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ORIGINAL ARTICLE

EFFICIENCY MARK OF POSTOPERATIVE PAIN MANAGEMENT AND NORMALIZATION OF ADAPTATION STATUS IN PATIENTS WITH REPRODUCTIVE SYSTEM ONCOPATHOLOGY

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ABSTRACT

Purpose of the study. Studying possible management of postoperative pain and normalization of adaptation status in patients with reproductive system onychopathology using xenon-oxygen therapy.

Patients and methods. The study included 97 patients receiving surgical treatment for reproductive cancer at National Medical Research Centre for Oncology in 2016–2020. All patients were divided into the main and control groups depending on the performed corrective therapy with xenon-oxygen mixture (XOM). Inclusion criteria were: established diagnosis – endometrial cancer, cervical cancer or ovarian cancer at the surgical stage of antitumor treatment, absence of decompensated concomitant pathology. In addition to general clinical tests, the intensity of symptoms in patients was assessed using a standardized Edmonton questionnaire, adaptation status and data of a numerical rating scale of pain were recorded, the severity of endogenous intoxication was measured using calculated lymphocytic, leukocyte, nuclear and leukocyte shift index. Stages of the study included functional assessment of the patient's condition before surgical treatment and on the 1st and 5th days of the postoperative period.

Results. An analysis showed statistically significant differences between the groups: in the group of patients receiving xenon-oxygen therapy, 12.9% of patients complained of pain, while in the control group – 34.2%, on mild exertion 17.1% and 39.9%, respectively ($p<0.05$). The therapy with XOM demonstrated its high significance in the adaptive status regulation and regression of negative clinical manifestations in patients after oncogynecological surgeries.

Conclusion. The effectiveness of the chosen therapy with XOM demonstrates the possibility of anesthesia and normalization of the adaptive status of oncogynecological patients who underwent surgical treatment for reproductive cancers.

Keywords:
reproductive cancers, postoperative pain, xenon-oxygen therapy, adaptation status, psychological status, rehabilitation treatment.

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ОРИГИНАЛЬНАЯ СТАТЬЯ

ОЦЕНКА ЭФФЕКТИВНОСТИ КУПИРОВАНИЯ ПОСЛЕОПЕРАЦИОННОЙ БОЛИ И НОРМАЛИЗАЦИЯ АДАПТАЦИОННОГО СТАТУСА У ПАЦИЕНТОК С ОНКОПАТОЛОГИЕЙ РЕПРОДУКТИВНОЙ СИСТЕМЫ

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РЕЗЮМЕ

Цель исследования. Исследовать возможности купирования послеоперационной боли и нормализации адаптационного статуса у пациенток с онкопатологией репродуктивной системы с применением ксенон-кислородной терапии.

Пациенты и методы. В исследование включено 97 пациенток, находившихся на хирургическом лечение по поводу злокачественной опухоли репродуктивной системы в отделении онкогинекологии ФГБУ «НМИЦ онкологии» Минздрава России в период 2016–2020 гг. Данные пациентки в зависимости от проведенной корригирующей терапии ксенон-кислородной смесью были разделены на основную и контрольную группы. Критерии включения: наличие у пациенток установленного диагноза (рак тела матки, рак шейки матки, рак яичников) на хирургическом этапе противоопухолевого лечения, отсутствие декомпенсированной сопутствующей патологии. Помимо общеклинических исследований у пациенток оценивали интенсивность симптомов при помощи стандартизированного опросника ESAS (The Edmonton Symptom Assessment System), фиксировали адаптационный статус и данные числовой рейтинговой шкалы боли, выраженность эндогенной интоксикации проводили с помощью расчетных лимфоцитарного, лейкоцитарного, ядерного индекса сдвига лейкоцитов крови. Этапы исследования включали: функциональную оценку состояния пациенток до хирургического лечения, затем на 1-е и 5-е сутки послеоперационного периода.

