533-2020-1-3-1

ORIGINAL ARTICLE

DEVELOPMENT OF POSTCASTRATION SYNDROME AND CORRECTIVE EFFECT OF XENON IN EXPONENTIAL DOSE REGIMEN IN YOUNG PATIENTS WITH GYNECOLOGICAL CANCERS

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ABSTRACT

Purpose of the study. Investigation of possible optimization of treatment in patients with breast cancer and cervical cancer with low-dose xenon therapy.

Patients and methods. The study included 156 patients with pT1B2N0M0 cervical cancer (CC) and pT2N1M0 breast cancer (BC) of the reproductive age (29–45 years) after radical treatment, including forced surgical castration in hormone-positive breast cancer with concomitant gynecological pathology. Since the formation of pathological syndromes, 1 cycle (5 sessions) of low-dose xenon inhalation therapy (XT) was performed, with an algorithm for xenon dose calculation and exposure according to the exponential pattern of decreasing concentration and increasing exposure, with an individual approach. Together with general clinical and laboratory examinations, we used international scales for assessing the severity of the patient condition by the Kupperman menopausal index (MMI), ESAS, quality of life (MOS-SF-36), in a modification of the Russian International Center, pain (VAS); the types of general adaptive reactions were identified by the method of L.Kh.Garkavi.

Results. Important advantages of a new method associated with a rapid regression of pathological psychosomatic symptoms were revealed after XT. MMI values (p<0.05) decreased, 96.8% of patients reported no pain at all on activity, manifestations of neurovegetative disorders significantly decreased (p=0.02–0.04), and the coefficient of antistress reactions to stress increased, which was congruent with the data on improving the quality of life.

Conclusion. High efficiency of the technology demonstrated possible prevention of surgical menopause development and clinical manifestations of postcastration syndrome in order to improve the quality of life and social rehabilitation of young patients with gynecological cancers.

Keywords:
cervical cancer, breast cancer, postcastration syndrome, xenon therapy, exponential dose regimen, adaptive reactions

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Information about funding: the work was carried out with the support of the National Medical Research Centre for Oncology of the Ministry of Health of Russia.
Conflict of interest: authors report no conflict of interest.

For citation:
Kit O.I., Popova N.N., Shikhlyarova A.I., Frantsiyants E.M., Moiseenko T.I., Menshenina A.P., Goncharova A.S., Zhukova G.V., Protasova T.P., Arapova Yu.Yu. Development of postcastration syndrome and corrective effect of xenon in exponential dose regimen in young patients with gynecological cancers. South Russian Journal of Cancer. 2020; 1(3): 6-17. https://doi.org/10.37748/2687-0533-2020-1-3-1

Received 30.12.2019, Review (1) 20.03.2020, Review (2) 01.07.2020, Accepted 01.09.2020

Южно-российский онкологический журнал 2020, т.1, №3, с. 6-17
https://doi.org/10.37748/2687-0533-2020-1-3-1
ОРИГИНАЛЬНАЯ СТАТЬЯ

РАЗВИТИЕ ПОСТКАСТРАЦИОННОГО СИНДРОМА И КОРРИГИРУЮЩЕЕ ДЕЙСТВИЕ КСЕНОНА В ЭКСПОНЕНЦИАЛЬНОМ ДОЗОВОМ РЕЖИМЕ У ПАЦИЕНТОК МОЛОДОГО ВОЗРАСТА С ОНКОПАТОЛОГИЕЙ РЕПРОДУКТИВНЫХ ОРГАНОВ

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РЕЗЮМЕ

Цель исследования. Исследовать возможность оптимизации лечения больных РМЖ и РШМ при помощи низкодозной ксенонотерапии.