Результаты. При проведении анализа данных установлены статистически значимые отличия, так в группе пациенток с применением терапии ксенон-кислородной смесью жалобы на боль предъявляли 12,9% пациенток, тогда как в контрольной группе – 34,2%, при незначительной нагрузке 17,1% и 39,9% соответственно (p<0,05). Применение терапии ксенон-кислородной смесью продемонстрировало высокую значимость метода в регуляции адаптационного статуса и в регрессе негативных клинических проявлений у пациенток после онкогинекологических операций.

Заключение. Эффективность выбранной терапии ксенон-кислородной смесью позволяет продемонстрировать возможность обезболивания и нормализации адаптационного статуса онкогинекологических пациенток перенесших хирургическое лечение опухолевых процессов репродуктивных органов.

Ключевые слова:
опухоли репродуктивной системы, послеоперационная боль, ксенон-кислородная терапия, адаптационный статус, психологический статус, восстановительное лечение.

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According to the International Agency for Research on Cancer, published in 2018, it was noted that 18.1 million new cases and 9.6 million deaths from malignant neoplasms were registered worldwide. In 2019, more than 600 thousand new patients diagnosed with cancer were identified in Russia. Among the female population, tumors of the reproductive system account for the largest share of all malignancies, so breast cancer was diagnosed in 18.3%, uterine body cancer in 7.0%, cervical cancer in 4.7%, ovarian cancer in 4.5% of women. Consistently high rates in the structure of oncological morbidity of tumors of the reproductive system lead to an annual increase in the number of women who have undergone radical surgical treatment and need early rehabilitation measures [1, 2].

Most gynecological operations are considered to be moderately traumatic, however, according to the rating of the 2013 cohort study of painful surgical interventions, obstetric and gynecological operations took the first place in terms of pain intensity in the early postoperative period [3]. These statements partly explain the research of Gerbershagen HJ (2014), who in his work notes gender differences in the perception of postoperative pain. Moreover, women emphasize the high intensity of pain regardless of the type of surgical intervention [4]. The multicenter generalizing data of Schnabel A (2020) became the basis for the formation of prognostic risk factors for postoperative pain, which include: age less than 54 years, female gender, preoperative chronic pain and opioid use, duration of surgery more than 90 minutes, depression and anxiety in the preoperative period. The presence of three risk factors leads to an increase in pain symptoms, which can cause adverse postoperative consequences in the form of dysfunctional disorders and the development of chronic pain [5]. According to the research work of Brandsborg B. (2012), insufficiently relieved acute pain after hysterectomy forms the risk of developing chronic pain syndrome in 18–32% of women [6].

Undoubtedly, it is necessary to take into account psychological factors in the formation of pain syndrome, which play an important role during the postoperative period, as noted in the research work Sobol-Kwapinska M. (2016). So, the psychological correlates of postoperative pain include depression, waiting for surgery and pain, anxiety, low level of optimism. As a result of this study, it was revealed that negative situational aspects before the operation, then are prerequisites for a higher level of pain activity in the postoperative period [7]. Negative psychotraumatic factors in the preoperative period in cancer patients are uncertainty and waiting for surgery, the formation of anxiety-depressive symptoms, lack of motivation to continue treatment, loss of vital energy and personal meanings [8].

In oncogynecology, surgical treatment in combination with other antitumor therapy is the dominant method regardless of the stage of the process [9]. When performing radical surgical treatment of tumors of the genital system, it is preferable to perform organ-preserving operations. However, in some clinical cases, the most appropriate is the total removal of an organ affected by a tumor with suspected metastatic foci. The high risk of implantation metastasis makes it necessary to perform an extended volume of surgery with the removal of the ovaries. The data of the study by Kolbasova EA (2014) indicate that the localization of the tumor in hormone-dependent and hormone-producing organs provokes the development of a complex of neuroendocrine and psychoemotional symptoms that are difficult to predict and correct [10]. In oncogynecology, the postoperative period is complicated by postovariectomy syndrome, where the main pathogenetic factor is hypoestrogenism. Forced surgical suppression of the ovaries is accompanied by various functional changes in the tissues and organs, provoking a sharp change in hemostasis, disorders of the functions of the neuroendocrine, cardiovascular and other systems of the body with the formation of maladaptive adaptive reactions with a complex of deviations in the psychoemotional sphere [11].