Пациенты и методы. В исследование включено 156 онкологических больных раком шейки матки (РШМ) pT1B2N0M0 и раком молочной железы (РМЖ) pT2N1M0 репродуктивного возраста (29–45 лет) после радикального лечения, включая вынужденную хирургическую кастрацию при гормонпозитивном РМЖ с сопутствующей гинекологической патологией. С момента формирования патологических синдромов применяли 1 курс (5 процедур) ингаляционной низкодозной ксенонотерапии (КсТ), включающей алгоритм расчетных доз ксенона и экспозиции воздействия в соответствии с экспоненциальной закономерностью снижения концентрации и увеличения экспозиции с учетом персонализированного подхода. Наряду с общеклиническими и лабораторными исследованиями использовали международные шкалы оценки степени тяжести состояния по менопаузальному индексу (ММИ) Kupperman, ESAS, качества жизни (MOS-SF-36), в модификации Российского Межнационального Центра, боли (ВАШ); идентифицировали тип общих адаптационных реакций по Л.Х.Гаркави.

Результаты. После проведения КсТ были установлены важные преимущества нового метода, связанные с быстрым регрессом патологической психосоматической симптоматики. Значительно снизились показатели ММИ (p<0,05), 96,8% пациенток отметили полное купирование болевых ощущений при нагрузке, достоверно снизились проявления нейровегетативных нарушений (p=0,02–0,04), увеличилось соотношение антистрессорных реакций к стрессу, что совпадало с данными повышения качества жизни.

Заключение. Высокая эффективность используемой технологии демонстрирует возможность предупреждения развития хирургической менопаузы с клиническим проявлением посткастрационного синдрома для улучшения качества жизни и социальной реабилитации пациенток молодого возраста с онкопатологией репродуктивных органов.

Ключевые слова:
рак шейки матки, рак молочной железы, посткастрационный синдром, ксенонотерапия, экспоненциальный режим дозирования, адаптационные реакции

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Информация о финансировании: работа проведена при поддержке ФГБУ «НМИЦ онкологии» Минздрава России.
Конфликт интересов: авторы заявляют об отсутствии конфликта интересов.

Для цитирования:
Кит О.И., Попова Н.Н., Шихлярова А.И., Франциянц Е.М., Моисеенко Т.И., Меньшенина А.П., Жукова Г.В., Протасова Т.П., Арапова Ю.Ю. Развитие посткастрационного синдрома и корригирующее действие ксенона в экспоненциальном дозовом режиме у пациенток молодого возраста с онкопатологией репродуктивных органов. Южно-российский онкологический журнал. 2020; 1(3): 6-17.
https://doi.org/10.37748/2687-0533-2020-1-3-1

Получено 30.12.2019, Рецензия (1) 20.03.2020, Рецензия (2) 01.07.2020, Принята к печати 01.09.2020

In the modern structure of oncological diseases in women, about 40% are occupied by tumors of the reproductive system [1, 2], among which the absolute leader is breast cancer (BC) — 20.9%, the second place is cervical cancer (CC) with a frequency of 5.9% [3, 4]. These problems become particularly relevant due to the increase in the number of young women of reproductive age among cancer patients who found themselves after surgical castration in the epicenter of their own systemic disorders of neuroendocrine regulation, inversion of metabolic processes and psychological status [5–8].

First of all, such events are associated with the carcinolytic effects of the tumor on the state of the internal environment. Secondly, after radical treatment of the tumor and disabling ovarian function the trigger mechanism changes. Precisely, the leading pathogenetic factor becomes hypoestrogenia, which forms an equally complex metabolic picture of the post-castration syndrome long before the onset of the natural menopausal period. The frequency of occurrence of this symptom complex is from 50 to 100% among operated women [9]. For young women, ovarian removal is an irreversible loss of reproductive function and, unlike natural menopause, it is always stressful when the body is neither physiologically nor psychologically prepared for the onset of premature menopause [10, 11]. In other words, in contrast to the natural processes of extinction of reproductive function, one-time total shutdown of ovarian function is accompanied by acute neuro-hormonal and metabolic restructuring of the body [12]. The scenario of breast cancer, which has a catastrophic acceleration of spread among young women, is also developing, affecting the most important systemic regulatory and Executive mechanisms of neuro-hormonal status [13, 14]. This requires constant improvement and development of new treatment approaches, including the use of technologies of restorative medicine [15–19]. Replacement therapy with natural estrogens is used as an alternative correction of estrogendeficiency states. At the same time, neurovegetative manifestations are leveled, but the risk of developing cardiovascular and metabolic-endocrine disorders remains [20–22].