The imbalance of psychological functioning and acute changes in homeostasis with the manifestation of pain symptoms after surgical treatment in cancer patients, undoubtedly, requires a timely solution to this problem in the provision of necessary and reasonable medical care. Modern achievements and significant changes in medical technologies determine the tactics of accompanying and restor-

ative treatment. The goal of adequate analgesia in the early postoperative period is the regression of the stress response to surgical aggression, the possibility of reducing the risk of functional complications, and the maximum recovery of the patient after surgery [12]. At the same time, the basic principles of analgesia in the early postoperative period should meet the needs of the patient with the provision of adaptation of therapy depending on the functional state, effectiveness and safety. Analgesic measures should be carried out within the framework of a "multimodal approach", which provides for the use of drugs from different pharmacological groups to ensure optimal functional and emotional recovery of patients who have undergone surgical treatment. To increase the effectiveness of analgesic therapy, it is necessary to improve organizational and methodological approaches and use modern achievements of anesthesiology, resuscitation and surgery [13, 14].

Thus, the strategy of leveling pain after gynecological cancer operations should be based, first, on knowledge of the characteristics operations in oncological pathology characterized by aggressive surgical approach with the formation of extensive wound surfaces and demonstration of the surgical stress response with production of inflammatory mediators [3], and secondly, be aware of the emotional imbalance that occurs in 42–68% of women with loss of fertility and reproductive functions [10, 15]. It is obvious that the need to eliminate pain and normalize the psychoemotional state equally are important components of the early restoration of the functional balance of the body of patients after radical surgical treatment in oncogynecology.

The data of modern literature reflect the multidirectional methods and techniques that are united by a common goal of regression of pathological disorders with compensatory possibilities of restoring the functionally balanced state of the body of women after hormone-reducing operations. Thus, the use of plasmapheresis and xenon therapy in cancer patients with the manifestation of postovariectomy syndrome led to an improvement in the clinical condition, normalizing hormonal parameters, reducing reactive anxiety, and improving the quality of life [16]. The use of xenon therapy in oncology is based on its analgesic, detoxifying properties, as well as on the ability to influence the mechanisms of adaptation by means of implementing the action on the stress-limiting and stress-implementing systems of the body, including in persons in a state of psychoemotional stress. It is known that when dosed, xenon is able to block the processes of lipid peroxidation and reduce the activity of epinephrine and glucocorticoids, and also contributes to the suppression of the activity of NMDA receptors in the structures of the nociceptive system. This feature of xenon is used to relieve pain in cancer patients with nociceptive pain, as well as during painful surgical manipulations [17–20].

Taking into account the unique properties of this inert gas, we made the choice of using a course of therapy with a xenon-oxygen mixture (XOM) as the main component of therapy for the correction of a complex complex of postoperative changes, regression of pain symptoms and altered psychoemotional signs with normalization of the adaptive status in oncogynecological patients.

Purpose of the study: to investigate the possibilities of postoperative pain relief and normalization of adaptive status in patients with oncopathology of the reproductive system using xenon-oxygen therapy.

PATIENTS AND METHODS

The study included 97 patients who were undergoing surgical treatment for a malignant tumor of the reproductive system in the Department of Oncogynecology of the National Medical Research Centre for Oncology of the Ministry of Health of Russia of the Ministry of Health of the Russian Federation in the period 2016–2020. Part of this study was carried out within the framework of the grant of the President of the Russian Federation "New technologies of molecular detoxification and cellular immunotherapy in the complex of treatment and rehabilitation of cancer patients with malignant tumors of the genitals". All patients received informed consent for the study and processing of personal data, in accordance with the ethical standards of the Helsinki Declaration (1964, as amended in 2013). The cancer diagnosis was confirmed in accordance

with the accepted clinical recommendations based on the examination data, objective methods of examination and morphological analysis [9]. The criteria for inclusion in the study were the presence of an established diagnosis in the patients: cancer of the uterine body, cervical cancer, ovarian cancer at the surgical stage of antitumor treatment, and the absence of decompensated concomitant pathology. The exclusion criteria were the presence of decompensated pathology and mental illness. The patients, depending on the corrective therapy with XOM, were divided into the main and control groups. In the postoperative period, on the 2nd, 3rd and 4th days, in the main group, in addition to the standard pain relief therapy recommended by WHO, in order to regress pain and normalize the adaptive status, the patients were treated with XOM. The patients of this group were provided with information about the possibilities of xenon therapy in oncology, about the absence of carcinogenicity and toxicity of the gas, the essence of manipulations, indications and contraindications were described in detail. In addition to standard general clinical studies, patients were assessed the intensity of symptoms using the standardized ESAS questionnaire (The Edmonton Symptom Assessment System), recorded the adaptation status according to L.H.Garkavi and analyzed the data of the numerical pain rating scale (NRS), the severity of endogenous intoxication was carried out using calculated lymphocyte (LI), leukocyte (LII), nuclear (NI) and the white blood cell shift index (ISL). The stages of the study included: functional assessment of the patients' condition before surgical treatment, on the 1st and 5th days of the postoperative period.

The main group was represented by 49 patients with a diagnosis of cervical cancer 21 (42.8%), uterine body cancer 16 (32.6%), ovarian cancer 12 (24.6%). Median age 53.1 years, mean age 47.2±1.8 years, range 30–75 years, underwent surgical treatment, according to clinical recommendations [9]. All patients received a course of xenon-oxygen therapy. The control group consisted of 48 patients diagnosed with cervical cancer 22 (45.7%), uterine body cancer 19 (39.8%), ovarian cancer 7 (14.5%). Age median 51.4 years, mean age 49.1±1.4 years, range 29–72 years, with similar surgical treatment without XOM therapy. The prevalence of the tumor process (TNM classification, 2011) in the main group is represented by the following indicators: stage II-24 (48.9%), stage III – 21 (42.8%), stage IV – 4 (8.3%), in the control group stage II – 22 (45.7%), stage III – 22 (45.7%), stage IV – 4 (8.6%). In the main group, concomitant pathology is presented: oncological disease in anamnesis in 2 (4.2%) patients, cardiovascular pathology in 26 (53.1%) patients, cerebral circulation disorders and other neurological nosology in 4 (8.3%) patients, gastrointestinal diseases in 5 (10.2%) patients, burdened allergic history in 4 (8.3%) patients. In the control group, the manifestation of concomitant diseases was represented by: pathology of the cardiovascular system in 24 (49.9%) patients, neurological pathology in 3 (6.2%) patients, gastrointestinal diseases in 3 (6.2%) patients, oncopathology in the anamnesis in 3 (6.2%) patients, allergic reactions in the anamnesis in 6 (12.5%) patients. The clinical and anamnestic data of the patients in the main and control groups showed no statistically significant differences in the localization and stage of the tumor process, as well as concomitant pathology. The obtained data were processed using standard computer techniques (Statistuca 10, Microsoft Excel). In comparison of the groups, the Student's parametric T – test and the nonparametric Mann-Whitney U – test were used, and the critical significance level of p was assumed to be 0.05.

Therapy with XOM was carried out in the morning hours by specialists who have passed certification training in this medical technology. The legal basis for this therapy was a permit for the use of medical technology FS No. 2010/227 "Method for the correction of acute and chronic stress disorders based on the inhalation of therapeutic doses of xenon brand "Xemed"" [17]. Indications for the use of this medical technology is the relief of pain and stress disorders of any etiology. Technical support of the procedure was carried out using the CPC-1 – therapeutic circuit for xenon inhalation with gas flow regulation (TU 9444–002–39791733–2009) (License No. 64/0125-L/02, LLC "KseMed", Russia, Moscow region, Khimki, Michurinsky 1st dead end, 20; Registration certificate No. FSR 20006037 of 05.11.2009). For monitoring the concentration of the gas flow of xenon and oxygen in the respi-