Existing treatment and rehabilitation programs with the use of plasmapheresis, relaxation, auto-training, phytotherapy, healing fitness massage, as well as the appointment of anti-anxiety agents from the group of high-potential benzodiazepine tranquilizers, including tricyclic and tetracyclic antidepressants and neuroleptics, do not always have a positive result in achieving full normalization of the disturbed neurovegetative and psychoemotional status.

Taking into account the problem of choosing an adequate accompanying therapy for relieving the complex of side effects, our attention was drawn to the medical experience of using an inert gas — xenon, which is considered to be a highly promising factor in correcting functional disorders in various pathologies, including cancer. It is known that xenon does not have teratogenic and mutagenic properties, and its clinical effect is characterized by nootropic, antidepressant, antihypoxic, immunostimulating, and anti-inflammatory effects [23–25]. Moreover, during the rehabilitation period, it is recommended to use sub-narcotic doses of this biologically active factor.

It would seem that given the antistress effect of xenon, no special testing of individual sensitivity and dose selection is required. However, such a standardized approach for patients with hormone-positive BC and CC at an early stage after surgical treatment is not quite appropriate. This is due to the development of an inadequate response against the background of the formation of post-mastectomy and postovariectomy syndromes or their simultaneous course, which was noted in practice in the form of high reactivity and violent vegetative manifestations after subnarcotic doses of xenon therapy, refusal of medical care.

Due to these circumstances, in order to create an adequate dose regime, we took as a basis the theory of General non-specific adaptive reactions of the body, which contains ideas about a multilevel periodic response system, principles and technologies of activation therapy, as a scientifically based approach to managing the processes of increasing the body's resistance [26].

The purpose of the study: to investigate the possibility of optimizing the treatment of patients with BC and CC using low-dose xenon therapy.

PATIENTS AND METHODS

The criteria for inclusion in the formation of study groups were reproductive age (up to 45 years), diagnosis — locally advanced BC and CC, comprehensive treatment in the FGBU "RNIOI" of the Ministry of health of the Russian Federation in 2016–2018, the stage of surgical treatment. All research protocols were prepared in accordance with the ethical standards of the Declaration of Helsinki (1964, as amended in 2013) and approved by the ethics committee of the FGBU "RNIOI" the Ministry of health.

In the first main group included 60 women with locally developed CC, hospitalized in the oncological Department of the FGBU "RNIOI" of the Ministry of health for comprehensive treatment, including a modified hysterectomy with appendages (classification by Piver III), which in the early postoperative period developed signs of post-castration syndrome. The degree of prevalence of the process according to the TNM classification corresponded to $pT_{1b}N_0M_0$ (n=14), $pT_{2a}N_0M_0$, according to histological analysis — squamous cell cancer of various degrees of differentiation. The second main group consisted of 60 patients of reproductive age hospitalized in the Department of tumors of the skin, soft tissue and breast cancer No. 1 FGBU "RNIOI" of the Ministry of health in order to perform surgical treatment in the form of radical mastectomy by Madden. The degree of prevalence of the process according to the TNM classification corresponded to T2N0M0 st II, histological analysis data — infiltrating carcinoma. The third main group included 36 patients with hormone-positive (luminal) subtypes of breast cancer and such concomitant genital pathologies as uterine fibroids (23 people, 64.3%), endometriosis (9 people, 25.1%), ovarian cyst (4 people, 11.2%). Previously, these patients received combined treatment (surgery in the volume of Madden mastectomy and hormone therapy), and then — surgical treatment in the volume of laparoscopic extirpation of the uterus with appendages. The operation was preceded by obtaining consent from the patients to complete the fertility function. The degree of prevalence of the process according to the classification of TNM corresponded to pt2n3m0 st III, according to histological analysis was diagnosed: infiltrating carcinoma.