ratory mixture and measuring the volumetric the combined medical gas analyzer "GKM-03-Insovt" (CJSC "Insovt", Moscow) was used in the binary gas mixture. St. Petersburg, Russia) and a medical xenon dosimeter (DKM-01) (manufactured by AKE-LA-N LLC, Russia). Inhalation of the mixture was carried out through a mask tightly attached to the patient's face. In the first 2 minutes, the inhalation mixture contained air with an increased concentration of medical oxygen of 35–40%. Then, at a gas flow rate of 5–6 l/min, xenon was gradually added to the inhaled mixture to 14–15% and the mixture concentration was maintained for 20 minutes, subsequent procedures proceeded with an increase in the xenon concentration to 20%, and then 25% with a reduction in the time exposure to 15 minutes and in the final procedure to 10 minutes. The criteria for sufficient exposure and achieving the effect of xenon were the appearance of signs of superficial sleep with a decrease in the respiratory rate and heart rate. To prevent possible complications from the respiratory and cardiovascular systems, constant monitoring of blood oxygen saturation was carried out, and hemodynamic parameters were monitored.

RESEARCH RESULTS AND DISCUSSION

The negative consequences of radical surgical treatment of oncogynecological pathology are manifested by irreversible stress-induced systemic disorders in the body of women, which requires the development of a comprehensive approach to recovery measures at all stages of antitumor treatment. Undesirable clinical manifestations in the early postoperative period and side effects of antitumor treatment significantly worsen the quality of life of women, which undoubtedly has a dominant character in the choice of the patient's decision to continue therapy [21]. The fact of a high risk of neurovegetative and psychoemotional disorders in women with oncopathology of the reproductive organs after hormone-reducing operations is proven.

In our work, we pursued two goals of applying a course of therapy with XOM, to stop postoperative pain and to minimize the manifestations of psychoemotional manifestations of postovariectomy syndrome in patients who underwent radical oncogynecological intervention.

The analysis of the analgesic effect of XOM was carried out taking into account the assessment of the adequacy of anesthesia in 97 patients in the early postoperative period after radical oncogynecological surgery. All patients, on the eve of the evening and immediately before the operation, were prescribed a drug from the benzodiazipine group in order to normalize their psychological state. In the main group, the following surgical procedures were performed: extended extirpation of the uterus with appendages (type Piver III) in 21 (42.8%) patients, extirpation of the uterus with appendages and resection of the large omentum in 12 (24.6%) patients, extirpation of the uterus with appendages in 16 (32.6%) patients. In the control group, the following operations were performed: extended extirpation of the uterus with appendages (type Piver III) in 22 (45.7%) patients, extirpation of the uterus with appendages and resection of the large omentum in 7 (14.5%) patients, extirpation of the uterus with appendages in 19 (39.8%) patients. General combined anesthesia in the main group was 53.1%, in the control group – 54.3%, spinal-epidural anesthesia in the main group – 46.9% and in the control group – 45.7%. The average duration of operations in the groups was 78.2±0.45 minutes in the main group and 86.1±0.21 minutes in the control group. The average intraoperative blood loss had no statistical differences and was: in the main group 210.1±0.21 ml, in the control group 242.4±0.11 ml. Postoperative analgesia in the groups was carried out in accordance with WHO recommendations. The duration of operations, the volume of intraoperative blood loss and the type of anesthesia did not have significant differences in the groups. For all indicators, the groups are comparable, the differences in the indicators are not statistically significant (p<0.2).

Pain intensity was assessed at rest and with moderate physical activity (changes in the position of the body in bed) according to the subjective data of the questionnaire of the numerical rating scale of pain on the 1st and 5th days after surgery. The indicators were evaluated in points, with 0 points-no pain, with 10 points-the most pronounced pain syndrome. It was found that on the 1st day after the operation, the

patients assessed the level of pain, which was 3.9 points (range 3–4), which was regarded as average pain. Pain in the area of the postoperative wound on the first day at rest was recorded by 46.5% of patients, and 65.2% of patients-with a slight load, the data are shown in the table 1.