Specifically for this study, based on the principles of activation therapy, we developed a new exponential dose algorithm for xenon inhalation therapy, aimed at modeling the harmonious adaptive response of the body by gradually increasing small doses of xenon exponentially with a coefficient of 0.7 and reciprocally reducing the time of each procedure. This excluded the possibility of overdose and provided a soft, but productive recovery of indicators of the functional state of cancer patients after surgical castration for locally advanced BC and hormone-positive CC. We used medical xenon-Xemed, dosage form-compressed gas, produced by AKELA-N LLC, Russia, Moscow region, Khimki, no. 99/363/4, registration certificate LS-000121–240810. Instructions for the use of xenon (Pharmacopoeia article 42–2891–97 of 8.10. 1999 and Pharmacopoeia article of the enterprise no. 42–0523–5109–04. Hazard class-4 according to GOST 12.1007). Order of the Ministry of health of the Russian Federation No. 363 of 10.10. 1999. application of xenon in medical practice. Technology has included the implementation of 5 sessions of xenotherapy (KsT), starting from the third day after surgical castration, carried out every other day in the morning. In the first procedure, the dose algorithm started with the supply of xenon concentration of 12–14% in the volume of the inhaled xenon-oxygen mixture for 20 minutes. Then, during the following procedures, the xenon concentration and exposure value changed reciprocally: the 2nd procedure-14–16%, 17min, the 3rd — 16–18%, 15min, the 4th-18–20%, 12 min., the 5th — 20–22%, 10 min. In other words, the exponential mode of gradual increase in small doses of xenon was accompanied by the reverse mode-an exponential decrease in exposure.

The criteria for the effectiveness of the method were considered to be clinical manifestations in the form of surface sleep, calm breathing and a decrease in heart rate relative to the initial data. The severity of the post-castration symptom complex was assessed based on the results of the modified menopausal index (MMI) Kupperman (1959), modified by E.V. Uvarova (1983), estimated in points [27]. At the stages of treatment, various types of adaptive reactions (signaling criteria for blood morphological composition) were identified by Garkavi.

The adequacy of analgesia was determined based on subjective indicators of questionnaires with an assessment of the degree of pain intensity on a graphical visual-analog scale (VAS):

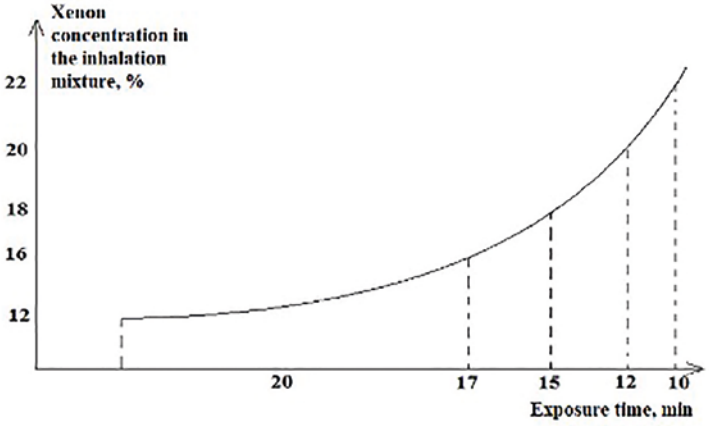

Fig. 1. Calculated exponential curve of the phase algorithm of xenon therapy, reflecting an increase in the concentration of xenon in the xenon-oxygen mixture (vertically), coupled with a decrease in exposure (horizontally).

Table 1. Structure of clinical manifestations of post-castration syndrome in patients with CC, depending on the treatment, with or without xenon therapy, %

Indicators	After surgery , *n*=60	Main group with KcT, *n*=32	Control group , without XT, *n*=28
	%	%	%
Increase in blood pressure	62.7	56.2	71.4
Headache	56.1	56.2	71.4
Dizziness	56.1	50.0	64.2
Sweating	72.6	37.5*	78.5
Hot flushes	59.4	43.7*	78.5
Arrhythmia	33.9	37.5	35.7
Sleep disorders	59.4	25.0*	100.0
Apathy	100.0	18.7*	85.6
Increased fatigability	72.6	12.5*	78.5
Reduced performance	56.1	12.5*	85.6
Anxiety	66.6	25.0*	71.4
Decreased appetite	13.2	12.5	14.2
Psycho-emotional complaints	85.8	18.7*	78.5
Pain in muscles	49.5	12.5	21.4
Violation of carbohydrate metabolism	13.2	12.5	14.2

Note: * – statistically significantly different from the values in the control group, $p<0.05$

0 points — no pain, 10 points — maximum pain. Patients determined their pain after 6 hours, 24 hours, and on the third day after surgery [28]. Postoperative analgesia was considered satisfactory if the level of pain intensity was not higher than 4 points according to VAS. The obtained data were processed using standard computer techniques (Statistica, 8. Microsoft Excel). When comparing the groups, the student's parametric T — test and the nonparametric Mann — Whitney U-test were used. the critical significance level of p was assumed to be 0.05.

RESEARCH RESULTS AND DISCUSSION

The dynamics of the main multi-time menopausal neurovegetative and emotional disorders in patients with a diagnosis of CC, due to the development of post-castration syndrome, and the state of symptoms after standard treatment and after the use of CT are presented in the table 1.

Analysis of clinical data showed that in the early postoperative period, all patients were characterized by a predominance of psychoemotional disorders: apathy in 100%, psychoemotional complaints in 85.8%, increased fatigue in 72.6%, anxiety in 66.6%, sleep disorders in 59.4%. Neurovegetative symptoms also included quite pronounced manifestations: high blood pressure, sweating and hot flashes were observed in patients in 65–72%, headache and dizziness-56.3%, which corresponded to well-known literature sources.Comparative analysis of groups after XT showed the advantage of a new method associated with rapid regression of pathological symptoms: such vegetative manifestations as sweating and hot flashes decreased by 2 times; anxiety by 2.8 times; sleep disorders by 4 times; psychoemotional complaints decreased by 4.2 times; decreased performance by 6.8 times; increased fatigue decreased by 6.2 times.

Table 2. Structure of clinical manifestations of post-castration syndrome in patients diagnosed with BC and forced castration with or without xenon therapy, %

Indicators	After the surgery , *n*=36	Main group with XT, *n*=19	Control group without XT, *n*=17
	%	%	%
Increase in blood pressure	61.6	36.8*	75.4
Headache	78.4	36.8*	52.2
Dizziness	78.4	26.3*	52.2
Sweating	67.2	26.3*	75.4
Hot flushes	67.2	26.3*	75.4
Arrhythmia	42.0	13.2*	29.0
Sleep disorders	100.0	36.8*	87.0
Apathy	86.8	26.3*	75.4
Increased fatigability	25.2	13.2*	75.4
Reduced performance	100.0*	36.8*	58.8
Anxiety	95.2*	26.3*	58.8
Decreased appetite	25.2	36.8	34.8
Psycho-emotional complaints	100.0	26.3*	87.0
Violation of carbohydrate metabolism	25.2	26.3	29.0

Note: * – statistically significantly different from the values in the control group, $p<0.05$

As for patients with hormone-positive (luminal) subtypes of BC, the multivariance and severity of clinical symptoms of post-castration changes after forced surgical castration are poorly studied and insufficiently reflected in the literature. In our study, we analyzed the most actively manifested clinical signs of post-castration syndrome and their reduction using XT. This data is presented in the table 2.

Analysis of the results showed that the use of personalized exponential programming technology for low-dose xenotherapy in patients with hormone-positive BC after total ovarian removal significantly differs from the results of patients with a similar diagnosis and treatment without xenotherapy. This is reflected in the positive dynamics and regression of pathological symptoms on the part of neurovegetative disorders. First of all, we managed to normalize the level of blood pressure, reduce the frequency of arrhythmia episodes, headache and dizziness by 2 times, vegetative crises by 3 times, reduce the frequency of anxiety by 2.5 times, sleep disorders by 2.3 times, apathy by 3 times, psychoemotional complaints by 3.5 times, increased fatigue by 6 times.