When analyzing the data, it was found that on the 5th day of the postoperative period, statistically significant differences were revealed, so in the group of patients with the use of XOM, complaints of pain at rest were presented 2.7 times less than in the control group. During exercise, a similar trend was observed: in the main group, the pain decreased by 3.8 times compared to the first day, while in the control group it was only 1.6 times (data processing using standard methods (Statistica, 10. Microsoft Excel) using the parametric T – student test and non-parametric U – Mann-Whitney test, the critical level of significance p=0.05).

The analysis of the leaves of the purpose of anesthesia is established that in the group with application of XOM anesthesia drugs NSAIDs decreased by 2.2 times compared with the control group, and the introduction of narcotic analgesic was not done at all. These indicators demonstrate the effectiveness of the analgesic effect when using XOM therapy in the early postoperative period.

It is proved that the activity of sex hormones is associated with the psychological state and behavioral reactions in women, which is manifested by emotional disorders in the form of depression and anxiety [22]. To determine the dynamics of the functional state, the intensity of symptoms and the psychological status of patients after radical operations in oncogynecology on the 1st and 5th days of the postoperative period, we used the indicators of the standardized ESAS questionnaire recommended for assessing the functional state of cancer patients [23]. The questionnaire data includes the 8 most common clinical symptoms in cancer patients at the stages of antitumor treatment (nausea, weakness, shortness of

Table 1. Indicators of the rating scale of pain in oncogynecological patients with the use of XOM therapy

Indicator	1st day after surgery, n=97		Main group (5th day), n=49		Control group (5th day), n=48		p
	%	Score	%	Score	%	Score	
Pain in rest	46.5	3.9±1.2	12.9	2.1±0.2	34.2	2.6±0.1*	0.02
Pain in strain	65.2	4.8±1.1	17.1	2.1±0.3	39.9	3.1±0.2*	0.01

Note: * – statistically significant difference between the indicators in the control group and the main group (p<0.05).

Table 2. Indicators of the standardized ESAS questionnaire in oncogynecological patients at the stage of surgical treatment with the use of XOM

Indicator	After surgery, n=97		Main group, n=49		Control group, n=48		p
	%	Score	%	Score	%	Score	
Feeling bad	57.3	3.8±1.1	26.5	1.4±0.1	41.0	4.7±0.1*	0.03
Dyspnea	18.5	0.8±0.1	11.2	0.4±0.1	13.1	0.7±0.2	0.4
Nausea	79.21	3.9±0.9	5.2	1.7±0.1	22.9	4.9±0.2*	0.03
Weakness	82.1	4.4±1.2	38.1	2.7±0.2	33.9	3.6±1.1	0.2
Depression	55.0	4.1±1.1	14.2	1.9±0.1	35.1	4.9±1.2*	0.02
Sleep disturbance	59.2	5.2±1.2	15.5	2.0±0.2	62.0	3.1±1.1	0.4
Appetite disturbance	43.6	2.9±0.8	22.6	1.8±0.1	24.4	2.1±0.1	0.6
Anxiety	66.5	5.9±1.6	22.1	3.0±1.2	50.8	5.9±0.2*	0.01

Note: * – statistically significant difference between the indicators in the control group and the main group (p<0.05).

breath, general health, as well as depression, anxiety, sleep disorders and appetite). The data are shown in table 2.

As a result of the study, it was found that in the group with the use of XOM, there was a statistically significant decrease in clinical manifestations of depression by 2.9 times, nausea by 4.1 times, poor health by 1.9 times, and anxiety by 2.3 times (p<0.05). Weakness, loss of appetite and sleep-there were no statistical confirmations. The data of the ESAS questionnaire analysis show a positive trend in the regression of psychoemotional and autonomic disorders when using XOM therapy.