The score coefficient allowed us to determine the frequency of detection and severity of MMI in patients who underwent forced castration, data on which are shown in table 3.

As can be seen from table 3, the level of MMI, which characterizes a mild degree of psychoemotional and somatic disorders in patients diagnosed with BC after forced castration, was found with the lowest frequency and level of score compared to those in patients with moderate and severe MMI. The data show that during this period, the vast majority of patients had moderate and, especially, severe MMI. A different situation appeared when comparing the indicators obtained after the XT with the group without the use of xenon. It was noted that in the main group, the frequency of moderate and severe MMI decreased significantly (by 4.8 and 2.4 times, respectively) and the level of score significantly decreased.

Table 3. Determining the severity of post-castration syndrome in patients diagnosed with breast cancer and forced castration using xenon therapy

The severity of MMI	After the surgery , *n*=36		Main group with XT, *n*=19		Control group without XT, *n*=17	
	%	Points	%	Points	%	Points
Mild degree	5.6%	22.6±3.5	73.6%	19.3±2.8	11.8%	24.4±2.9
Middle degree	19.6%	41.2±3.1	12.2%	37.2±2.0*	58.5%	44.2±3.4
Severe	72.8%	61.3±4.2	12.2%	54±3.6	29.5%	66.1±6.1

Note: * – statistically significantly different from the values in the control group, $p<0.05$

Table 4. Relief of pain in the postoperative period in CC patients during xenon therapy

Indicators	After the surgery, *n*=60	Main group with XT, *n*=32	Control group without XT, *n*=28
	%	%	%
Pain in rest	59.2	12.6*	31.5
Pain in minor activity	70.4	19.2*	45.5

Note: * – statistically significantly different from the values in the control group, $p<0.05$

This coefficient clearly demonstrated the effectiveness of the xenotherapy technology used in the conditions of a simultaneous course of post-mastectomy and post-castration syndrome in young patients diagnosed with hormone-positive BC.

We took into account that in the complex of combined treatment of cancer patients, the surgical component is one of the main ones. Postoperative pain is an unavoidable symptom of the operated patient due to surgical tissue damage, the presence of drains and, in some cases, the development of postoperative complications. However, postoperative pain is usually underestimated and can lead to cardiorespiratory, thromboembolic, and other complications with poor quality of life [29]. Cancer patients, more than others, need protection from operational aggression associated with radicalism, the removal of regional lymphatic collectors, with the actualization of the issue of effective methods for relieving pain in the early postoperative period. To assess the severity of subjective manifestations of pain syndrome, the intensity of pain was assessed at rest and with moderate physical activity on the 3rd and 9th days after surgery. In the main group of patients, it was suggested to determine their pain before and after a session of xenon therapy.

On the example of determining the severity of pain in patients with a diagnosis of CC, it was found that on the 3rd day after surgery, before the start of xenotherapy, the average level of pain in all patients studied was 3 points (range 2–4). At the same time, 59.2% of patients registered pain in the area of the postoperative wound at rest and 70.4% of patients — pain with a slight load (when moving in bed).

At the end of the course of xenon therapy, no more than 12.6% of patients diagnosed with CC complained of pain, while in the control group, the relative number of such patients was 44.8% (table 4).

When analyzing the results of the analgesic effect of xenon in patients with luminal subtypes of BC in the early post-castration period, was noted that after the first procedure with xenon, almost all patients - 96.8% - noted complete relief of pain symptoms at rest and a significant reduction in pain during exercise. The pronounced analgesic effect was maintained for 10-12 hours. That's noteworthy, that migraine pain is reduced in 4 cases, without the use of additional medications, even after a single procedure with xenon–oxygen mixture.

To determine the adaptive status, we used an algorithm that included, first, an individual assessment of the type of AP at different stages of the study and the formation of a General group structure of AP, second, calculating the quantitative share and cluster formation of each reaction in the group, and finally, calculating the ratio of the total cluster of antistress reactions to that for stress (K=AC/S). In fact, this coefficient represented the relative digital equivalent of the dominant adaptive state and allowed us to objectify the effectiveness of the xenon therapy used.

When studying the structure of AP in a group of patients with CC in the early postoperative period, deep changes in the reactivity of the body of a pathological nature were noted. In the vast majority of patients, a General non-specific stress reaction in acute form was identified. The frequency of detection of this reaction increased by more than 2 times relative to the background (before the operation). On the contrary, the frequency of development of an integral reaction of calm activation of the physiological type decreased by almost 4 times, and increased activation was not detected in any case. During the recovery postoperative period, the situation did not change dramatically under the standard regime of accompanying therapy, namely, the stress reaction prevailed, which acquired a chronic form.

The use of programmed modes of low-dose xenon therapy in the early postoperative period in patients with CC contributed to the formation of the AP structure. The dominant link was antistress type reactions, the detection rate of which was close to 80%. Of these, the predominant type was the training response, characterized by the severity of anabolic processes, the development

of protective inhibition in the CNS, the functional activity of the endocrine and thymic-lymphatic system within the lower half of the norm, and a gradual increase in non-specific, including antitumor resistance. In the interpretation of L.H. Garkavi, M.A. Ukolova, E.B. Kvakina, the normotype of this reaction is characterized by an increase in the anti-inflammatory potential, which is of great importance for accelerating the healing and restoration of protective systems.

Speaking about the change in the integral indicator of adaptive status, represented by K=AC/S, it can be seen that its initial values decreased by 8.7 times after surgery, which indicated a natural shift in the ratio towards the pathological type of AR-stress. During recovery therapy without xenon, the value of K=AC/S increased only 1.6 times compared to the previous level. In contrast, the dynamics of the AR/C ratio increased significantly after the use of programmed modes of low-dose xenon therapy, exceeding the K values after surgery by 17.5 times. This indicator demonstrated the high significance of the biotropic effect of xenon for regulating the adaptive status of the body and, consequently, the possibility of regression of post-castration syndrome in women of reproductive age after radical oncogynecological operations. These changes in the AP ratio at the stages of treatment of CC patients can be illustrated by a graphical curve (continuous line) reflecting the course of adaptive processes as a result of an individualized approach using the developed modes of low doses of xenon (fig. 2).

For comparison, we analyzed the structure of AR in BC patients with post-mastectomy syndrome, whose complex treatment included radical breast surgery. An important point in the group of patients with BC was the comparison of the structure of AR 9 days after surgery, when the recovery period passed without the use of low-dose xenon therapy. According to the data obtained, no cases of chronic stress were observed in the group of patients without xenon, while the structure of antistress reactions was completely restored, which was close to the original one. The difference was that in the initial state, the reaction of increased activation dominated, and in the subsequent recovery period, it developed in 1.4 times fewer cases. At the same time, the largest cluster was the reaction of training, which represented a symptom complex that leads not to exhaustion, but to the accumulation of reserves with small energy expenditures and moderate functional activity of regulatory systems whose activity is balanced.

When studying the structure of AR in BC patients with post-mastectomy syndrome, the situation was almost identical after low-dose xenon

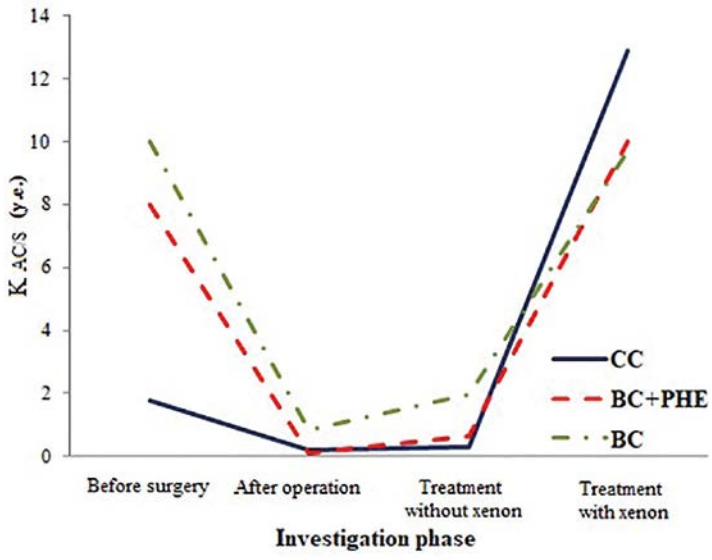

Fig. 2. Dynamics of the ratio of antistress reactions and stress in young patients with reproductive oncopathology in the development of post-castration syndrome and xenotherapy.