Numerous literature sources indicate the functional features of cancer patients, which are expressed in a decrease in the reserves of the metabolic and detoxification systems with clinical manifestations in the form of polypocal functional disorders of homeostasis [24]. Detoxification and anti-inflammatory properties of xenon therapy should be considered as the trigger components of restorative treatment. In order to objectify the study, for rapid assessment of the body's reactivity to surgical intervention in oncogynecological patients and the possibility of anti-inflammatory effects of XOM therapy, we analyzed the indicators of the blood leukocyte formula, taking into account the generally accepted intoxication indices, the data are presented in the table 3.

Changes in the leukocyte formula of the blood on the 1st day after surgery indicated local reactive processes, an increase in the monocyte and lymphocyte links, and a decrease in immature forms of elements in the blood determine the activation of immune processes that provide detoxification. Comparable numerical values of the nuclear index (NI) indicated the state of intoxication at various stages of the study, which corresponded to the moderate severity of the clinical manifestation of the inflammatory reaction [25]. On the 5th day, the NCI index in patients with XOM therapy decreased by 42% compared to the 1st day after surgery, and in the control group by 14%, i. e., 3 times less. Such dynamics, in cases of the use of XOM therapy, indicated the restoration of neutrophil and monocyte regeneration. The lymphocytic index (LI) after surgery in patients with oncogynecological disease had the lowest level of values, close to the lower limits of the norm, indicating immunosuppression (table 3). However, on the 5th day of the postoperative period, LI indicators increased 4.1-fold in the group with XOM therapy, and in the control group increased 2-fold (p<0.001), which indicates the recovery potential of XOM therapy. The index of the shift of white blood cells (ILC), as an indicator of the body's reactivity to irritation, clearly showed a significant dynamics of values with an increase relative to the initial values on the 1st day of the postoperative period, with the achievement of the normal level in the treatment of XOM compared to the control group (table 3).

Thus, the dynamics of calculated indicators of intoxication indices indicated that after surgery in oncogynecology, patients have a pronounced reaction from the blood system. As a result of XOM therapy, the estimated indicators of intoxication indices were close to the baseline level, in contrast to the group without XOM therapy. The obtained data suggest that the detoxification effect of xenon therapy is manifested in the form of a decrease in the accumulation of endotoxins and products of incomplete metabolism in the body of cancer patients.

Table 3. Dynamics of calculated indicators of intoxication indices in oncogynecological patients using XOM therapy, c.u.

Indicator	Condition before surgery, n=97	1st day after surgery, n=97	Main group (5th day), n=49	Control group (5th group), n=48
LII	2.09±0.33	4.71±1.09	2.02±0.31[1,2]	4.56±1.09
NI	0.27±0.03	0.67±0.14	0.23±0.01[1,2]	0.46±0.03
LI	0.41±0.11	0.14±0.03	0.58±0.09[1,2]	0.29±0.05
ILC	1.91±0.32	3.65±0.43	1.49±0.12[1,2]	3.26±0.73

Note: LII – leukocyte intoxication index; NI – nuclear index; LI – lymphocytic index; ILC – index of the shift of blood leukocytes; [1] – differences between the indicator after surgery and the treatment of XOM in the main and control groups are significant, p<0.05; [2] – differences in the indicators in the main and control groups are significant, p<0.05.

The psychopharmacotherapeutic effect of xenon in small doses is applicable for the correction of adaptive disorders and the elimination of stress syndrome of various origins [17, 26]. To objectify the effectiveness of XOM therapy in oncology, we used the determination of the adaptive status of patients before surgery (baseline), on the 1st and 5th days of the postoperative period. Determining the type of general non-specific adaptive response of the body is an indicator of the level of health with an assessment of the immune and neuroendocrine systems. When conducting a parametric analysis of the cell composition of the leukogram, we determined the type of adaptive response and the level of reactivity. The calculation of the quantitative share and the formation of the cluster of adaptive status in the groups was analyzed using the calculated coefficient of the ratio of the total cluster of antistress and stress reactions (K = AS/S) [27].