therapy. The structure of AR consisted only of clusters of antistress reactions with twice the frequency of development of the training reaction over calm and increased activation, the representation of each of which was the same. In this case, it seemed appropriate to compare the level of values of K=AC/S when using xenon therapy and without it in BC, which showed equally stable indicators of the dominance of antistress reactions. This parallel led to the conclusion that there is no need to include this technology of rehabilitation and rehabilitation therapy in this group of patients.

On the contrary, against the background of these results with BC, the situation was clearly manifested, which indicated the mandatory inclusion of xenotherapy in hormone-positive subtypes, when surgical treatment is not limited to mastectomy, but in the presence of a pronounced pathology of the genitals is accompanied by surgical castration. Thus, when considering the as/S ratio in the period after 9 days after ovarian removal in BC patients without xenon, the value of K=AC/S was 12 times less than the initial value, although it exceeded the postoperative level of values (fig. 2).

In the same period of time after the end of the developed programmed mode of low-dose xenon therapy after surgical castration, it was demonstrated that it was possible to achieve the highest K=AC/S, exceeding that without the use of xenon by 15.2 times. It was this co-ordinal difference that emphasized the need for effective use of such a biologically active factor as xenon, which has a regulatory effect on the integral adaptive mechanisms of the body as a whole.

It should be noted that the inclusion of mechanisms that limit or completely suppress the development of stress under the influence of adequate functional load primarily affects the higher regulatory centers of the CNS, in particular the hypothalamic-pituitary regulation of the thyroid and sex glands, the adrenal cortex, inter-system immune-hormonal relations, the processes of metabolism, proliferation, and apoptosis. In other words, small launcher reason, the role of which in this case executes the xenon, is able to launch the cascade of complex functional transformations on the level of regulatory and Executive systems of the body, helping maintain the structure of physiological reactions through the processes of self-organization. Due to the possibility of developing various discrete States, the organism, as a complex open nonlinear system, makes phase transitions to the most favorable state at the moment. When a stress reaction is protected by damage and high energy consumption, and with physiological loads, such a response is biologically impractical and even a small impact (xenon) against the background of a large one (antitumor treatment) will cause an adequate ONAR of a physiological type of another level of reactivity, which was confirmed by us. However, it should be taken into account that the severity of the stress effect will differ when performing BC surgical treatment followed by surgical castration or limited only to radical breast surgery.

CONCLUSION

Thus, the research allowed us to justify the effectiveness of using a personalized approach to xenon therapy by developing a programmable exponential algorithm for dosing the xenon-oxygen mixture. As a result, a pronounced regulatory effect was obtained, which consists in restoring the adaptive status against the background of removal of the reproductive system organs in women of childbearing age. This effect demonstrates its importance for justifying the prevention of the development of surgical menopause with the clinical manifestation of post-castration syndrome in the form of functional psychoemotional and neurohumoral disorders in order to improve the quality of life and social rehabilitation.

Authors contribution:

Kit O.I. – determination of a relevant direction to study, general management of the study.

Popova N.N. – study performing, processing and analysis of results, manuscript writing.

Shikhlyarova A.I. – formulation of the purpose of the study, establishment of the study design and exposure algorithm, analysis of results, manuscript writing.

Frantsiyants E.M. – analysis of results.

Moiseenko T.I. – statement of specific clinical objectives of the study, monitoring of patients.

Menshenina A.P. – direct formation of patient groups and clinical support of the study.

Zhukova G.V. – analysis of results, manuscript writing.

Protasova T.P. – assessment of the adaptive status of patients.

Arapova Yu.Yu. – assessment of parameters of the psychosomatic status of patients.

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