The analysis of the dynamics of the structure of adaptive reactions in oncogynecological patients showed significant changes. Thus, in the majority of patients, acute stress after radical surgery was identified in 71.9% of cases (more than 2.2 times relative to the background state before surgery) and with an anti-stress/stress ratio of 0.39, which is 5.1 times less than the level before surgery. Integral indicators of the adaptive status of antistress/stress indicated a natural shift in the ratio towards pathological reactions after surgery. The frequency of balanced reactions of quiet activation decreased by 4 times, and increased activation was not recorded in any case (table 4).

The recovery period without XOM therapy had almost no positive dynamics, the stress response prevailed in 66.3% of patients, and the anti-stress/stress ratio did not actually change in comparison with the 1-day postoperative period. The frequency of the training response was 2.8 times less than the stress response. The use of XOM therapy contributed to the formation of a different adaptive status. The dynamics of the antistress/stress ratio increased significantly, exceeding the postoperative values by 6.5 times and reaching the initial level. The dominant type was the training reaction, which is characterized by the predominance of anabolic processes with the development of protective inhibition in the central nervous system, functional activity of the endocrine system with an increase in non-specific, including antitumor resistance [27].

CONCLUSION

Thus, the study showed that the majority of patients with oncogynecological pathology after radical surgical treatment and standard treatment on the 1st day experience moderate pain at rest in 46.5%, with a slight load in 65.2%. After the use of sessions of xenon-oxygen therapy on the 2nd, 3rd, and 4th day of the postoperative period, the relief of pain was noted in 2.7 times more patients than in the group without this therapy. Complaints of pain in the main group were presented by 12.9% of patients, while in the control group – 34.2%, with a slight load of 17.1% and 39.9%, respectively (p<0.05). When conducting an objective rapid assessment of the indicators of intoxication indices in the group with XOM therapy, the approach of these indicators to the initial level before surgical treatment was noted, which indirectly determines

Table 4. Structure of adaptive reactions in oncogynecological patients when using therapy in the postoperative period

Adaptive reaction types	Condition before surgery, n=97	1st day after surgery, n=97	Main group (5th day), n=49	Control group (5th day), n=48
Stress, %	33.1	71.9	28.2	66.3
Training response, %	8.4	21.3	56.2	28.2
Rest activation, %	20.6	6.8	8.8	-
Increased activation, %	37.9	-	6.8	5.5
K = AS/S, c.u.	2.02	0.39	2.54	0.5

Note: AS – antistress, S – stress.

the decrease in the body's systemic response to surgical trauma.

The use of XOM therapy demonstrated the high significance of the method in the regulation of the adaptive status and in the regression of negative clinical manifestations in patients after oncogynecological operations. According to the ESAS questionnaire revealed a positive trend in the recovery of psychosomatic well-being in group therapy XOM, there was a statistically significant decrease in symptoms of depression 2.9 times of illness 1.9 times, anxiety 2.3 times, nausea 4.1-fold (p<0.05). The data of the questionnaires were objectified by indicators of the dynamics of adaptive reactions during treatment with xenon therapy. Thus, in the postoperative period, the adaptive status in oncogynecological patients was functionally low reactivity with the identification of acute stress in 71.9% of cases, which is more than 2.2 times higher than the background state. On the 5th day of the postoperative period, no positive dynamics were observed in the group without XOM therapy, the acute stress response was recorded in 66.3% of patients, with no changes in the antistress/stress ratio. Xenon therapy helped to restore the adaptive status of oncogynecological patients in the form of a predominance of a balanced training response and normalization of the antistress/stress ratio, which reached the initial indicators and exceeded the postoperative value by 6.5 times, which undoubtedly indicates the recovery capabilities of XOM therapy.

Authors contribution:

Rozenko D.A. – determination of research objectives, study design, analysis of results.

Shikhlyarova A.I. – conduction of the study, assessment of the adaptation status of patients.

Popova N.N. – direct conduction of the study end conducting xenon-oxygen therapy, assessment of parameters of the psychosomatic state of patients, manuscript writing.

Verenikina E.V. – determination of research design, participation in the analysis of results.

Menshenina A.P. – setting clinical research objectives, monitoring patients' condition.

Ardzha A.Yu. – formation of patient groups and clinical support of the study.

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